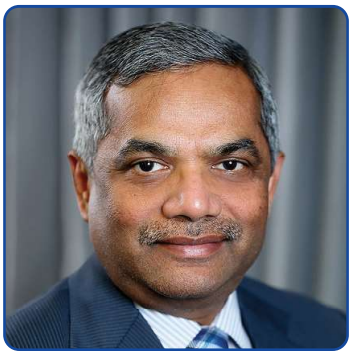
Global Eye Genetics Consortium

Newsletter #03

From the desk of Dr. Gyan "John" Prakash, US National Eye Institute



The journey of the Global Eye Genetics Consortium (GEGC) began unexpectedly in an ophthalmology clinic during a routine eye examination in 2009. At that time, I could not have imagined that a simple question would lead to the creation of a global phenomenon. When my ophthalmologist suspected an eye condition but could not provide a specific risk score due to a lack of data for my ethnicity, it left a void in me and a compelling need to address this issue. It was hard to believe that scientific discoveries could be limited by geography and ethnicity. I had always thought that good science anywhere should mean good science everywhere.

This desperation to understand what was happening within my genes triggered a series of meetings and discussions with key figures in the field of eye genetics across the Asian countries. My goal was to comprehend the ecosystem and explore the potential for promoting data generation in the regional geographies representing as many ethnicities as possible to enrich the scientific database for research and clinical application. From 2009 to 2014, after countless rounds of ideation in meetings, the concept of the Asian Eye Genetics Consortium was finally born during the South Asian Academy of Ophthalmology meeting. The credit for the final push to take concrete action goes to my wife, who encouraged me and a few of my collaborators to just start, reminding us that the most difficult step is often the first one.

A Collaborative Research Agreement between the US National Eye Institute (NEI) of the National Institutes of Health (NIH) and Japan's National Institute of Sensory Organs (NISO) of the National Hospital Organization at Tokyo Medical Center (NHOTMC) to work on genetic eye diseases in Asia was signed during the World Ophthalmology Congress in Tokyo, Japan, on April 5, 2014. At that time, the director of NEI, Dr. Paul Sieving, and the president of NHOTMC, Dr. Junzo Takeda, signed the agreement. The aim was to jointly address genetic eye diseases in Asia, the most densely populated and diverse region in the world. The signing ceremony was witnessed by Dr. Yozo Miyake, director of NISO, Dr. Takeshi Iwata, Prof. Dr. S. Natarajan, and me.

We have come a long way from our most humble beginnings with four members from three countries to now boasting over 225 members from 38 countries. Recognizing its global outreach, the Asian Eye Genetics Consortium was renamed the Global Eye Genetics Consortium (GEGC) in May 2018 at ARVO in Honolulu. The collective efforts of all the founders, the executive team, and the consortium members have led to this significant achievement. Despite the challenges posed by the pandemic, our activities have resulted in the formation of a vast global network of scientists, clinicians, and policymakers. Over the past ten years, several collaboration training and scientific exchange programs have taken place between the GEGC members. The consortium has also produced four volumes of Advances in Vision Research (Publ: Springer Nature), thus bringing several hundred eye researchers from more than thirty countries sharing their common interests on a single global platform.

I am deeply grateful to everyone who has shared in the vision and mission of GEGC. While the nostalgia of past accomplishments brings immense satisfaction, what matters now is how we will advance in the next ten years. On a personal level, I applaud the efforts of GEGC executives who have worked passionately to advance the genetic eye research to the next level.

Dr. Gyan "John" Prakash
Director
International Programs, National Eye Institute
Patron, Past President GEGC

Upcoming Sessions of GEGC in Gobal Forums

SCIENTIFIC CONFERENCE
JULY 27-29, 2024

AFRICAN OPHTHALMOLOGY COUNCIL

International Council of Ophthalmology

World Ophthalmology Congress
16-19 August, 2024, Vancouver, Canada

The place where the *future of sight* is shaped.

