AMERICAN UVEITIS SOCIETY
FALL MEETING
SUNDAY, OCTOBER 28, 2018
7:00 PM

AAO 2018
CHICAGO, IL

CHICAGO DOWNTOWN MARRIOTT
MIRACLE MILE

SCHEDULE – AMERICAN UVEITIS SOCIETY – SUNDAY, OCTOBER 28, 2018

7:00-7:55 PM	**Social Hour**
7:55-8:00 PM	**Introduction to the Plenary Session** Nisha Acharya, MD, MS Program Chair, AUS Fall Meeting
8:00-8:45 PM	**Plenary Session** Year in Review: Uveitis Basic and Clinical Science **Russell N. Van Gelder, MD, PhD** **Professor and Chair, Dept of Ophthalmology** **University of Washington School of Medicine**
8:45 PM	**Business Meeting and Break**
	Free papers
9:00 PM	**Elisabetta Miserocchi, MD:** MYD88 L265P Mutation Detection in the Aqueous Humor of Patients with Vitreoretinal Lymphoma
9:07 PM	**Rhett Nance:** Visual Acuity and Optical Coherence Tomography Findings in Pediatric Patients with Uveitic Macular edema
9:14 PM	**John Sheppard:** PP-001, a new small molecule for intraocular treatment of uveitis – first results of a prospective multicenter clinical trial
9:21 PM	**Shaivi Patel:** Uveitis demographics: main versus satellite clinics of a tertiary referral center
9:28 PM	**Shiri Shulman:** Late Intraocular Lens Subluxation in Chronic Uveitis
9:35 PM	**Michal Kramer:** Severe visual loss in malignancy: CAR or Immuno-therapy related?

SCHEDULE – AMERICAN UVEITIS SOCIETY – SUNDAY, OCTOBER 28, 2018

9:42 PM	**Heather Tamez**: Ophthalmic Implications of Immune Checkpoint Inhibitor Therapies
9:49 PM	**Siva Raman Bala Murugan, MS:** Analysis of Vitamin A and D levels in Vogt-Koyanagi-Harada (VKH) panuveitis in South India
9:56 PM	**Noy Ashkenazy:** The effect of patient compliance on remission rates in pediatric non-infectious uveitis
10:03 PM	**Robert Purgert:** Management of uveitic and steroid-induced glaucoma with minimally invasive glaucoma surgery (MIGS)

MYD88 L265P Mutation Detection in the Aqueous Humor of Patients with Vitreoretinal Lymphoma

Miserocchi, Elisabetta, MD[1]; Ferreri, Andrés J. M., MD[2]; Giuffrè, Chiara, MD[1]; Cangi, Maria G., PhD[3]; Ponzoni, Maurilio, MD[3]; Bandello, Francesco M., MD[1]; Modorati, Giulio M., MD[1]

Institutions: 1. Ocular Immunology and Uveitis Service, Department of Ophthalmology, University Vita-Salute, San Raffaele Scientific Institute, Milan, Italy. 2. Unit of Lymphoid Malignancies, Department of Onco-Hematology, San Raffaele Scientific Institute, Milan, Italy. 3. Pathology Unit, San Raffaele Scientific Institute, Milan, Italy.

Purpose: to detect the presence of MYD88 L265P mutation in the aqueous humor of patients with cytologically proven vitreoretinal lymphoma.

Methods: eight consecutive patients with bilateral vitreoretinal lymphoma (16 eyes) were prospectively evaluated. Genomic DNA was extracted from aqueous samples after paracentesis, and vitreous humor samples after diagnostic vitrectomy. MYD88 codon 265 mutation was investigated by both amplification-refractory mutation system polymerase chain reaction approach and pyrosequencing assay in the aqueous humor of all patients and in the vitreous of six patients. A control group of eight age-matched patients with established diagnosis of noninfectious uveitis was also tested for the presence of MYD88 L265P mutation in the aqueous humor.

Results: eight patients (3 males, 5 females) with mean age of 69.5 years (range 50-85) were considered. All the patients tested for MYD88 L265P in the vitreous (six) were positive, and this result was consistent with cytological examination in all samples but one. The MYD88 L265P mutation was found in the aqueous of six patients (75%) and in three of them the mutation was present in both eyes. Results of MYD88 L265P mutation in aqueous and vitreous sample were consistent in seven of the eight eyes with available samples. The aqueous humor of the noninfectious uveitis control group was negative for the detection of MYD88 L265P mutation.

