225 Barrier function of the ocular surface - Minisymposium
Monday, May 08, 2017 11:00 AM–12:45 PM
Ballroom 2 Minisymposium
Program #/Board # Range: 1562–1569
Organizing Section: Cornea
Contributing Section(s): Immunology/Microbiology

Program Number: 1562
Presentation Time: 11:00 AM–11:02 AM
Welcome and Introduction
Jun Shimazaki. Department of Ophthalmology, Tokyo Dental College, Ichikawa, Japan.
Presentation Description: The aim of the mini-symposium "Barrier function of the ocular surface" will be presented, followed by introduction of the speakers.
Commercial Relationships: Jun Shimazaki, None

Program Number: 1563
Presentation Time: 11:02 AM–11:03 AM
Welcome and Introduction
Thomas A. Ferguson. Ophthal & Vis Sciences, Washington University, St Louis, MO.
Presentation Description: Welcome and Introduction
Commercial Relationships: Thomas A. Ferguson, F. Hoffmann-La Roche Ltd (C)

Program Number: 1564
Presentation Time: 11:03 AM–11:20 AM
Ocular surface glycocalyx barrier function
Pablo Argueso. Schepens Eye Research Institute and Massachusetts Eye and Ear, Harvard Medical School, Boston, MA.
Presentation Description: Carbohydrates have been traditionally considered sources of energy for the living organism. However, it is now becoming evident that carbohydrates also play important roles in determining cell function. A large number of carbohydrates are located on the cell surface, where they modulate a wide variety of cell-cell and cell-pathogen interactions. This communication results in a varied spectrum of cellular events, such as secretion of bioactive substances, recruitment of immune cells to areas of cellular damage, or cancer cell metastasis. We are interested in elucidating the structure and function of transmembrane mucins, a group of highly glycosylated, high-molecular-weight glycoproteins that constitute a major component of the protective biofilm on epithelial cell surfaces. Due to their extremely large size, they extend above other components of the plasma membrane, therefore constituting the outermost interface between the epithelial cell and the external environment. Our current studies involve investigating the interactions between transmembrane mucins and multivalent carbohydrate-binding proteins in the ocular surface epithelial glycocalyx. This field of investigation is yielding clues to the understanding of the pathogenesis of ocular surface diseases in which the glycocalyx barrier is compromised.
Commercial Relationships: Pablo Argueso, None
Support: NIH Grants EY024031 and EY026147

Program Number: 1565
Presentation Time: 11:20 AM–11:37 AM
Barrier function in dry eye diseases
Stephen C. Pflugfelder. Ophthal-Ocular Surf Ctr, Baylor College of Medicine, Houston, TX.
Presentation Description: The ocular surface is the most exposed mucosal tissue in the body. It is subjected to desiccation, chemical and particulate matter and a variety of microbes. There are elaborate barriers to these insults, including the lacrimal function unit that regulates production and clearance of tears that contain antimicrobial factors, glycocalyx and membrane mucins on the apical ocular surface epithelia and epithelial tight junctions. Tear dysfunction disrupts ocular surface barrier via alterations in tear volume and composition, decreased mucin production, altered epithelial differentiation and accelerated epithelial desquamation and apoptosis.
Commercial Relationships: Stephen C. Pflugfelder, Allergan, Inc. (C), Shire, Inc. (C), Senju (C)
Support: NIH Grant EY11915 (SCP), NIH Core Grants-EY002520 & EY020799

Program Number: 1566
Presentation Time: 11:37 AM–11:54 AM
Protection of the ocular surface barrier
M Elizabeth Fini[1, 2]. [1]USC Institute for Genetic Medicine, University of Southern California, Los Angeles, CA; [2]Proteris Biotech, Inc., Pasadena, CA.
Presentation Description: CLU (clusterin) is a highly conserved, homeostatic glycoprotein, first described in 1983 as a secreted factor that stimulates the 'clustering' of cells *in vitro*. Later it was discovered that CLU functions as an extracellular molecular chaperone, promoting proteostasis, cytoprotection and anti-inflammation in tissues throughout the body. CLU is especially prominent at fluid-tissue interfaces, including the ocular surface epithelia and tears. Recently, using a preclinical mouse model that mimics human dry eye disease, our team made the novel discovery that topical CLU prevents and ameliorates ocular surface barrier disruption caused by desiccating stress. It appears to do so by binding selectively to damaged cells. Positioned in this way, topical CLU protects both the cells and the protein components of the barrier. Results of knockout mouse studies suggest that endogenous CLU does the same, but that its protective action is overwhelmed in disease. Recognition of the novel 'sealing and healing' properties of CLU at the ocular surface has led us to propose that supplementation with topical CLU could serve as an innovative treatment for dry eye. It has been known for some time that endogenous CLU is depleted from the ocular surface epithelia in a variety of inflammatory conditions that lead to squamous metaplasia, thus CLU supplementation might further aid in maintaining mucosal differentiation. These ideas are now being tested.
Commercial Relationships: M Elizabeth Fini, Proteris Biotech, Inc. (S), Proteris Biotech, Inc. (P), Proteris Biotech, Inc. (E)
Support: NIH grants EY009828, EY012651, EY025890, EY026479