ISER 2024

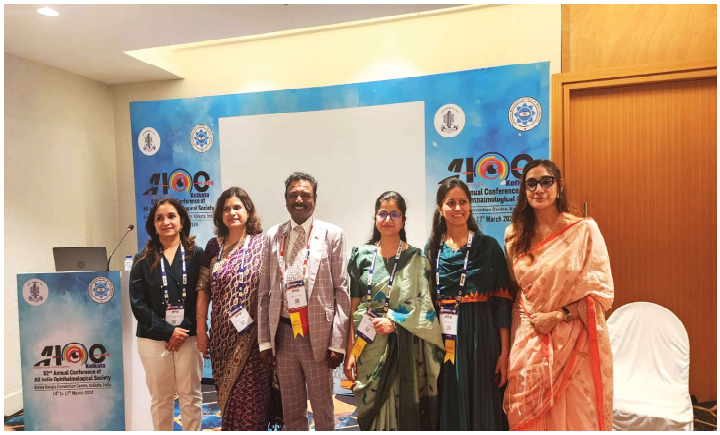
XXVI Biennial Meeting of the International Society for Eye Research
20 - 24 October 2024 / Buenos Aires, Argentina

Recent Event

AIOC 2024 Kolkata
Envisioning the Future together

The Global Eye Genetics Consortium (GEGC) session at AIOC March 2024, titled "Genetic Implications of Eye Diseases – What Every Ophthalmologist Should Know," aimed to educate ophthalmologists about the genetic aspects of eye disorders. The GEGC is dedicated to spreading knowledge and awareness about genetic eye disorders, recognizing that nearly half of the patients seen in clinics are affected by conditions with genetic implications. The eye, after the brain, is the second most common organ impacted by genetic diseases, which ranges from single gene disorders like retinitis pigmentosa and pediatric cataract to multifactorial disorders such as myopia and diabetic retinopathy. These genetic disorders often have systemic implications requiring referrals to other subspecialties. With advancements in clinical and molecular diagnosis, and the growing potential of gene therapy, it is crucial for ophthalmologists to understand the genetic basis of various eye conditions to ensure precise diagnoses, timely referrals, genetic counseling, appropriate testing, and effective management.

The session lasted 90 minutes and included the lectures from eminent ophthalmologists and genetic counsellor from India. At the outset, Dr. Prof. S. Natrajan, Vice President of GEGC introduced GEGC. Dr Shailja Tibrewal from Dr. Shroff's Charity Eye Hospital, New Delhi, and Secretary General of GEGC spoke on genetic implications of Anterior Segment and Whole Globe Anomalies.Dr Suneeta Dubey, Head of Glaucoma services at Dr. Shroff's Charity Eye Hospital, New Delhi, provided an overview of the Developmental Glaucomas and its Genetics. Insights into Diagnosis and Treatment of Inherited Retinal Disorders was well covered by Dr. Praveen Sen a well-known retina specialist from Dr. Agarwal's Eye Hospital, Chandigarh. Dr Sima Das, head of Ocular Oncology at Dr. Shroff's Charity Eye Hospital, New Delhi spoke on implications of a Genetic Diagnosis in Retinoblastoma. The critical aspect of Genetic counselling and testing was well covered by Dr. Dipanjana Datta from Organisation of Rare Disease India. Finally, Dr. Prof. S. Natrajan enlightened everyone on what's New in Therapeutics in Genetic Disorders.



