Global Eye Genetics Consortium

Newsletter #08

Upcoming events

HOST

CO-HOST

New Delhi, India
April 3 – 6, 2025

2025 APAO

The 40th Asia-Pacific Academy of Ophthalmology Congress
In Conjunction with
The 83rd Annual Conference of
the All India Ophthalmological Society

Members speak

Mônica Barbosa de Melo, PhD - Researcher
Center for Molecular Biology and Genetic Engineering
University of Campinas, Campinas, SP, Brazil

The GEGC session at International Society for Eye Research annual meeting (Argentina) was held on 21st October 2024. We covered the details of this meeting in our previous newsletter. Dr Mônica Barbosa de Melo (Campinas, Brazil) spoke about the Genetic Profile of Congenital and Primary Open Angle Glaucoma in this session. She discussed the progress of research on congenital and primary open-angle glaucoma in Brazil. Below is an excerpt of her talk.

Genetic Profile of Congenital and Primary Open Angle Glaucoma in Brazil

Brazil, a country of continental dimensions, is characterized by a highly admixed population derived from three ancestral roots: Europeans, Africans, and Native Americans. The proportional contribution of these ancestries varies across the country. This extensive admixture, coupled with the relatively recent formation of the Brazilian population compared to Europeans and Asians and the underrepresentation of admixed populations in genetic research, underscores the value of conducting genetic studies in this context. This presentation aimed to discuss recent findings and future perspectives on glaucoma genetics in Brazil, with a focus on congenital glaucoma, juvenile open-angle glaucoma (JOAG), and primary open-angle glaucoma (POAG).

Studies on congenital glaucoma in Brazil have revealed a variant frequency in the CYP1B1 gene ranging from 22% to 50%, predominantly in compound heterozygosity. Additionally, novel variants have been identified. The presence of CYP1B1 mutations was associated with a worse clinical prognosis, characterized by earlier disease onset, younger age at diagnosis, higher intraocular pressure (IOP), and a greater number of surgical interventions.

For JOAG, research has centered on mutations in the MYOC gene, which were detected in 34% of unrelated patients. These mutations were also related to a poor prognosis, including earlier age at diagnosis, higher IOP, increased need for trabeculectomies, and positive family history. Among the variants identified, Cys433Arg was the most prevalent, accounting for 79.5% of cases with MYOC mutations. This variant, unique to Brazil, exhibits a founder effect and high penetrance after the age of 40. Analysis of microsatellite markers and single nucleotide polymorphisms (SNPs) suggests that this variant originated between 560 and 1520 years ago, likely within the Native American population.

Investigations into POAG have primarily aimed at replicating findings from previous genome-wide association studies (GWAS). In these efforts, nine of fourteen previously identified SNPs were successfully validated. Furthermore, the Brazilian cohort contributed to a GWAS on POAG patients of African ancestry, which identified a variant in the APBB2 gene with an odds ratio of 2.05 (1.38-3.07).
Given the underrepresentation of Latin American and admixed populations in GWAS, a collaborative POAG study is underway between Brazilian researchers and the Genome Institute of Singapore. To date, 1,500 patients and 1,500 controls from four states and the Federal District have been analyzed using GSA microarrays. The goal is to include at least 4,000 patients and 4,000 controls from all Brazilian regions. This study aspires to advance our understanding of glaucoma genetics in Brazil and contribute to the development and refinement of polygenic risk scores.

Ocular Genetics Trivia

Here are 5 eye genetics-based fun word guessing questions with ophthalmology clinical syndromes. So, guess away!

1

Causing vision loss, with no repair,
I'm a syndrome that's quite rare.
My name starts with an "L" so fine,
And I'm linked to the RP gene's decline.

2

Causing ectopia lentis, and a tall, slender crew,
I'm a condition that's autosomal dominant too.
My name starts with an "M", so strong and so grand,
And I'm linked to the FBN1 gene's command.

3

Causing night blindness, and a loss of vision's decree,
I'm a syndrome that's X-linked recessive, you see.
My name starts with a "C", so unique and so rare,
And I'm linked to the RPGR gene's lair.

4

Causing retinal detachments, and a loss of vision's flow,
I'm a condition that's autosomal dominant, don't you know.
My name starts with an "S", so strong and so bold,
And I'm linked to the COL2A1 gene's story to be told.

