Global Eye Genetics Consortium

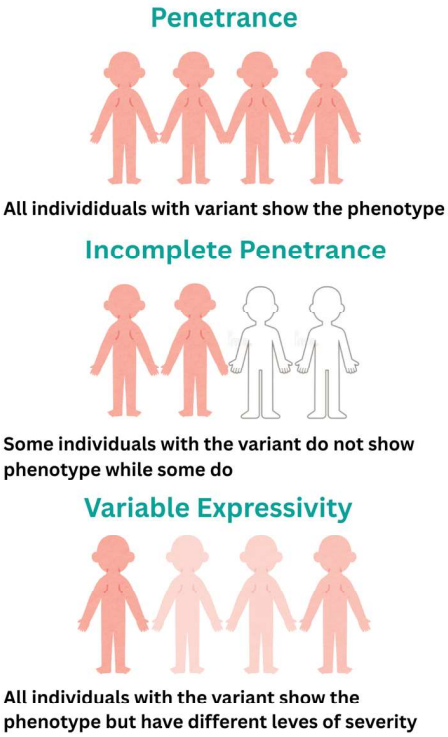
Newsletter #13

Jan to Mar 2026

Genetics 101 | Penetrance and Expressivity

Penetrance and Expressivity in Ophthalmic Genetics

In clinical genetics, the presence of a pathogenic variant does not always translate into a predictable phenotype. Two related concepts help explain this variability: penetrance, which refers to whether a genotype is clinically expressed at all, and expressivity, which refers to the degree or pattern of expression among affected individuals.



Incomplete penetrance is especially relevant in ophthalmic genetics because a disease-causing variant may be present in an individual with no obvious clinical signs at examination, or even throughout life. Variable expressivity, in contrast, is seen when the same variant produces different severities or combinations of ocular findings, ranging from subtle structural changes to severe visual impairment.

Why It Matters in Ophthalmology

These concepts are not merely academic; they directly influence diagnosis, counseling, and family screening. Inherited eye disorders often show substantial intrafamilial variability, making it unwise to assume that one family member's presentation predicts another's outcome. Genotype-positive relatives may therefore need continued surveillance even when they appear clinically unaffected.

A classic example is PAX6-related aniridia, where the disorder is generally highly penetrant but clearly variable in expressivity, with phenotypes ranging from near-complete iris absence to milder anterior segment and foveal abnormalities. Similarly, CYP1B1-associated primary congenital glaucoma may show high penetrance in some families, yet the clinical spectrum can still include apparently unaffected individuals who later manifest disease.

What Shapes the Phenotype

Penetrance and expressivity are influenced by more than the causal variant itself. Modifier genes, differences in gene expression, regulatory variation, mosaicism, and environmental or developmental factors all contribute to phenotypic diversity. This is one reason why monogenic eye disease is often more complex than textbook Mendelian inheritance suggests.

Clinical Takeaway

The practical message is clear: a pathogenic variant is not a fixed clinical destiny. Penetrance tells us who manifests disease, while expressivity tells us how that disease appears. In counseling, this distinction helps set realistic expectations, supports risk-based surveillance, and prevents overconfident predictions.

Upcoming Events

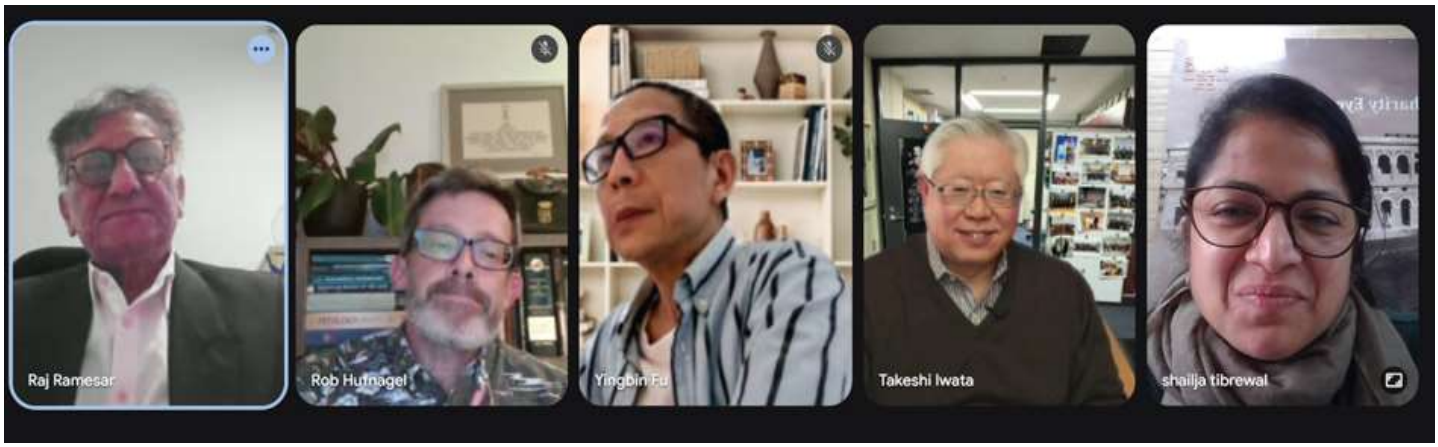
The GEGC Annual Business Meeting shall be held at the ARVO meeting 2026, in Denver, Colorado

