19th Annual
Winter Symposium

January 17-19, 2015
Canyons Grand Summit Hotel
Park City, Utah

Program Chairman: Glenn J. Jaffe, MD
**Guest Speakers**

**Douglas A. Jabs, MD, MBA**  
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Professor of Medicine  
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**Todd P. Margolis, MD, PhD**  
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**Glenn J. Jaffe, MD**  
Professor of Ophthalmology  
Chief, Vitreoretinal Service  
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using the chi-square test, and p values were corrected for multiple hypotheses testing using permutation. All analyses were conducted with PLINK.

**Results:** Two SNPs, rs1891467 in transforming growth factor beta (TGF) - β2 and rs479777 upstream of CCDC88B were associated with ocular sarcoidosis involvement. Specifically, the G allele of rs1891467 (OR=4.6, p=0.035) and the T allele of rs479777 (OR=4.2, p=0.002) were found to be more prevalent in ocular sarcoidosis cases. These associations remained after multiple hypothesis correction (p values of 0.03517 and 0.002677, respectively). The TGF-β2 59941 G allele has previously been associated with increased risk of pulmonary fibrosis, and the rs479777 T allele has been linked with an increased susceptibility to sarcoidosis in European populations.

**Conclusions:** The rs1891467 and rs479777 polymorphisms were associated with an increased risk of ocular involvement in sarcoidosis. Further investigation is necessary to confirm this initial finding.

8:29-8:34AM **Discussion**

8:34-8:41AM **HLA-A29+ Birdshot Chorioretinopathy in an African American Patient**

Pauline T. Merrill, MD

8:41-8:46AM **Discussion**

8:46-8:58AM **Automated Measure of Retinal Vascular Leakage on Ultra-Widefield Fluorescein Angiography in Patients with Uveitis**

Paula E. Pecen, MD

Santen, Inc. travel grant awardee

**Purpose:** 1. To demonstrate the utility of ultra-widefield fluorescein angiography (FA) as an objective measure of inflammatory activity in patients with uveitis.

2. To develop a method to quantify retinal vascular leakage on ultra-widefield FA in patients with uveitis.

3. To correlate retinal vascular leakage analysis with inflammatory status in patients with uveitis based on clinical exam.

**Methods:** Patients with uveitis were evaluated with ultra-widefield FA Optos® 200Tx between May 2012 and December 2013. Clinical data was collected to assess uveitis status as active or inactive inflammation based on clinical examination. Images were initially graded to identify those with or without leakage. One late phase widefield FA image from each eye was transformed into a standardized projection to accurately represent the 3-dimensional globe in a 2-dimensional image. A custom designed image analysis software was developed to automatically and objectively quantify retinal vascular leakage by eliminating the retinal vessels and optic nerve, and quantified only hyperfluorescent perivascular leakage (white areas within the image); the total leakage area was then divided by the total area of the retinal surface in the standardized image.

**Results:** An initial set of 254 patients with uveitis and a total of 1053 eye images were reviewed. Corresponding eye exams were reviewed for each imaging session and revealed 607 eye images deemed clinically active. Of the 1053 eye images, 628 eye images were identified with leakage. All 607 eye images (100%) which were clinically active were also found to have leakage. Automated leakage analysis was then performed on a subset of 164 images (93 eyes with active inflammation and 71 with inactive inflammation). The mean leakage area percentage in eyes with active inflammation was 4.4% of the total area of the retina, whereas the mean leakage area of eyes with inactive inflammation was 0.9% (p < 0.0001).

**Conclusions:** Retinal vascular leakage on ultra-widefield FA accurately identifies and correlates with active inflammation in patients with uveitis. Automated retinal vascular leakage analysis highly correlates with inflammatory status based on clinical examination. Based on automated retinal vascular leakage, an objective measure of inflammation may not only guide therapeutic decisions, but may also help identify subclinical inflammation and may be used as an objective endpoint of future clinical treatment trials in uveitis.

8:58-9:03AM **Discussion**

9:03AM-9:10AM **Case unknown**

Douglas A. Jabs, MD, MBA
immune battleground in routine orolabial HSV-1 infection, but, as for ocular syndromes, we can only speculate if boosting these local T-cell responses will be helpful or harmful. Acyclovir resistance is still a problem, and suppression of shedding and transmission by current nucleoside therapy is incomplete. Antivirals with a newer target, the viral helicase/primase have promising activity in recurrent genital HSV infection, including at prolonged dosing intervals.