5

Causing vision loss, and a loss of hair,
I'm a syndrome that's autosomal recessive, so rare.
My name starts with a "B", so unique and so fine,
And I'm linked to the BBS gene's decline.

Meet Our Members

Dr.Yang Pan Yang Pan is a prominent researcher at the National Hospital Organization Tokyo Medical Center, where she is at the forefront of studying retinal diseases. Her work primarily focuses on age-related macular degeneration (AMD), glaucoma, and inherited retinal diseases (IRD). These conditions pose significant challenges to vision health, and Yang is dedicated to unraveling the complex molecular mechanisms that contribute to their onset and progression.

With a strong background in Medical Science, Yang aims to bridge the gap between molecular biology and clinical applications. By identifying specific molecular pathways involved in retinal diseases, she hopes to pave the way for innovative therapeutic strategies that can enhance treatment options and improve patient outcomes.

Currently, Yang holds a Postdoctoral position in the Molecular and Cellular Biology Division at the National Hospital Organization Tokyo Medical Center. Her affiliation with the Osaka University Graduate School of Medicine in Osaka, Japan, further strengthens her research endeavors. Here, she collaborates with leading experts in the field, contributing to a vibrant academic environment focused on cutting-edge research.

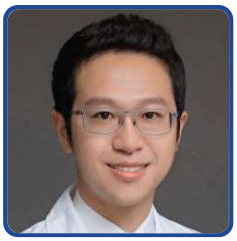
Yang's commitment to advancing our understanding of retinal diseases positions her as a valuable asset to the scientific community, and her work has the potential to transform therapeutic approaches for patients affected by these debilitating conditions

Dr. Paisan Ruamviboonsuk Dr. Paisan Ruamviboonsuk is a distinguished figure in the field of ophthalmology. He earned his medical degree from Mahidol University, Thailand, in 1987 and vitreo-retina fellowship certificate at Albert Einstein College of Medicine/Montefiore Medical Center in New York in 1994-1995. Currently, He is a Clinical Professor of Ophthalmology at the College of Medicine, Rangsit University, Rajavithi Hospital in Bangkok.

He is a former President of the Thai Retina Society (2009-2014) and a former President of the Royal College of Ophthalmologists of Thailand (2011-2016). His contributions extend internationally as an International Trustee-at-Large of the Board of Trustees of the American Academy of Ophthalmology (AAO) in 2025-2027, the Vice-President of the Asia-Pacific Tele-Ophthalmology Society since 2021, the Scientific Secretary of the Asia-Pacific Vitreo-Retina Society (APVRS) since 2017, a council member of the Asia-Pacific Academy of Ophthalmology (APAO) since 2014, and the Secretary General of the ASEAN Ophthalmology Society since 2015.

Dr. Ruamviboonsuk has received numerous accolades for his impactful work, including the United Nations Public Service Award in 2012 and the World Health Organization Sasakawa Health Prize in 2022 for his project on prevention of blindness from diabetic retinopathy in primary health care and communities. He has also been honored with the AAO Achievement Award in 2018, APAO Distinguished Service Award, APAO Achievement Award, and APAO Senior Achievement Award in 2007, 2014, and 2024, respectively. He also delivered the APAO Arthur Lim Award Lecture in 2018 and APVRS Dennis Lam Award Lecture in 2024.

As a pioneer in the research of diabetic retinopathy and polypoidal choroidal vasculopathy, Dr. Ruamviboonsuk has made significant contributions to the prevention of blindness from these leading diseases in the Asia-Pacific region. He is frequently invited to speak at international ophthalmology meetings and serves as a reviewer for many peer-reviewed journals.



Dr. Jia-Horung Hung Dr. Jia-Horung Hung, an accomplished ophthalmologist specializing in uveitis and retinal disorders. Dr. Hung is an active member of several prestigious professional societies, including The Ophthalmological Society of Taiwan, the American Academy of Ophthalmology, the Taiwan Retinal Society, and the Taiwan Ocular Inflammation Society , where he served as Secretary General from 2020 to 2023.

Dr. Hung's research interests are diverse, encompassing ocular inflammation, infections, surgical techniques, hereditary ocular diseases, and ophthalmic big-data analysis. His contributions to the field have garnered recognition, including the Young Investigator Research Award in Clinical Medicine from the School of Medicine at National Cheng Kung University, as well as Best Presentation awards at various academic meetings. Additionally, he has been celebrated for his teaching efforts and was part of a team that won a Gold Medal and Best Hardware at the 2020 International Genetically Engineered Machine competition.