The details of the meeting are as follows

Date: May 4th (Monday)
Timing: 01:15 pm – 02:45 pm
Venue: Room 107/109, The Colorado Convention Center, 700 14th St., Denver, Colo., 80202
Agenda: The GEGC educational website and other activities

Recent Events

GEGC Educational Activities Planning Meeting – Key Highlights



A virtual meeting of the Global Eye Genetics Consortium (GEGC) was held on 6 January 2026, bringing together the executive members global leaders to discuss the formal registration of GEGC as a society and the development of its educational initiatives. A key focus was the registration of GEGC as a society in Japan, with discussions around sustainable models for membership fees and their utilization for website development and educational activities. While there was support for structured funding, the importance of maintaining equitable and accessible education was emphasized.

The group outlined a vision for a dynamic GEGC digital platform, which would serve as a central hub for webinars, courses, fellowships, and global resources in ocular genetics. Rather than duplicating existing efforts, there was consensus on leveraging and linking high-quality international educational resources.

Education will follow a phased approach, beginning with webinars and expanding into structured programs. Proposed topics include genomics, genotype–phenotype correlations, patient education, and emerging technologies such as AI in genetics. The need for genetics-focused training for ophthalmologists and strengthening genetic counselling capacity globally was strongly highlighted. Plans were also made to establish dedicated subcommittees (education, outreach, AI, genomics, and website development) to drive these initiatives.

The meeting concluded with clear action points, including membership communication, resource mapping, webinar planning, and committee formation, with a target timeline of March 2026 for initial deliverables.

AIOC 2026 | GEGC Special Session

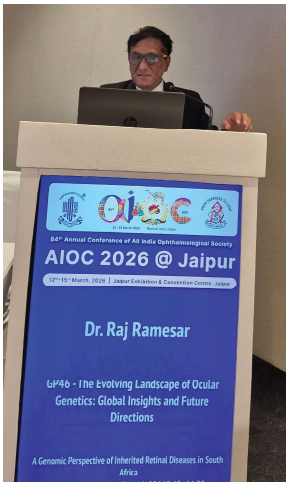
The Evolving Landscape of Ocular Genetics: Global Insights and Future Directions

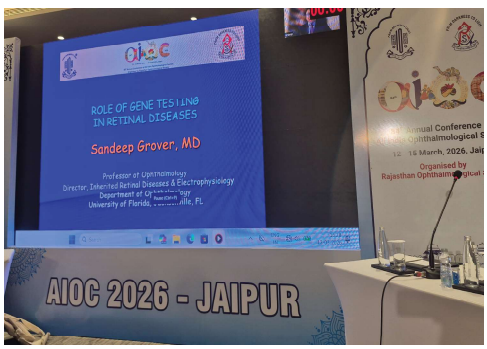
Setting the Stage: GEGC's Expanding Global Vision

The session opened with GEGC Secretary General of Shailja Tibrewal, Senior Consultant, Dr Shroff's Charity Eye Hospital, New Delhi, who presented a concise update on GEGC's expanding initiatives. She highlighted the consortium's growing international footprint, collaborative research efforts, and its role in building educational capacity for ocular genetics.

