
IN OUR DNA
COLUMBIA | OPHTHALMOLOGY

PRECISION OPHTHALMOLOGY 2025

COLUMBIA


THE ANSWERS LIE IN OUR DNA

The Department of Ophthalmology

AT COLUMBIA UNIVERSITY
IRVING MEDICAL CENTER

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is a leading international center for innovative clinical care of eye disorders, the advancement of medical knowledge through state-of-the-art research, and the education of tomorrow's leaders in ophthalmology and vision science. It is truly In Our DNA to discover, to educate, and to provide care!

We are continually pushing the boundaries of what is possible in vision research, and we bring that research to our patients through compassionate and multidisciplinary clinical medicine. Our expanding faculty of clinicians and scientists strive to improve the human condition by providing care across the full range of ophthalmic subspecialties. The Department consistently ranks among the top institutions in the world in external grant funding for vision science, and our donors have provided the generous resources that allow our investigators to attack even the most vexing problems in our field. Our educational mission is equally distinguished and viewed as a model for others, with a growing training program for every level of learner, from students to residents to postdoctoral researchers, as well as established clinical fellowships in retina, cornea, glaucoma, orbital and ophthalmic plastic surgery, neuro-ophthalmology, and pediatric ophthalmology.

We push forward with the understanding that not only are the eye disorders that we seek to prevent, treat, and cure rooted in our genetic underpinnings, but it is "in our DNA" as a leader in ophthalmic medicine to pursue precision genomics and unlock the mysteries of ocular disease. Our commitment to advanced education, discovery science, and superlative clinical care reflects the very essence of who we are as part of a world-class university and academic medical center.

Capza2
Myh9
Dst
Cdh5
Adam10
Adam15
Eps15
Shank3
Picalm
Map3k11
Rock2
Exoc5
Abca1
Ybx1
Rac1
Vav3
Arrb1
Ndrg1
Tmsb4x
Actr2
Tpm4
Capza2
Hip1

CONTENTS

01 Our Impact Across Time 06

02 Foundational Biology 16

03 Disease Mechanisms 24

04 Complex Inheritance + Applied Genetics 32

05 Clinical + Translational Science 40

06 Data Science, Bioinformatics + Artificial Intelligence 54

07 Columbia Ophthalmology + Vision Science 62

08 Department Statistics + Faculty 70

FROM THE CHAIR

Dear Friends,

It has been nearly ten years since we introduced the concept of *Precision Ophthalmology*™: customized genetic, diagnostic, and translational clinical care that uses a patient's own genetic profile to tailor a personalized course of treatment—or even prevention—for even the most challenging eye conditions. This book, *In Our DNA*, is the third in a series focused on how we are delivering on the promise of Applied Genetics in ophthalmology.

We begin with the foundational building blocks that are essential to delivering on the promise of *Precision Ophthalmology*™: Discovery science, and how underlying biology relates to disease mechanisms and the enormous influence that genetics and heritability have in the chain of events that lead to eye disease. During these most uncertain times, we want to reestablish the importance of funding and performing discovery science as the first step in finding therapies of tomorrow.

We then exploit that foundational science to implement translational clinical trials, making use of advances that have come into their own over the past decade, including synthetic biology and genome engineering, as well as big data, bioinformatics, and artificial intelligence. All of these tools are fundamental to our efforts to understand and leverage genetic patterns and inheritance and will allow us to accelerate the process of moving from ideas to therapies.

For example, our Applied Genetics program, launched in 2019, uses a highly individualized interdisciplinary approach to evaluate ophthalmic disorders of genetic origin, with experts from multiple subspecialties reviewing each case and connecting patients with the latest research studies right here in our own Clinical Trials Unit as well as nationally and internationally. To date, we have identified patients with variants in more than 300 genes, and the list is sure to grow exponentially in the near future. Through our Applied Genetics efforts, we are also training the leaders in science and medicine that will continue the search for cures.

Columbia Ophthalmology is driving the future of *Precision Ophthalmology*™—a future that, in many ways, is already here. In the previous two reports, we explored the imminent promise of an individualized genetic approach to eye care and eye disease. Here, we share the many ways in which that promise is rapidly being realized. As we seek to develop transformative vision treatments, the answers truly do lie in our DNA.

G.A. (Jack) Cioffi, MD
Edward S. Harkness Professor
Jean and Richard Deems Professor
Chair, Department of Ophthalmology

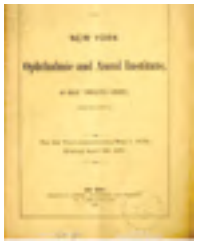
01

Our Impact Across Time

The Edward S. Harkness Eye Institute, on 165th Street, under construction in 1932.

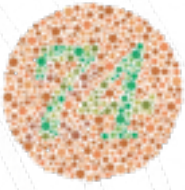
01 Our Impact Across Time

1866 Cornelius R. Agnew, MD, establishes an ophthalmology clinic at the College of Physicians and Surgeons.



1869 Herman J. Knapp, MD, establishes the New York Ophthalmic and Aural Institute, which later becomes the Herman Knapp Memorial Hospital.

1903 Arnold H. Knapp, MD, son of Herman, appointed professor of ophthalmology at P&S and becomes the third clinic director.



1911 Edmund B. Wilson, PhD, maps color blindness onto the X chromosome.

1928 Presbyterian Hospital moves to 168th Street, and the Vanderbilt Clinic—the clinical care unit of P&S, with its Ophthalmology service—moves uptown with it. John M. Wheeler, MD, DSc, becomes the first chair of the Department of Ophthalmology.

1933 The Department moves into the Edward S. Harkness Eye Institute on 165th Street.

1888 Dr. Herman Knapp is appointed professor of ophthalmology at P&S and becomes the second clinic director.

1867 Dr. Agnew is appointed the first professor of ophthalmology at P&S, marking the official beginning of the program.

1911 Herman Knapp Memorial Eye Hospital, founded by Arnold Knapp, opens at 10th Avenue and 57th Street, two blocks from P&S. The Eye staff at P&S hold appointments at the new hospital.

1931 Edward S. Harkness pledges money to build a separate Eye Institute at the new medical center.

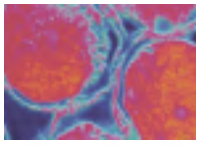
1933 Ramon Castroviejo, MD, performs the first corneal transplant on a human.

1st Clinic Director
CORNELIUS R. AGNEW, MD
1867-1888

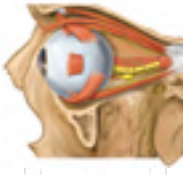
2nd Clinic Director
HERMAN J. KNAPP, MD
1888-1902

3rd Clinic Director
ARNOLD H. KNAPP, MD
1903-1928

1st Department Chair
JOHN M. WHEELER, MD, DSC
1928-1939



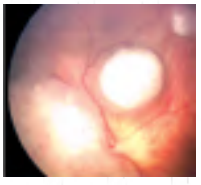
1935-36
Discovery of hyaluronic acid by Dr. Karl Meyer. Phillips Thygeson, MD, OphD, describes the microbiologic transmission of trachoma.



1936 The Muscle Clinic becomes the Eye Institute's first subspecialty clinic.

1939 Dr. Thygeson becomes the fourth clinic director, serving until 1945.

1943 Raymond L. Pfeiffer, MD, is the first to delineate the landmarks of the ocular orbit on plain x-rays.



1947 First retinoblastoma, pediatric, and adult ocular tumor clinics are established by Dr. Algernon B. Reese.

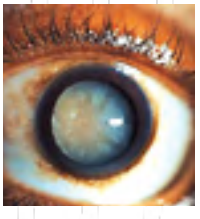
1948 The pupillography laboratory is established by Otto Lowenstein, MD, PhD, a pioneer in the quantitative measurement of pupil function.

1955 American Optical releases the AO HRR color vision test, developed by LeGrand Hardy, MD, director of the Knapp Memorial Physiological Optics Laboratories, and M. Catherine Rittler, working with Gertrude Rand, PhD, of Johns Hopkins.

1938
Dr. Castroviejo urges people to will their eyes to science, leading to the development of today's eye banks.

1940-41 New methods for quantitative analysis of intracellular sugars are developed by Dr. Zacharias Dische. The Knapp Hospital closes, and the Knapp Memorial Library of Physiological Optics opens.

1948 Willis Knighton, MD, establishes a glaucoma clinic on the newly remodeled fifth floor of the Eye Institute.

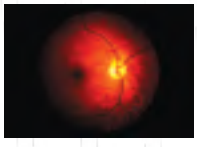


1956 George Merriam Jr., MD, with Elizabeth Focht, MD, of NYU, establishes a relationship between cataract formation and radiation. This leads to the development of standards of ocular radiation safety still in use today.

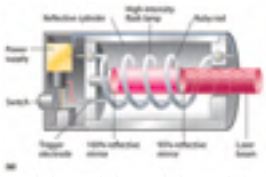
2nd Department Chair
JOHN H. DUNNINGTON, MD
1946-1959

01 Our Impact Across Time

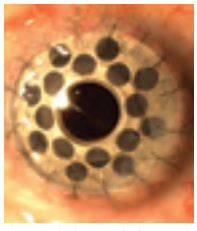
1957 Irene Loewenfeld, PhD, and Dr. Lowenstein build an “electronic pupillograph” that incorporates infrared technology. It is the first device to accurately measure and analyze the diameter of the pupils.



1961 Frank Carroll, MD, a leader in research on diseases of the optic nerve, establishes an optic nerve clinic.



1961 Dr. Campbell is first to use the ruby laser in humans, working with Rittler and Charles Koester, MD. Fight for Sight Children’s Eye Clinic is added to the Eye Institute, headed by Phillip Knapp, MD.



1962 First keratoprosthesis, developed by Hernando Cardona, MD, is presented to the 19th International Congress of Ophthalmology.

1965 Black Medical Research Building is completed. From 1965 to 1969, the 15th floor is heavily utilized for ophthalmology laboratories.

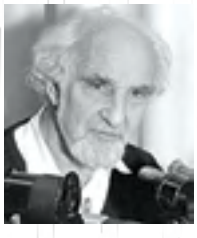
1966 Saiichi Mishima, MD, develops a system for preserving corneas until transplantation.

1966 Max Forbes, MD, describes indentation gonioscopy in closed-angle glaucoma.

1958 World’s first retina clinic is established by Charles J. Campbell, MD, PhD.

1962 John W. Espy, MD, creates the Eye Institute’s Contact Lens Clinic, which he directs for 25 years.

1964 First basic and clinical corneal research center is established by Drs. Gerard DeVoe and Anthony Donn.



1968 David Maurice, MD, and Dr. Donn are first to use confocal microscopy to detect new structural features of the eye. American Optical Company releases its monocular indirect ophthalmoscope, developed in part by Dr. Campbell.

3rd Department Chair
A. GERARD DEVOE, MD
1959-1974

1968 First argon laser is used to treat human disease by Francis L'Esperance Jr., MD. Harold Spalter, MD, is among the first to publish on the use of lasers for the treatment of diabetic macular edema and central serous retinopathy.

1969 Dr. Phillip Knapp describes a muscle transposition procedure for paralytic strabismus that becomes known as the "Knapp procedure" and remains in common use to this day.

1973 Using the ultrasound he developed, Dr. Coleman demonstrates that operating at an earlier stage in ocular trauma can vastly improve the patient's prognosis for recovery.

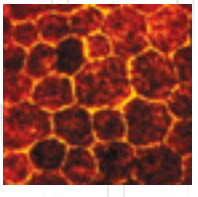
1969 D. Jackson Coleman, MD, develops the first commercially available hand-operated ultrasound B-scan system for ophthalmic evaluation.

1972 Abraham Spector, PhD, publishes research on protein aggregation and cataract formation. His laboratory will become one of the world's leading cataract research laboratories.

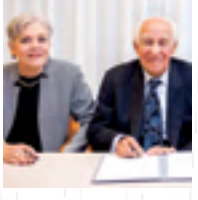
1980 Stephen Trokel, MD, publishes findings on techniques for submillimeter resolution CT scanning of orbital diseases.

1983 Dr. Trokel publishes a major paper introducing the idea of using the laser to reshape or sculpt the cornea. Dr. Trokel and Dr. L'Esperance (pictured) patent the excimer laser for vision correction.

1986 Basil V. Worgul, PhD, who directs Columbia's Eye Radiation and Environmental Research Lab, is named American director of the Ukrainian/ American Chernobyl Ocular Study.



1980 Charles Koester, MD, develops the first wide-field specular microscope, which proves to be invaluable for studying the corneal endothelium.

