

June 28 (Friday) 17:20-18:20 Room 2 (Small Auditorium)

## Rapid Fire-Day 1

Chairs: John Gonzales (*USA*)  
Ko-Hei Sonoda (*Japan*)  
Yoko Ozawa (*Japan*)

- RF1-1**     **Anti-Vascular Endothelial Growth Factor Agent Reduces Inflammation in Diabetic Macular Edema**  
Hidetaka Noma (*Japan*)
- RF1-2**     **Hyperreflective Foci in DME with Serous Retinal Detachment: Association with Dyslipidemia**  
Kihwang Lee (*South Korea*)
- RF1-3**     **Diabetic Proliferative Fibrous Membrane Formation-Histopathological Study**  
Po-Ting Yeh (*Taiwan*)
- RF1-4**     **Effect of triamcinolone acetonide on retinal inflammation and angiogenesis**  
Tomohiro Otsuka (*Japan*)
- RF1-5**     **Dynamics of Soluble VEGF Receptors and their Ligands in Aqueous Humour During Ranibizumab for AMD**  
Ryosuke Motohashi (*Japan*)
- RF1-6**     **Choroidal thickness and blood flow velocity in a patient with acute macular neuroretinopathy**  
Yuki Hashimoto (*Japan*)
- RF1-7**     **Widefield fluorescein angiography findings in patients with retinal edema after cataract surgery**  
Sohee Jeon (*South Korea*)
- RF1-8**     **Ocular Toxoplasmosis in a tertiary referral centre. Clinical features, treatment and prognosis**  
Peter McCluskey (*Australia*)
- RF1-9**     **Usefulness of vitreous biopsy for steroid-resistant intermediate uveitis**  
Mitsunao Ide (*Japan*)
- RF1-10**    **Retinal complications in uveitis patients in Taiwan**  
Yu-Hsuan Huang (*Taiwan*)
- RF1-11**    **Inflammatory characteristics in TAO using 3D human organoid**  
Fumihito Hikage (*Japan*)
- RF1-12**    **Povidone-Iodine/Dexamethasone Eye Drops in Adenoviral Conjunctivitis Treatment: A Systematic Review**  
Herdanti R Putri (*Indonesia*)

## Rapid Fire-Day 1

**RF1-1 Anti-Vascular Endothelial Growth Factor Agent Reduces Inflammation in Diabetic Macular Edema**Hidetaka Noma, Kanako Yasuda, Ryosuke Motohashi,  
Ryosuke Matsushima, Masahiko Shimura*Hachioji Medical Center, Tokyo Medical University, Tokyo, Japan*

## [Purpose]

To investigate the correlations among the aqueous flare value (an indicator of inflammation), functional-morphologic parameters, and aqueous humor levels of factors/receptors were investigated in patients with diabetic macular edema (DME) who received intravitreal ranibizumab injection (IRI).

## [Methods]

Aqueous humor levels of 10 cytokines or growth inflammatory/factors were measured in 46 DME patients receiving IRI. Aqueous humor levels of vascular endothelial growth factor (VEGF), soluble VEGF receptor (sVEGFR), and other cytokines/inflammatory factors were measured by the suspension array method. Aqueous flare values were measured with a laser flare meter and center macular thickness (CMT) was examined by optical coherence tomography.

## [Results and Discussion]

Compared with before treatment (baseline), the aqueous flare value showed a significant decrease at 1 month after IRI therapy. There were significant correlations between the aqueous flare value and the aqueous levels of sVEGFR-1, placental growth factor, monocyte chemoattractant protein 1, soluble intercellular adhesion molecule-1, interleukin-6, and interferon-inducible 10-kDa protein. In addition, a significant correlation was noted between the change of the aqueous flare value and improvement of CMT at 1 month after IRI.

## [Conclusions]

These findings suggest that IRI reduces inflammation and that the aqueous flare value is influenced by inflammatory factors/cytokines. In addition, the change of the aqueous flare value may be an indicator of CMT in DME patients receiving IRI therapy.

**RF1-3 Diabetic Proliferative Fibrous Membrane Formation-Histopathological Study**

Po-Ting Yeh, Chung-May Yang, Chang-Hao Yang

*Department of Ophthalmology, National Taiwan University Hospital, Taipei, Taiwan*

**Purpose:** To investigate the clinical and histopathological features of the proliferative fibrous membrane after diabetic vitrectomy.