Global Genomics in Focus

A powerful global perspective was brought in by Raj Ramesar, Professor and Head, Division of Human Genetics, University of Cape Town, South Africa. His talk, "A Genomic Perspective of Inherited Retinal Diseases in South Africa," underscored the importance of studying underrepresented populations. He demonstrated how African genomic data is reshaping variant interpretation and broadening our understanding of disease mechanisms.





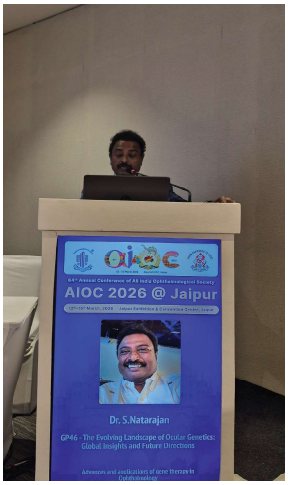
Complementing this, Sandeep Grover, Professor of Ophthalmology, UF Health Jacksonville, USA, delivered a clinically grounded talk on "Role of Gene Testing in Retinal Diseases." He emphasized the transition of genetic testing from a research tool to a clinical necessity, guiding diagnosis, prognosis, and eligibility for emerging therapies.

From Bench to Bedside: Translational Innovations

Bridging cutting-edge science with clinical application, Rajarshi Pal, Chief Scientist, Eyestem Research, Bengaluru, presented on induced pluripotent stem cell-derived retinal cells, highlighting their therapeutic promise and translational potential.

P Sundaresan, Senior Scientist, Aravind Medical Research Foundation, explored the complex interplay of mitochondrial and nuclear genetics in Leber's Hereditary Optic Neuropathy, offering new insights into disease variability.

Adding a translational dimension, Fulya Tuncay, University of Health Sciences, Ankara, Turkey, presented "Familial Exudative Vitreoretinopathy: From Bedside to Bench," illustrating how clinical observations can drive molecular discoveries.



The session concluded with Vice President & Treasury Dr. Natrajan Sundaram, Professor and Head, Aditya Jyot Eye Foundation, Mumbai, who discussed advances and applications of gene therapy in ophthalmology, highlighting both current successes and future directions.

Looking Ahead

The GEGC session at AIOC 2026 was more than a scientific exchange—it was a testament to the power of global collaboration in advancing ocular genetics. As genomics becomes increasingly integrated into routine ophthalmic care, such platforms are critical in shaping a future where precision medicine is accessible, inclusive, and impactful.

Bridging Continents Through Genomics:
A Distinguished Visit by Dr Raj Ramesar

The Global Eye Genetics Consortium (GEGC) had the privilege of facilitating a highly enriching academic visit by Raj Ramesar, Professor of Human Genetics at the University of Cape Town, South Africa, to leading ophthalmic institutions in India. Internationally recognized for his pioneering contributions to human genetics and inherited retinal diseases, Dr. Ramesar's visit marked a significant step toward strengthening global partnerships in ocular genomics.

Advancing Ocular Genetics at Dr Shroff's Charity Eye Hospital

At Dr Shroff's Charity Eye Hospital, Dr. Ramesar delivered a compelling lecture titled "Genomics of Inherited Retinal Dystrophies – An African Perspective." The session drew keen interest from clinicians, fellows, and researchers, reflecting the growing relevance of genomics in everyday ophthalmic practice. This lecture also marked the beginning of the "Distinguished Lecture" series – an educational initiative of the GEGC. His lecture highlighted the importance of incorporating diverse population datasets into genetic research. By presenting insights from African cohorts—often underrepresented in global genomic studies—he demonstrated how expanding the genetic evidence base can refine variant interpretation, improve diagnostic accuracy, and ultimately enhance patient care worldwide.

Beyond the formal lecture, Dr. Ramesar engaged in in-depth discussions with clinicians, genetic counsellors, and laboratory scientists. These interactions explored practical challenges in implementing next-generation sequencing, interpreting variants of uncertain significance, and integrating genomic insights into clinical workflows. The exchange of ideas fostered a collaborative environment and inspired new avenues for research and capacity building.

Fostering Academic Exchange at Aditya Jyot Eye Hospital

Dr. Ramesar's visit also extended to Aditya Jyot Eye Hospital, led by Prof. S Natarajan, where he continued academic engagements with experts in ophthalmology and vision science. The discussions here focused on translational research, emerging gene-based therapies, and the future of precision medicine in ophthalmology.

