102 Homologies between the brain and the eye: Can ocular researchers lead the way or are we following our ‘brainy’ colleagues?
Sunday, May 07, 2017 8:30 AM–10:30 AM
Ballroom 4 Symposium
Program #/Board # Range: 7–12
Contributing Section(s): Biochemistry/Molecular Biology, Glaucoma, Immunology/Microbiology, Physiology/Pharmacology, Retinal Cell Biology

Program Number: 7
Presentation Time: 8:30 AM–8:36 AM
Introduction - Developmental and anatomical homologies:

Setting the scene
Paul McMenamin. Dept of Anatomy & Dev Biology, Monash University, Melbourne, VIC, Australia.

Presentation Description: Since this symposium will aim to illustrate the strong homologies between the eye and the brain, this introduction will briefly remind participants of the shared embryological origins of the neural parenchyma and retina, the homologies between the corneasceral envelope and the dura mater and the uveal tract and the pia-arachnoid. The shared nature of blood barriers and the lack of lymphatics in the neural environment and the constraints of immune surveillance that both these features impose on the immune system will be discussed. A brief outline of the homologies in the anatomy and physiology of the CSF and aqueous humour will be given. Whilst the introduction may simply act as a reminder for the audience of knowledge gained during their education and training it will hopefully serve to paint the scene for the remaining speakers and stimulate a new appreciation of the features of the eye that are unique and those that are less so.

Commercial Relationships: Paul McMenamin, None

Program Number: 8
Presentation Time: 8:36 AM–8:58 AM
Immune surveillance in the brain
Britta Engelhardt. University of Bern, Bern, Switzerland.

Presentation Description: Our improved understanding of immune surveillance of the central nervous system (CNS) has repeatedly provoked dismissal of the existence of immune privilege of the CNS. Understanding immune privilege of the CNS requires intimate knowledge of its unique anatomy. This will be discussed in the context of immune cell entry into the CNS across the brain barriers.

Commercial Relationships: Britta Engelhardt, None

Program Number: 9
Presentation Time: 8:58 AM–9:20 AM
Autimmune disease of the CNS: Multiple Sclerosis and Experimental Autimmune Encephalitis (EAE)-lesson from the brain
Claude C. Bernard. Australian Regenerative Medicine Institute, Monash University, Clayton, VIC, Australia.

Presentation Description: Multiple Sclerosis (MS) is an inflammatory disease of the central nervous tissue (CNS) characterized by localised myelin destruction and axonal loss. This results in progressive neurological deficits, which most often manifest as impaired vision, ataxia and signs of paralysis, among others. The cause of MS is still unknown but is believed to involve both cell-mediated and humoral immune responses directed against components of the CNS. EAE is a well-established model that recapitulates many clinical and physiological aspects of MS, including optic neuritis. That MS and ocular pathology are associated is not surprising, given that the eye is an extension of the brain and that the expression of defined-myelin antigens are higher in the optic nerve than in the spinal cord. An important conceptual development in the understanding of EAE and MS has been the compartmentalization of the mechanistic process into two distinct but overlapping connected phases, inflammatory and neurodegenerative. The extension of these findings to ocular research will no doubt enhance our understanding of their pathophysiology as well as their potential treatments.

Commercial Relationships: Claude C. Bernard, None

Support: National Health and Medical Research Council of Australia (APP1053621) and the Department of Industry, Commonwealth of Australia (AISRF06680).

Program Number: 10
Presentation Time: 9:20 AM–9:40 AM
Lymphomas of the eye and brain – very close cousins (or the same entity?)
Sarah E. Coupland. Molecular and Clinical Cancer Medicine, University of Liverpool, Liverpool, United Kingdom.

