Global Eye Genetics Consortium

Newsletter#02

Foreword

We are pleased to hear positive responses for the launch of GEGC newsletter. This year marks the 10th year of GEGC and hope to complete the global network this year by having GEGC sessions in Africa and South America. As we complete the global networking, we are now in the next phase of global research conducted by GEGC. Global research can be potentially designed at different levels from sharing of phenotype information to sharing of DNA or iPSC samples. From our observations of past visits to different countries, we are likely to face challenges in each global region with lack of eye geneticists, lack of research funding, and government regulations in sharing of patient information or samples. Each componentis essential to initiate productive international genetic eye research collaboration. At the coming annual GEGC meeting during ARVO 2024 on May 6, 1:15-2:45 pm (Chelan4, Seattle Convention Center), we will have presentations and discussions to address these obstacles and possible ways to overcome them. We will hear presentations from Dr. Yingbin Fu (Baylor College of Medicine) and Dr. Kapil Bharti (National Eye Institute) about the next phase of GEGC global research. We hope to see all GEGC members participating ARVO to attend this GEGC meeting and share their experience of global collaborations or propose various ideas for the next phase of GEGC global research and international collaboration.

ARVO 2024
May 5 – 9 | Seattle
Vision for the Future

Dr. Takeshi Iwata, PhD, FARVO

Upcoming Sessions of GEGC in Gobal

SCIENTIFIC CONFERENCE
JULY 27-29, 2024

AOC
AFRICAN OPHTHALMOLOGY COUNCIL

International Council of Ophthalmology
WOC
World Ophthalmology Congress
16-19 August, 2024, Vancouver, Canada
The place where the *future of sight* is shaped.

ISER 2024
XXVI Biennial Meeting of the International Society for Eye Research
20 - 24 October 2024 / Buenos Aires, Argentina

Recent Event

The meeting between the Global Eye Genetics Consortium (GEGC) and the Chairman of the African Ophthalmological Council (AOC) was a pivotal moment in fostering future collaborations to advance eye health research and genetic studies. The gathering took place on 23rd February 2024, during the 39th Asia Pacific Academy of Ophthalmology Meeting in Bali. Representatives from both organizations came together to discuss shared goals and potential areas of cooperation. GEGC was represented by Dr Gyan "John" Prakash from NEI, USA and Prof S Natarajan from Aditya Jyot Eye Hospital, India. Dr Ciku Mathenge, Head of Rwanda International Institute of Ophthalmology, and treasurer of the AOC, participated in the meeting from the AOC. This meeting was a continuation of the efforts by the GEGC team to establish collaborations in Africa. Just a week before this in-person meeting, an online meeting was held between the GEGC team ((Dr John Prakash, Dr Takeshi Iwata (NISO, Japan), Dr Rob Hufnagel (NEI, USA), Dr Shailja Tibrewal (SCEH, New Delhi)) and the AOC ((Lisa Roberts (Cape Town, South Africa) and Dr Ciku Mathenge (Kigali, Rwanda)).

The agenda of both the meetings included discussions on the latest advancements in eye genetics research, ongoing projects, and the potential impact of collaborative efforts. GEGC representatives emphasized the importance of a global approach to understanding and addressing eye-related genetic disorders. Dr Ciku Mathenge highlighted the unique challenges and opportunities within the African context, shedding light on the diversity of eye health issues faced by the continent's population. This included considerations such as genetic variations specific to African populations, socio-economic factors influencing eye health, and the need for tailored approaches to address prevalent eye diseases.

Discussions during the meeting focused on establishing a framework for collaborative initiatives, such as joint research projects, data sharing, and capacity-building programs. They recognized the importance of inclusivity and the need to engage researchers and healthcare professionals from diverse backgrounds to ensure a comprehensive understanding of eye genetics on a global scale.

The meeting concluded with a commitment to hold a GEGC session in the upcoming AOC congress in Kigali in July this year. Dr Ciku Mathenge who is the president of the 2024 AOC congress promised to support the GEGC in their endeavours in Africa. She said that this session would serve as a blueprint for joint research efforts, resource-sharing mechanisms, and the exchange of expertise. Both parties expressed enthusiasm for the potential positive impact of this collaboration on advancing knowledge, improving diagnostics, and developing targeted treatments for eye-related genetic conditions, especially in the African context.

