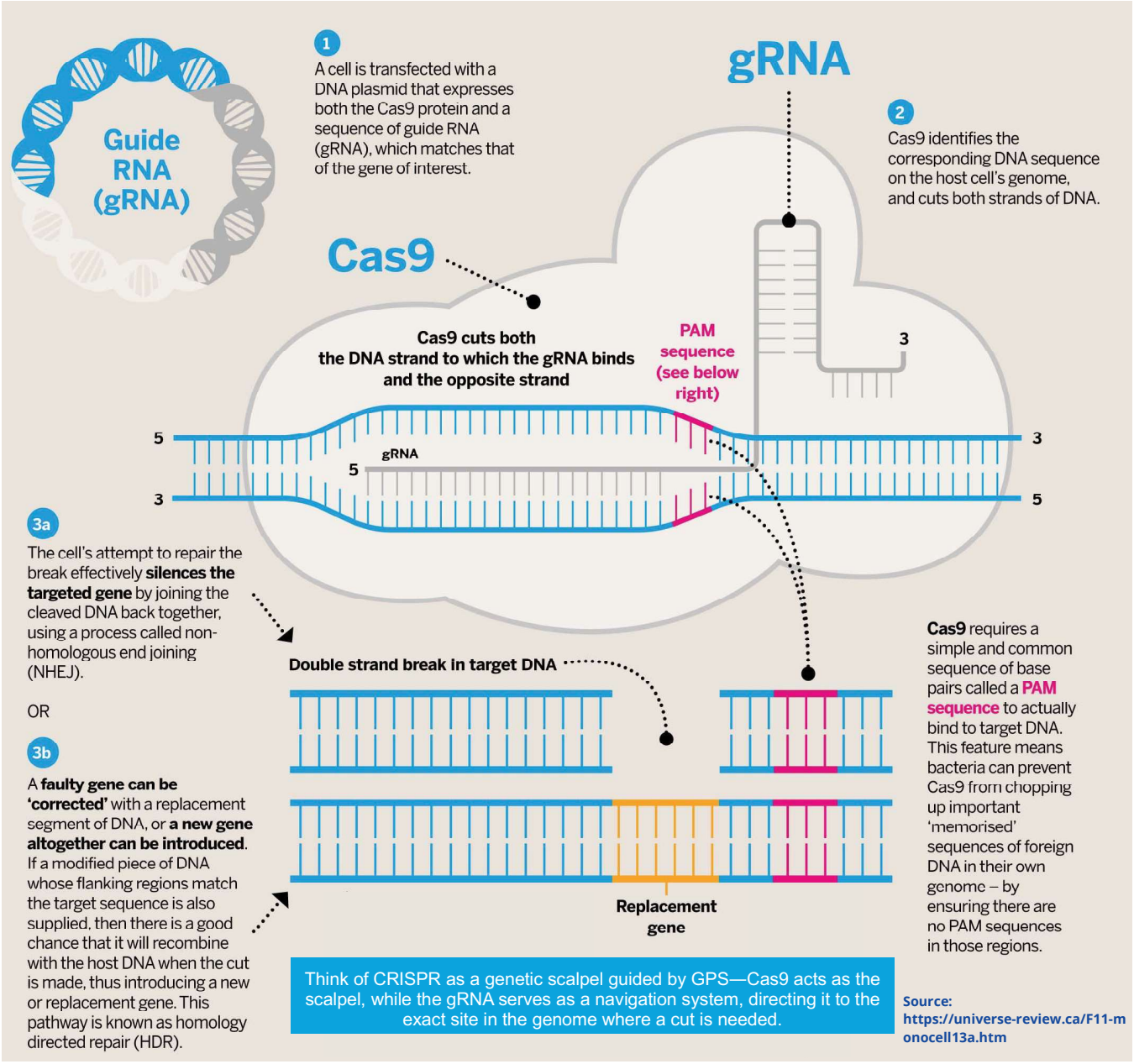
Global Eye Genetics Consortium

Newsletter #09

Genetics 101 | A New Segment in Focus

Welcome to Genetics 101, our new segment dedicated to unpacking key concepts in genetics. Each issue, we'll spotlight a fundamental or emerging topic shaping the future of biomedical science and clinical research. Whether you're refreshing core knowledge or staying current with new tools, this space is designed for professionals who work with—or are simply fascinated by—the blueprint of life.

