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Review Article

Highlights from the 21st International Ocular Surface Society meeting

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1. Introduction

1.1. About the International Ocular Surface Society annual meeting

Scheffer Tseng, Andrew Huang, and Stephen Pflugfelder started the International Ocular Surface Society in the mid-1990s while they were at the Bascom Palmer Eye Institute. The mission of the society is to provide an open venue for the exchange of basic science and clinical information about various aspects of ocular surface diseases. The annual meeting format includes brief presentations followed by a discussion of each talk, an Award Lecture by a noted researcher in the field, followed by mini-Symposium in the afternoon. Each year the Mini-Symposium theme changes.

Annual meetings are held on the Saturday before Association for Research in Vision and Ophthalmology (ARVO) annual meetingd. The first few IOSS meetings were held at the Bascom Palmer Eye Institute when ARVO was in Ft. Lauderdale. Subsequently, the meetings have been at venues in the various cities hosting ARVO.

Meeting attendees are from around the world, including the Americas, Europe, and Asia. The annual meeting is sponsored by dues, meeting registrations, and independent medical education grants from industry. Society presidents have generally served a 5-year term. Scheffer Tseng served as the first president, followed by Kazuo Tsubota, Stephen Pflugfelder, and the current president, Cintia de Paiva. The society has co-sponsored several symposia with the European Contact Lens Society in the past.

2. 2018 annual meeting

The 21 s t Annual Meeting was held on April 28, 2018, at the Dole Cannery, Pomaikai Ballrooms in Honolulu, Hawaii. The specific goals of this meeting were to gain new knowledge and skills for treating ocular surface disorders and to promote interaction and networking among the participants.

The 2018 meeting program featured sessions in the morning and afternoon on a variety of clinical and basic ocular surface topics. There was ample time for discussions and interactions. The award lecturer was Dr. Mary Ann Stepp, Ph.D., and the title of her lecture was, “Intraepithelial Corneal Nerves and Dry Eye: too many, too few, or too depolarized?” The afternoon mini-symposium had a theme of “Lacrimal gland pathology and regeneration” by three investigators in the field: Dr. Cintia de Paiva, Dr. Driss Zoukhri, and Dr. Stefan Schrader.

2.1. Keynote Speaker

Dr. Mary Ann Stepp (Professor at the Department of Anatomy and Cell Biology and Department of Ophthalmology, George Washington University School of Medicine and Health Sciences, Washington DC) was selected as the 2018 Keynote Speaker. Her lecture was entitled “**Intraepithelial corneal nerves and dry eye: too many, too few, or too depolarized?**”, and her summary is below. Her co-authors were Alexa Williams, Gauri Tadvalkar, and Sonali Pal-Ghosh.

“It is an exciting time to be studying the ocular surface. Pharmacy shelves are overflowing with over the counter topical treatments for dry eye and vitamins for the eyes. The public is reminded of the importance of having comfortable eyes every time they turn on their radios and

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televisions. The numbers of patients in doctors' offices with ocular surface problems far exceeds those with other complications. Why is all of this good for basic and translational research on the eye? Because it reminds everyone every day that without a clear, pain-free refractive surface, we all suffer.

A few weeks ago, my lab manager called me from her local pharmacy asking me what eye drop to get for her son and his allergic itchy eyes. She was in the aisle looking over all the dry eye medications and could not find any eye drops for allergic symptoms. As it turned out, they were all sold out of every single bottle of every single company's product for allergic symptoms. The medications that research on the ocular surface have developed comfort to millions of people every day and get more effective all the time because of the work people are doing to understand the cornea and ocular surface.

It was an honor to give the Award Lecture at the meeting of the International Ocular Surface Society this year in Honolulu the day before ARVO meeting started. I have long admired the science done by many of those who attended, who asked questions and gave presentations. I was thrilled to see so many new faces and at the attention being given to the importance of the corneal sensory nerves in ocular surface health.

The ocular surface is covered by stratified squamous corneal epithelial cells that are in cell: cell contact with the plasma membranes of a dense network of nerve fibers whose somas are located in the trigeminal ganglion. These axons act as sentinels. They are early responders to chemical and mechanical injuries that can lead to blindness and they release trophic factors that nourish corneal epithelial cells and regulate their differentiation. The sheerness of the cornea makes it susceptible to superficial abrasions. Cell migration compromises adhesion of the healing epithelium to its substrate and the cell membranes of re-innervating sensory axons.

While often referred to as subbasal nerves, the intraepithelial corneal nerves are composed of two distinct populations of axons [1]. The majority extends between the membranes of the basal cells running parallel to the ocular surface and constitute the subbasal nerves. They enter into the epithelium from stromal nerves. Branching from the subbasal nerves, are the intraepithelial nerve terminals. They extend between the basolateral membrane of basal, suprabasal, and wing cells. Right before they reach the tight junction barrier formed by the apical squames, they turn and, once again, extend parallel to the ocular surface. They express GAP43 (Fig. 1), a protein expressed in growing axons [2,3], and live-cell imaging shows them extending, severing, and extending again [4,5], proving that they are continuously growing. As apical squames desquamate, their associated axons break and get phagocytosed by adjacent epithelial cells or are shed in the tears.