**Methods:** The patients with diabetic retinopathy (PDR) who had to undergo vitrectomy were enrolled as the PDR group. In addition, patients with proliferative vitreoretinopathy (PVR) who needed to undergo vitrectomy were included as the control group. The patients in the PDR group were further divided into: 1. Active PDR with bevacizumab pre-treatment; 2. Active PDR without bevacizumab pretreatment; 3. Mainly fibrotic PDR. Proliferative fibrous membrane and vitreous fluid of PDR or PVR were collected during surgery and further processed for pathological and ELISA analysis.

**Results and Discussion:** Immunohistochemistry analysis showed that CD45 and GFAP staining were more obvious in PDR than in PVR ( $p < 0.05$ ); alpha-SMA and TGF-beta were significantly prominent in active PDR than in fibrotic PDR and PVR ( $p < 0.05$ ). In the vitreous fluid, CTGF and TGF-beta were significantly higher in active PDR than in fibrotic PDR and PVR ( $p < 0.05$ ).

**Conclusions:** Immunohistochemistry study showed that the proliferative fibrous membranes in PDR mainly consist of glial cells and their formation may be related to inflammatory responses. Alpha-SMA, TGF-beta and CTGF were more prominent in active PDR than in PVR and fibrotic PDR; therefore, the membranes are prone to have fibrotic contraction and induce tractional retinal detachment clinically.

**RF1-2 Hyperreflective Foci in DME with Serous Retinal Detachment: Association with Dyslipidemia**Kihwang Lee<sup>1</sup>, Yoo-Ri Chung<sup>1</sup>, Seung Yeop Lee<sup>1</sup>, Young Ho Kim<sup>1</sup>,  
Hye-Eun Byeon<sup>2</sup>, Jeong Hun Kim<sup>3,4,5</sup>

<sup>1</sup>Department of Ophthalmology, Ajou University School of Medicine, Suwon, South Korea, <sup>2</sup>Institute of Medical Science, Ajou University School of Medicine, Suwon, South Korea, <sup>3</sup>Fight against Angiogenesis-Related Blindness (FARB) Laboratory, Clinical Research Institute, Seoul National University Hospital, Seoul, South Korea, <sup>4</sup>Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, South Korea, <sup>5</sup>Department of Ophthalmology, Seoul National University College of Medicine, Seoul, South Korea

**[Purpose]:** To investigate the presence of hyperreflective foci (HF) and their association with dyslipidemia in serous retinal detachment (SRD)-type diabetic macular edema (DME) to support the idea that HF on optical coherence tomography (OCT) findings of DME patients could be indicative of activated microglia.

**[Methods]:** The medical records and OCT findings were retrospectively reviewed in 33 eyes with SRD-type macular edema associated with diabetic retinopathy (DR) and compared with 22 eyes with branch retinal vascular occlusion (BRVO). The mean number of HF, the mean choroidal thickness, and lipid profiles were analyzed and compared between groups.

**[Results and discussion]:** The mean number of HF and the mean choroidal thickness were significantly higher in DR group compared to BRVO group. Significant correlation of HF were noted with total cholesterol ( $r = 0.496$ ,  $P = 0.006$ ), as well as with triglycerides ( $r = 0.639$ ,  $P = 0.002$ ). Among lipid profiles, triglycerides remained significantly associated with HF by multiple linear regression ( $\beta = 0.004$ , 95% CI: 0.001 - 0.019,  $P = 0.030$ ).

**[Conclusions]:** HF on OCT of DME patients could be indicative of activated microglia. HF are associated with dyslipidemia, especially high triglycerides, suggesting inflammatory reaction from dyslipidemia in diabetic retina. Further studies concerning the effect of lipid-lowering therapy to HF and associated inflammation may be needed.