4:50-5:00PM Discussion

5:00-5:45PM Herpes, the Infection that Keeps Giving
Todd P. Margolis, MD, PhD
The human herpes viruses are well established causes of recurrent and chronic uveitis, from iritis to retinitis. HSV, VZV and CMV are the most common causes and in the first half of this talk I will discuss the presentation and management of these diseases with an eye on the pathophysiology of recurrent ocular disease.

The concepts that I will be presenting will derive from a number of different sources including clinical trials, personal clinical experience, and an understanding of human anatomy, immunology, the molecular biology of the virus, and animal models of disease. In the second half of the talk I will discuss animal model based mechanisms of HSV-1 latency in the nervous system, including a new model of the regulation of HSV latency that we recently discovered in our lab.

5:45-5:55PM Discussion

5:55-6:15PM Break

6:15-7:29PM CASE PRESENTATIONS/ FREE PAPERS

6:15-6:22PM Proliferative Retinopathy in Acute Retinal Necrosis
Shilpa Kodati, MD

6:22-6:27PM Discussion

6:27-6:34PM Recurrent Acute Retinal Necrosis
Lana Rifkin, MD

6:34-6:39PM Discussion

6:39-7:19PM Treatment of Cytomegalovirus Retinitis with CMV-Specific T-Lymphocyte Infusion
Szilard Kiss, MD
Cytomegalovirus retinitis is a blinding infection that affects immunocompromised patients who are unable to generate a T-cell response against the organism. Infusion of CMV-specific leukocytes has been shown to be effective in patients with systemic CMV infection, especially those resistant to standard therapies or those who are unable to tolerate the side effects of systemic pharmacotherapy. We have developed a protocol for the specific treatment of CMV retinitis that includes infusion of third-party donor derived CMV pp65-specific T-cells. Several cases will be presented to highlight a potential role for CMV-specific leukocyte infusion in the treatment of CMV retinitis.

7:19-7:29PM Discussion

7:29-7:34PM INDUSTRY PARTNER PRESENTATIONS

7:29-7:34PM Santen, Inc.

7:34-7:39PM Allergan, Inc.

7:39PM End of Session 2

7:45-10:00PM Dinner at The Canyons Grand Summit Hotel

SUNDAY
JANUARY 18

7:00-8:00AM Breakfast

7:00-9:20AM Exhibits

8:00-8:05AM Introduction
Glenn J. Jaffe, MD

8:05-9:37AM CASE PRESENTATIONS/ FREE PAPERS

8:05-8:12AM White Out: Bilateral Retinitis in a 9 Year Old
Marissa Bucci, MD

8:12-8:17AM Discussion

8:17-8:29AM Human Ocular Surface Microbiome Composition Revealed by Next-Generation Sequencing
Thuy Doan, MD
Santen, Inc. travel grant awardee

Purpose: Human mucosal surfaces are thought to be colonized by a diverse community of microorganisms that help shape the immune system and when altered may lead to infections or cause inflammation in the host. Conventional culture techniques have failed to identify the composition and to characterize the diversity of these communities because a majority of these microbes are unculturable. Unlike the skin, GI tract, or oral mucosa, where next-generation sequencing techniques have been successfully applied to understand native microbial communities, the ocular surface microbiome remains incompletely characterized. In this study, we sought to characterize the ocular surface bacterial community in healthy subjects by using 16S rRNA gene deep sequencing on the Illumina platform. Quantitative PCR for Torque Teno Virus (TTV) was also performed. Data were analyzed in R.