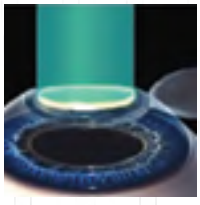


1983 Endre Balasz, MD, Malcolm P. Aldrich Research Professor and Director of Research in the Department, develops Healon, a hyaluronic acid polymer that transforms cataract and corneal surgery.

4th Department Chair
CHARLES J. CAMPBELL, MD, PHD
1974-1987

01 Our Impact Across Time

1994 Peter Gouras, MD, PhD, performs the first human retinal cell transplants.



1987 Stephen Trokel, MD, performs the first human excimer laser surgery for vision correction.

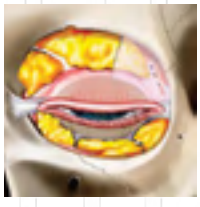
1997 Latanoprost (Xalatan™) for the treatment of glaucoma, developed by Dr. László Z. Bitó, is marketed worldwide.

1998 NewYork-Presbyterian is formed, becoming the Ophthalmology Department's partner and the number-one hospital system in New York City.

2005 The Bernard and Shirlee Brown Glaucoma Research Laboratory opens.

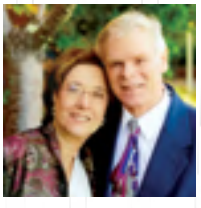
2000 John Flynn, MD, joins the Department as the first Anne S. Cohen Professor of Pediatric Ophthalmology.

2005 Janet Sparrow, PhD, named Anthony Donn Professor of Ophthalmic Science.

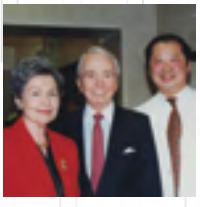


1993 Dr. Trokel describes orbital fat removal for orbital decompression.

1996 The FDA approves the use of perfluorocarbons for retinal surgery, based on the work of Stanley Chang, MD. In 1996, Dr. Chang succeeds Anthony Donn, MD (above left), as Department Chair, building on a robust legacy in ophthalmology research.

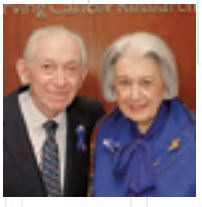


1998 R. Duff and Carol Kurland establish the Anne S. Cohen Professor of Pediatric Ophthalmology.



1998 The Flanzer Eye Center opens on the Harkness Eye Institute's first floor, and the Low Vision Clinic is established under Dean Hart, OD.

2004 The Louis V. Gerstner Jr. Clinical Research Center in Vision, home to the Russell Berrie Diabetic Retinopathy and Starr Foundation Retina Research Units, opens with Stanley Chang, MD, Mrs. Robin Gerstner, and Henry Kissinger in attendance.

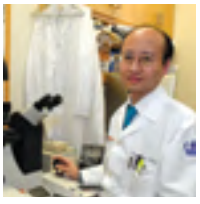


2005 Mr. and Mrs. Herbert Irving endow the new Florence and Herbert Irving Translational Vision Research Laboratory.

5th Department Chair
ANTHONY DONN, MD
1987-1996

6th Department Chair
STANLEY CHANG, MD
1996-2012

2006 Rando Allikmets, PhD, and the AMD Study Group discover factors H and B, genes contributing to age-related macular degeneration.

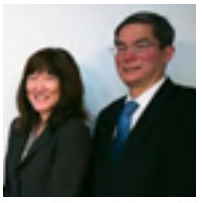


2012 Stephen Tsang, MD, PhD, is named László Z. Bitó Professor of Ophthalmology.

2012 The Jean and Richard Deems Professorship of Ophthalmology & Endowment Fund is established, leading to the recruitment of G.A. (Jack) Cioffi, MD, as the 7th Department Chair.

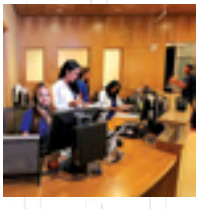
2013 Donald Hood, PhD, elucidates structure-function relationship of glaucomatous damage to the macula.

2014 Lauren Yeager, MD, examines a young patient at the Stephen Ross Pediatric Eye Center at the Morgan Stanley Children's Hospital, which opened in 2014.



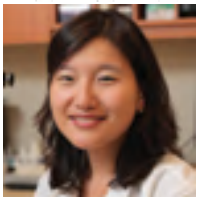
2015 Jean and Kent Sheng establish a glaucoma fellowship endowment.

2015 Jeffrey Liebmann, MD, joins the Department as Vice-Chair, Glaucoma Division Director and the Shirlee and Bernard Brown Professor of Ophthalmology.

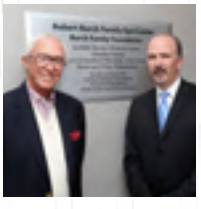


2010 The Columbia Laser Vision Correction Center and the Gloria and Louis Flanzer Vision Care Center open.

2012 Jason Horowitz, MD, is appointed A. Gerard DeVoe-B. Dobli Srinivasan Director of the Residents' Eye Clinic at Harkness.

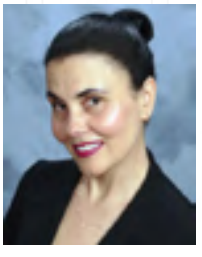


2012 Leejee H. Suh, MD, is named Miranda Wong Tang Associate Professor of Ophthalmology and Chief of the Cornea Service.



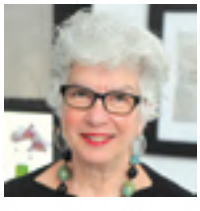
2014 The Robert Burch Family Eye Center opens at the Lighthouse Guild International on the Upper West Side of Manhattan.

2015 Tongalp Tezel, MD, joins the Department as Chang Family Professor of Ophthalmology to lead the retina service.



2015 Gülgün Tezel, MD, Laboratory founded.

2016 Basic Science Course in Ophthalmology (BSCO) celebrates 75 years of training residents from around the world in the fundamentals of vision science.

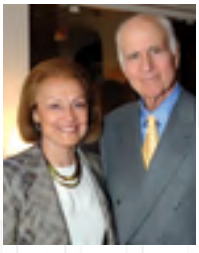


2011 Vision neuroscientist Carol Mason, PhD, is elected to the Institute of Medicine.

7th Department Chair
G.A. (JACK) CIOFFI, MD
2012-PRESENT

01 Our Impact Across Time

2016 Ronald Silverman, PhD, develops an advanced ultrasound technology to measure ocular blood flow.



2017 Jonas Children's Vision Care program opens to provide advanced care to children with sight-threatening disorders.

2017 Precision Ophthalmology™ is coined by the Department launching Precision Medicine Initiative.

2019 Simon John, PhD, a Howard Hughes investigator in glaucoma and other neurodegenerative diseases, is appointed Robert L. Burch III Professor of Ophthalmic Science.

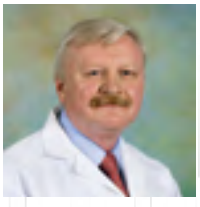
2020 Applied Genetics at Columbia Ophthalmology is launched.

2020 Columbia Ophthalmology expands collaboration with Centers for Disease Control and Prevention, under the leadership of Lisa Hark, PhD, MBA.

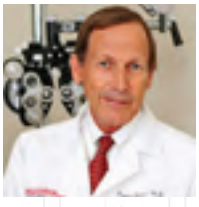
2017 Brian Marr, MD, is named John Wilson Espy, MD, Professor of Ophthalmology, leading a relaunch of the Division of Ocular Oncology.

2017 Irene Maumenee, MD, joins the Department and receives the Laureate Recognition Award from the American Academy of Ophthalmology for her lifelong contribution to ophthalmic genetics.

2019 David and Victoria Foley establish the Foley Retina Research Fund and the Foley Clinical Retinal Fellowship Endowment.

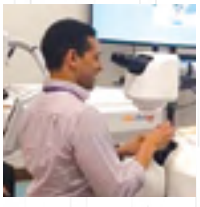


2019 Konstantin Petrukhin, PhD, develops tinlarebant, a new drug for Stargardt disease and dry AMD that begins a Phase 3 clinical trial.



2020 American Society of Ophthalmic Trauma is founded by James Auran, MD.

2020 Noga Harizman, MD, is appointed Chief of Ophthalmology at Harlem Hospital.



2020 HelpMeSee surgical virtual simulation lab opens for resident and fellowship training. Ives (Tony) Valenzuela, MD, becomes the first certified trainer at Columbia Ophthalmology.

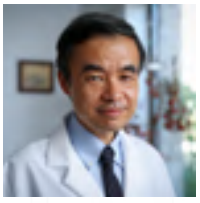
7th Department Chair
G.A. (JACK) CIOFFI, MD
2012-PRESENT

2021 Aliaa Abdelhakim, MD, PhD, and Qing Wang, MD, PhD, are selected as inaugural Chang-Burch Scholars.

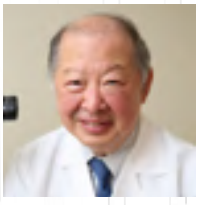
2022 Surya N. Mohapatra, PhD, endows the Mohapatra Pediatric Ophthalmology and Strabismus Fellowship.

2023 Artificial Intelligence for Vision Science Laboratory opens, led by Kaveri Thakoor, PhD.

2023 New, state-of-the-art ophthalmology laboratories open at Hammer Health Sciences Center.



2024 Xin Zhang, PhD, is appointed the new Director of Vision Science Research.



2024 Stanley Chang, MD, receives American Academy of Ophthalmology Laureate Recognition Award.

2025 Robert Burch Family Eye Center relocates to Lincoln Center with support from Robert Burch and Louis V. Gerstner, Jr.

2021 Steven Rosenberg, MD, joins the Department as Anne S. Cohen Professor of Ophthalmology to lead the Pediatric Ophthalmology Division.

2022 Danielle Trief, MD, MSc, establishes pediatric cornea service.

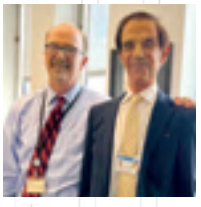
2022 Through the generosity of Leonard A. Lauder, Aakriti G. Shukla, MD, MSc, is recruited as the inaugural Leonard A. Lauder Professor.

2023 George Florakis, MD, is appointed the Malcolm Aldrich Clinical Professor leading the Westchester Ophthalmology Division.

2024 Lisa Park, MD, is appointed Director of Comprehensive Ophthalmology and Eye Care.

2024 Lora Glass, MD, is appointed Director of Ophthalmic Plastic and Reconstructive Surgery Division.

2024 Royce Chen, MD, with G.A. (Jack) Cioffi, MD, and Jean Sheng, is chosen to lead new Education Division as Jean Sheng Associate Professor of Ophthalmology and Vice Dean of Education.



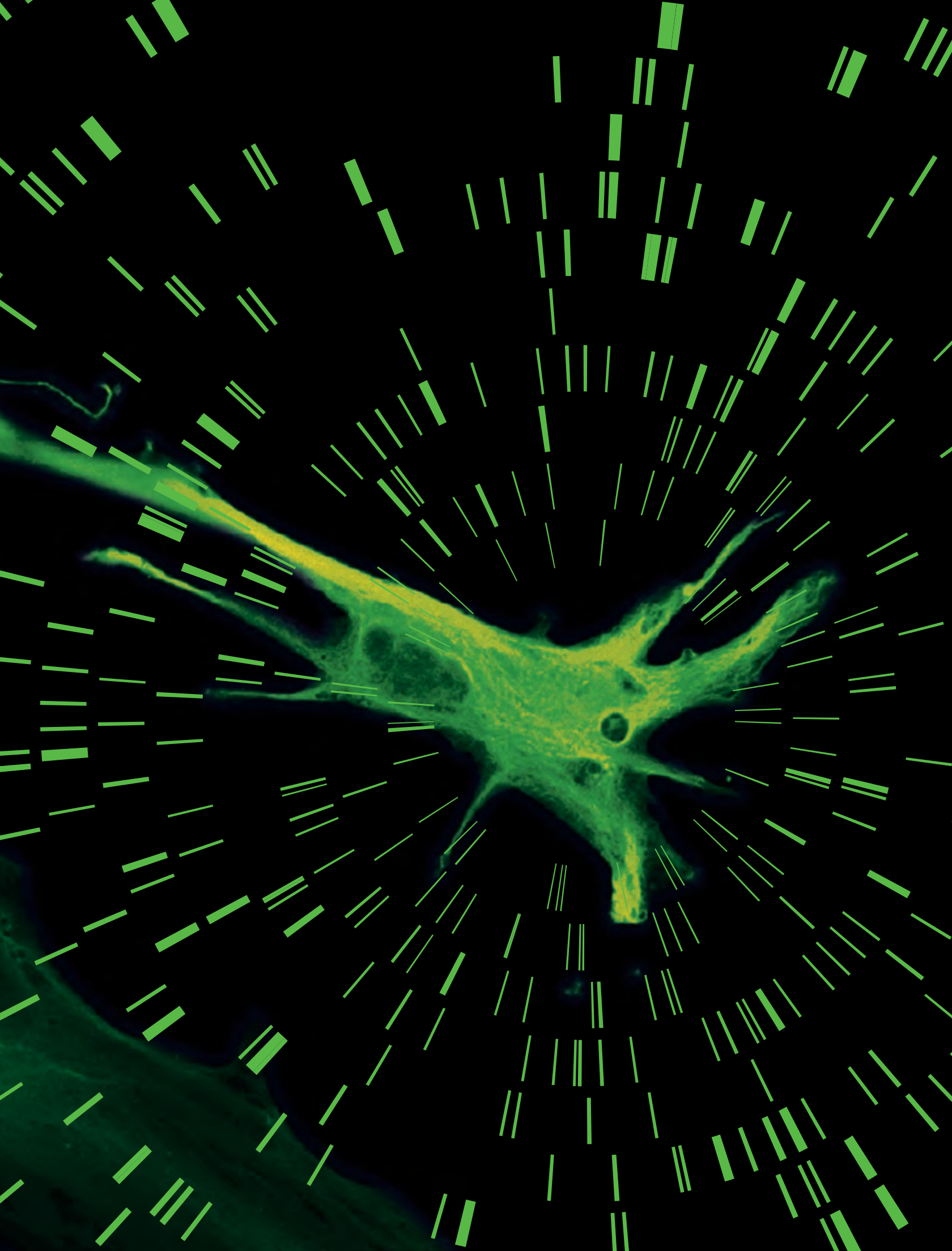
2025 Danny H.-Kauffmann Jokl, MD, endows the Danny H.-Kauffmann Jokl Neuro-Ophthalmology Professorship and Fellowship.