Conclusion: MYD88 mutation was detected in the aqueous humor of 75% of patients with cytologically proven vitreoretinal lymphoma. This technique may be considered as an additional diagnostic tool in the detection of vitreo-retinal lymphoma.

Disclosures: None.

Visual Acuity and Optical Coherence Tomography Findings in Pediatric Patients with Uveitic Macular edema

Nance, Rhett; Eyler, Stephen; Kopplin, Laura J.

Institution: Department of Ophthalmology & Visual Sciences, Medical College of Wisconsin Eye Institute

Purpose: To evaluate visual acuity outcomes in pediatric patients treated for uveitic macular edema and to assess the relationship of acuity with structural retinal changes on optical coherence tomography (OCT).

Methods: We completed a single institution retrospective chart review of pediatric patients treated for uveitic macular edema with available OCT imaging between April 2006 and April 2016. Demographic data and Snellen visual acuity were collected from first diagnosis with macular edema through resolution of edema. OCT images from this interval were reviewed for the presence of intraretinal or subretinal fluid, ellipsoid zone disruption, or hyperreflective retinal foci and central subfield thickness was recorded. Visual acuity was converted to the logMAR scale and OCT findings summarized as percentages. Data was compared using t-test or Fisher's exact test as appropriate.

Results: 29 eyes from 17 patients were evaluated. Mean logMAR acuity at the time of diagnosis with macular edema was 0.55 (SD = 0.36). With resolution of macular edema, logMAR acuity improved to 0.32 (SD = 0.26, p=0.0009). OCT of all eyes demonstrated intraretinal fluid and 12 eyes (41%) also had subretinal fluid present at initial diagnosis. After resolution of macular edema, 16 eyes (51%) continued to demonstrate intraretinal hyperreflective foci within 1 mm of the fovea and 11 eyes (38%) had ellipsoid zone disruption within 500 microns of the fovea. Ellipsoid zone disruption or hyperreflective foci were both overrepresented in patients with visual acuity >20/40 after resolution of macular edema compared to patients with acuity ≤ 20/40; however, this was not statistically significant in either case.

Conclusions: Pediatric patients with uveitic macular edema demonstrate improvement in acuity with resolution of retinal edema. The relationship between ellipsoid zone changes, hyperreflective foci and visual recovery should be explored further; this will require larger cohort to fully delineate.

Disclosures: None.

PP-001, a new small molecule for intraocular treatment of uveitis - first results of a prospective multicenter clinical trial

Sheppard, John[1]; Thurau, Stephan[2]; Pleyer, Uwe[3]; Deuter, Christoph[4]; Heiligenhaus, Arnd[5]; Van Calster, Joachim[6]; Talin Barisani-Asenbauer, Talin[7]; Obermayr, Franz[8]

Institutions: 1. Virginia Eye Consultants and Eastern Virginia Medical School, Norfolk, Virginia, USA. 2. University Eye Hospital, Ludwig-Maximilians-Universität, Mathildenstr. 8, 80336 München, Germany. 3. Eye Hospital, Charité, Mittelallee 4, 13353 Berlin, Germany. 4. University Eye Hospital, Eberhard-Karls-Universität, Elfriede-Aulhorn-Straße 7, 72076 Tübingen, Germany. 5. Department of Ophthalmology, St.-Franziskus-Hospital, Hohenzollernring 74, 48145 Münster, Germany. 6. Department of Ophthalmology, University Hospitals Leuven, Kapucijnenvoer 33, 3000 Leuven, Belgium. 7. Medical University of Vienna, Kinderspitalgasse 15, 1090 Wien, Austria. 8. Panoptes Pharma Ges.m.b.H., Reisnerstraße 34/1, 1030 Wien, Austria

Purpose: To investigate safety, tolerability and potential therapeutic effects of intravitreal PP-001, a novel, small-molecule DHODH-inhibitor, which targets activated T-cells, in the treatment of chronic noninfectious posterior segment uveitis.