Meet Our Members

Aftab Taiyab, Canada "Aftab Taiyab, an Assistant Professor in the Department of Pathology and Molecular Medicine at McMaster University, focuses on understanding ocular diseases such as Glaucoma and Posterior Capsular Opacification (Secondary Cataract), which are increasingly prevalent due to the aging global population. These conditions significantly contribute to blindness worldwide, making Taiyab's research critical. Utilizing various model systems alongside cell, molecular, biophysical, and engineering techniques, his work aims to unravel the mechanisms behind the initiation and progression of these diseases. A significant part of his research involves deciphering gene regulatory networks that may contribute to glaucoma in animal models and correlating these findings to human cases, with the goal of developing innovative treatments. Taiyab's multifaceted approach integrates multiple scientific disciplines to address the complex challenges of these eye diseases. His extensive affiliations at McMaster University include positions within the Faculty of Health Sciences, the McMaster Institute of Aging Research, and the Neuroscience department. His laboratory is currently funded by NIH and Canadian federal agencies. He holds a BSc Hons from Ranchi University, an MSc from Madurai Kamaraj University, and a PhD from the Center for Cellular and Molecular Biology in Hyderabad, India. Taiyab's diverse academic and research background establishes him as a leading figure in ocular disease research, dedicated to reducing blindness and improving quality of life for affected individuals."

Dr. Subhabrata Chakrabarti is currently the Associate Director of Research at the L V Prasad Eye Institute, Hyderabad. He is a Molecular Geneticist largely trained in India and at the National Eye Institute (NEI), NIH, and has contributed to the understanding of the molecular mechanisms in complex eye diseases. His major work on functional genomics of primary congenital glaucoma (PCG) that affects children in the developing world, has convincingly demonstrated the underlying mechanisms in disease pathogenesis and ocular development. His works have also provided evolutionary insights on the geographical structuring and migrations of these disease-associated mutations worldwide. This led to the initiation of bilateral grants with Brazil, Tunisia, Portugal, Australia and USA to understand the nature-nurture dialectics in PCG. The dissections of the genetic and physical interactions along with genotype-phenotype correlations in PCG have provided insights for predictive testing. Further, his group is currently involved in studying the genetic epidemiology of age-related and rare eye diseases in a longitudinal cohortwith an overarching component of translation from bench to bedside to community. He has published widely in reputed peer reviewed journals and has been well funded by national and international grants.

Dr. Chakrabarti's work has also provided him recognitions in the form of several honours and awards; notable among them being the 'Fellow' of ARVO (Association for Research In Vision and Ophthalmology; globally the largest body involved in eye research, education and training); 'Research Recognition Award' of the World Glaucoma Association (WGA); Young Affiliateships of all the three Science Academies of India (INSA, NASI and IASc) and TWAS (The World Academy of Sciences) and as an elected member of the GRC. He serves on multiple leadership roles of ARVO, ISER (International Society for Eye Research), WGA; federal and international funding agencies (like the Royal College of Ophthalmology, Fight for Sight) and on various editorial boards and scientific bodies on eye and vision research.He is the Associate Editor of IOVS (Investigative Ophthalmology and Visual Sciences, a premier journal of ARVO)andan expert onthe Glaucoma Variant Curation Expert Panel of ClinGen, which is an NIH initiative. He also serves on the working group of Global Eye Health Research and Training Consortium of the National Eye Institute (NEI), NIH.

Mark Radford "Prof. Mark Radford has held the positions of Executive Director and Chief Executive Officer (CEO) at the Queensland Eye Institute since March 2010. His academic journey began with an undergraduate degree from Flinders University of South Australia in 1978. He furthered his education with a Doctor of Medicine from Nagasaki University School of Medicine in 1992, supported by a Japanese Government (Mombusho) Fellowship. Additionally, during this time, he completed a PhD at Flinders University in 1989.Prof.