Results: Sequencing resolution to the genus and species levels were obtained for 140 conjunctiva samples from 35 healthy volunteers. Propionibacterium acnes, Arthrobacter fusiformis, Corynebacterium tuberculostearicum, and Enterobacter hormaechei were the most abundant species comprising of 8.3%, 7.8%, 5.3%, and 4.9% of the identified reads, respectively, across all samples. Principal component analyses showed that the genera responsible for the majority of the variance across all conjunctiva samples were Corynebacterium, Propionibacterium, Staphylococcus, Neisseria, Stenoyxobacter, and Streptococcus. TTV was detected in 63% of the patients (17/27). Subgroup analyses revealed that the TTV load was statistically higher in men compared to women (0.012 TTV copy/epithelial cell ± 0.0028 TTV copy/epithelial cell vs. 0.001 TTV copy/epithelial cell ± 0.0006 TTV copy/epithelial cell, mean ± SEM, p = 0.0078). However, TTV load was not dependent on age (0.012 TTV copy/epithelial cell ± 0.0035 TTV copy/epithelial cell ≤60 years old) vs. 0.005 TTV copy/epithelial cell ≤0.0018 TTV copy/epithelial cell ≤30 years old, p = 0.9623).

Conclusions: The ocular surface microbiome bacterial composition in healthy volunteers is diverse. The variability across samples is largely determined by Corynebacterium, Propionibacterium, Staphylococcus, Neisseria, Stenoyxobacter, and Streptococcus. Low TTV levels are found in the majority of the samples and TTV viral load is dependent on gender. Future experiments using unbiased next-generation sequencing to characterize the bacterial, fungal, and viral composition of the ocular surface will further our understanding of ocular infectious and inflammatory diseases.

8:29-8:34AM Discussion

8:34-8:46AM The Influence of Race and Gender on the Risk of Hair Loss Secondary to Methotrexate
Sarah M. Escott, MD
Many uveitides, particularly the more severe intermediate, posterior, and panuveitides, are chronic diseases with a low rate of spontaneous remission. As such they typically require chronic medical therapy. Conventional immunosuppressive agents (aminopterin, calcineurin inhibitors) and biologic agents have a low rate of inducing a sustained, drug-free remission.

The only immunosuppressive agents which appear to be able to induce a sustained, drug-free remission are alkylating agents, where a drug-free remission can be induced in 70-90% of patients with a relapse rate of <5%/year. However, these agents are associated with a likely increased risk of malignancy and typically are reserved for diseases where other agents do not work adequately well.

More recent data from the SITe Study suggests that therapeutic vitrectomy may double to triple the rate of remission in intermediate uveitis. Well analyzed case series also suggest that peripheral retinal ablative therapy (e.g. cryotherapy, photocoagulation) also may induce a remission in patients with intermediate uveitis. These data suggest that surgical approaches may have benefit in the management of patients with intermediate uveitis.

8:46-8:51AM
Discussion

8:51-9:03AM
Studies of Purified Triamcinolone
William R. Freeman, MD

9:03-9:08AM
Discussion

9:08-9:20AM
Retinoschisis in Pars Planitis
Julia F. Malalis, MD

9:20-9:25AM
Discussion

9:25-9:32AM
Severe H1N1 Retinopathy
Mark W. Johnson, MD

9:32-9:37AM
Discussion

9:37AM
End of Morning Session

3:30-4:00PM
Après Ski Refreshments

3:30-7:28PM
Exhibits

4:00-5:55PM
SCIENTIFIC SESSION 2: MECHANISMS OF UVEITIS REMISSION

4:00-4:05PM
Introduction
Glenn J. Jaffe, MD

4:05-4:50PM
Long-term Drug-Free Remissions in Uveitis
Douglas A. Jabs, MD, MBA

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5:45-5:55PM
Discussion

5:55-6:15PM
Break

6:15-7:18PM
CASE PRESENTATIONS/ FREE PAPERS

6:15-6:27PM
Long Term Drug-free Remission After Chlorambucil Therapy
Debra A. Goldstein, MD

6:27-6:32PM
Discussion

6:32-6:44PM
Characteristics of Chronic Uveitis in the Elderly
Wanda Martinez, MD

6:44-6:49PM
Discussion

6:49-6:56PM
Double Trouble
Ashwini Reddy, MD

6:56-7:01PM
Discussion

7:01-7:13PM
The Role of the Gut Microbiota in Immune-mediated Uveitis
Phoebe Lin, MD, PhD

7:13-7:18PM
Discussion

7:18-7:28PM
INDUSTRY PARTNER PRESENTATIONS

7:18-7:23PM
Bausch+Lomb

7:23-7:28PM
XOMA Corp.

7:28PM
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