The meeting set the stage for a long-term partnership between the Global Eye Genetics Consortium and the African Ophthalmological Council, exemplifying the importance of international collaboration in addressing complex health challenges.

Meet Our Members

Dr. Rita S. Sitorus is a Professor and Senior Consultant in the Paediatric Ophthalmology Division at the Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo Hospital, Jakarta. She completed her PhD at Vrije University medical center, Amsterdam, and conducted post-doctoral research at the University of Giessen, Germany. Dr. Sitorus has spent 5 years in Germany, Japan, and the Netherlands on fellowships in Pediatric Ophthalmology, researching clinical and molecular aspects of genetic eye diseases.She has published articles in Pediatric Ophthalmology, participated in the International Retinoblastoma Staging Working Group, and established blindness prevention programs in Indonesia and Asia. Dr. Sitorus is a board member of various international and national ophthalmology societies, including APSPOS and IPOSS. She led the development of National Guidelines for ROP screening in Premature Babies in Indonesia. Her recognitions include an Achievement Award from the Asia Pacific Academy of Ophthalmology in 2013 and being ranked as the 6th most productive researcher at Universitas Indonesia in 2020. She serves on the Health Research Ethics Committee and is a member of the Global Forum for Research Ethics & Integrity. Currently, she is contributing to the founding of the Indonesian Genetic Eye Disease Association (InaSGED), focusing on the clinical and genetic aspects of IRD and Stargardt's disease.

Dr. Kenneth Mitton is affiliated with the Eye Research Institute (ERI) at Oakland University, founded by V. Everett Kinsey, PhD, in 1968. Kinsey championed the NEI at NIH and co-chaired the selection of its inaugural director, earning the Lasker medical prize for pioneering multicenter clinical trials on ROP. Dr. Mitton's research at ERI focused on photoreceptor gene expression and collaboration with Associate Retinal Consultants (ARC) clinicians, Michael Trese, MD, and Kimberly Drenser, MD PhD. Together, they developed a DNA targeted sequencing service for FEVR, Norrie Disease, and Retinoschisis patients, leveraging Wendy Dailey's expertise in human DNA sequencing. Their work explored the role of Norrin (NDP) in neural retinal vasculature development, with contributions from research groups like Ohlmann and Nathans' labs. Dr. Mitton's biochemistry background facilitated the production and confirmation of a FZD-binding protein based on human Norrin, named "Noregen" by Caeregen Therapeutics. Supported by NEI funding, their STTR Phase-1 study evolved into an SBIR Phase-II award for pre-clinical research on Noregen, currently in GMP manufacturing development for future human trials. Their research exemplifies human genetic discoveries guiding disease understanding and novel therapy development, fostering interdisciplinary research and applied human genetics training for science and medical students.

Dr. Xunlun Sheng is a research director of Laboratory of Genetic Eye Diseases in Gansu Aier Eye Optometry Hospital and a leader of the Basic and Clinical Research Innovation Team for Hereditary Eye Diseases in Ningxia Eye Hospital, People's Hospital of Ningxia Hui Autonomous Region (Third Clinical Medical College of Ningxia Medical University ,Yinchuan, China). The work of the team aims to identify genetic defects in a large number of patients with inherited retinal diseases (IRDs) with new technologies such as whole exome sequencing (WES) and whole genome sequencing (WGS) and to study the function of novel discovered gene related to IRDs. The team is also interested in studying genetic factors of early-onset high myopia (eoHM) and in identifying candidate genes associated with eoHM in a large number of patients with eoHM. Professor Sheng has long been engaged in genetic research on inherited retinal diseases (IRDs) for more than twenty years. She is an active member of the Chinese Branch of Global Eye Genetics Consortium (GEGC), a member of Chinese Ophthalmological Association, Member of China Optometry Association, and vice president of ophthalmology branch of Chinese Society of Geriatrics.