These interactions emphasized the importance of aligning clinical expertise with genomic innovation. The exchange of perspectives between international and Indian experts underscored a shared commitment to advancing care for patients with inherited retinal

Dr Natrajan's Visit to Tokyo & FujiRetina 2026 – Advancing Global Collaborations in Retina

Dr. Sundaram Natarajan's recent visit to Tokyo marked a significant step in strengthening global academic and clinical collaborations in vitreoretinal sciences. The visit combined a fruitful academic exchange at Dr. Takeshi Iwata's laboratory with active participation as International Faculty at the prestigious FujiRetina 2026 meeting, held from March 27–29, 2026.

During his visit, Dr. Natarajan had the opportunity to engage with Dr. Takeshi Iwata and his team at the National Hospital Organization Tokyo Medical Center. The interactions focused on cutting-edge research in retinal diseases, genetics, and translational approaches, fostering meaningful dialogue on future collaborations between Indian and Japanese research ecosystems. This exchange highlights the growing importance of cross-border partnerships in accelerating innovation in ophthalmology.

Dr. Natarajan was invited as International Faculty at FujiRetina 2026, an increasingly influential global meeting in vitreoretinal science.

The conference, led by Prof. Kazuaki Kadonosono, continues to evolve as a major international forum, bringing together experts from across the world. As highlighted in the President's address, FujiRetina aims to:

- Advance retinal science in Japan and the Asia-Pacific region
- Build strong global collaborations
- Support the next generation of ophthalmologists
- Improve patient care worldwide

With participation from over 1,500 delegates across 30+ countries in previous editions, the meeting reflects the rapid progress and global integration of retinal research. Set against the backdrop of Tokyo's iconic cherry blossom season, FujiRetina 2026 provided not just an academic platform but also an inspiring environment for exchange of ideas, innovation, and collaboration.
This visit underscores the importance of international engagement in shaping the future of retinal care. Strengthening such collaborations will be instrumental in advancing research, improving clinical outcomes, and driving innovation in the management of retinal diseases.

Emerging Genetic Evidence Linking Reticular Pseudodrusen to Severe Age-Related Macular Degeneration.

According to a study funded by the National Health and Medical Research Council through a Synergy Grant and recently published in Nature Communications, it has been reported that genetic factors associated with reticular pseudodrusen-retinal deposits that contribute to vision loss and are present in up to 60% of individuals with advanced AMD. These Australian scientists have, for the first time, identified genetic alterations that heighten the risk of severe, vision-threatening forms of age-related macular degeneration (AMD). The investigation, conducted by researchers from the Centre for Eye Research Australia, Walter and Eliza Hall Institute of Medical Research, and the University of Melbourne, identifies a potential therapeutic target for managing the most severe manifestations of AMD, including Geographic Atrophy. AMD, a condition resulting from degeneration of photoreceptor cells in the macula, the retinal region responsible for central vision, is among the leading causes of irreversible blindness in individuals aged over 50 worldwide. Globally, more than 196 million people are affected by AMD. Current treatments are limited to slowing disease progression after substantial retinal damage has already occurred. In a large international collaboration led by the Australian research team, investigators identified a distinct genetic pattern in individuals with reticular pseudodrusen. Specifically, they found a strong association with genetic variants located on Chromosome 10, while no association was observed with the well-established AMD-related gene variants on Chromosome [1].

Retinal imaging of individuals carrying these Chromosome 10 variations also revealed a thinner retina, a finding that requires additional study. Co-lead investigator Melanie Bahlo from WEHI emphasized that this study represents the first genome-wide investigation of the genetic mechanisms underlying reticular pseudodrusen. Earlier work in 2005 had linked AMD to genetic changes on Chromosome 1, particularly involving the Complement Factor H (CFH), which plays a role in immune regulation. More recent therapies targeting these pathways have demonstrated modest benefits in slowing disease progression. According to study co-lead Robyn Guymer of the Centre for Eye Research Australia, the findings reinforce the view that AMD is not a single disease entity but rather a spectrum of related conditions that may require different therapeutic strategies. She noted that reticular pseudodrusen, which are detectable on retinal imaging, have previously been associated with poorer visual function and less favorable responses to treatment. These new findings suggest that reticular pseudodrusen are primarily influenced by biological pathways related to Chromosome 10 rather than the well-known Chromosome 1 genes associated with AMD. This discovery underscores the importance of investigating how Chromosome 10 variants influence retinal structure and developing treatments that extend beyond complement-based therapies to prevent the formation of sight-threatening retinal deposits.