Methods: In a prospective, multicenter phase-1 study a total of 11 patients received a single dose of 300, 600 and 1200 ng, respectively, of intravitreal PP-001. All patients maintained their systemic medication during the study. The main outcome measures were ocular and systemic safety, pharmacokinetics in peripheral blood and efficacy.

Results: No major systemic or ocular side effects were observed, especially no increase of IOP. Minor side effects were related to the injection procedure but not to the study drug, which was well tolerated. Compared to baseline, visual acuity was increased in a dose dependent fashion in the treated eyes of all study groups at days 14 and 28 after injection; the fastest and highest increase of average 15 letters was observed in the 1200 ng group until the last follow up at day 28. Macular OCT showed either stability or improvement in all subjects.

Conclusion: In patients with noninfectious uveitis intravitreal PP-001 can improve VA and is safe and well tolerated without affecting IOP. The therapeutic effect lasts beyond the last visit at 4 weeks. Sustained release formulations are under investigation for prolonged efficacy.

Support: Panoptes Pharma, Vienna, Austria.

Disclosures: Dr. Sheppard is a consultant for Panoptes Pharma. Dr. Obermayr is an employee, and the remaining authors are clinical investigators.

Uveitis demographics: main versus satellite clinics of a tertiary referral center

Patel, Shaivi; Scott, Adrienne; Thorne, Jennifer; Berkenstock, Meghan

Institution: Drexel University College of Medicine (Ms.Patel); Wilmer Eye Institute, Johns Hopkins School of Medicine (Drs. Scott, Thorne, and Berkenstock)

Purpose: The types of and demographics of uveitis vary by location, region, and practice. The proportion and causes of infectious uveitis also change over time. Comparing the types of uveitis seen in an urban referral clinic and affiliate suburban clinics has previously been undocumented. We report the types of uveitis seen by the same group of uveitis subspecialty trained physicians at the main uveitis clinic compared with those seen at the satellite clinics. We secondarily examine changes in the rates of infectious uveitides.

Methods: A retrospective study of the medical records of 436 consecutive, new patients (687 eyes) with uveitis as identified by ICD-9 codes seen by eight uveitis specialists. Patients were either seen by one uveitis specialist at a tertiary referral center in Baltimore, Maryland or one of three affiliated satellite clinics in the greater Baltimore area from July 1, 2013 through March 31, 2017. All subjects were evaluated by one examiner at a minimum of two visits. Demographic information obtained for each subject included age at onset of uveitis, chronicity of uveitis, sex, race, associated systemic disease, and anatomic location of uveitis. Treatment with immunosuppressive medications was also recorded. Data from each of the satellites was pooled into one comparison group, as the demographics between each clinic did not differ by age distribution, sex, or race. Patients were assigned to the main or satellite clinic based on location of more than 50% of their visits.

Results: The mean age was significantly higher in the satellites (57 ± 17.4 vs 48.4 ± 18.7 y, $p<0.0004$). Caucasians were the most common race at both sites (55.7 and 49.6%). African Americans were the next most prevalent group, and were seen more frequently at the main clinic (39.2% vs 34.3%). However, the difference in race overall was not significant ($p=0.836$). Anterior uveitis was the most common anatomic location for inflammation overall, with more acute cases in the satellites ($p<0.0001$). The number of cases of anterior uveitis were significantly higher in the satellites compared to more cases of posterior uveitis at the main clinic ($p<0.0001$). More cases were unilateral at the satellites ($P<0.001$). There was no difference in the percent of uveitis with a known systemic cause between sites (38.6 vs 38%, $p= 0.938$). The most common infectious uveitis was due to syphilis. The amount of infectious uveitis seen in both locations was not significant (14.3 vs 13.9%, $p=0.938$). Use of immunosuppression was almost 12 times more common at the main clinic.

Conclusion: Similar to previous studies, the most common location of ocular inflammation was in the anterior chamber. More cases of unilateral, acute anterior uveitis were seen at satellite locations. Immunosuppressive medications were used more frequently at the main clinic. This reflects more patients seen, a larger proportion of chronic, bilateral conditions, and increased numbers of posterior and panuveitis managed at the main clinic. Infectious uveitis was treated in both sites, most frequently syphilis.

Disclosures: None.