**RF1-4 Effect of triamcinolone acetonide on retinal inflammation and angiogenesis**Tomohiro Otsuka<sup>1</sup>, Tomomi Masuda<sup>1</sup>, Yuji Takahashi<sup>1</sup>, Ayako Suzuki<sup>1</sup>,  
Akiyoshi Uemura<sup>2</sup>, Reijiro Arakawa<sup>1</sup>, Akira Naito<sup>1</sup>

<sup>1</sup>Drug Evaluation and Research Sagami Research Laboratories, Wakamoto Pharmaceutical Co., Ltd., Kanagawa, Japan, <sup>2</sup>Department of Ophthalmology and Visual Sciences, Nagoya City University, Nagoya, Japan

## [Purpose]

The objective of this study is to clarify the action mechanism of triamcinolone acetonide (TA) on retinal inflammation and angiogenesis using both in vitro and in vivo models.

## [Methods]

Retinal inflammation and abnormal angiogenesis caused by pericyte depletion in retinal veins were induced by intraperitoneal injection of anti-platelet derived growth factor receptor- $\beta$  (PDGFR- $\beta$ ) antibody at P1 in C57BL/6 mice. TA was injected into the vitreous at P7, and then retinal inflammation and angiogenesis were histologically analyzed at P10 and P13. Change in retinal gene expression in antibody-injected mice was analyzed by microarray at P13. Human retinal microvascular endothelial cells (HRMECs) were cultured with TA in the presence of VEGF or FGF, and then cell proliferation and migration were measured. Effects of TA on some angiogenic factors were also investigated.

## [Results and Discussion]

Injection of anti-PDGFR- $\beta$  antibody induced significant inflammation and disruption of retinal vascular integrity and morphology in mice. TA reduced inflammation and improved disruption of vascular morphology. As a result of microarray analysis, inflammation and angiogenesis related genes were found to be upregulated in antibody-injected mice. TA inhibited HRMECs proliferation and migration induced by VEGF or FGF in vitro.

## [Conclusions]

TA reduced retinal inflammation and abnormal angiogenesis in mice. Effect of TA may be partially mediated by inhibiting the proliferation and migration of vascular endothelial cells. Further investigations might be needed.

**RF1-5 Dynamics of Soluble VEGF Receptors and their Ligands in Aqueous Humour During Ranibizumab for AMD**

Ryosuke Motohashi, Hidetaka Noma, Kanako Yasuda, Masahiko Shimura  
Hachioji Medical Center, Tokyo Medical University, Tokyo, Japan

[Purpose] Intravitreal ranibizumab injection (IRI) is effective for patients with exudative age-related macular degeneration (AMD) and decreases intraocular levels of vascular endothelial growth factor (VEGF), but VEGF receptor intraocular dynamics after IRI are unclear. Therefore, we evaluated changes in the aqueous humor levels of soluble vascular endothelial growth factor receptor (sVEGFR)-1, sVEGFR-2, and their ligands for these receptors (VEGF) patients with AMD receiving IRI.

[Methods] The subjects were 24 patients with AMD (24 eyes) who received 3 doses of IRI at monthly intervals. Aqueous humor samples were obtained when each IRI dose was given (visits 0, 1, and 2 at 4-week intervals). Then the suspension array method was employed to measure sVEGFR-1, sVEGFR-2, VEGF, and placental growth factor (PlGF) in aqueous humor samples from the 24 AMD patients and 13 cataract patients (as controls). Best corrected visual acuity (BCVA) and central macular thickness (CMT) were also assessed over time.

[Results and Discussion]: At baseline, the aqueous humor levels of sVEGFR-1, sVEGFR-2, VEGF, and PlGF were significantly higher in the AMD group than in the control group. There was a significant correlation between VEGF and PlGF or between sVEGFR-1 and sVEGFR-2. BCVA and CMT both improved significantly after IRI, and the aqueous humor levels of VEGF, PlGF, and sVEGFR-1 also decreased significantly.

[Conclusions] VEGFRs may be involved in the pathogenesis of AMD. IRI improves clinical parameters in AMD patients by suppressing intraocular levels of VEGF, PlGF, and sVEGFR-1.

**RF1-7 Widefield fluorescein angiography findings in patients with retinal edema after cataract surgery**

Sohee Jeon  
Keye Eye Center, Seoul, South Korea

Purpose: To evaluate the ultra-widefield fluorescein angiography (UWFA) findings in patients with cystoid macular edema (CME) after cataract surgery.