CRISPR-Cas9: Precision in Genome Engineering



CRISPR-Cas9 is a gene-editing tool that uses guide RNA to direct the Cas9 enzyme to specific DNA targets, creating double-strand breaks. These breaks are repaired by the cell through non-homologous end joining or homology-directed repair. Its precision and versatility have made CRISPR essential in research and medical advancements.

Meet Our Members

Professor Mineo Kondo serves as the Chair of the Department of Ophthalmology at Mie University Graduate School of Medicine, Japan. He completed his medical degree at Kanazawa University School of Medicine in 1991 and obtained his doctoral degree in ophthalmology from Nagoya University in 2007. His academic journey also includes a research fellowship at the University of Michigan in Ann Arbor, USA, between 1999 and 2001. Following this fellowship, he joined the faculty of the Department of Ophthalmology at Nagoya University in 2001, where he contributed significantly to the department's growth and research initiatives.

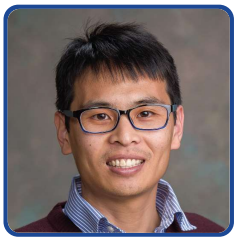
As a clinician-scientist, Professor Kondo is dedicated to advancing the understanding of retinal and macular diseases. His research interests focus on the physiology of the retina, both in healthy eyes and in those affected by various diseases. By combining electrophysiological, morphological, and molecular biological techniques, he has been able to develop advanced methods for diagnosing and characterizing retinal diseases. His work has made a considerable impact on the field, leading to better diagnostic techniques and a deeper understanding of retinal pathologies.

With over 200 peer-reviewed publications to his name, Professor Kondo is highly regarded in the scientific community. His research has enriched the field of ophthalmology and continues to inspire both clinical practice and further academic inquiry. Professor Kondo is also actively involved in editorial work, serving on the editorial boards of several respected journals in ophthalmology, including Translational Vision Science and Technology, Documenta Ophthalmologica, Current Eye Research, and the Japanese Journal of Ophthalmology. His ongoing contributions to both clinical practice and scientific research underscore his significant role in the field of ophthalmology.

Dr. Muthusamy Malaravan is an esteemed ophthalmologist based in Northern Sri Lanka, with a deep commitment to advancing eye care in the region. He holds an MBBS and an MD in Ophthalmology, complemented by a Fellowship in Anterior Segment and IOLs. Currently, Dr. Malaravan serves as a lecturer in the Department of Ophthalmology at Jaffna Teaching Hospital, where he plays a pivotal role in the education of medical students and healthcare professionals.

Dr. Malaravan has been instrumental in improving the Cataract Surgical Rate in the Northern Province of Sri Lanka, contributing to the broader initiative "Eye Health & SDGs - Insight 2030." His dedication to eye health extends beyond clinical practice, with a focus on enhancing educational opportunities for future ophthalmologists. He also holds teaching positions in Undergraduate Medical Education in Ophthalmology and Allied Health Science at the Faculty of Medicine, Jaffna, Sri Lanka, as well as in the BSc Nursing program at Aravind Eye Care Hospitals & Post Graduate Institute of Ophthalmology in India, a WHO Collaborating Centre.

An alumnus of the University of Colombo and University of Jaffna, Dr. Malaravan's career reflects his passion for improving eye health and training the next generation of healthcare professionals. His extensive publications and research contributions have earned him recognition, with over 2,369 reads and 13 citations. His work continues to inspire progress in ophthalmology and public health, particularly in the context of sustainable development goals for eye health in Sri Lanka.



