ARVO EDUCATION COURSE

Saturday, April 27, 2019
8am-12pm
Vancouver Convention Centre
Vancouver, British Columbia, Canada

Ocular immunology: Fundamentals, disease entities, and future therapeutic opportunities

Course organizers:

Lead organizer: Reza Dana, MD, Mass. Eye & Ear Infirmary / Harvard Medical School

Sunil Chauhan, PhD, Harvard Medical School

Daniel Saban, PhD, Duke University School of Medicine

Presentations

Presenters and presentations may change.

8-8:15am

Introduction- Spectrum of Ocular Immunopathologies

Reza Dana, MD, Mass. Eye & Ear Infirmary / Harvard Medical School

The spectrum of ocular immunpathologies include a wide range of conditions that encompass both the globe as well as adnexal structures (e.g. lacrimal gland and eyelids) that provide critical support for the functioning of the eye and visual system. These conditions include the various ocular atopic (allergic) disorders, dry eye disease, immune-mediated glaucoma syndromes, various uveitic disorders and some retinopathies, among others. This introductory lecture will provide the audience with a high-level overview of ocular immune mediated disorders and describe the areas of highest unmet medical need and relevant therapeutic strategies.

8:15-8:30am

Ocular Immune Privilege

Jerry Niederkorn, PhD, Univ Texas Southwestern Med Ctr

This presentation will review the concept of ocular immune privilege – a condition in which immune responses that occur at extraocular sites are either blocked or suppressed within the eye. Studies in mice have revealed that multiple anatomical, physiological, and immunoregulatory processes conspire to tightly regulate immune-mediated inflammation in the eye. Corneal transplants are beneficiaries of ocular immune privilege and enjoy a success rate that is unrivaled in the field of organ transplantation. This presentation will also briefly discuss the major strategies that protect ocular tissues from immune-mediated inflammation and coincidentally promote the survival of corneal transplants. The presentation will describe conditions in which immune privilege is terminated in order to protect the host from life-threatening infections even at the risk of blindness.

8:30-8:45am

Dry Eye Disease

Cintia De Paiva, MD, Baylor College of Medicine

Dry eye is a multifactorial disease where inflammation plays a key role. We will summarize the current knowledge about dry eye, including the most recent findings from humans and animal models with emphasis on the crosstalk of epithelial and immune cells.

8:45am-9am

Autoimmune posterior uveitis – lessons from animal models

Rachel R Caspi, PhD FARVO

Non-infections uveitis, believed to be of autoimmune origin, can cause severe vision los. Its etiology and the basic mechanisms involved in pathogenesis are unclear, and are difficult to study in humans for logistic and ethical reasons. We therefore turn to animal models, of which several have been developed that differ in their mode of induction as well as their clinical appearance and course. This presentation will describe different models of autoimmune uveitis, dissect the immunological responses that drive them, and discuss their relevance to human disease.

9am-9:15an

Corneal Transplantation and Beyond

Victor Perez, MD, Foster Center for Ocular Immunology at Duke Eye Center

Transplantation and acceptance of allogeneic tissue in the eye is what every transplant immunologist and surgeon wants to understand. In fact, corneal transplantation is the most common solid organ transplant performed in the United States and immune response to these can lead to new discovery in tolerance induction and immune-modulatory approaches to other allogeneic transplanted tissue as well. In contrast to other solid organ transplants, the eye provides a unique opportunity to have access to the transplanted tissue and assess readily clinically survival end-points, develop novels way of visualizing immune responses to allo-antigens, build pre-clinical models to understand immune mechanisms of rejection and deliver novel immune-therapies to prevent these and induce tolerance. In this session, we will exploit our models to visualize immune responses in vivo, which we have used to understand mechanisms of immune responses to allo-antigens in the eye, especially in the context of high risk corneal vascularized corneal transplant, which represent a model to other solid organ transplants. Moreover, in the context of other allotransplants performed in the eye, that include stem cells, understanding inflammatory responses will also be reviewed. In total, we believe that the development of novel approaches to regulate specific local immune- early after transplantation is an innovative approach to regulate ocular allo-immune responses and prevent long-termed rejection by exploiting the immune-regulatory responses of the eye to induce immune-tolerance to transplant rejection reactions.

9:15-9:30am

Development of inflammatory hypoxia and the prevalence of glycolysis in herpes simplex virus-induced stromal keratitis

Susmit Suvas, PhD, Wayne State University School of Medicine, Wayne State University School of Medicine

Herpes stromal keratitis (HSK) is a chronic immunoinflammatory condition, which develops in response to recurrent corneal infection with herpes simplex virus (HSV). Immune cell influx, neovascularization, loss of corneal sensation, and the stromal opacity in HSV-1 infected cornea are the hallmarks of HSK. In United States, HSK is a major cause of infection-induced blindness and the current treatments involve long-term use of anti-virals and the topical application of corticosteroids. Considering the importance of immune cell influx in the

development of HSK, the focus of this presentation will be to highlight the novel role of neutrophils and altered cellular metabolism in pathogenesis of HSK.