Methods: Retrograde chart review was done. 33 patients who showed CME after cataract surgery were included. Ophthalmologic examinations, including UWFA, were performed. UWFA was scored according to a system suggested by the Angiography Scoring for Uveitis Working Group (ASUWG). Demographic characteristics were compared between patients with normal and abnormal UWFA findings. Factors associated with a high ASUWG score were evaluated. UWFA findings in an eye with CME after cataract surgery and factors associated with the ASUWG score.

Results: Thirty-three eyes (100.0%) of 33 eyes showed abnormal UWFA findings, including optic disc staining (27 eyes, 81.8%), capillary leakages at peripheral or posterior pole (33 eyes, 100.0%), pinpoint leakage (28 eyes, 84.8%), peripheral retinal vascular leakage (8 eyes, 24.2%), and retinal staining or subretinal pooling (2 eyes, 6.1%). Univariate regression analysis showed that the age (beta=-0.690, p=0.001) and the presence of ERM (p=0.029) were associated with high ASUWG score. Multiple regression analysis revealed that after adjustments for other factors, age was independently associated with a higher ASUWG score (beta=-0.690, p=0.001).

Conclusions: Patients with CME after cataract surgery shows generalized inner and outer blood retinal barrier (BRB) breakage. Particular attention is required for cataract surgery with patients with young age and preoperative retinal abnormalities.

**RF1-6 Choroidal thickness and blood flow velocity in a patient with acute macular neuroretinopathy**

Yuki Hashimoto<sup>1,2</sup>, Wataru Saito<sup>2,3</sup>, Michiyuki Saito<sup>2</sup>, Yuka Hasegawa<sup>2</sup>, Takeshi Yoshitomi<sup>1,4</sup>, Susumu Ishida<sup>2</sup>

<sup>1</sup>Fukuoka International University of Health and Welfare, Fukuoka, Japan, <sup>2</sup>Department of Ophthalmology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan, <sup>3</sup>Kaimeido Eye and Dental Clinic, Sapporo, Japan, <sup>4</sup>Department of Ophthalmology, Akita University Graduate School of Medicine, Akita, Japan

Background: To quantitatively examine sequential changes in the morphology and circulation hemodynamics of the choroid using EDI-OCT and laser speckle flowgraphy (LSFG) in a patient with acute macular neuroretinopathy (AMN).

Case presentation: A 15-year-old boy was referred to our hospital due to AMN in his right eye alone. The next day AMN developed OS. Three months later, bilateral AMN lesions spontaneously resolved and the morphology of macular photoreceptors improved. Central choroidal thickness (CCT) of the right eye decreased by 86 µm after three months, compared with that at the initial visit. In the left eye, similarly, CCT increased by 16 µm after the AMN onset at 1 week compared with a pre-onset value at the first visit and thereafter decreased by 57 µm at 3 months. Macular MBR increased by 20-55% OD and 51-71% OS during the follow-up until 3 months.

Conclusions: We found that the choroid at the macula thickened at the onset of AMN and became thin with the regression of disease. Our EDI-OCT and LSFG results suggest that choroidal circulation impairment plays a role in the pathogenesis of AMN.

**RF1-8 Ocular Toxoplasmosis in a tertiary referral centre. Clinical features, treatment and prognosis**

Peter McCluskey<sup>1,3,4</sup>, Will Yates<sup>1,3</sup>, Fabian Chiong<sup>2,5</sup>, Sophia L Zagora<sup>1,3</sup>, Jeffrey J Post<sup>2,5</sup>, Denis Wakefield<sup>6,7</sup>

<sup>1</sup>Save Sight Institute, University of Sydney, Sydney, Australia, <sup>2</sup>Department of Infectious Diseases, Prince of Wales Hospital, Sydney, Australia, <sup>3</sup>Sydney Eye Hospital, Sydney, Australia, <sup>4</sup>St Vincent's Clinic, Darlinghurst, Australia, <sup>5</sup>Prince of Wales Clinical School, University of UNSW, Randwick, Australia, <sup>6</sup>School of Medical Sciences, University of NSW, Sydney, Australia, <sup>7</sup>NSW Health Pathology, NSW Health, Sydney, Australia