Radford commenced his career as a research academic, serving as a lecturer and later an Associate Professor at Hokkaido University in Japan. From 1993 to 2003, he acted as a consultant for various government and private organizations globally. He then returned to Hokkaido University in 2003 as a Professor within the Department of Behavioral Science.In 2006, Prof. Radford transitioned back to Australia to assume the roles of CEO and Managing Director at Symbiosis Group Limited, a life science investment, management, and commercialization company headquartered in Brisbane. Subsequently, he joined the Queensland Eye Institute, bringing his extensive experience in research, medical research investment, and commercialization to the organization.Prof. Radford's expertise spans diverse areas such as clinical research, research ethics, clinical trials, governance, leadership, and decision-making. He has made significant contributions to these fields through his publications and teaching endeavors. Prof. Radford is affiliated with several professional associations and holds honorary Fellowships with the Royal Australian & New Zealand College of Ophthalmologists, the Australian Institute of Company Directors (AICD), and the Australian Institute of Management (AIM). His multifaceted career reflects his commitment to advancing medical research, governance, and leadership within the field of ophthalmology."

Dr. Pall Singh is an experienced ophthalmologist with a keen interest in Neuro Ophthalmology, Orbit, and Vitreo-Retinal specialties. He has extensive experience in treating various eye conditions such as Dry Eyes, Diabetic Retinopathy, Retinal Detachment, and Age-related Macular Degeneration. Dr. Pall remains updated with the latest technological advancements, ensuring that he utilizes the most current treatment options to facilitate quick and comfortable vision restoration for his patients.

Dr. Pall Singh was the Associate Professor and Head of Department of Ophthalmology at the National University of Malaysia before resigning in September 1990 to join the Tun Hussein Onn National Eye Hospital where he is still the Senior Consultant Ophthalmologist.

Dr. Pall Singh has held multiple prestigious positions within the field of ophthalmology. He served as the President of the College of Ophthalmologists, Academy of Medicine Malaysia, and was a member of the Specialty Committee for Ophthalmology National Specialist Register. Additionally, he was a member of the Conjoint Committee of Ophthalmology of the Universities. At present, Dr. Pall is the Chairman of the Medical Advisory Committee at the Tun Hussein Onn National Eye Hospital and is part of the Teaching Staff. Furthermore, he serves as a medical advisor for ophthalmology in Medical Defence Malaysia, a mutual medical defense organization.

His expertise encompasses various procedures including Retina Surgery, Vitrectomy, Vitreoretinal Surgery, Intravitreal Injection, Laser Photocoagulation, and Vitreolysis."

Trivia

Find the hidden 'SYNDROMES'

S A L W J G E L Y O N G X H S K R L L W
B F H J O O S J P L J N T R D E P A T A
E I X X J L V D V J Y U E V G F D T R R
E T G B B D F Z R L Q L N E Y A S I O H
H I N D N E T R P O K F I G R O Q G P V
W B P R M N V M A C A R Y A L T K I L V
U S R C Q H J Y I M D Y H X I N W D A O
B S D J L A C T M L K I J S U P D O U N
O C H A G R S Z E P G D T E C I F T Y H
A A W E T A J F F A B U T E R H E N P I
Y H I M R B N X N A F P S V S I I E T P
Z X A B C E X A R G K D H Q L A K D N P
G E K G X I Y D I D B P D I S X N O W E
C R P A K O E C Z K B X P R I S N L P L
S W F O K T X O C H L Q R C R T P U K L
D M C T B N U R E O K W E V S X J C K I
A T G I E V S T U R G E W E B E R O B N
P O E E W K C I P N N A M E I N O L J D
V D E C H A R L E S B O N N E T O F T A
L W A A R D E N B U R G Q S Y W A L V U

Ophthalmic genetic news around the world

CRISPR-based gene therapy for Leber congenital amaurosis

An experimental CRISPR-based gene editing technology has shown promising results for treating a rare form of inherited blindness. The BRILLIANCE Phase I/II clinical trial, led by researchers at Oregon Health & Science University (OHSU), tested EDIT-101, an experimental CRISPR-based gene therapy for Leber congenital amaurosis (LCA). LCA is a rare genetic retinal disorder affecting individuals from birth or early infancy, with at least 20 different forms caused by mutations in various genes linked to retinal development and function.