02

Foundational Biology

"In recent years, through basic research, our understanding of visual perception and the causes of visual disorders have made possible better defined and more effective clinical care."

Torsten N. Wiesel, MD
Nobel Laureate



02 Foundational Biology

Foundational research at Columbia Ophthalmology is providing essential new knowledge that allows broad and fundamental discoveries regarding the function of the eye and its internal structures and is the basis of progress in understanding and treating eye diseases. We exploit the latest technologies to dig deeply into the biology of the eye, to uncover previously unknown control mechanisms, as well as to provide new molecular information about disease processes. This research is not only transforming understanding of conditions like glaucoma and macular degeneration but also stimulating new approaches for preventing and treating a wide range of ocular diseases.

Technological advances in areas such as single-cell genetic sequencing, genomics, gene therapy, and artificial intelligence (AI) are accelerating the pace of progress and permitting more comprehensive discovery than has been possible at any time in the past. For example, modern genomic technologies allow us to interrogate the eye's cellular and molecular landscape in unprecedented detail, including the discovery of previously undescribed subclasses of ocular cells. This allows the identification of previously unknown disease mechanisms and new therapeutic targets, leading to more effective treatments.

Novel gene therapy tools, such as genome editing and viral vectors, promise to revolutionize the treatment of eye disease, permitting us to precisely target genetic mutations that cause eye disease. We are developing gene therapeutics with the aim of restoring normal gene function, offering the possibility of long-term improvements for patients. Beyond gene therapy, the potential for stem cell therapies, and especially the directed differentiation of induced pluripotent stem cells (iPSC), to create specific cell types holds tremendous promise. New experimental and therapeutic strategies to repair, regenerate, and protect diseased tissues are possible with iPSCs. The directed differentiation of stem cells is directly informed by foundational discoveries in ocular development and will ultimately lead to novel therapies. Dysfunctional genes or pathways may be repaired in stem cells derived from a patient's own tissues, implanted in the eye, and used for tissue repair.

In addition to gene therapy and stem cell research, our fundamental research is delineating crucial roles of ion channels, metabolism, and immune pathways in the eye, while our genetic research implicates unexpected new disease genes and molecular processes. Ongoing research is revealing the importance of metabolic changes, oxidative stress, and inflammation in both childhood and age-related diseases. Our research into the role played by mitochondrial dysfunction and cellular energy imbalances in ocular disease is leading to novel therapeutic strategies, aimed at inducing cellular resilience by rebalancing energy homeostasis and protecting cells from damage. Resilience strategies include metabolic and nutritional support therapies and the use of antioxidants and mitochondrial enhancers to provide new opportunities to preserve vision. Overall, these broad and exciting basic science research efforts offer a brighter future for vision health.

Simon John, PhD

Overleaf: Confocal microscopy image of a murine astrocyte (green, GFAP) cultured by Gülgün Tezel's lab.

SCHLEMM'S CANAL IN INHERITED GLAUCOMA

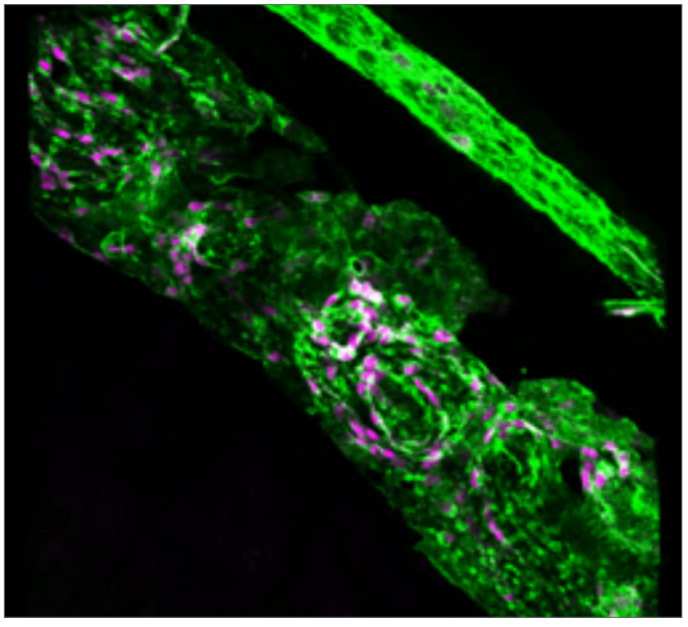


Figure. Image of Schlemm's canal in the adult mouse eye, staining with PECAM1 in green and APLNR in magenta.

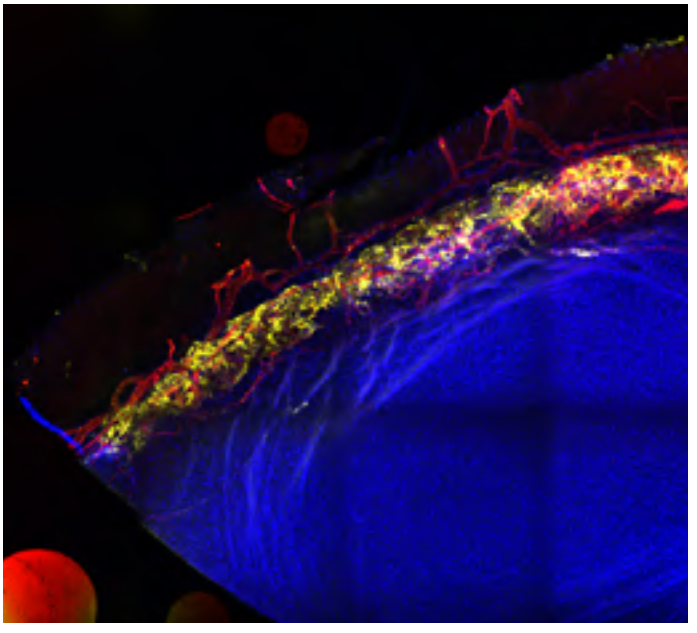


Figure. Image of an adult mouse eye showing the Schlemm's canal in yellow (stained with PROX1) and limbal vasculature in red (stained with PECAM1).

Elevated intraocular pressure is a major risk factor for glaucoma, a leading cause of blindness that affects nearly 80 million people worldwide. The Balasubramanian Lab investigates the molecular biology involved in the development of Schlemm's canal and trabecular meshwork, the aqueous humor outflow tissues that regulate intraocular pressure.

Patients with pediatric forms of glaucoma, most of which are associated with a genetic etiology, exhibit morphological and functional defects in Schlemm's canal and the trabecular meshwork, leading to decreased aqueous humor outflow and elevated intraocular pressure. To understand the disease etiology and improve treatment options for both congenital glaucoma and adult forms of glaucoma, it is crucial that we understand the underlying biology of outflow tissue development and how genetic changes in disease impact these tissues. We use a combination of mouse genetics, single cell transcriptomics, hiPSC models, confocal microscopy, and ocular physiology to derive a deeper understanding of outflow tissue development and biology. Images above are high-resolution confocal microscopy views of Schlemm's canal and genes expressed in the cells of Schlemm's canal.

Revathi Balasubramanian, PhD

02 Foundational Biology

PRECISION OPHTHALMOLOGY VIA INTEGRATED DNA ANALYSIS

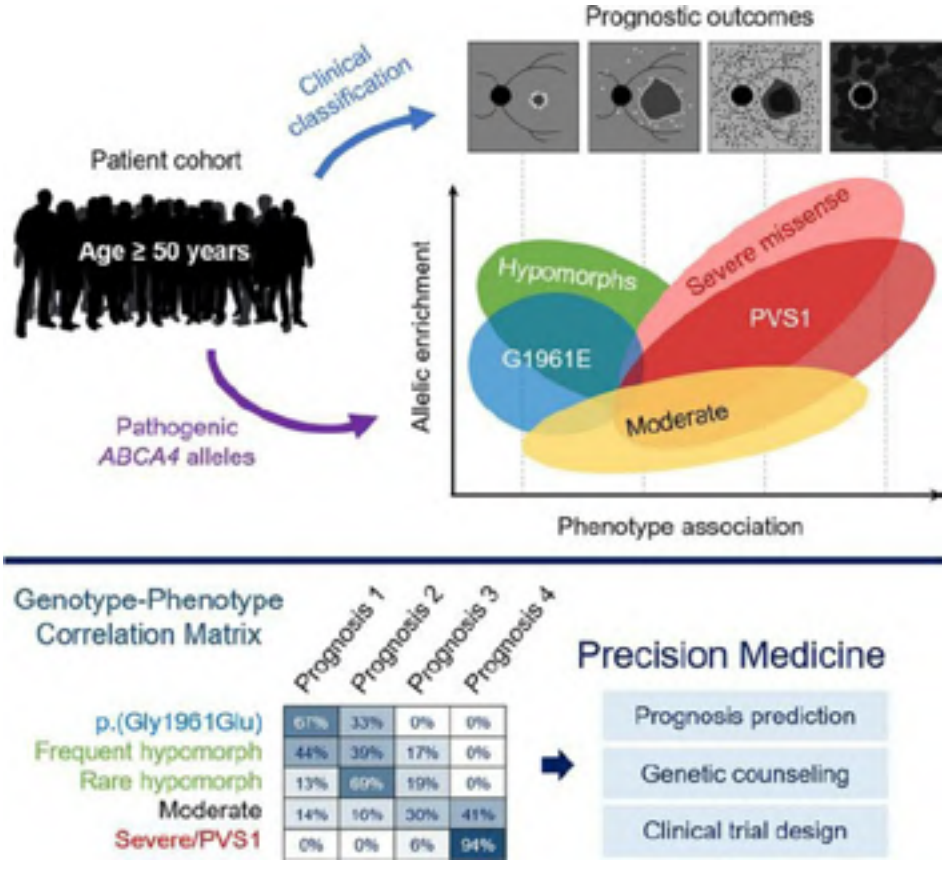


Figure. By defining four major prognostic outcome groups of comprehensively screened (including whole genome analyses) ABCA4 disease patients, classifying ABCA4 mutations by severity and tabulating these data, we were able to create a powerful tool for geneticists, clinicians, genetic counselors, and clinical trial designers.

The Allikmets Lab performs detailed genetic analyses of monogenic and complex retinal diseases. Earlier results include identifying causal genes for many Mendelian macular dystrophies and retinitis pigmentosa. Similarly, we have identified major genetic associations in complex traits such as macular degeneration (CFH, CFB, etc.) and MacTel (SPTLC1, PHGDH, etc.). More recently, we have made major progress in detailed analysis of a myriad of phenotypes caused by variation in the ABCA4 gene, including identifying cis- and trans-modifiers, which have substantially facilitated our understanding of Stargardt disease and all other associated disease entities, now collectively called ABCA4 disease. Most importantly, an integrated analysis of clinical and genetic data led to the development of a genotype-phenotype correlation matrix that aids both clinicians and patients in understanding individual disease expression and long-term progression. In addition, these analyses allow more advanced genetic counseling and targeted clinical trial design for specific treatment modalities.