Late Intraocular Lens Subluxation in Chronic Uveitis

Shulman, Shiri; Trivizki, Omer; Abu-Manhal, Muhamad

Institutions: Ophthalmology Division, Tel Aviv Medical Center, affiliated to Sackler Faculty of Medicine, Tel Aviv University, Israel

Purpose: To report a case series of 4 patients with chronic uveitis who had in-the-bag late intraocular lens (IOL) subluxation.

Methods: Retrospective data and literature review.

Results: We reviewed the data on all patients with uveitis in our institution between 2007-2018 and identified four patients (three females) with intraocular lens (IOL) subluxation which was attributed mostly to a history of uveitis. Two patients had idiopathic pan uveitis, one had chronic anterior uveitis, and one had sympathetic ophthalmia. All four were treated systemically, and two were also treated with intravitreal triamcinolone injections. No patients had pseudoexfoliation or high myopia. Two had presented with posterior subluxation: one of them with inferior subluxation, the other with nasal decentration, and neither had active uveitis. The mean age of the patients at cataract operation was 55.4 ± 15.6 years, and the mean interval since the subluxation diagnosis date was 10.5 ± 6.0 years. Two patients underwent a successful secondary surgical reposition, one needed an IOL exchange procedure, and one chose to continue medical follow-up only. All four patients maintained their original visual acuity before the occurrence of subluxation. A literature review yielded 22 other cases of IOL subluxation due to uveitis with few common clinical features, although they all had intermediate posterior involvement and the mean time to subluxation was also around 10 years.

Conclusion: IOL subluxation in chronic uveitis is rare. The risk of subluxation should be borne in mind prior to recommending surgery. IOL reposition and fixation procedures may be challenging in this group of patients, but they do maintain their visual acuity and therefore it should be considered as a reasonable option.

Disclosures: None.

Severe visual loss in malignancy: CAR or Immuno-therapy related?

Kramer, Michal[1,2]; Weinberger, Yehonatan[1]; Kalish, Hadas[1,2]

Institutions: 1. Department of Ophthalmology, Rabin Medical Center, Petah-Tikva, Israel. 2. Sackler School of Medicine, Tel-Aviv university, Tel Aviv, Israel

Purpose: To describe a case of severe visual loss in an oncology patient, and discuss both diagnostic and treatment dilemmas.

Case presentation: A 60-year-old male presented with a 2-months' history of decreased vision in both eyes. Medical history was remarkable for oligo-metastatic lung adenocarcinoma (treated with radiation and Pembrolizumab), hypertension, and peripheral vascular disease.

Upon presentation, his visual acuity was 1/36 in the right eye (RE) and 6/8.5 in the left eye (LE), with no RAPD, yet complete loss of color vision in the RE and partial loss in the LE. Slit lamp examination was normal, and multimodal ocular Imaging (color fundus, FA, OCT) were unremarkable. Visual field examination revealed a central scotoma in the RE and a concentric field defect in the LE. Electroretinogram showed mild decrease in photopic response in the LE, and scotopic decrease in both eyes, suggesting predominantly rods' dysfunction. Pembrolizumab was discontinued. Anti- recoverin antibodies were negative. Other anti-retinal antibodies still pending. Brain MRI demonstrated the known brain metastasis which were unrelated to visual pathways. Despite no improvement after pulse corticosteroid therapy and plasmapheresis, the significant deterioration that occurred after cessation of treatment suggested some favorable effect. Plasmapheresis was resumed with additional IVIG, and continuing brain radiation.

Current working diagnosis is cancer associated retinopathy (CAR), though immunomodulation mediated retinopathy could not be ruled out.

Discussion will include literature review of the following points:
1. Can these entities be differentiated?
2. Is there a preferential treatment for each, after cessation of immunotherapy? The case will be open for discussion.

Disclosures: None.

Ophthalmic Implications of Immune Checkpoint Inhibitor Therapies

Tamez, Heather; Shieh, Christine; Longmuir, Reid; Salem, Joe-Elie; Moslehi, Javid: Johnson, Douglas; Kim, Stephen; Gangaputra, Sapna

Institution: Vanderbilt University Medical Center, Nashville, TN

Purpose: To report the spectrum of ocular adverse events related to immune checkpoint inhibitor (ICI) therapy.