Purpose: To determine the severity and clinical course of ocular toxoplasmosis in an Australian tertiary referral centre. Methods: Retrospective review of patient files who presented to Sydney Eye Hospital between 2007 and 2017 with clinical features consistent with ocular toxoplasmosis. Baseline risk factors and treatment details were recorded and analysed. Visual acuity and relapse rate compared to other studies in ocular toxoplasmosis. Results: 48 patients with ocular toxoplasmosis who presented to Sydney Eye Hospital during the period of observation. The median age was 35.5 (IQR 21-50) with 29 (60%) having no previous symptomatic episodes or evidence of chorioretinal scarring. Visual acuity at presentation was 0.51 or 6/19 (SE 0.096) and at follow up 0.31 or 6/9 (SE 0.094). 9 patients experienced a recurrence during the period of observation with time to recurrence 2.2 years (SE 0.45). The relapse rate (1 or more) 0.09/person-year. Location of lesion was predominantly within the vascular arcades (n=44) with macular involvement in 9 patients. Most patients received clindamycin therapy (n=34) with pyrimethamine and sulfadiazine used for those with macula involvement. Conclusion: Patients with ocular toxoplasmosis had fewer recurrences compared with other published series and had better visual recovery. The majority of patients received clindamycin and oral prednisolone which was well tolerated with pyrimethamine and sulfadiazine reserved for those with macula involving disease

**RF1-9 Usefulness of vitreous biopsy for steroid-resistant intermediate uveitis**

Mitsunao Ide<sup>1,2</sup>, Hiroshi Takase<sup>1</sup>, Kyoko Ohno-Matsui<sup>1</sup>

<sup>1</sup>Ophthalmology & Visual Science Tokyo Medical and Dental University, Tokyo, Japan, <sup>2</sup>Japanese Red Cross Musashino Hospital, Tokyo, Japan

**Purpose:** To investigate the usefulness of vitreous biopsy for steroid-resistant intermediate uveitis of unknown etiology.

**Methods:** Thirty eyes of 30 patients (male ratio = 56%, mean age = 61 y.o.) who underwent vitreous biopsy. Comprehensive analysis including cytology, immunoglobulin heavy chain (IgH) gene rearrangement, cytokine concentration, polymerase chain reaction (PCR) for various infectious agents, and Goldmann-Witmer coefficient (GWC) of rubella virus (RV) were performed. Data regarding patients' demographics, ocular manifestations, final diagnosis, and biopsy results were retrospectively collected from the medical records.

**Results:** The final diagnosis of the 30 patients included intraocular lymphoma (7 patients) diagnosed by the combination of cytology, IgH rearrangement, and interleukin (IL)-10/IL-6 ratio (>1), and RV associated uveitis (8 patients) diagnosed by GWC. Among the 15 patients in whom no significant results were obtained by biopsy, diagnosis of sarcoidosis (2 patients) and ocular tuberculosis (1 patient) were eventually made by systemic investigations.

**Conclusion:** Patients with steroid-resistant intermediate uveitis included certain number of intraocular lymphoma as well as RV-associated uveitis. Vitreous biopsy was useful to diagnose such diseases as well as to exclude other infectious uveitis.

**RF1-11 Inflammatory characteristics in TAO using 3D human organoid**

Fumihito Hikage<sup>1</sup>, Kaku Itoh<sup>1</sup>, Yosuke Ida<sup>1</sup>, Haruka Ida<sup>1</sup>, Chiaki Ohta<sup>1</sup>, Arisa Takahashi<sup>1</sup>, Tae-Hwa Chun<sup>2</sup>, Hiroshi Ohguro<sup>1</sup>

<sup>1</sup>Sapporo Medical University, Sapporo, Japan, <sup>2</sup>University of Michigan, Ann Arbor, USA

**[Purpose]** Thyroid-associated ophthalmopathy (TAO) is one of the major complications often associated with Graves' thyrotoxicosis. During the progression of TAO, retrobulbar orbital connective tissue becomes inflammatory and fibrotic. In this study, we aim to develop a 3D human organoid model to recapitulate tissue remodeling and gene expression observed in TAO.

**[Methods]** Human orbital fibroblasts were cultured from tissues obtained from patients with TAO and from those undergoing surgeries for other noninflammatory eye conditions (Graves' =5, Normal=5). The 384-well hanging droplet culture was used to generate 3D organoids. The deposition of ECM was assessed with immunofluorescent (IF) staining. Tissue rigidity was measured using the microsquisher.