By defining four major prognostic outcome groups of comprehensively screened (including whole genome analyses) ABCA4 disease patients, classifying ABCA4 mutations by severity, and tabulating these data, we were able to create a very helpful tool for geneticists, clinicians, genetic counselors, and clinical trial designers.

Rando L. Allikmets, PhD

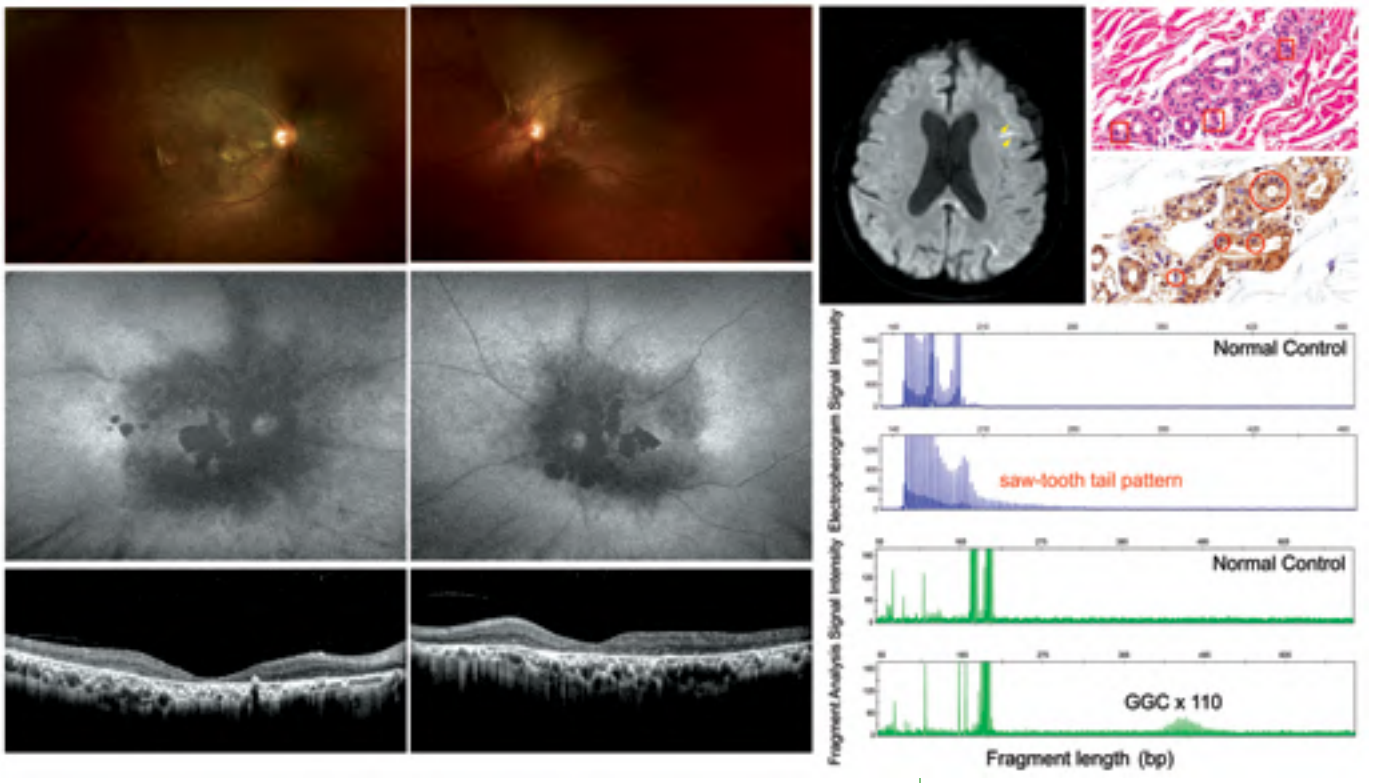


Figure. A patient with neuronal intranuclear inclusion disease (NIID) presented with retinal degeneration and dementia. Whole exome and genome sequencing were negative. Brain MRI showed corticomedullary junction hyperintensity (yellow arrows). Skin biopsy revealed eosinophilic intranuclear globules in eccrine glands (red squares), confirmed by ubiquitin immunostaining (red circles). Triplet repeat primed PCR of NOTCH2NLC showed a saw-tooth pattern, with 110 GGC repeats.

Dr. Wang is a specialist in identifying genetic mutations in inherited eye diseases, especially in patients with negative whole exome sequencing results. Using advanced techniques (illustrated in the figures above), he draws on his clinical expertise, electrophysiology background, genetic knowledge, and understanding of the limitations of various genetic tests.

His research focuses on mitochondrial function in cellular metabolism and apoptosis, with particular emphasis on retinal diseases. Although mitochondria are present in all cells, photoreceptors are more resilient to dysfunction than retinal ganglion cells. The roles of energy insufficiency and oxidative stress remain unclear. His NIH-funded laboratory is developing patient-specific and conditional overexpression knock-in mouse models to study mitochondrial involvement in inherited retinal dystrophies. These models hold strong potential for advancing therapies to preserve vision in diseases such as retinitis pigmentosa and retinal ganglion cell degeneration through mitochondrial reprogramming.

Nan-Kai Wang, MD, PhD

02 Foundational Biology

ANION CHANNELS IN THE EYE

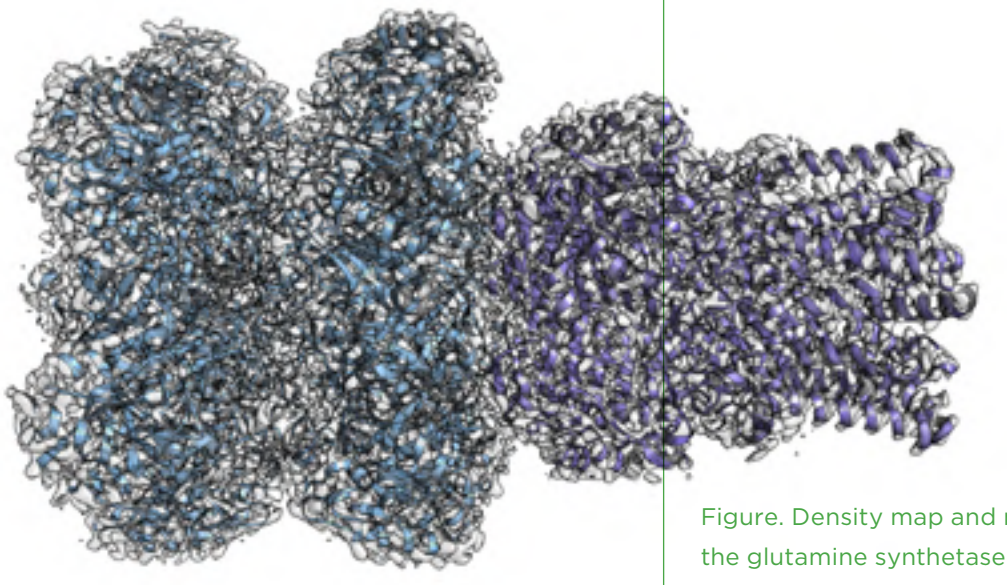


Figure. Density map and model of the glutamine synthetase (GS)-bound bestrophin2 (Best2) cryo-EM structure from the side view. Best2 and GS are labeled with purple and blue, respectively.

The Yang Lab focuses on anion transporting, particularly the bestrophin proteins, which are an ancient family of ion channels widely distributed from bacteria to mammals, with four paralogs in humans (Best1-4). In metazoans, they function as Ca2+-activated anion channels with critical (patho) physiological roles in the eye.

Best1 predominantly expresses in the retinal pigment epithelium, generating a vision-related electrical signal named “light peak,” and its mutations are genetically linked to at least five retinal degenerative disorders collectively known as bestrophinopathies. With no treatment available at the moment, patients are susceptible to progressive vision loss and even blindness. Best2 is highly expressed in non-pigmented epithelium of the ciliary body regulating aqueous humor formation and drainage. Knockout of Best2 in mice leads to a reduction of intraocular pressure (IOP), suggesting the pharmaceutical potential of Best2 inhibitors for relieving ocular hypertension, which is a major risk factor for various eye diseases, including open-angle glaucoma.

Our accomplishments include solving the first Best1 and Best2 structures and the first co-structure of a bestrophin channel in complex with a protein partner, deciphering their regulatory mechanisms and physiological roles in the eye and brain, elucidating disease-causing mechanisms of patient-derived mutations, and developing treatment strategies for bestrophin-associated eye diseases.

Tingting Yang, PhD

SIGNALING MECHANISMS IN OCULAR DEVELOPMENT

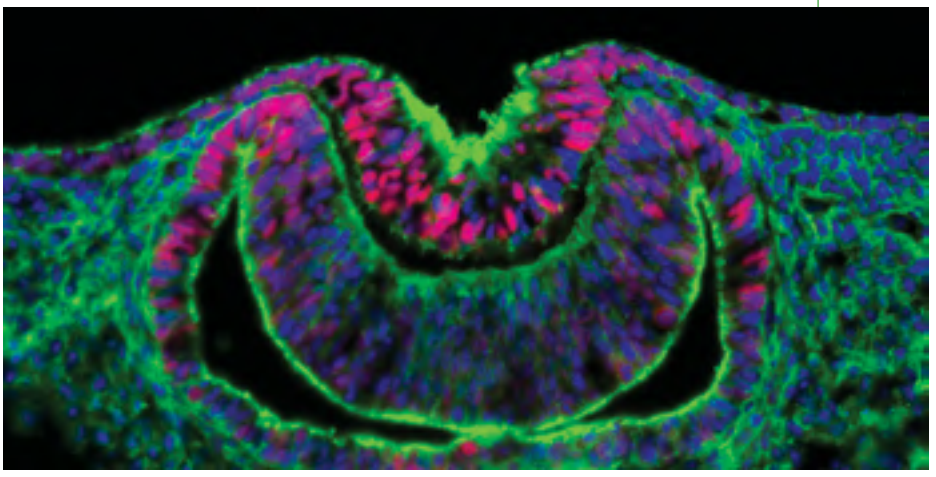


Figure. Embryonic day 9.5 eye stained for Pax6 (red), F-actin (green), and nuclei (blue).

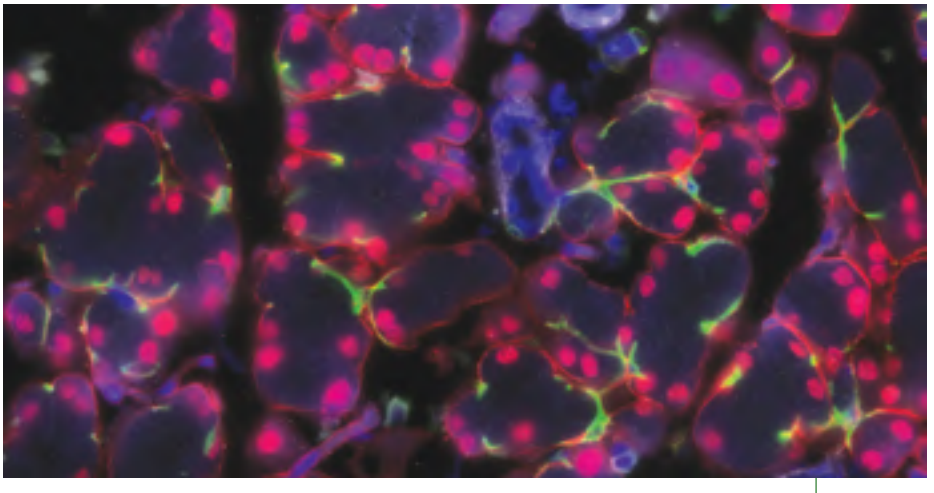


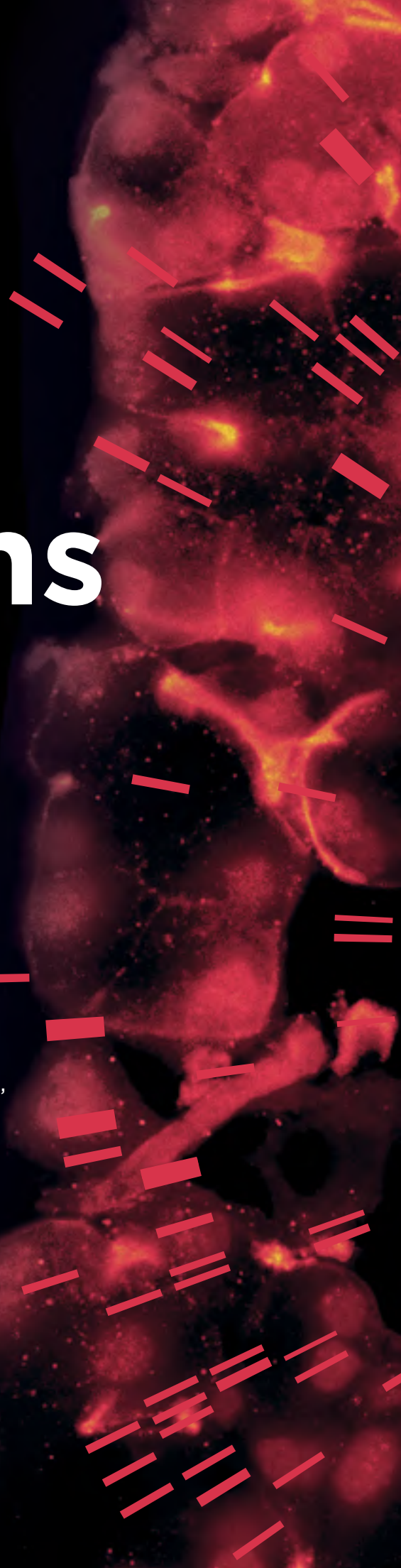
Figure. Adult lacrimal gland stained with antibodies against Mist1 (red) for acinar cells, smooth muscle actin (green) for myoepithelial cells, and P-cadherin (white) for ducts.