Sources consulted:
1)Farashi S, Fletcher EL, Guymer RH, Bahlo M, et al. HTRA1/lncRNA HTRA1-AS1 dominates in age-related macular degeneration reticular pseudodrusen genetic risk with no complement involvement. Nature Communications. 2025;16:10854. doi:10.1038/s41467 025-65903-9.
2) Centre For Eye Research Australia (CERA). Australian scientists reveal new genetic risk for severe macular degeneration. . Published December 8,2025.Accessed March 11,2026. https://www.cera.org.au/ Australian-scientists- reveal- new -genetic- risk- for- severe- macular- degeneration | CERA

Promising novel oral treatment for Stargardt disease Type 1?

Belite Bio has completed its Phase 3 DRAGON trial (NCT05244304) evaluating Tinlarebant, an oral drug treatment for adolescents with Stargardt disease type 1 (STGD1), an inherited form of macular degeneration. Tinlarebant is taken orally and aims to reduce retinal accumulation of bisretinoids—vitamin A–related toxins implicated in Stargardt disease and also in geographic atrophy associated with Age-Related Macular Degeneration.

The DRAGON study was a multicenter, randomized, double-masked, placebo-controlled trial with a 2:1 allocation favoring tinlarebant over placebo. Its primary objective was to determine whether the drug slows the growth of atrophic retinal lesions while also assessing its safety and tolerability. Tinlarebant works by reducing levels of retinol binding protein-4 (RBP4), the main transporter of vitamin A from the liver to the eye, thereby limiting the formation of toxic vitamin A–derived compounds in the retina. A total of 104 participants aged 12–20 years were enrolled across 11 regions worldwide, including the United States, the United Kingdom, Germany, France, Australia, China, and several European and Asian locations. Eligible participants had genetically confirmed STGD1 with at least one mutation in the ABCA4 gene and measurable retinal atrophy. Tinlarebant significantly slowed the growth of retinal atrophy, a key marker of disease progression, by about 35% compared with placebo. It also met important secondary goals showing a similar reduction in lesion growth on imaging. The most common side effects included changes in colour vision, slower dark adaptation, night-vision difficulties, and headaches. With no approved treatments currently available for STGD1, the results represent a major step toward the first potential treatment for Stargardt disease, with the company planning to submit the drug for approval to the US Food and Drug Agency in 2026.Tinlarebant has received multiple regulatory incentives, including fast-track and rare pediatric disease designations in the United States and orphan drug status in several regions.

Sources consulted:
1. Belite eyes tinlarebant approval after late-stage Stargardt success. Clinical Trials Arena. Published December 2, 2025. Accessed March 12, 2026. https://www.clinicaltrialsarena.com/news/belite-bio-stargardt-disease/
2. Belite Bio concludes phase 3 DRAGON study for Stargardt disease. Published September 16, 2025. Accessed March 12, 2026. https://ophthalmologytimes.com/view/belite-bio-concludes-phase-3-dragon-study-for-stargardt-disease

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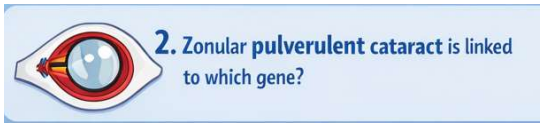

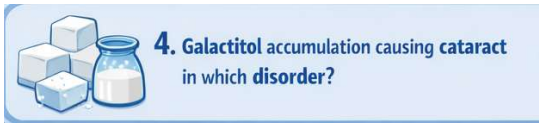

Know our members

Dr. Muhammad Iqbal is a leading researcher in Molecular Biology and Human Genetics. He earned his PhD from the National Centre of Excellence in Molecular Biology (NCEMB), University of the Punjab, Lahore in 2010. His doctoral work led to the discovery of a novel locus (RP51) and identification of the TTC8 gene as a cause of non-syndromic autosomal recessive Retinitis pigmentosa in the Pakistani population.