Methods: The WHO VigiLyze database of individual case safety reports (ICSRs) was queried for reported eye disorders associated with ICIs (ipilimumab, pembrolizumab, nivolumab, avelumab, atezolizumab, durvalumab, and tremelimumab) from 2009 to April 15, 2018. These events were categorized as intraocular (dry eye, uveitis), external (eyelid, extraocular muscle, orbital disease), or subjective visual changes (blurry vision).

Results: A total of 846 patients with ocular ICSRs were identified: 448 (53%) were intraocular, most commonly uveitis; 165 (19.5%) were external, primarily ptosis and diplopia; 233 (27.5%) were visual changes. Most patients received nivolumab (N=314, 37.1%), ipilimumab (N=241, 28.5%), pembrolizumab (N=189, 22.3%), or a combination of ipilimumab and nivolumab (N=74, 8.7%). With nivolumab, 155 patients (49.4%) had intraocular events, 76 (24.2%) had external disease, and 83 (26.4%) experienced visual changes. Of the patients receiving ipilimumab, 136 (56.4%) had intraocular events, 33 (13.7%) had external disease, and 72 (29.9%) experienced vision changes. Of the patients treated with pembrolizumab, 97 (51.3%) had intraocular events, 42 (22.2%) external disease, and 50 (26.5%) experienced vision changes. Of the patients treated with a combination of nivolumab and ipilimumab, 46 (61.2%) had intraocular events, 7 (9.5%) external disease, and 21 (28.3%) experienced vision changes.

Conclusions: ICIs are increasingly used for metastatic malignancies however, the frequency of ocular adverse events has not been fully described. Despite its limitations, the WHO Viglyze database highlights the various ocular irAEs that have been reported globally. We advocate for establishing ophthalmic screening guidelines for patients receiving these medications to give them the best chance of survival with optimum ocular health.

Support: RPB unrestricted grant to Vanderbilt Eye Institute

Disclosures: None.

Analysis of Vitamin A and D levels in Vogt-Koyanagi-Harada (VKH) panuveitis in South India

Bala Murugan, Siva Raman, MS; Murthy, Somasheila, MD; Diaz, Jose MD; Powell, Jonathan; Jwo, Kevin, MD; Gritz, David C, MD; Venkatesh, Rengaraj, DNB

Institution: Aravind Eye Hospital, LV Prasad Eye Institute, Albert Einstein College of Medicine

Background Statement: Low Vitamin D levels have been reported in the patients with uveitis and have shown to be related to increased inflammation. Additionally, Vitamin A deficiency has shown to be related to inflammation, including ocular inflammation in animal models.

Purpose: Evaluation of serum vitamin A and D levels in VKH panuveitis in 2 referral centres in South India.

Methods: Prospective case-control study in 2 tertiary eye care centers in South India evaluating vitamin A (Retinol and Transthyretin) and D levels (25-Hydroxy cholecalciferol)for patients satisfying the revised International VKH criteria, divided into 4 groups: (1)Active acute inflammation (2)Chronic phase active inflammation (3)Inactive inflammation on immunosuppression,(4)Inactive inflammation, off medication and (5)Age-matched (to group 1) controls

Results: Vitamin A and D levels were low in all the groups. The VKH subgroups and the control group were not statistically significant ($p>0.05$).

Conclusion: The difference in the levels of Vitamin A and D levels in each of the subgroups needs a large sample size to validate their usage as a therapeutic option

Support: Albert Einstein College of Medicine, New York

Disclosures: None.

The effect of patient compliance on remission rates in pediatric non-infectious uveitis

Ashkenazy, Noy; Saboo, Ujwala S; Robertson, Zachary M; Cao, Jennifer H

Institution: University of Texas Southwestern Medical Center (Dallas, TX); Children's Medical Center Dallas (Dallas, TX)

Purpose: To identify barriers to compliance in chronic pediatric non-infectious uveitis requiring immunomodulatory therapy, and to examine its association with ability to achieve disease remission.

Methods: A retrospective analysis was performed on pediatric patients with chronic non-infectious uveitis on immunomodulatory therapy at University of Texas Medical School and Children's Medical Center (Dallas, TX) between September 2015 and March 2018. A fellowship-trained uveitis provider (JHC) examined and directly managed all treatment. Compliance barriers, subcategorized based on the WHO classification, were compared to rates of achieving disease remission, steroid free remission, and durable remission.