The Zhang Lab investigates the developmental biology of the visual system, focusing on how embryonic cells differentiate into specialized ocular structures. Their research explores the signaling mechanisms that govern eye formation, particularly how fibroblast growth factor (FGF) and Wnt pathways regulate retinal cell fate determination through phase transitions. Their findings have advanced the field's understanding of how these signals guide the development of the neural retina, retinal pigmented epithelium, and ciliary margin. Additionally, they study lacrimal gland development through PI3K, MAPK, and mTOR signaling networks, with implications for treating dry eye disease. By integrating developmental biology, genetics, and regenerative medicine, their work provides insights into congenital eye disorders and establishes foundations for novel therapeutic approaches targeting ocular diseases.

Xin Zhang, PhD

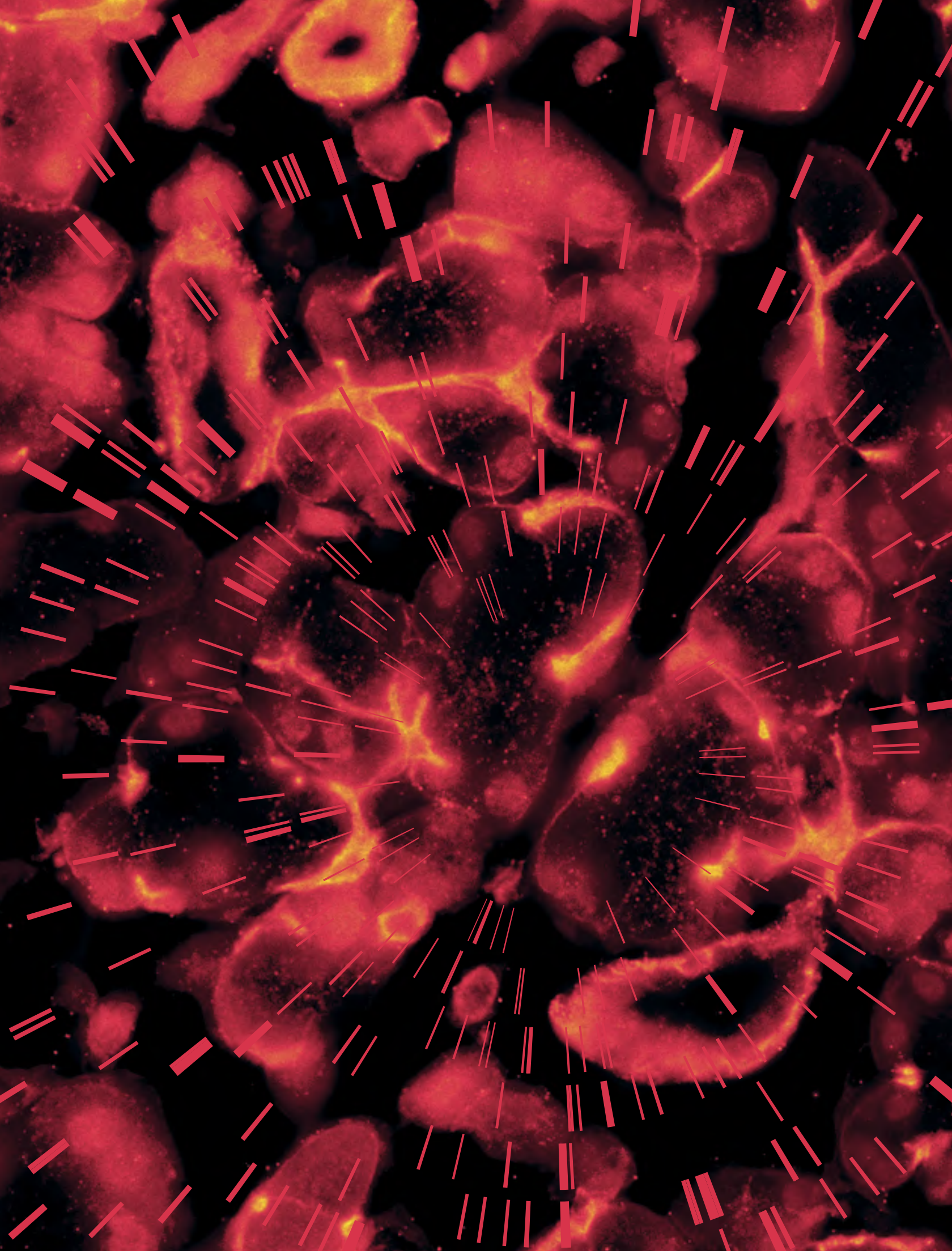
03

Disease Mechanisms



"Advances in imaging, even to the subcellular level, are providing unprecedented views of the metabolic activities of ocular cells—the molecules that signal cellular development—and how the eye perceives and processes light in both health and disease, allowing scientists to tease apart the mechanisms underlying the diseases that afflict the visual system."

Carol A. Mason, PhD
Professor, Columbia University



03 Disease Mechanisms

To develop effective treatments for blinding disease, it is essential to understand how the disease develops, its observable features (phenotype), and its natural history. We are addressing these critical questions at Columbia Ophthalmology, with funding from the National Eye Institute of the National Institutes of Health, other governmental agencies, private foundations, and generous donors.

When the disorder is inherited, efforts are directed towards the identification of the causative gene. Our scientists have identified genetic variations causing single-gene diseases, such as retinitis pigmentosa and recessive Stargardt disease. Disease-causing genetic errors associated with the vitamin A cycle are responsible for multiple early-onset visual deficits.

Other diseases, such as primary open-angle glaucoma and age-related macular degeneration, are more complex and have onset later in life. These disorders are caused by a combination of age-related changes and genetic variations, as well as risk factors such as diet and smoking. Unlike many other tissues, environmental light exposure can also play a role in eye disease. Scientists are increasingly aware of the contributions from immune system dysregulation to disease onset and progression. Lessons learned about disease mechanisms ultimately illuminate features that can be used to measure treatment outcomes during the development of novel therapies. While gene therapy to correct a genetic error can potentially cure a disease, a single gene can have multiple different mutations, with each defect requiring a different set of tools. Other therapeutic approaches that have broad applicability include metabolic reprogramming to restore disabled photoreceptor cells and approaches that target the products of disease processes.

Models that mimic at least some of the pathological features of eye disease have played crucial roles in understanding ocular disease in preclinical studies. At Columbia Ophthalmology, our scientists have altered relevant genes in the mouse to understand disease mechanisms, complementing gene discovery in patients. Retinal organoids—three-dimensional multicellular structures grown in a dish—are increasingly moving to the forefront of research. These miniature organs are particularly instructive if the original cells are derived from an individual patient. Organoids and other cell culture systems have been instrumental in unveiling disease mechanisms and can be used to test novel therapeutics.

Advances in high-resolution retinal imaging have enhanced our capabilities for early detection and phenotyping of ocular disease. Optical coherence tomography (OCT) is a non-invasive tool that allows us to assess the layers of the retina and visualize glaucomatous changes in the optic nerve head and blood vessel patterning. Short-wavelength blue autofluorescence imaging detects and quantifies toxic products of the vitamin A cycle that manifest at higher levels in genetic diseases such as recessive Stargardt disease, Best disease, and some forms of retinitis pigmentosa.

Janet R. Sparrow, PhD

Overleaf:
The adult lacrimal gland is composed of secretory acinar cells enveloped by contractile myoepithelial cells and connected to a network of transporting ducts. Xin Zhang, PhD

IOP REGULATION, METABOLISM, AND RESILIENCE IN GLAUCOMA

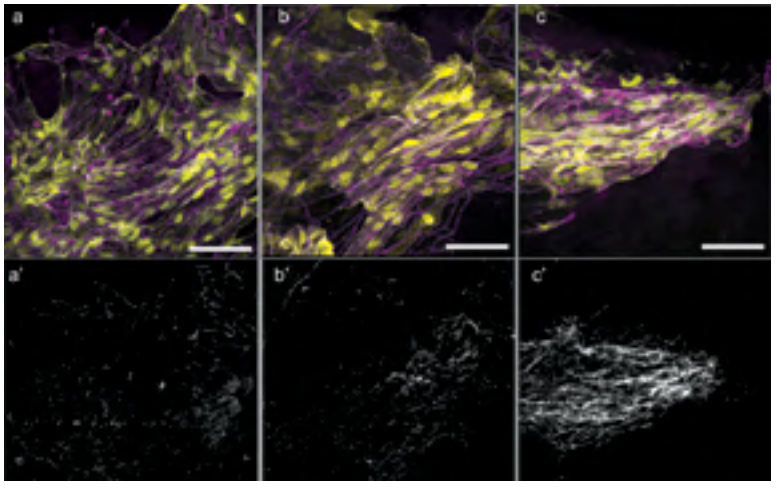


Figure. Mechano-responsive phosphorylation of the junctional molecule VE-CADHERIN (CDH5) increases with higher intraocular pressure (IOP) in Schlemm's canal endothelial cells (SECs). Phosphorylation at amino acid 658 increases the permeability of cell junctions, allowing more fluid to drain from the eye and lowering IOP. *a-c* SC with GFP and CDH5 labeling, and *a'-c'* colocalization of pY658CDH5 and CDH5 at cell-cell junctions at the different IOPs. Scale bars: 20 µm. *Adapted from Kizhatil et al., 2025 Nat Comms.*

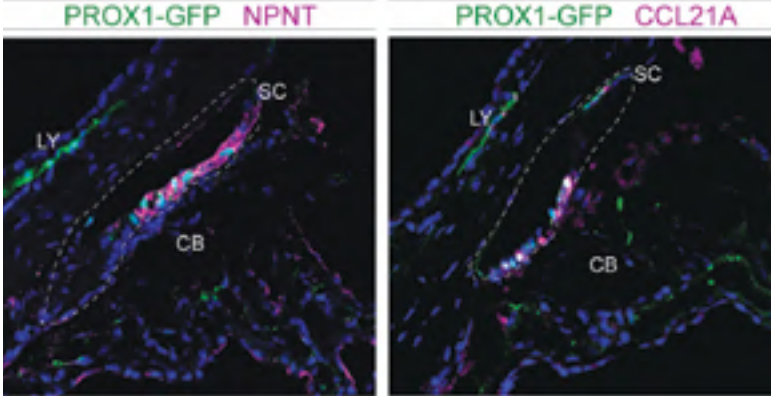


Figure. Immunofluorescence (IF) reveals regional differences in gene expression within Schlemm's canal (SC). In frozen sections, NPNT expression is prominently observed in the anterior portion of the SC, while CCL21A expression is elevated in the posterior portion. This suggests that the expression of NPNT and CCL21A may be influenced by local environmental factors, such as variations in aqueous humor flow rates. *Adapted from Balasubramanian et al., 2024 eLife.*

The John Lab is advancing glaucoma research by investigating intraocular pressure (IOP) elevation and glaucomatous neurodegeneration using diverse molecular and physiological approaches, including cutting-edge single-cell genomics. By characterizing ocular drainage tissues, Schlemm's canal, and the trabecular meshwork, at single-cell resolution, the lab has provided the foundational biology and scientific information on their molecular composition and function in fluid regulation, identifying key signaling molecules that regulate Schlemm's canal and uncovering potentially differential molecular responses to local ocular fluid drainage dynamics (see Figures). They have also shown that IOP increases trigger mechano-signaling that destabilizes cell junctions and promotes pressure-lowering fluid flow into Schlemm's canal.