Program Number: 1567
Presentation Time: 11:54 AM–12:11 PM
Ocular Surface inflammation is regulated by innate immunity
Mayumi Ueta. Department of Frontier Medical Science and Technology for Ophthalmology, Kyoto Prefectural University of Medicine, Kyoto, Japan.
Presentation Description: As in the intestines and air way, on the ocular surface, the surface epithelium serves a critical function as the front-line defense of the mucosal innate immune system. An exaggerated epithelial host defense reaction to endogenous bacteria may initiate and perpetuate inflammatory mucosal responses, although the detection of microbes is arguably the most important task of the immune system.
I present about ocular surface inflammation due to disordered innate immunity and about our hypothesis that the onset of Stevens-Johnson syndrome (SJS) with severe ocular surface complications, a devastating ocular surface inflammatory disease, is strongly associated with abnormality of the innate immune system.

There is a possibility that some ocular surface inflammatory diseases are pathogenetically related with a disordered innate immune response, and focusing on the innate immunity of the ocular surface might help to elucidate the pathogenesis of various ocular surface diseases.
Commercial Relationships: Mayumi Ueta, None
Support: This work was supported by grants-in-aid from the Ministry of Education, Culture, Sports, Science and Technology of the Japanese government (BioBank Japan Project), and by the JSPS Core-to-Core Program (A. Advanced Research Networks), and partly by grants-in-aids for scientific research from the Japanese Ministry of Health, Labor and Welfare

Program Number: 1568
Presentation Time: 12:11 PM–12:28 PM
Microbial infections at the ocular surface
Eric Pearlman. Ophthalmology and Visual Sciences, University of California, Irvine, CA.
Presentation Description: Bacterial and fungal infections of the cornea can result in severe visual impairment and blindness. Fortunately, the ability of these microbes to penetrate the corneal stroma is limited by barrier functions at the ocular surface, including antimicrobial peptides and enzymes in tears, a dense glycocalyx at the corneal surface, and tight junctions formed by the corneal epithelium. The mechanisms and consequences of breaching these ocular defenses by pathogenic microbes will be discussed.
Commercial Relationships: Eric Pearlman, None
Support: NIH grants EY18612 and EY14362

Program Number: 1569
Presentation Time: 12:28 PM–12:45 PM
Allergic disease and ocular surface barrier
Andrea Leonardi. Neuroscience, Ophthalmology, University of Padua, Padova, Italy.
Presentation Description: Ocular allergy is a common ocular surface disorder that is increasing in incidence and causes considerable ocular morbidity. Conjunctival and corneal epithelial cells form a barrier to the outside world and are at the front line of mucosal immunity. Disruption of cell-cell junctions is required to initiate epithelial immune responses. Therefore, in order for allergens to pass from the external environment and interact with the conjunctival and corneal immune cells, they need to cross the conjunctival epithelium and enter the submucosal space. Defective epithelial barrier function may facilitate this process and might be linked to TH2 polarization in allergic patients. In fact, recent studies have emphasized the importance of epithelium-derived cytokines in promoting TH2 immune responses, at least in part by conditioning local dendritic cells (DCs). Moreover, conjunctival fibroblasts and epithelial cells activities and phenotypes in vitro can be modulated by diverse mediators involved in the ocular allergic reaction, such as histamine, IL-4, TGF-b1, and TNF-a but also by UV-B. The overall response of the two conjunctival layers to stimuli is delicately coordinated and orchestrated to produce well-defined sets of Hsps, whose imbalances may drive the course of the ocular allergic disease toward progression–aggravation or toward stabilization–remission. Several studies have revealed that these cytokines and other inflammatory mediators directly impair the barrier function of corneal epithelial cells and increase the expression of chemokines and adhesion molecules by corneal stromal fibroblasts, effects that may enhance allergic inflammation. Using conjunctival impression cytology samples, we collected sufficient RNA from conjunctival surface cells from normal subjects and vernal keratoconjunctivitis (VKC) patients, allowed successful transcriptome-wide expression analysis. Factors involved in both innate and adaptive arms of the immune system were found over-expressed in VKC samples. The increased expression of several chemotactic factors and co-stimulatory signals required for T cell activation and survival, confirms the complexity of this pathology. Therefore, maintenance or restoration of barrier function of the ocular surface is a potential goal for the treatment of ocular allergic reactions.
Commercial Relationships: Andrea Leonardi, Medivis (C), Santen (F), Dompè (C), Alcon (C), Santen (C)
Support: DOR1634548/16, 60A07-1101/15 from Italian Ministery of Health, and from a research unrestricted grant from Santen