Results: Fifty-seven patients with non-infectious uveitis were included. Thirty-three (58%) patients were compliant. Barriers to compliance identified to have a statistically significant adverse effect on remission rates included patient/parent negligence, transportation issues, family strife, and having a systemic autoimmune disease associated with uveitis ($p<0.05$). At a mean follow-up of 24.5 (range 12-31) months, a total of 29 (51%), 28 (49%), and 2 (3.5%), achieved disease remission, steroid remission, and durable remission, respectively. Poor compliance was associated with decreased rates of disease remission (12%, vs. 39%, $p=0.005$) and steroid-free remission (11%, vs. 39%, $p=0.002$). Having three or more compliance barriers was associated with decreased remission rates ($p<0.05$).

Conclusions: Pediatric patients with chronic non-infectious uveitis who were non-compliant with their immunomodulatory therapy were found to have lower rates of disease remission and steroid-free remission on immunomodulatory therapy.

Support: This research supported in part by an unrestricted research grant from Research to Prevent Blindness (New York, New York) as well as a Core research grant from the University of Texas Southwestern Medical School. The funding organizations had no role in the design or conduct of this research.

Disclosures: None

Management of uveitic and steroid-induced glaucoma with minimally invasive glaucoma surgery (MIGS)

Purgert, Robert; Lowder, Careen; Eisengart, Jonathan

Institution: Cleveland Clinic Cole Eye Institute

Purpose: The clinical course of uveitic patients may be complicated by uveitic and/or steroid-induced glaucoma. We examined the efficacy of two minimally invasive glaucoma surgery (MIGS) devices, gonioscopy assisted transluminal trabeculotomy (GATT) and Kahook dual blade (KDB), in treating uveitic and steroid-induced glaucoma.

Methods: Medical records of patients that underwent GATT or KDB surgery by a single surgeon at Cleveland Clinic since 2015 were reviewed. Individuals were included if they were ≥ 18 years old with uveitic and/or steroid-induced glaucoma with uncontrolled intraocular pressure (IOP). Paired and unpaired t-tests were used for within- and between-subject comparisons, respectively.

Results: 20 eyes from 18 consecutive patients were included. Age was 51 ± 4 years (range 18-81). Gender was 65% female. Efficacy at 3 months for each glaucoma type was as follows. Steroid-induced glaucoma patients had IOP reduction of 21.7 ± 4.4 mmHg ($n = 6$, $p = 0.004$) and reduction of 1.5 ± 0.5 medications ($n = 6$, $p = 0.03$). Uveitic glaucoma patients had IOP reduction of 9.8 ± 5.2 mmHg ($n = 4$, $p = 0.16$) and reduction of 1.5 ± 0.6 medications ($n = 4$, $p = 0.10$) that approached statistical significance. Patients with both steroid + uveitic glaucoma had IOP reduction of 11.8 ± 4.8 mmHg ($n = 9$, $p = 0.009$) and reduction of 2.0 ± 0.5 medications ($n = 9$, $p = 0.004$). Efficacy at 3 months for each MIGS device was as follows. Patients that underwent KDB had IOP reduction of 9.6 ± 2.5 mmHg ($n = 8$, $p = 0.01$) and reduction of 1.4 ± 0.5 medications ($n = 8$, $p = 0.03$). Patients that underwent GATT had IOP reduction of 18.0 ± 6.3 mmHg ($n = 11$, $p = 0.0005$) and reduction of 2.0 ± 0.5 medications ($n = 11$, $p = 0.0004$). Comparable efficacies were observed at 6 months in each respective group.

Conclusions: Uveitic and steroid-induced glaucoma can be effectively managed with GATT and KDB. Both achieve approximately 10 mmHg IOP reduction and elimination of 1-2 glaucoma medications.

Support: Research to Prevent Blindness (New York, New York) unrestricted grant to the Cole Eye Institute (RPB1508DM), Foundation Fighting Blindness (Columbia, Maryland) grant to the Cole Eye Institute (CCMM08120584CCF), and National Eye Institute/National Institute of Health (Bethesda, Maryland) P30 Core Grant (IP30EY025585).

Disclosures: None.

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23rd Annual American Uveitis Society Winter Symposium

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Sincerely,

Alan Palestine, MD
Albert T. Vitale, MD
AUS Winter Symposium Program Co-chairs