Dr. Iqbal joined The Islamia University of Bahawalpur soon after his PhD, where he has been actively engaged in teaching and research. He developed and teaches advanced courses in Human Molecular Genetics and leads a research group investigating genetic disorders such as hereditary vision loss, hearing impairment, and intellectual disability—conditions especially prevalent in South Punjab due to high consanguinity. His work extends into the community through genetic counseling, aiming to reduce the recurrence of inherited disorders in families through education and support.

Dr. Iqbal has also gained international recognition. He was awarded training fellowships by the National Human Genome Research Institute (NIH, USA) in 2019 and the University of Geneva, Switzerland in 2021, where he advanced his skills in genome data analysis and built global collaborations. Through his research, teaching, and outreach, Dr. Iqbal is playing a vital role in improving genetic literacy and reducing the burden of genetic diseases in underserved regions of Pakistan.

Dr. Passant Abdelrahman MBA MBBCh MSc is an ophthalmology post-residency trainee at Eye Care Center based in Maadi, Cairo, Egypt, pursuing her specialization in Retina. She is also an Egyptian Board-certified healthcare management physician specialist and a global health researcher by virtue of completing an MSc Global Health at the University of Manchester, UK and having other current projects. Her studies have helped her gain deeper insight into ophthalmology, leadership in healthcare, vulnerability, medical ethics, health systems, and healthcare disparities.

She currently serves as the Resident and Associate Society (RAS) Liaison to the Advisory Council of Ophthalmic Surgery at the American College of Surgeons (ACS) and to the Egypt Chapter of ACS. Her interests include active engagement in international dialogues, surgical leadership, advancements in ophthalmology including AI and robotics, and advocacy. She is also an active member of the American Academy of Ophthalmology (AAO) International Meetings Committee and has represented AAO as faculty at different Retina symposiums held by international host societies, and regional societies like the Asia Pacific Academy of Ophthalmology (APAO). Her roles as session chair have further helped her develop both scientific and clinical knowledge, communication and leadership skills. Dr Passant is also an AAO Resident Self-Assessment Committee member, one of AAO's Clinical Education committees.

Dr. Abdelrahman began her medical journey after completing her International General Certificate of Secondary Education (IGCSE), earning a place at Benha University Faculty of Medicine before continuing her studies after 3 months at Cairo University's Kasr Al Ainy School of Medicine where she graduated in 2016, and completed medical internship in 2017. Early exposure to patients from underserved and rural communities shaped her commitment to equitable healthcare and strengthened her sense of social responsibility. She was among the first candidates in Egypt to pass the Royal College of Ophthalmologists' newly introduced hybrid Refraction Certificate examination format. Dr. Passant is a member of the Global Young Ophthalmologist Alliance (GYOA). She has founded the Young Ophthalmologists in Egypt online Group (YO-EG), seeking research collaborations, innovations and global YO networking and meeting participation.

Dr. Jaspreet Sukhija is a distinguished ophthalmologist and Professor at the Advanced Eye Centre, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, one of India's leading medical and research institutions.

With a clinical focus on pediatric ophthalmology, strabismus, and neuro-ophthalmology, Dr. Sukhija leads comprehensive services that combine state-of-the-art surgical care with evidence-based clinical practice for children and adults alike. He has made noteworthy contributions to the field through innovative surgical techniques and academic scholarship that have influenced practice patterns in complex pediatric conditions.

Dr. Sukhija's research has earned national recognition, including the Prof. Hanumantha Reddy Award for the best pediatric ophthalmology paper at the All-India Ophthalmology Society conference. His work on modified surgical approaches for pediatric cataract and strabismus has helped improve safety and outcomes in challenging cases. He has delivered prestigious orations such as the Dr. R. N. Gandhewar Oration at the Annual Conference of the Vidarbha Ophthalmological Society, where he highlighted evolving trends in pediatric cataract surgery to clinicians from across India.

An active academician, Dr. Sukhija has authored numerous peer-reviewed publications and regularly participates in national conferences and educational forums. He serves as a mentor to residents and fellows, fostering clinical excellence and research inquiry in the next generation of ophthalmologists. Under his leadership, the Pediatric Ophthalmology Unit at PGIMER also engages in community outreach and awareness initiatives—such as campaigns to address rising childhood myopia—reflecting his commitment to preventive eye care and public health.

Dr. Sukhija's blend of clinical expertise, scholarly achievement, and dedication to patient-centered care distinguishes him as a leading figure in ophthalmology both in India and beyond.

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