Presentation Description: Vitreoretinal lymphomas (VRL) and central nervous system lymphomas (CNLS) are aggressive high-grade lymphomas, which often occur together or are subsequent to each other. They have very similar morphological, immunophenotypical and genetic characteristics. For example, according to the WHO Lymphoma classification, most VRL and CNSL can be subtyped as diffuse large B-cell lymphomas (DLBCL) with most of being the activated B-cell genetic type (ABC), typically associated with a poor prognosis. They have a similar immunoprofile with positivity for B-cell antigens (CD79a, CD20 and PAX5), ABC-related DLBCL markers (MUM1/IRF4 and BCL6), for C-MYC and BCL-2 proteins, and have a high Ki-67 growth fraction. The number of somatic mutations of the immunoglobulin gene in both VRL and CNSL is high. Further, aberrant somatic hypermutation is also seen in CNSL targeting several other genes (e.g. PIM1, TTF, MYC, KLH14, OSPL10, SUSD2). Epigenetic studies reveal frequent gene silencing through hypermethylation. Interestingly, both VRL and CNSL have a propensity to stay within the CNS (i.e. without dissemination to lymph nodes), possibly due to the expression pattern of chemokine receptors and their ligands, and the supportive immunosuppressive environments present in the eye and brain. Very few studies have had the opportunity to study paired CNSL and VRL samples: those that have, together with the associated clinical histories, would suggest that CNS and VRL indeed represent the same entity, with occasional cases demonstrating that the lymphomatous lesions within the eye and brain in the same patient have arisen from the same B-cell clone. And yet, there are cases that have remained purely within the eye or in the brain, without involvement of the other organ, suggesting some degree of anatomical compartmentalization. Animal models for both VRL and CNSL are available but require improvement for a true understanding of the pathogenesis of these diseases, and for the investigation into more effective therapies.

Commercial Relationships: Sarah E. Coupland, None

Program Number: 11
Presentation Time: 9:40 AM–10:00 AM
Brain and retinal degenerative diseases: Is there a common thread?
Catherine Bowes Rickman. Ophthal & Cell Biology, Duke University Medical Center, Durham, NC.

Presentation Description: The overlap of Alzheimer’s disease (AD) and age-related macular degeneration (AMD) will be considered. Both diseases are late-onset, heterogeneous, neurodegenerative
diseases resulting from a constellation of overlapping risk factors including aging, environmental risk factors and genetic susceptibility. AD is the most common cause of dementia in older adults, incurable and characterized by loss of learning and memory. It is characterized by neuropathologic accumulation of amyloid plaques and neurofibrillary tangles in the brain. In developed countries, AMD is the leading cause of irreversible blindness in the elderly and there are no treatments for the majority of patients. Early AMD is characterized by the formation of protein- and lipid-rich, sub-retinal pigmented epithelium (RPE) deposits. There is mounting evidence that these diseases share some pathogenic and pathophysiological elements. AD pathogenesis is driven by two processes that contribute to neural loss: extracellular deposition of beta amyloid (Aβ) and intracellular accumulation of tau protein. Therapies targeting Aβ in AD have been tested in clinical trials, without any clear indication that these drugs can improve AD symptoms. In AMD, Aβ accumulates and co-localizes with activated complement within sub-RPE deposits. In animal models immunotherapy targeting Aβ has shown promising results as was demonstrated for AD. Currently clinical trials targeting Aβ in AMD are underway. Will the differences in the sites and type (oligomeric or fibrillar) of Aβ accumulation in the eye versus the brain increase the potential for a positive outcome in these trials?

Commercial Relationships: Catherine Bowes Rickman, None
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Program Number: 12
Presentation Time: 10:00 AM–10:20 AM
Connections between aqueous humor/cerebral spinal fluid dynamics and disease
W Daniel Stamer. Duke University, Durham, NC.
Presentation Description: Physiologically there are many similarities between the dynamics of aqueous humor of the eye and cerebral spinal fluid of the brain. These are clear, specialized circulatory fluids that serve hydromechanical, environmental as well as transport functions. Delivering hormones and nutrients, while removing wastes requires constant formation and removal. The neuroepithelia of the ciliary processes and choroid plexi actively secrete aqueous humor and cerebral spinal fluid, respectively; while the trabecular/uveoscleral outflow pathways of the eye and arachnoid villi/lymphatic pathways of the brain drain these humors. Not surprisingly, the functional anatomy of these corresponding structures is strikingly similar, with production and removal rates into/from these closed compartments resulting in intraocular and intracranial pressure. Imbalances in the relative magnitude of intraocular pressure or intracranial pressure due to aging, obesity, obstruction of drainage or space flight results in pathology located at the lamina cribrosa of the optic nerve head. Susceptibility resides in the fact that the lamina cribrosa separates the intraocular and orbital subarachnoid compartments, which is continuous with the intracranial space. Alterations in this pressure gradient are thought to damage unmyelinated retinal ganglion cell axons as they pass through the lamina cribrosa, leading to glaucoma or papilledema; depending upon the force vector. Understanding the relationship between intraocular and intracranial pressure regulation will aid in developing targeted ways to minimize the pressure gradient across the lamina cribrosa and preserve vision.

Commercial Relationships: W Daniel Stamer, Aerie (C), Bausch and Lomb (C), Ironwood (F), Nicox (C), Inotek (F), Aerie (F), Allergan-Activas (F)
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