Building on their discovery of metabolic disturbances in glaucoma, the lab is developing therapies that enhance cellular resilience to prevent or treat the disease. They discovered that dietary supplementation with nutrients/metabolic intermediates like nicotinamide (vitamin B3) and pyruvate strongly protects against both IOP elevation and glaucomatous neurodegeneration in mice. In collaboration with Dr. Louis Pasquale, they found that these metabolites are resilience factors against high genetic risk for human glaucoma. These findings have spurred clinical trials around the world, highlighting the promise of resilience-based therapies to complement existing treatments and improve patient outcomes.

Simon John, PhD

03 Disease Mechanisms

PLATFORMS FOR PRECISION THERAPY IN INHERITED RETINAL DISEASES

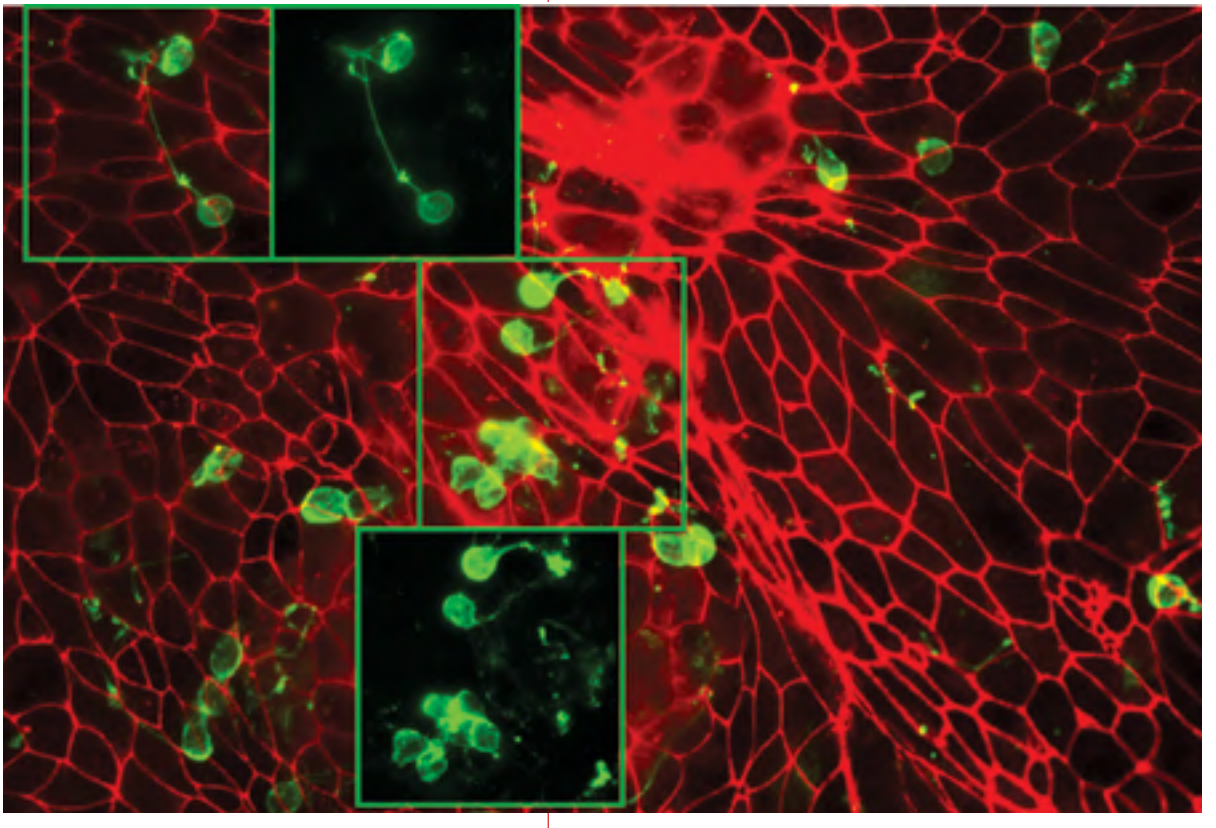


Figure. Human postmortem photoreceptor co-cultured with human induced pluripotent stem cell-derived retinal pigmented epithelial cells. Green: human rhodopsin, Red: ZO-1.

The Jonas Children's Vision Center (JCVC) Lab, under the direction of Stephen Tsang, MD, PhD, studies inherited retinal diseases using integrated platforms that span genome-engineered animal models, patient-derived induced pluripotent stem cells (iPSCs), gene editing, and metabolic therapies. The lab investigates a broad range of disease genes—including but not limited to RS1 and ABCA4—to understand mechanisms of retinal degeneration and develop precision treatments. Our research includes ex vivo modeling using human photoreceptor-RPE co-cultures, in vivo functional validation in transgenic animals, and CRISPR-mediated gene correction. We also explore metabolome engineering as a therapeutic strategy. By combining cutting-edge reprogramming tools with translational models, JCVC aims to restore vision in children (and adults) affected by a wide spectrum of monogenic retinal disorders.

Stephen H. Tsang, MD, PhD

IMAGING REVEALS VISUAL CYCLE IMPAIRMENT

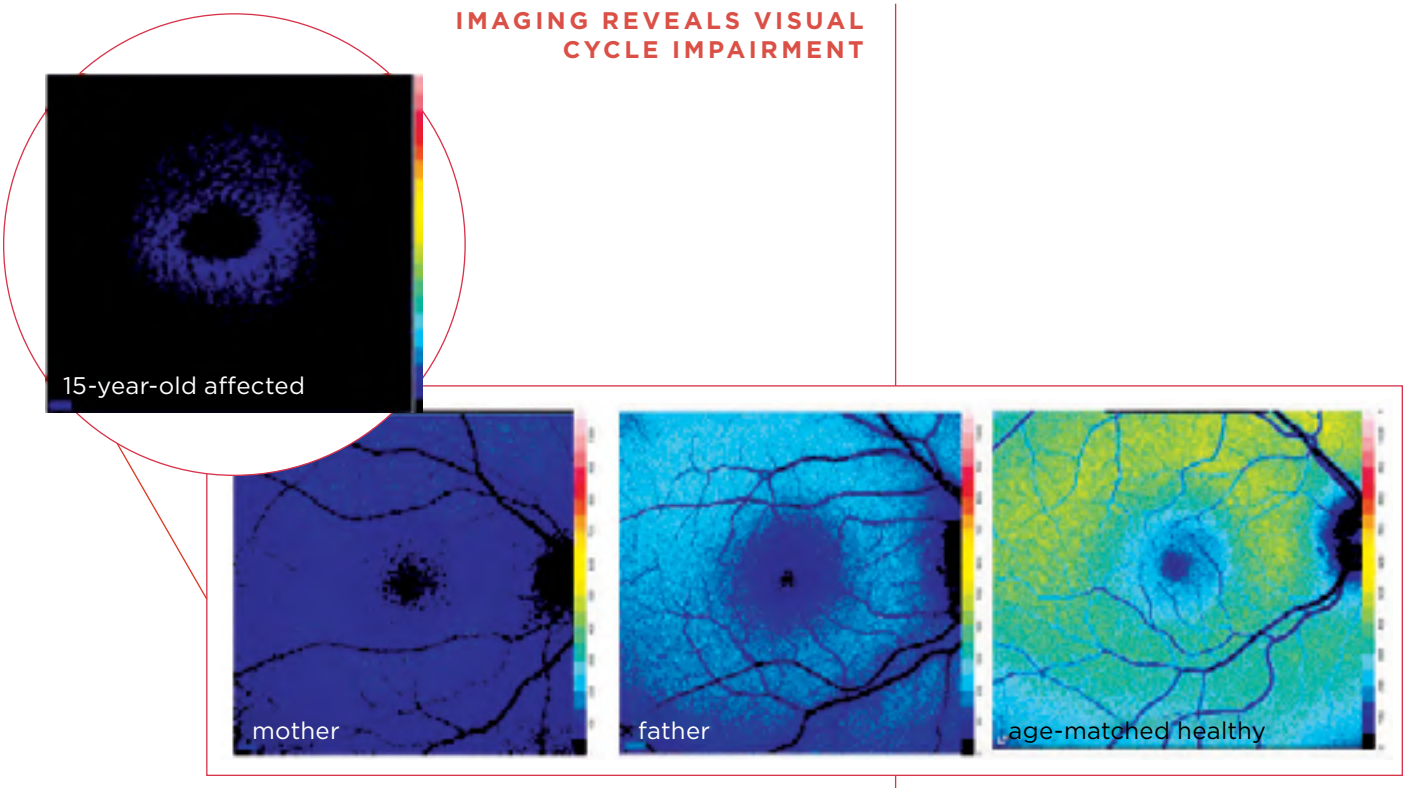
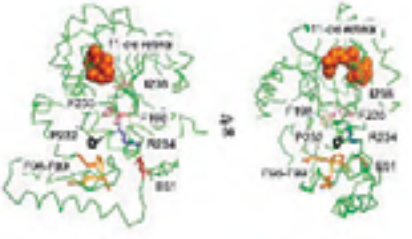
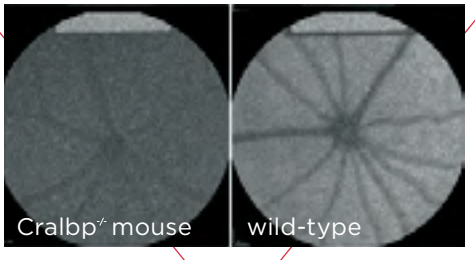


Figure. Quantitative autofluorescence (qAF) retinal imaging serves to monitor both deficiencies in the visual cycle and the accumulation of vitamin A byproducts. The darkness of this image, from a 15-year-old who carries mutations in the visual cycle protein CRALBP, is consistent with the protein function. The parents are asymptomatic, yet differences in their qAF images when compared with a healthy eye provided the first indication that the visual cycle failed to provide healthy levels of CRALBP. These data were corroborated by qAF imaging in a mouse model of CRALBP deficiency and by structural studies of the CRALBP protein.





Vision is initiated by the absorption of a photon of light by a vitamin A-derived chromophore housed in the retina's photoreceptor cells. The visual cycle generates a supply of the chromophore for continued light detection. Some retinal diseases are the result of genetic deficiencies in visual cycle proteins. Conversely, the demands of the visual cycle also produce toxic vitamin A byproducts called bisretinoids that accumulate in photoreceptor cells. These molecules are the primary disease-causing agents in some retinal diseases, such as recessive Stargardt disease. Accelerated formation of bisretinoids can also be a secondary factor in other retinal diseases. The laboratory of Janet Sparrow, PhD, has led the vision science community in understanding the retinal disease consequences of these byproducts, the processes governing how they form, how they react to light in ways that can be harmful, and their contributions to fundus autofluorescence.

Janet R. Sparrow, PhD

03 Disease Mechanisms

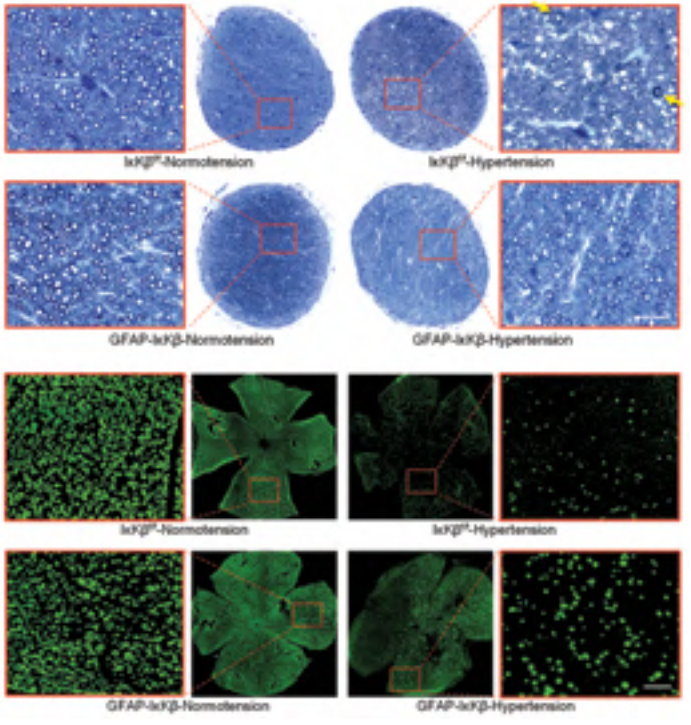


Figure. Glial cell responses in glaucoma promote neuroinflammation, creating an additional damaging force on retinal ganglion cells and their axons in the optic nerve. By comparatively analyzing neuroinflammatory and neurodegenerative outcomes of glaucoma in mice with or without deletion of specific genes in astroglia (GFAP-IκKβ$^{f/f}$ versus IκKβ$^{f/f}$), Dr. Tezel's recent research identified NF-κB as a valuable glial treatment target to provide immunomodulation and protect neurons against inflammatory injury. By decreasing neuroinflammation, cre/lox-based inhibition of astroglial NF-κB (a common transcriptional activator of multiple inflammation pathways co-playing in glaucoma) increased the survival of optic nerve axons (blue) and retinal ganglion cell somas (green) in mouse eyes with experimentally induced ocular hypertension.