Dr. Shicheng Guo, is a renowned leader in biopharmaceuticals with a career spanning prestigious institutions. He has held key roles, including Principal Scientist at Johnson & Johnson's Central Data Science Department, and has contributed significantly to genetics and pharmacology research at the University of Texas Health Science Center at Houston, the University of California, San Diego, and the University of Wisconsin-Madison. Dr. Guo earned his Ph.D. from Fudan University and has authored over 100 publications, receiving numerous accolades for his pioneering work in gene and RNA therapies. He is Director of Translational Genetics at Arrowhead Pharmaceuticals

Beyond his academic and professional accomplishments, Dr. Guo has been an active volunteer and leader within the Chinese-American BioPharmaceutical Society (CABS). He has held several roles, including EC member in O2 & BCD (2023) and Co-Chair of O2 (2024), and has been instrumental in maintaining CABS platforms, launching the CABS Data Science Summer Intern Program, and contributing to the 2023 and 2024 CABS Biopacific Conferences. In recognition of his contributions, he received the 2023 "Special Contribution" and "Co-Chairs' Picks" awards.

Dr. Guo's vision for CABS includes empowering innovation by providing team training in AI-driven project management and automation, positioning CABS as a global leader in biopharmaceutical innovation, expanding its influence across the Bay Area and Pacific Rim, and enhancing funding through partnerships with nonprofits and academic institutions. Additionally, he aims to boost CABS's visibility in the biopharma sector and offer training, certifications, scholarships, and internships within the CABS community.

Through these efforts, Dr. Guo strives to elevate CABS's role in advancing the global biopharmaceutical industry.

Professor Adekoya Bola Josephine is a distinguished academic at Lagos State University, where she serves as a Professor in the Department of Ophthalmology. Specializing in ophthalmology, glaucoma, and surgery, she is a leading expert in the medical treatment of glaucoma, with a particular focus on improving eye care in Nigeria. Professor Adekoya earned a Master of Science (M.Sc) in Public Health in Eye Care with distinction from the University of London, UK, in 2010, which laid the foundation for her impactful work in both clinical practice and research.

Her research primarily focuses on the epidemiology and medical treatment of glaucoma, a leading cause of blindness globally. She has worked extensively on identifying at-risk patients, improving diagnosis, and enhancing the quality of care for glaucoma sufferers. In addition to her glaucoma work, she is deeply involved in public health initiatives aimed at raising awareness about eye care, particularly through collaborations with governmental and non-governmental organizations to secure funding and advocate for better care. Professor Adekoya also researches ocular injuries, exploring the epidemiology of eye injuries in both adults and children.

Professor Adekoya has an impressive portfolio of academic publications, including chapters in Illustrated Clinical Surgery and numerous articles in prestigious journals. Some of her notable publications include her research on cataract surgery techniques, virtual reality simulations for

evaluating daily living activities in glaucoma patients, and the status of glaucoma care in Sub-Saharan Africa. Her work also addresses psychiatric comorbidities associated with glaucoma, as well as clinical outcomes related to cataract surgery and the implantation of iris claw lenses.

In addition to her academic contributions, Professor Adekoya has collaborated with various institutions on research projects, including a histopathological study of ophthalmic tumors in Kebbi, Nigeria, and an analysis of glaucoma services in Lagos State in partnership with the London School of Hygiene and Tropical Medicine. These collaborations highlight her commitment to global research and improving eye care, both locally and internationally.

Beyond her research, Professor Adekoya is a dedicated advocate for glaucoma awareness and rehabilitation. She actively works to educate both the public and healthcare professionals on the importance of early glaucoma detection and treatment. Her efforts extend to providing rehabilitative services for blind glaucoma patients and promoting patient support networks. Professor Adekoya continues to shape the future of eye care in Nigeria and beyond, making significant contributions to both the clinical and public health aspects of ophthalmology.