Aging reduces intraepithelial corneal nerves density in humans [6], and mice [7,8]. Mouse studies show that aging leads to reduced expression of genes by corneal epithelial that promote axonal elongation [9]. Recent studies also indicate that intraepithelial corneal nerves function is reduced in dry eye disease [9,10] and studies are currently underway to determine whether loss of intraepithelial corneal nerve function is a cause or consequence of dry eye disease.

The intraepithelial corneal nerves are millimeters long in humans, but along their entire length, they are deprived of the protection of glial cells. In the peripheral nervous system, non-myelinating glial cells called Schwann cells wrap around axons providing structural support and protection and facilitating axonal repair after injury. Corneal epithelial cells perform these functions for the intraepithelial corneal nerves [1]. It should not surprise us that when corneal epithelial cells are damaged, axon function is impaired. Exactly how sensory axons are impaired in dry eye, allergy, and aging and how we can help them recover are important topics for research going forward. The ocular surface community will play important roles in leading these efforts."

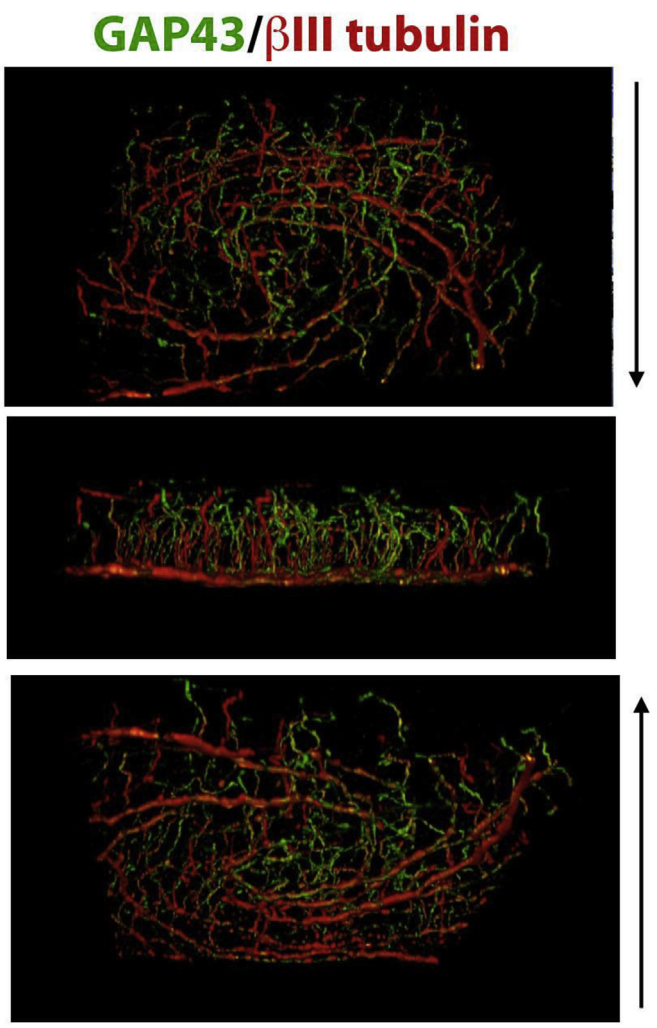

Fig. 1. Representative image of the subbasal nerves and the intraepithelial nerve terminals of an unwounded adult mouse cornea revealed using antibodies against beta III tubulin (red) and growth associated protein (GAP) 43 (green). Subbasal nerves and intraepithelial nerve terminals together make up the intraepithelial corneal nerves. Images were obtained from whole mount corneas as described [1]. The 3D cross sectional view shown in the center image and generated using Volocity has been rotated approximately 45° up (top) and 45° down (bottom) to highlight the apical extension of the nerve terminals. Intraepithelial nerve terminals branch from the subbasal nerves and grow continuously as highlighted by their apical staining with GAP43.

2.2. 2018 Mini-Symposium: Lacrimal Gland Pathology and Regeneration

1- Dr. Cintia de Paiva (Baylor College of Medicine, Houston, TX) presented her work on how inflammation participates in the development of age-related dry eye disease. She summarized her published studies with the Sjögren syndrome-prone NOD.B10−H2^{b} mouse strain, in which male mice develop dacryoadenitis. Her studies showed that these mice have a spontaneous worsening of dry eye phenotype and lacrimal gland inflammation with aging up to 2 years of age. Surprisingly, this was accompanied by an accumulation of regulatory T cells that maintained their Foxp3 expression while acquiring effector qualities, such as production of interferon-gamma in lacrimal gland and cervical lymph nodes. She also demonstrated that regulatory T cells, when isolated from aged NOD.B10·H2^{b} mice, lose their suppressive capacity in mixed lymphocyte reactions. Furthermore, adoptive transfer of aged regulatory cells induced similar T cell infiltration in lacrimal gland and goblet cell loss than aged effector cells in immunodeficient hosts, while no disease induction was observed in young donors. These