**[Results]** IF staining demonstrated significantly higher accumulation of type3 and 4 collagens in Graves' organoids than normal controls. These Graves' organoids displayed increased tissue stiffness compared with normal controls. Gene expression analysis showed the increased expression of connective tissue growth factor (CTGF), and lysyl oxidase (LOX). Despite the pro-fibrotic and pro-inflammatory characteristics of Graves' organoids, these organoids were highly adipogenic compared with normal controls. Increased CTGF and LOX activities coupled with hypoxic microenvironments may contribute to the tissue stiffness and proinflammatory characteristics of Graves' orbital connective tissues.

**[Conclusions]** Human 3D model system should allow us to further understand the disease mechanisms underlying the enigmatic TAO.

**RF1-10 Retinal complications in uveitis patients in Taiwan**

Yu-Hsuan Huang<sup>1</sup>, De-Kuang Hwang<sup>1,2</sup>, Yu-Mei Chung<sup>1</sup>

<sup>1</sup>Department of Ophthalmology, Taipei Veterans General Hospital, Taipei City, Taiwan, <sup>2</sup>School of Medicine, National Yang-Ming University, Taipei City, Taiwan

**[Purpose]** To evaluate the incidence and risk factors for developing retinal complications in uveitis patients in Taiwan.

**[Methods]** The National Health Insurance Research Database was used in this study. A million registered beneficiaries were randomly selected from the database. All uveitis patients who were newly diagnosed between 2002 and 2011 were identified. Retinal complications in this study was identified based on ICD-9 codes, which included macular hole, macular pucker, and retinal detachment. Patients who underwent vitrectomy were further identified. Clinical and demographic factors including age, gender, anatomical types of uveitis were analyzed to explore the risk factors for incidence of these retinal complications.

**[Results]** There were totally 10,936 newly onset uveitis patients identified from the database. Among them, 261 (2.4%) develop retinal complications after uveitis. Only 23% (n=60) of them received vitrectomy for treatment. Older age, posterior and pan-uveitis were significant risk factors for developing these complications.

**[Conclusions]** Although retinal complications rarely happened in the first few years after uveitis occurred, a quarter of them may need surgical treatment. Clinicians should follow up retina and macular carefully in elder patients and those whose uveitis mainly involve posterior segment of eye.

**RF1-12 Povidone-Iodine/Dexamethasone Eye Drops in Adenoviral Conjunctivitis Treatment: A Systematic Review**

Herdanti R Putri<sup>1</sup>, Meuthia R A Primaputri<sup>1</sup>, Rina L D Nora<sup>2</sup>

<sup>1</sup>Faculty of Medicine, Universitas Indonesia, Depok, Indonesia, <sup>2</sup>Department of Ophthalmology, Cipto Mangunkusumo-Kirana National Hospital, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

**INTRODUCTION**

Adenoviral conjunctivitis is a common eye disease. Until now the main treatment is supportive. Povidone-iodine/dexamethasone (PVP-I/Dexa) showed a promising therapeutic agent for adenoviral conjunctivitis in the previous studies. This systematic review aims to study whether PVP-I/Dexa enhances the clinical resolution of conjunctivitis in human better than artificial tears alone.

**METHODS**

Literature searching was conducted using keywords and MeSH headings to identify published articles on Cochrane, PubMed, Science Direct, EBSCO, and Proquest. Articles included was full-text randomized control trial on adult human subjects.

**RESULTS**

Three RCTs were included in this systematic review. The preparation combination ranges from PVP-I 0.1% to 1.0% and dexamethasone 0.1% with control groups including artificial tears, dexamethasone, and PVP-I alone. 3 RCTs evaluated clinical resolution by direct eye examination and questionnaire or global clinical score. Combination of PVP-I/Dexa group demonstrated superiority that PVP-I/Dexa slightly fasten symptoms improvement (eye redness, tearing, watery discharge, itching, and foreign body sensation) compared to control groups. However, the clinical resolution was not statistically significant. Adverse events such as subepithelial corneal infiltrate (SCI) and superficial punctate keratitis (SPK) were also observed. The incidence of adverse event varies in these three studies.

**CONCLUSION**

There is a superiority of using combination PVP-I/Dexa eye drop in improving symptoms of adenoviral conjunctivitis.