Dr. Deepshikha Agrawal, the Director of MGM Eye Institute, Raipur, Chhattisgarh, has dedicated 32 years to combating blindness in Central India, marked by poverty and under-development. Her commitment led to the establishment of MGM Eye Institute in 2004, aiming to provide high-quality eye care irrespective of financial status. Dr. Agrawal's leadership propelled the institute forward, achieving recognition for its DNB Course by the National Board of Examination and as a training center for ophthalmologists from government medical colleges. The institute offers fellowships and training internships, endorsed by international bodies like IOFF and IOC. Dr. Agrawal's academic journey includes MBBS from NSCB Medical College Jabalpur (MP), MS from S.S Medical College, Rewa (MP), and a cornea anterior segment fellowship from LV Prasad Eye Institute (LVPEI), Hyderabad. She actively contributes to ophthalmic research and education, with over 95 publications and presentations. Her leadership extends to organizing CME courses and guiding DNB students. Recognitions for her contributions include the Distinguished Service Award by the Asia-Pacific Academy of Ophthalmology, Streeshakti Samman Award by the Chhattisgarh Urban Bank Federation, and the PBMA H.V. Desai Hospital Golden Eye ACOIN Award. Recently, she received "THE SUSRUTA AWARD" at the APAO Conference 2024 in Bali, Indonesia, further acknowledging her outstanding contributions to the field.