9:30-9:45am: Questions and Answers

9:45 -10am: Break

10-10:15am

Innate immunity in bacterial and fungal keratitis

Eric Pearlman, PhD, University of California, Irvine

Corneal infections caused by pathogenic bacteria and fungi are major causes of visual impairment and blindness worldwide. This presentation will cover recent advances in our understanding of the cellular and molecular events that underlie early stage host responses to these organisms.

10:15-10:30am

Interplay between adaptive and innate immune responses in chronic allergic eye disease (AED) and Meibomian gland dysfunction (MGD)

Daniel Saban, PhD, Duke University School of Medicine

The two major branches of the immune system are the 1) innate and 2) adaptive responses. In general terms, the former is fast-acting and nonspecific, whereas the latter is antigen-specific and long-lasting. While these two branches are considered distinct, functionally they can act in an inter-dependent fashion to carry out an immune process in disease states, which will be the focus of the current presentation. Additionally, I will show recent work from our lab demonstrating that the T helper cell compartment (adaptive) can orchestrate recruitment of neutrophils (innate) to drive ocular surface inflammation. Importantly, this coordinated response causes MGD in the 'chronic-like' AED model in mice. Similarly, MGD severity in patients is positively correlated with tear neutrophil quantity (Reyes NJ. 2018, Science Translational Medicine). Hence, the interplay between adaptive and innate immunity is an important area of study in ocular surface disease and may be key to better understanding the unresolved clinical problem of MGD in patients.

10:30-10:45am

Ocular Immune Modulation by Adult Stem Cells

Sunil Chauhan, PhD, Harvard Medical School

Mesenchymal stem cells are adult stem cells that possess extraordinary capacity to modulate tissue inflammation and regeneration. The objective of this educational talk is to discuss the mechanisms and factors by which adult stem cells regulate the immune response in inflamed ocular tissues.

10:45-10:55am: Questions and Answers

10:55 – 11am: Quick break to stretch

11-11:15am

Innate Immunity and Uveitis

James Rosenbaum, MD, Devers & Casey Eye Institutes

The innate immune system is strongly implicated in uveitis. Observations that support a major role for the innate immune system include: 1) uveitis is a manifestation of several autoinflammatory syndromes including Blau syndrome; 2) activation of TLR4 by bacterial endotoxin is a standard rodent model for anterior uveitis; and 3) an adjuvant that activates the innate immune system is generally required in most animal models of T cell dependent uveitis. The intestinal microbiome is an obvious potential source for ligands that could potentially activate the innate immune system within the eye.

11:15-11:30am

Complement Dysregulation/ Age-Related Macular Degeneration

Catherine Bowes Rickman, PhD, Duke University Medical Center

As part of innate immunity, the complement system normally functions to enhance pathogen-host defense by promoting inflammation, phagocytosis and cell membrane attack. Interestingly, however, genetic variants in complement system proteins, particularly complement factor H (CFH) on Chromosome 1, are strongly associated with risk for development and progression of Age-related macular degeneration (AMD). AMD is the leading cause of irreversible central blindness in elderly populations of industrialized nation. Risk for AMD is conferred predominantly by advanced aging and is modulated by this and genetic risk factors, as well as environmental stresses. An overview of the genetic impact of the CFH risk and the direct biological effect of the CFH risk variant in causing AMD will be presented.

11:30-11:45am

Type II cytokines, immune activation and regulation of metabolism

Andrew Dick, MD, University of Bristol, UCL-Institute of Ophthalmology

The outer retina and choroid are rich in traditional and non-traditional immune cells. We are increasingly understanding that their role is extending beyond response to sterile inflammation or infection. The interaction of Type II cytokines (IL4, 13) as well as other inflammasome enabled cytokines (IL-33), are in consort with myeloid cells (Microglia and monocytes) to in turn inhibit Type II cytokine reponses, such as fibrosis or angiogenesis. An emerging notion is that intracellular cytokine activation regulates and acts as a checkpoint inhibiting aerobic glycolysis and maintaining mitochondrial health and thus cell survival. This is pertinent to chronic insidiious degenerative conditions such as AMD where immune activation is a positive response to ensure cell survival.

11:45-11:55am: Questions and Answers

11:55am-12pm

Wrap up

Reza Dana, MD, Mass. Eye & Ear Infirmary / Harvard Medical School

Quick summary of the day.