Gülgün Tezel, MD, is a scientist with a long-standing interest in the cellular and molecular mechanisms of neurodegeneration in glaucoma for a better understanding of this blinding disease and treating glaucoma patients. Her goal is to better understand "the big picture" of glaucoma and the involvement of multiple pathogenic processes, feeding into a vicious

TARGETING NEUROINFLAMMATION AND DEGENERATION IN GLAUCOMA

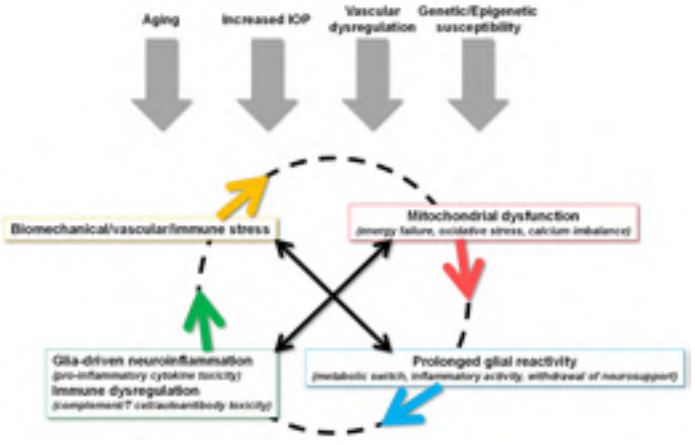


Figure. Dr. Tezel's laboratory investigates the molecular components and interdependence between different pathogenic routes, such as those with inflammatory or mitochondrial origin, to guide new treatment strategies with multitarget potential, since the best therapeutic benefit for a multifactorial neurodegenerative disease like glaucoma can be gained from multitarget treatments acting against multiple etiological paths for broader treatment effects.

cycle of neurodegeneration (see schematic above). Using in vitro and in vivo experimental models of glaucoma, Dr. Tezel's laboratory has analyzed cell type-specific responses to elucidate pathogenic processes, new treatment targets, and biomarkers. Her NIH/NEI-supported research, testing pharmacological and transgenic treatments through structural, molecular, and functional analyses, has provided translational insights into therapeutic modulation of neuroinflammation and neurodegeneration. For guiding immunomodulatory and neuroprotective treatment of glaucoma, Dr. Tezel's current projects specifically focus on the molecular regulation of glia-driven neuroinflammation and retinal ganglion cell-astroglia-microglia interactions, augmenting neurodegenerative inflammation with connection to mitochondria and metabolic regulation. Ongoing research also applies artificial intelligence and machine learning approaches to analyzing retinal SD-OCT scans in mice and developing strategies for preclinical enhancement of the present toolbox for clinical testing.

Gülgün Tezel, MD

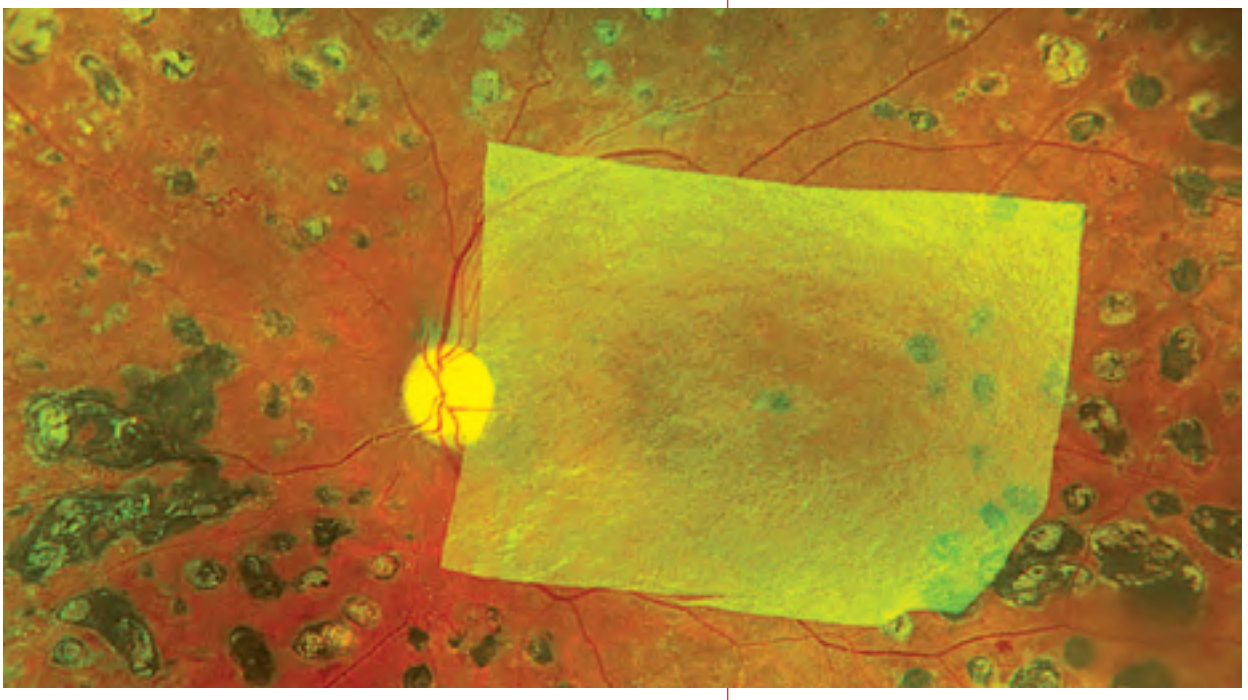


Figure. Image of an amniotic membrane grafting in a previously untreatable disease. Color fundus photograph of an epiretinal human amniotic membrane graft patched to treat a large macular hole. Patient previously had two failed macular hole repair surgeries. The hole closed, and the patient's visual acuity improved to 20/50.

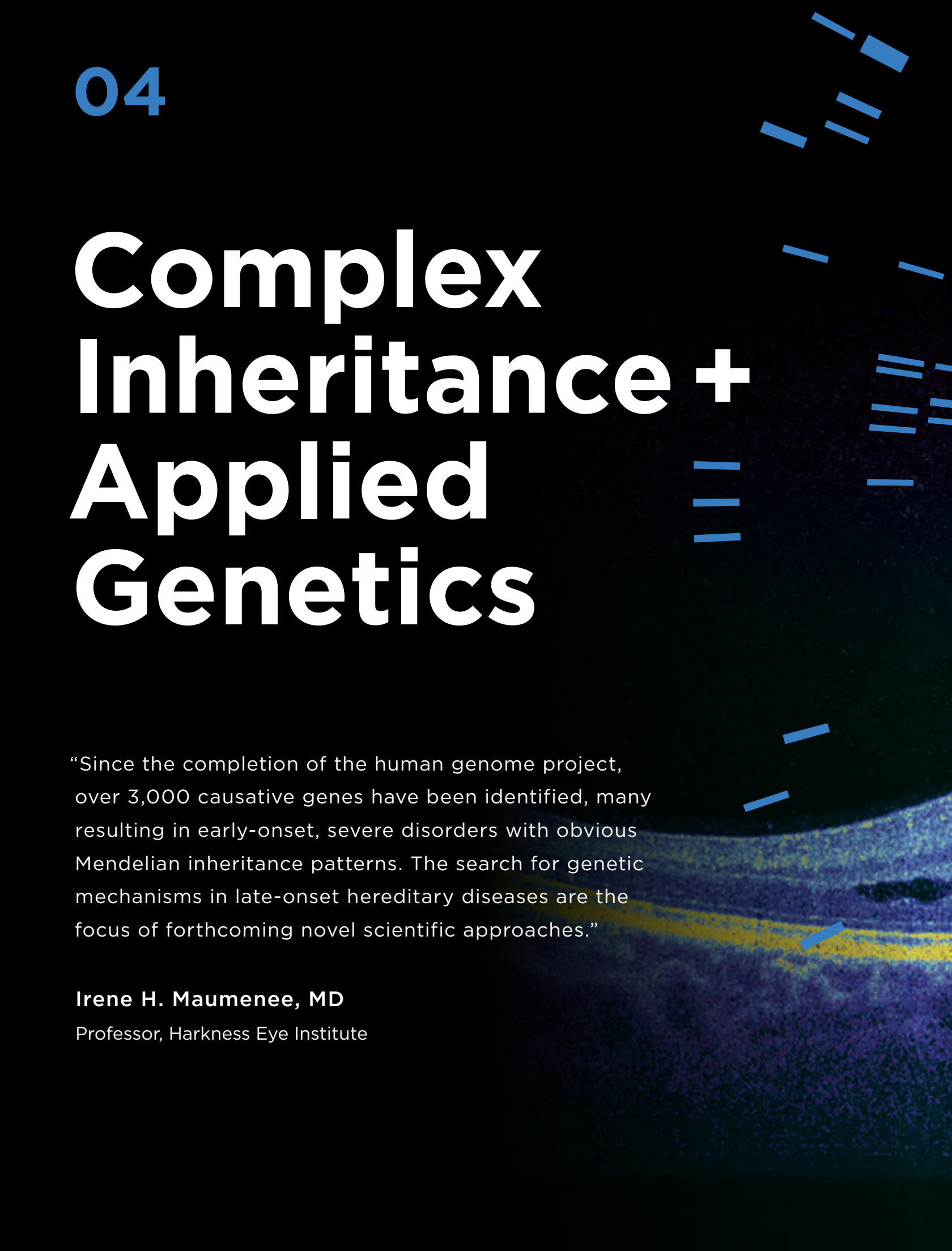
Dr. Tongalp Tezel has championed novel therapeutic approaches that apply learnings from the basic science laboratory to the clinical world, such as epiretinal amniotic membrane grafting. This surgical technique allows vitreoretinal surgeons to treat complex retinal diseases, such as large macular holes, myopic foveoschisis, macular telangiectasis, and myopic posterior pole detachments, with high success rates.

Initial protein and gene analyses on experimental models in the Tezel laboratory have shown that patched human amniotic membrane induces a wound-healing response by controlling the migration and proliferation of the retinal glial cells to the injured retina. Dr. Tezel has shared this technique with colleagues worldwide through conferences and didactic seminars.