EDIT-101's CRISPR-Cas9 gene editing system targets the CEP290 gene, associated with the Type 10 variation of LCA. The BRILLIANCE trial involved 12 adults and two children receiving the pioneering treatment through retinal injections, administered only in their worse eye.

The trial's primary aim was to determine the treatment's safety profile, while also evaluating EDIT-101's efficacy based on four outcomes: visual acuity, ability to see colored lights, ability to navigate a maze under different light levels, and self-reported quality of life improvements. Participants experienced no serious adverse events or dose-limiting toxic effects. Notably, 11 participants (79%) showed improvement in at least one assessed area, and 6 participants (43%) reported enhanced vision-related quality of life.

"This research demonstrates that CRISPR gene therapy for inherited vision loss is worth continued pursuit in research and clinical trials," explained Eric Pierce, a corresponding author of the paper. "While more research is needed to determine who may benefit most, we consider the early results promising. To hear from several participants how thrilled they were that they could finally see the food on their plates – that is a big deal. These were individuals who could not read any lines on an eye chart and who had no treatment options, which is the unfortunate reality for most people with inherited retinal disorders."

The authors aim to proceed with further clinical trials to determine the most effective administration of the CRISPR gene editing treatment.

SOURCE
Pierce EA, Aleman TS, Jayasundera KT et al. Gene editing for CEP290-associated retinal degeneration. N. Engl. J. Med. doi:10.1056/NEJMoa2309915 (2024).

Generation and characterization of three CRISPR/Cas9 edited RB1 null hiPSC lines for retinoblastoma disease modelling:

Researchers from LV Prasad Eye Institute, India recently published their results of hiPSC lines for retinoblastoma disease modelling. The study focuses on generating RB1 knockout induced pluripotent stem cell (iPSC) lines to model retinoblastoma, a type of cancer caused by the complete loss of RB1 gene function. Using CRISPR/Cas9 gene editing technology, the researchers targeted exon 18 of the RB1 gene in a healthy human iPSC (hiPSC) line to create three RB1-/- iPSC lines.

The editing process involved introducing small insertions or deletions (in-dels) at the target site, disrupting the gene's function. Following the CRISPR/Cas9 editing, the cells were clonally expanded to isolate individual cell lines. These clones were then genotyped to confirm the specific mutations introduced into the RB1 gene. Among the generated mutant lines, two were compound heterozygous, meaning they had different in-del mutations in each allele of the RB1 gene. The third line was homozygous, with identical mutations in both alleles.

To ensure the validity and usefulness of the mutant lines, several key characteristics were assessed. First, the edited iPSC lines were evaluated for their ability to maintain stemness and pluripotency, which are crucial properties of stem cells that allow them to differentiate into various cell types. The lines successfully maintained these properties, indicating that the gene editing did not affect their fundamental characteristics. The formation of embryoid bodies, which are three-dimensional aggregates of pluripotent stem cells that can differentiate into cell types from all three germ layers (ectoderm, mesoderm, and endoderm), further confirmed the pluripotency of the edited iPSC lines.

Additionally, the researchers verified that the edited cell lines maintained a normal karyotype, meaning they had the correct number and structure of chromosomes, which is essential for ensuring that the observed phenotypes are due to the RB1 mutations and not chromosomal abnormalities. Finally, the loss of RB1 expression was confirmed in all mutant lines, establishing that the gene editing was effective in knocking out RB1 function.

This study is significant because it provides a robust in vitro model for studying retinoblastoma. By creating iPSC lines with precise RB1 knockout mutations, researchers can investigate the cellular and molecular mechanisms underlying retinoblastoma development. Moreover, these iPSC lines can be used to screen potential therapeutic compounds and explore gene correction strategies, contributing to the development of targeted treatments for retinoblastoma and enhancing our understanding of the role of RB1 in cancer biology.

SOURCE
https://doi.org/10.1016/j.scr.2024.103373
https://www.sciencedirect.com/science/article/pii/S1873506124000710?via%3Dihub

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