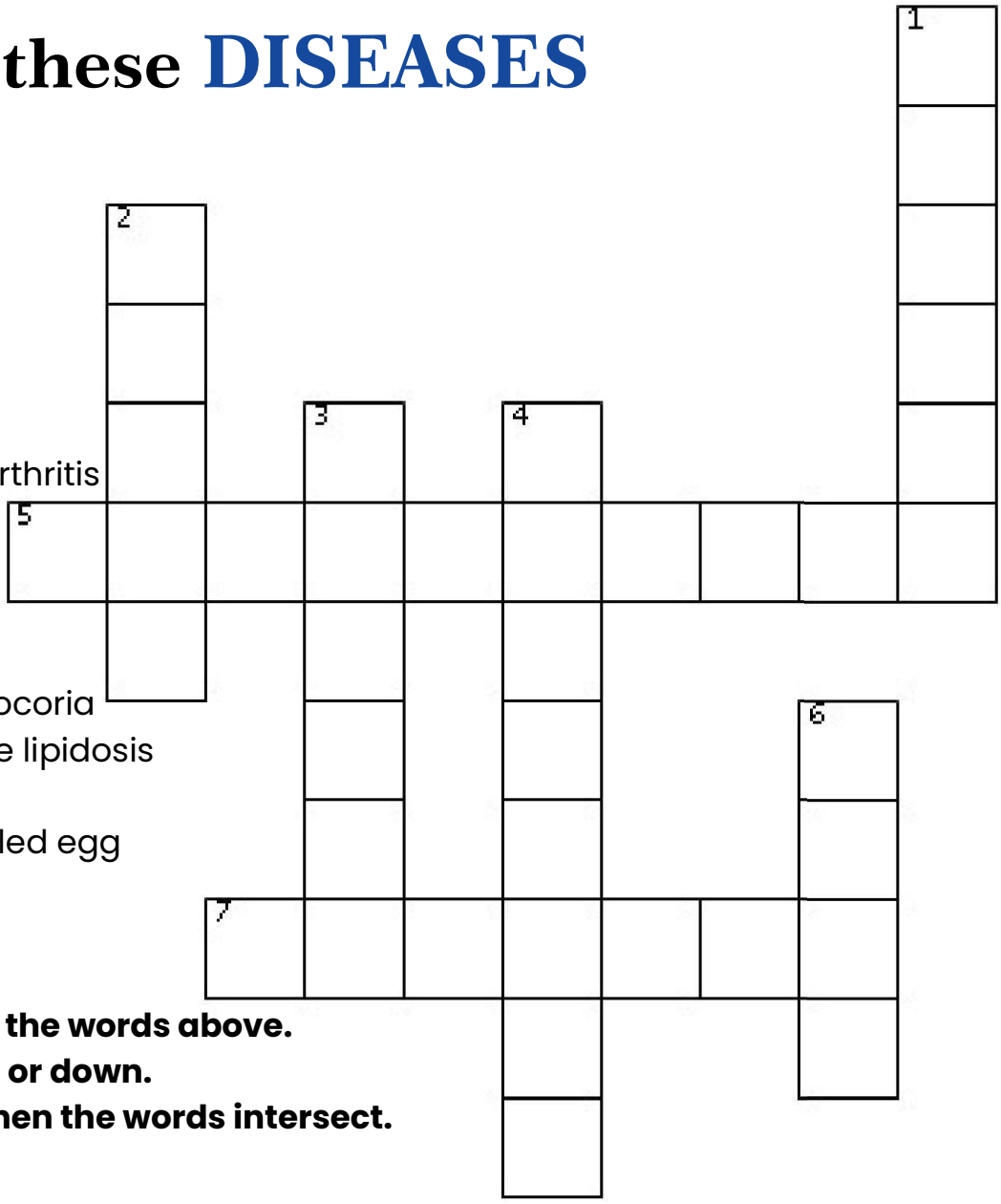
Diagnose these DISEASES

ACROSS

5. ABCA4
7. mucositis, uveitis, arthritis

DOWN

1. Anti AQP4
2. Differential for leucocoria
3. galactosylceramide lipidosis
4. Cherry red spot
6. Egg yolk to scrambled egg



Use the clues to fill in the words above.
Words can go across or down.
Letters are shared when the words intersect.

Ophthalmic genetic news around the world

CRISPR based genome engineering may correct a metabolic dysfunction across most Retinitis Pigmentosa variants

In a landmark study, the scientists at Columbia University Vagelos College of Physicians and Surgeons have provided hope for nearly 1.5 million people worldwide suffering from retinitis pigmentosa (RP). The most interesting part of their research is that this gene therapy could potentially treat RP patients irrespective of their genetic variation.

Retinitis pigmentosa is a heterogenous disorder with more than 80 different genes attributing to its pathogenesis. Developing Gene therapies for each of these variants is extremely challenging. Currently, FDA approved gene therapy is available for only one of these variants (RPE65). Scientists Stephen Tsang and Nicholas Nolan published the reports in Cell Reports Medicine, of their mouse model experiments using CRISPR-based genomic editing which delayed RP progression in mouse models by approximately one month, which is equivalent to approximately ten years in humans.

This treatment enhances glycolysis in rod cells and slows down the degenerative process, leading to reduced progression of the disease. Additionally, CRISPR-based gene therapy targets only the rod cells, minimizing potential side effects.

Electro-transfection: A non-viral gene therapy for severe retinal disease

PulseSight Therapeutics SAS, a newly launched ophthalmology biotech company, has secured seed financing from Pureos Bioventures and ND Capital. It aims to advance non-viral gene therapies with a minimally-invasive delivery system for treating major eye diseases, particularly wet and dry age-related macular diseases (AMD), including geographic atrophy (GA), leading causes of blindness in the elderly.

PulseSight's proprietary electro-transfection system delivers DNA plasmids encoding therapeutic proteins into the ciliary muscle to address genetic components of these conditions. Their lead program, PST-809, combines aflibercept and decorin to target wet AMD, offering potential advantages over current treatments. Another program, PST-611, targets GA in late-stage dry AMD using a plasmid encoding human transferrin protein.

The company's leadership includes experienced figures like Dirk Sauer, Dominik Escher, and Kostas Kaloulis, with Francine Behar-Cohen providing valuable expertise. Newly appointed CEO Judith Greciet brings over three decades of pharma and biotech experience. PulseSight aims to revolutionize AMD treatment and potentially address other neurodegenerative retinal disorders with its innovative approach.

Genetic determinants of comitant strabismus identified

Researchers at Boston Children's Hospital have made significant progress in understanding the genetic basis of strabismus, a common eye condition characterized by misalignment of the eyes. Their study identified chromosomal duplications on the second, fourth, and tenth chromosomes, which are prevalent in patients with both esotropia (inward eye turn) and exotropia (outward eye turn). This suggests shared genetic risk factors between the two conditions.

Led by Dr. Mary Whitman, MD, PhD, the research aims to uncover the underlying causes of strabismus to develop targeted treatments. Their findings, published in JAMA Ophthalmology, expand on previous research that identified genetic duplications increasing esotropia risk in white patients. The team broadened their investigation to include a diverse group of 234 patients with exotropia, revealing connections between these genetic markers and various forms of strabismus.

Contrary to expectations, the study did not identify specific deleted genes but rather duplicated regions that likely affect gene regulation. To further explore these findings, the researchers introduced these chromosomal variants into pluripotent stem cells for in-depth analysis of their impact on neuronal structure, function, gene expression, and chromatin rearrangement.

While direct treatment pathways are not yet established, this research offers promising insights for identifying at-risk individuals and potentially preventing strabismus development in the future.

(Sources: Cell Reports Medicine, Ophthalmology Times, Ophthalmology Breaking News)

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