Prof. (Dr.) Rajvardhan Azad is a distinguished clinician, educator, and researcher with over 40 years of expertise in eye care. He earned his MD in Ophthalmology from Dr. R.P. Centre for Ophthalmic Sciences, AIIMS, New Delhi, where he later became a Professor and served as Chief (2011–2014) of the Prestigious centre.

A Fellow of the Royal College of Surgeons, Edinburgh (FRCS), Academy of Medical Sciences (FAMS), college of ophthalmologist Sri Lanka and many other prestigious institutions, Prof. Azad has been advisor to Ministry of Health & Family Welfare, Government of India, Armed Forces Medical Services, and Vision 2020 India. He was also President of National Board of Examination NBE 2001-2004 and chairman of PG Program in MCI.

He was Secretary of AIOS for 6 yrs and then elected as President in 2009-2011.He also served as President of Vitreoretinal society of India. As Secretary General of the SAARC Academy of Ophthalmology (SAO), he played a key role in reviving SAO and introducing the ICO-SAARC fellowship for young ophthalmologists. He was also the Regional Secretary of the Asia Pacific Academy of Ophthalmology (APAO).

Currently, he serves as an Advisor to the National Task Force on Retinopathy of Prematurity (ROP) and the State Key Laboratory in Guangzhou, China. He is also an Honorary Professor at Zhongshan Ophthalmic Centre, Sun Yat-Sen University.

Prof. Azad is now Chairman of the Clinical and Research advisory board of Akhand Jyoti eye hospital and Raj Retina and Eye Care Centre in Patna and Director of ROP Services at Bharti Eye Hospital, New Delhi.

He is also the chairman of ophthalmic education committee of APAO and President of South Asian Academy of ophthalmology SAO. A leading vitreo-retinal surgeon, he specializes in pediatric retina, ROP, retinal detachment, diabetic retinopathy, and ARMD. His research has contributed to understanding the role of the Renin-Angiotensin System (RAS) in ROP, stem cell therapy, VEGF

mechanisms, and gene expression. He also identified new anti-angiogenic drugs from marine isolates in a rat model of ROP. His innovations include modified needle drainage for retinal detachment and ultrasound biomicroscopy (UBM) in late-stage ROP.

Prof. Azad was a Visiting Professor at institutions like the University of Texas and the University of Toronto. He has published 12 books,400 + peer reviewed research papers, and 60+ book chapters. He is on the editorial board of many leading ophthalmology journals and has received 50+ awards, including the De O'Campo Oration from APAO, Hose Rizal highest Award of APAO, Dr. B.C. Roy National Award. Latest in addition is International council of ophthalmology Award name Golden apple Award for 2025.

He also served as the first Indian President of APAO in 2013-2015. Currently He is a nominated member of Bihar legislative council as a lawmaker.

Dr. V. Vinod Mootha, M.D., is a distinguished Professor of Ophthalmology at the University of Texas Southwestern Medical Center (UT Southwestern). He leads a research team at the McDermott Center for Human Growth and Development, focusing on innovative treatments for corneal disorders.

Dr. Mootha's academic journey began at Baylor University, where he earned his B.S. in Biology, graduating summa cum laude. He then completed his M.D. at Johns Hopkins University School of Medicine. After a residency in Ophthalmology at the University of Wisconsin, he further specialized with a fellowship in Cornea and External Disease at UT Southwestern.

In 2004, Dr. Mootha joined UT Southwestern to develop less-invasive corneal transplant procedures for patients with Fuchs' endothelial corneal dystrophy (FECD) and other corneal diseases. His efforts were aimed at improving patient outcomes with advanced, minimally invasive techniques.

A major turning point in his career occurred in 2012, when Dr. Mootha received his first NIH grant. This grant supported his transition to becoming a surgeon-scientist, where he began exploring the molecular genetic basis of Fuchs' endothelial corneal dystrophy. That same year, he established his independent research laboratory at the Eugene McDermott Center for Human Growth and Development.