In the laboratory, Dr. Hung focuses on age-related macular degeneration, hereditary ocular diseases, and the innovative use of antimicrobial photodynamic therapy for treating eye infections. Since November 2023, he has been a visiting scholar at Professor Quan Dong Nguyen's lab at Stanford University. This experience is enriching his expertise in diagnosing and treating ocular inflammatory diseases while advancing his involvement in ophthalmology research and clinical trials.

Dr. Rajarshi Pal a prominent expert in stem cells and regenerative medicine, boasting 15 years of experience in both industry and academia. From 2011 to 2017, he served as Assistant Professor at the Manipal Institute of Regenerative Medicine (MIRM) in Bangalore. Before that, Dr. Pal worked at the National Institute of Immunology in New Delhi, Reliance Life Sciences in Navi Mumbai, and Stempeutics Research in Kuala Lumpur, Malaysia.

In 2014, he expanded his research efforts with a stint under the IUSSTF program, collaborating with Prof. Kapil Bharti at the NEI-NIH in Bethesda. His dedication to advancing biomedical science earned him the ICMR Young Biomedical Scientist Award in 2013.

Currently, Dr. Pal holds the positions of Visiting Scientist and Adjunct Professor at The University of Trans-Disciplinary Health Sciences and Technology (TDU) in Bangalore. His impressive accomplishments include 55 international peer-reviewed publications, 8 patents, and 5 book chapters, highlighting his significant contributions to the field.

Prof Clement Tan A/Prof Clement Tan, a Senior Consultant who heads the Neuro-Ophthalmology Service at National University Hospital. He also serves as a Senior Consultant for the Healthy Ageing Programme (Age Better) at Alexandra Hospital and is the Group Chief of Ophthalmology for the National University Health System. Additionally, he is the Director of the Division of Graduate Medical Studies.

His clinical specialties encompass Cataract Surgery, General Ophthalmology, and Neuro-Ophthalmology, with special interests in eye movement and pupil disorders. He receives referrals from fellow ophthalmologists, neurologists, and neurosurgeons, underscoring his expertise in managing complex cases.

After completing his basic and advanced ophthalmology training in Singapore, A/Prof Tan furthered his knowledge with a fellowship in Neuro-Ophthalmology at King's College Hospital and the National Hospital for Neurology and Neurosurgery in London, training under esteemed mentors Drs. Paul Riordan-Eva and Fion Bremner. His research interests are focused on neuro-ophthalmology, contributing valuable insights to the field.

A/Prof Tan's dedication has been recognized through prestigious awards, including the Long Service Medal in 2024 and the Public Administration Medal (Bronze) in 2023.

Dr. Audrey Chia a Senior Consultant and Head of the Pediatric Ophthalmology and Adult Strabismus Department at the Singapore National Eye Centre. A/Prof Chia graduated from the University of Sydney and completed her ophthalmology training at the Sydney Eye Hospital, and her Pediatric Ophthalmology fellowship at Great Ormond Street Hospital for Children in London.

Her research interests encompass strabismus, amblyopia, retinopathy of prematurity, and both medical and non-medical approaches to myopia control. As a Senior Clinical Investigator, she co-leads the Myopia Research Unit at the Singapore Eye Research Institute (SERI). A/Prof Chia also contributes to the SNEC-SERI Visual ElectroDiagnostic Laboratory, focusing on functional changes in myopia and amblyopia, retinal dystrophies, and drug-related toxicities.

In addition to her clinical and research roles, A/Prof Chia is passionate about training and educating the next generation of ophthalmologists and scientists, fostering growth at both SNEC and SERI. Her qualifications include an MBBS (Hons), FRANZCO, an MBA, and a PhD from the National University of Singapore.