Using both familial and trans-ethnic association studies, his group examined the role of intronic CTG triplet repeat expansions in the TCF4 gene in FECD. In 2015 his lab reported, that expanded CUG repeat-containing TCF4 transcripts form nuclear foci in the corneal endothelium of FECD patients with the triplet repeat expansions. In 2017, Mootha reported patients with myotonic dystrophy caused by a CTG repeat expansion in the 3' UTR of the DMPK gene are at increased risk for FECD and form CUG repeat foci in their corneal endothelium. These observations established CUG repeat foci as the genetic root cause of FECD. Dr. Mootha's lab is examining the potential of oligonucleotides targeting the CUG repeat RNA as a therapeutic strategy for FECD.

Dr. Mootha's contributions have been widely recognized. In 2016, he was named the Paul T. Stoffel / Centex Professor in Clinical Care, and in 2018, he received the Scholar-Innovator Award from the Harrington Discovery Institute.

With over 73 peer-reviewed papers to his name, Dr. Mootha has secured funding from the NIH, Research to Prevent Blindness, and the Harrington Discovery Institute. His research continues to shape the future of corneal disease treatment.

Ocular Genetics Trivia

Guess the condition/syndrome based on the emojis

Ophthalmic Genetics News

Around the World

Novel Gene therapy for X-linked Retinoschisis granted Regenerative Medicine Advanced Therapy Designation

With respect to the treatment of X-linked retinoschisis, the USA Food and Drug Administration (FDA) has granted a Regenerative Medicine Advanced Therapy (RMAT) designation to Atsena Therapeutics for its investigational gene therapy, ATSN-201. Atsena Therapeutics ("Atsena") is a clinical-stage gene therapy company developing best-in-class treatments for reversing or preventing blindness from inherited retinal diseases. XLRS is characterized by schisis, or abnormal splitting of retinal layers, which causes impaired visual acuity that is not correctable with glasses and leads to progressive vision loss and ultimately blindness. Currently, there are no approved treatments for XLRS, a condition typically diagnosed in early childhood that affects roughly 30,000 males in the US and Europe. The global prevalence of XLRS varies between 1 in 5000 and 1 in 30,000 males, with Finland consistently appearing to have the highest reported rates of this condition. This new therapy targets X-linked retinoschisis (XLRS) and uses Atsena's novel AAV.SPR capsid to effectively deliver the therapeutic gene to photoreceptor cells in the central retina. This delivery method aims to avoid the surgical complications linked to detaching the fovea.

The RMAT designation, created by the 21st Century Cures Act, is designed to speed up developing and reviewing promising regenerative medicines, such as gene therapies. To receive this designation, a therapy must be intended to treat a serious or life-threatening condition, and early clinical data must suggest it has the potential to meet unmet medical needs. This designation offers sponsors significant FDA guidance on efficient drug development, including discussions about alternative endpoints, ways to support accelerated approval, post-approval requirements, priority review of the BLA, and other opportunities to expedite the development and review process.

Atsena Therapeutics' CEO, Patrick Ritschel, appreciated the RMAT designation. He emphasized its potential to address the critical lack of approved treatments for XLRS, a rare inherited eye disease. He also noted that this regulatory progress, along with their recently completed $150 million Series C financing, strengthens their dedication to developing impactful gene therapies that could improve the vision and lives of individuals with XLRS and other inherited retinal conditions.

The safety and tolerability of ATSN-201 are being assessed in the ongoing LIGHTHOUSE study, a phase 1/2 clinical trial involving male patients aged 6 and older who have been diagnosed with XLRS due to mutations in the RS1 gene. Enrolment for this study is still underway. The FDA Fast Track designation marks a major step forward in developing ATSN-201 as a potential first-ever gene therapy for XLRS.

Sources:

Atsena Therapeutics Granted U.S. FDA Regenerative Medicine Advanced Therapy Designation for ATSN-201 Gene Therapy to Treat X-linked Retinoschisis. Accessed April 25,2025. https://atsenatx.com/press-release/atsena-therapeutics-granted-us-fda-regenerative-medicine-advanced-therapy-designation-for-atsn-201-gene-therapy-to-treat-X-linked-retinoschisis/

FDA Fast Tracks Atsena's Gene Therapy for XLRS OBN. Accessed April 26,2025 https://ophthalmologybreakingnews.com/atsena-receives-fda-fast-track-designation-for-atsn-201

FDA grants regenerative medicine advanced therapy designation to ATSN-201 for X-linked retinoschisis. Accessed April 26,2025. https://www.modernretina.com/view/FDA -grants -regenerative- medicine- advanced -therapy -designation- to- ATSN-201 -for- X-linked- retinoschisis

Does Reserpine have the potential to prevent vision loss in inherited blinding diseases?

Research on animals at the National Institutes of Health (NIH) indicates that the drug reserpine can protect the nerve cells in the retina that are crucial for sight, with a particularly strong effect in female animals. New studies using rats suggest that reserpine, a medication approved in 1955 for high blood pressure, could potentially be a treatment for retinitis pigmentosa, a rare inherited condition that causes blindness and usually begins in childhood. Currently, there is no cure for this disease.

The lead researcher of the NIH studies, Dr. Anand Swaroop, stated that the discovery of reserpine's effectiveness could significantly speed up the development of treatments for retinitis pigmentosa and other inherited retinal diseases. These diseases can arise from a wide variety of genetic mutations (over a thousand affecting more than 100 genes), but reserpine's protective action on nerve cells appears to work regardless of the specific genetic cause. These new findings build on earlier work showing that reserpine helps photoreceptor cells, the light-detecting neurons in the retina that die in retinitis pigmentosa and other retinal dystrophies, to survive. In 2023, Dr. Swaroop's lab demonstrated that reserpine could prevent vision loss in LCA10, a retinal dystrophy caused by mutations in the CEP290 gene.

In their most recent study, Dr. Swaroop's team tested reserpine in a rat model of a dominant form of retinitis pigmentosa caused by a mutation in the rhodopsin gene, a mutation commonly found in Irish Americans with the disease. Researchers found that reserpine helped preserve phototransduction, the process by which photoreceptor cells convert light into electrical signals that the brain uses for vision, in the rod photoreceptor cells (responsible for low-light vision) compared to untreated rats. They also observed that reserpine unexpectedly provided better protection to rod and cone photoreceptor cells (responsible for color vision in bright light) in female rats compared to male rats.

Dr. Swaroop noted that the reasons for these differences between sexes are currently unknown but warrant further investigation to potentially personalize treatments for retinal diseases in the future. Dr. Swaroop's lab is also working on developing newer, more potent drugs related to reserpine. The goal is to have options for treating slow-progressing inherited retinal dystrophies or to slow down vision loss in more aggressive forms of retinitis pigmentosa until more effective treatments that can reverse vision loss become available.

While reserpine is no longer commonly used for high blood pressure due to its side effects, the dosage needed for treating retinal degeneration would likely be very low and delivered directly into the eye. Because reserpine is a small molecule, it can be easily delivered to the target tissues in the eye.

Sources:

Repurposing a high blood pressure drug may prevent vision loss in inherited blinding diseases. Accessed April 28,2025. https://www.nei.nih.gov/about/news-and-events/news/repurposing-high-blood-pressure-drug-may-prevent-vision-loss-inherited-blinding-diseases#

Song HB, Campello L, Mondal AK, Chen HY, English MA, Glen M, Vanlandingham P, Farjo R, Swaroop A. "Sex-specific attenuation of photoreceptor degeneration by reserpine in a rhodopsin P23H rat model of autosomal dominant retinitis pigmentosa". March 27, 2025, eLife14:RP103888 https://doi.org/10.7554/eLife.103888.2

Answers to Ocular Genetics Trivia

- *Keratoconus*
- *Pigmentary dispersion syndrome*
- *Stickler syndrome*
- *Macular dystrophy*
- *Coloboma*