Ophthalmic Genetics News

Around the World

Genetic therapy restores vision in 4 blind children

Following a non-randomized, single-arm, clinical study conducted in the UK, four blind children aged between 1·0–2·8 years (from the US, Turkey, and Tunisia) have gained life-changing significant improvements in sight because of genetic therapy delivered via keyhole surgery at Great Ormond Street Hospital. They received therapy in only one eye. The NIHR Research Professorship, Meira GTx, and Moorfields Eye Charity funded the work. The four children were born with Leber Congenital Amaurosis type 4 (LCA4), a severe form of retinal dystrophy caused by mutations in the AIPL1 gene. Children with this rare genetic defect are typically certified legally blind from birth, and there are no conventional cures. Spectacles, contact lenses, medications, lasers, or surgery can't fix the problem because the root cause is a faulty gene preventing the eye's light-sensing cells from working properly. According to Prof Michel Michaelides, one of the researchers involved in the study and a consultant retinal specialist at Moorfields Eye Hospital/professor of ophthalmology at the UCL Institute of Ophthalmology, this new treatment is a potential paradigm shift for children suffering from this condition. The researchers designed a recombinant adeno-associated viral vector comprising the human AIPL1 coding sequence driven by a human rhodopsin kinase promoter region (rAAV8.hRKp.AIPL1). The product was manufactured under a Specials License from the Medicines and Health Products Regulatory Authority (UK) and made available to affected children with local ethics approval. The procedure consisted of a subretinal injection containing healthy copies of the AIPL1 gene into the retina of one eye during the delicate surgery. These copies were put inside a harmless virus, which helped them to enter the retinal cells and replace the defective genes. The children were prescribed oral prednisolone to protect against harm from inflammation. Outcome measures included visual acuity, functional vision, visual evoked potentials, retinal structure, and widefield fundus imaging). By about 3–4 years after the gene therapy, tests showed the treated eyes improved from essentially zero vision to roughly 20/200 on the Snellen vision chart.

Sources:
1)Genetic therapy improves sight for four blind children | NIHR Accessed March 2, 2025 https://www.nihr.ac.uk/news/
2) Doctors Restore Sight in Blind Children with Groundbreaking Gene Therapy. Accessed March 2, 2025 https://www.zmescience.com/medicine/genetic/gene-therapy-cures-childhood-blindness/
3)Michaelides, Michel et al. Gene therapy in children with AIPL1-associated severe retinal dystrophy: an open-label, first-in-human interventional study. The Lancet,2025, Volume 405, Issue 10479, 648 - 657

Ongoing OPGx-LCA5 trial achieves early clinical proof of concept.

Opus Genetics, Inc. (Nasdaq: IRD), a clinical-stage biotech company focused on developing gene therapies for inherited retinal diseases (IRDs) and other eye disorders, has announced that the first pediatric patient has been dosed in its ongoing Phase 1/2 clinical trial of OPGx-LCA5, an investigational gene therapy for Leber congenital amaurosis (LCA). OPGx-LCA5 aims to treat a form of LCA caused by biallelic mutations in the LCA5 gene, which encodes the lebercilin protein. This type of LCA is an early-onset severe inherited retinal dystrophy. Studies have shown that there is a dissociation between retinal structure and visual function in patients with this mutation, indicating a potential for therapeutic intervention through gene augmentation. OPGx-LCA5 uses an adeno-associated virus 8 (AAV8) vector to deliver a functional LCA5 gene to the outer retina.

Opus plans to release initial data from the pediatric cohort by Q3 2025. The ongoing trial has already shown early clinical proof of concept, with significant visual improvements observed as early as one month after treatment in the first three adult patients. This was evident in the 6-month data released in October 2024 and reviewed at a company-sponsored KOL event in December 2024. Opus plans to present the new 12-month data on these three adult LCA5 patients at a major medical conference in Q2 2025. An FDA Type D meeting is scheduled for March to discuss the proposed Phase 3 trial design and registrational endpoints for the OPGx-LCA5 program. For more information, visit clinicaltrials.gov (NCT05616793).

Source
https://www.globenewswire.com/news-release/2025/02/18/3027724/0/en/Opus-Genetics-Announces-Updates-on-OPGx-LCA5-Clinical-Program.Accessed March 1, 2025
https://ir.opusgtx.com/press-releases/detail/474/opus-genetics-announces-updates-on-opgx-lca5-clinical-program. Accessed February 28, 2025

Answers to Ocular Genetics Trivia

1. *LEBER CONGENITAL AMAUROSIS*
2. *MARFAN SYNDROME*
3. *CHOROIDEREMIA*
4. *STICKLER SYNDROME*
5. *BARDET-BIEDL SYNDROME*