Tongalp H. Tezel, MD

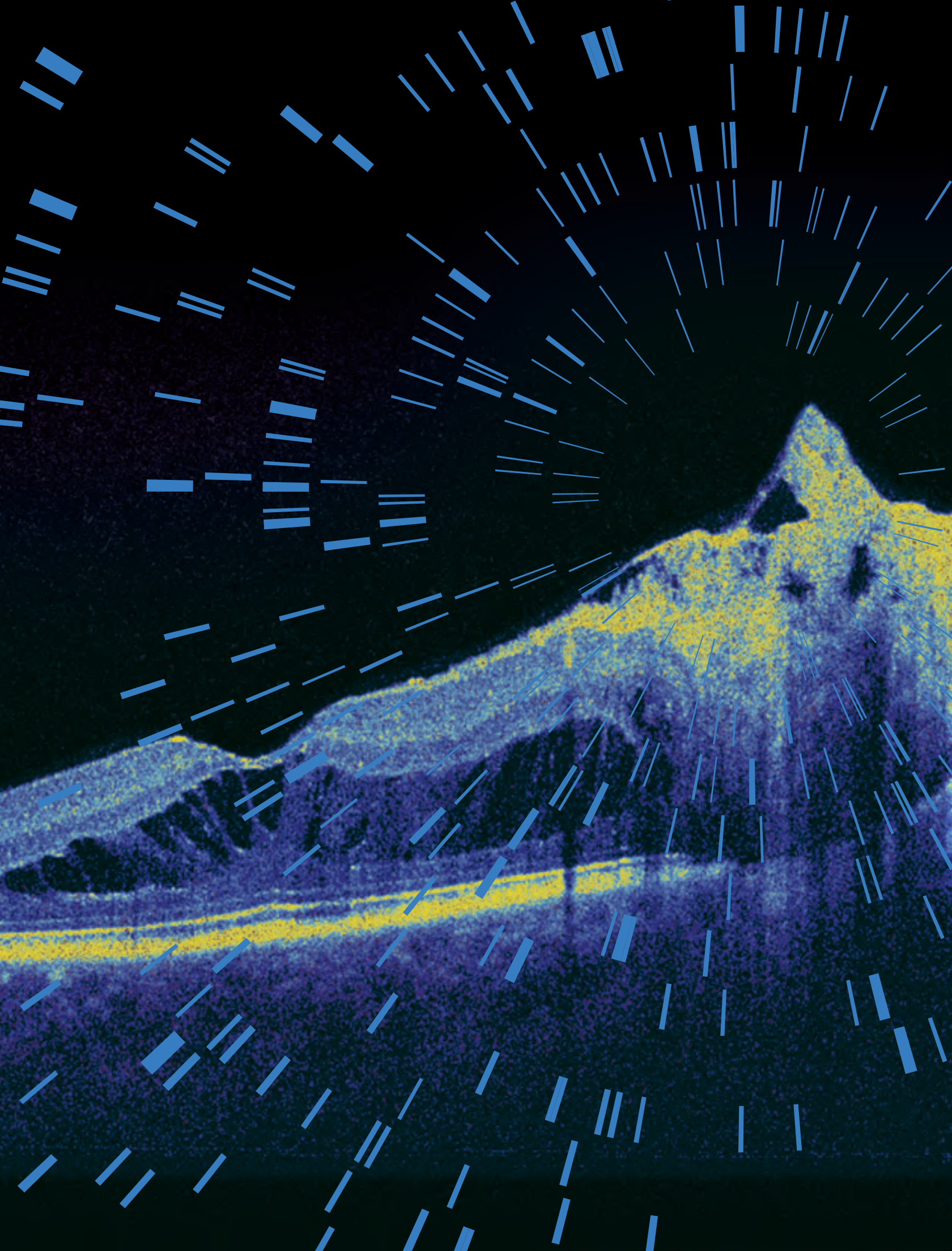
04

Complex Inheritance + Applied Genetics



"Since the completion of the human genome project, over 3,000 causative genes have been identified, many resulting in early-onset, severe disorders with obvious Mendelian inheritance patterns. The search for genetic mechanisms in late-onset hereditary diseases are the focus of forthcoming novel scientific approaches."

Irene H. Maumenee, MD
Professor, Harkness Eye Institute



04 Complex Inheritance + Applied Genetics

Nothing says “precision” in medicine more than a tailored approach to an individual patient’s genetic makeup, and that is part of our vision at Columbia Ophthalmology. As we advance in basic and clinical research, we uncover intricate genetic variations that influence the onset and progression of various eye conditions, from common refractive errors and glaucoma to macular degeneration and rare inherited retinal diseases. These insights are key to delivering personalized care, as they allow for more accurate diagnoses, tailored treatments, and better prognostic predictions. Without a deep understanding of these factors, physicians and healthcare providers may miss opportunities for early detection and targeted intervention, which are vital in preserving vision and improving the quality of life for patients.

Our department has led the way with discoveries that have revolutionized the way we look at the complexities of genetics and the mechanisms underlying inherited ophthalmic disease.

These seminal discoveries include the elucidation of the underlying genetic mechanisms of Stargardt disease and macular degeneration (Rando Allikmets, PhD), Best macular dystrophy (Konstantin Petrukhin, PhD), retinitis pigmentosa and novel methods to approach gene therapy (Stephen Tsang, MD, PhD), state-of-the-art imaging and image analysis in inherited retinal disease (Janet Sparrow, PhD), and ocular manifestations of inherited syndromes (Irene Maumenee, MD), among many other important discoveries and luminaries in the field. The inauguration of the Applied Genetics division has also brought an essential service to offer patients the best in care from both clinical and research perspectives.

In addition to our clinical and research focus, our department is uniquely positioned to help achieve our goals in precision medicine by providing a robust educational foundation in genetics and its applications in ophthalmic care. Through exposure during medical and graduate studies, residency and fellowship training, students and researchers at our institution have access to state-of-the-art genetic laboratories, clinical exposure, and advanced data analysis tools that will enable them to translate genetic knowledge into clinical practice. By offering specialized programs and fostering innovation in genetic research, we are training the next generation of ophthalmologists to be leaders in personalized eye care. This will not only advance the field but also ensure that the vision health of future generations is managed with precision and expertise, grounded in the latest genetic discoveries.

Aliaa H. Abdelhakim, MD, PhD

Overleaf:
Optical coherence tomography showing postoperative resolving tractional schisis in a patient with proliferative sickle retinopathy. Vision improved from light perception to 20/20. Royce W. S. Chen, MD

MOUSE AND HUMAN GENOMICS OF RETINAL DISEASES

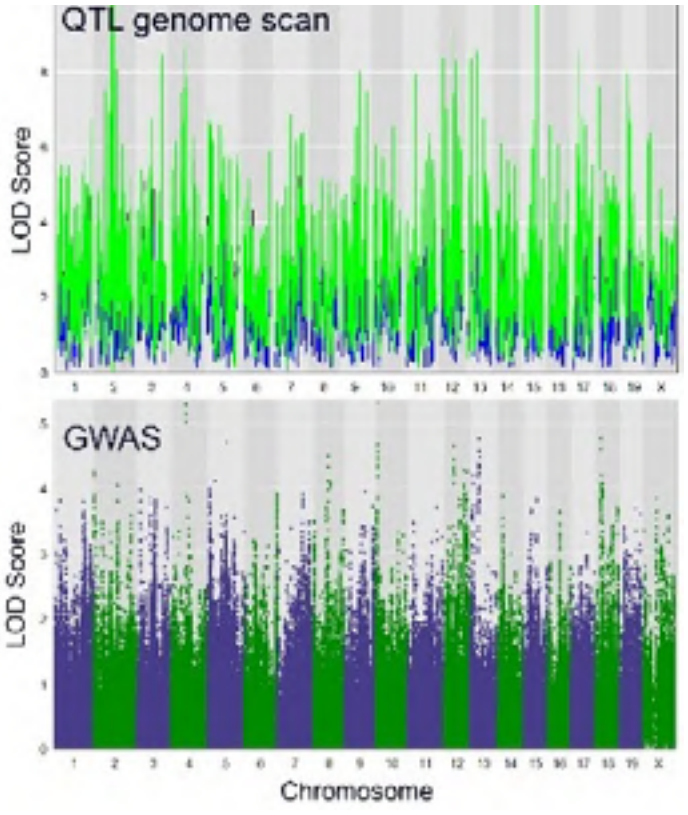


Figure. Marker mapping to determine locations in the mouse genome associated with fundus autofluorescence phenotype with 665 mice.

Figure. We are studying over 300 families with at least one MacTel-affected patient. Pedigree mapping, as shown in the figure, provides important information about the inheritance patterns in these families and drives further gene discovery.

Takayuki Nagasaki, PhD, in collaboration with investigators including Janet Sparrow, PhD, and Rando Allikmets, PhD, has demonstrated that the development of fundus autofluorescence is strongly associated with some retinal diseases, such as Stargardt disease. However, the precise molecular mechanisms are unknown. Clarification of this may assist in diagnosing and treating such diseases.

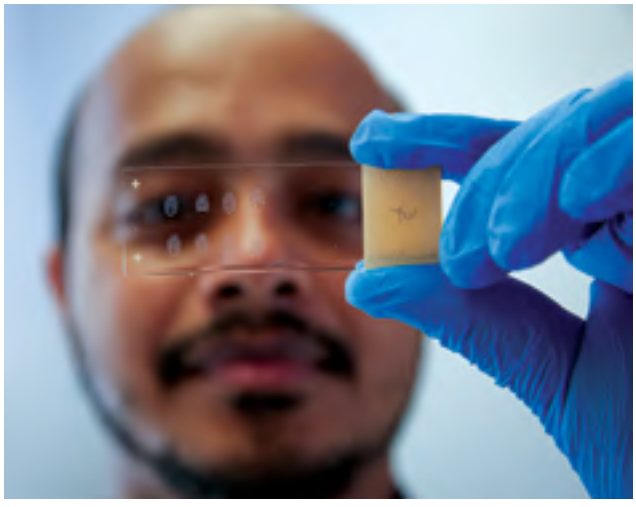
To this end, Columbia Ophthalmology determined fundus autofluorescence levels and genotypes of 665 mice and are analyzing them with techniques of statistical genetics to identify genes and gene networks associated with retinal diseases that are accompanied by fundus autofluorescence increase. These investigations will ultimately direct therapeutic studies that hold promise to mitigate blinding eye disease. Our ability to move back and forth between basic science laboratories and care of patients is a strength of Columbia Ophthalmology and is a method to accelerate the application of novel findings to clinical care.

Macular telangiectasia type II (MacTel) is a rare eye disease leading to gradual vision loss and is an example of the close collaboration of basic and clinical science at Columbia. We have recently identified, together with the international consortium, that mutations in genes such as SPTLC1 and PHGDH can be causal to a small fraction of the MacTel patients. However, the causes of the majority of MacTel patients remain unknown. To solve this problem, we have determined the genotypes of over 3,000 MacTel patients to dissect the polygenic nature of the disease.

Takayuki Nagasaki, PhD
in association with
Rando L. Allikmets, PhD

04 Complex Inheritance + Applied Genetics

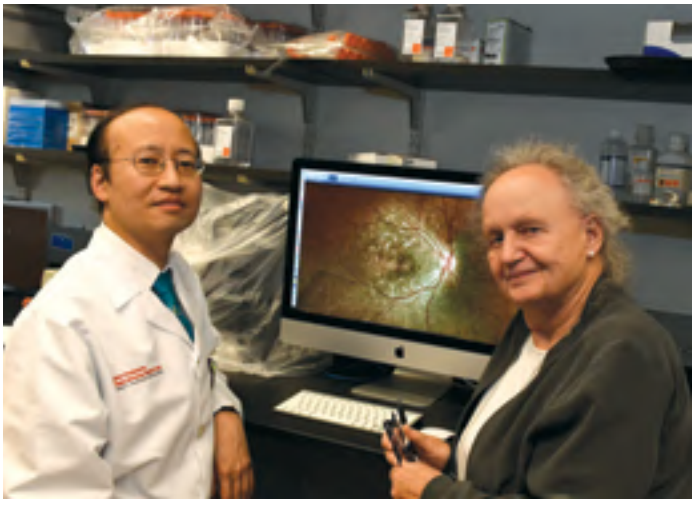
APPLIED GENETICS SERVICE AT COLUMBIA OPHTHALMOLOGY



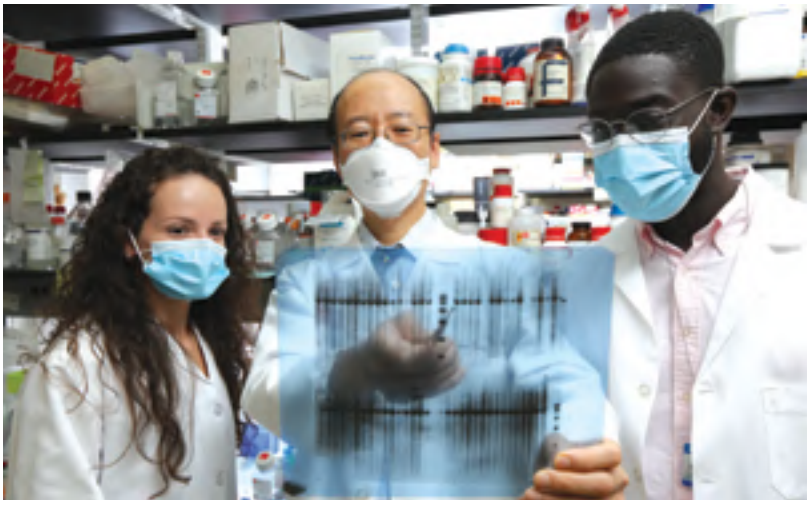
Abdul Hannan, PhD, Zhang Laboratory

Maribel Rodriguez tests a patient.

The Applied Genetics Service at Columbia Ophthalmology was created in 2019 to increase access to clinical genetics care for all patients with eye diseases and to connect them with the state-of-the-art research and clinical trials in the field. It is the only service of its kind in the New York region, serving over 20 million people. The program serves patients of all ophthalmic subspecialties and aims to create new intradepartmental collaborations. Patients undergo genetic counseling both before and after genetic testing to ensure they are active participants in the process. To date, over 2,000 genetic counseling appointments have taken place and over 1,000 samples have successfully been sequenced.



Stephen Tsang, MD, PhD, and Irene Maumenee, MD



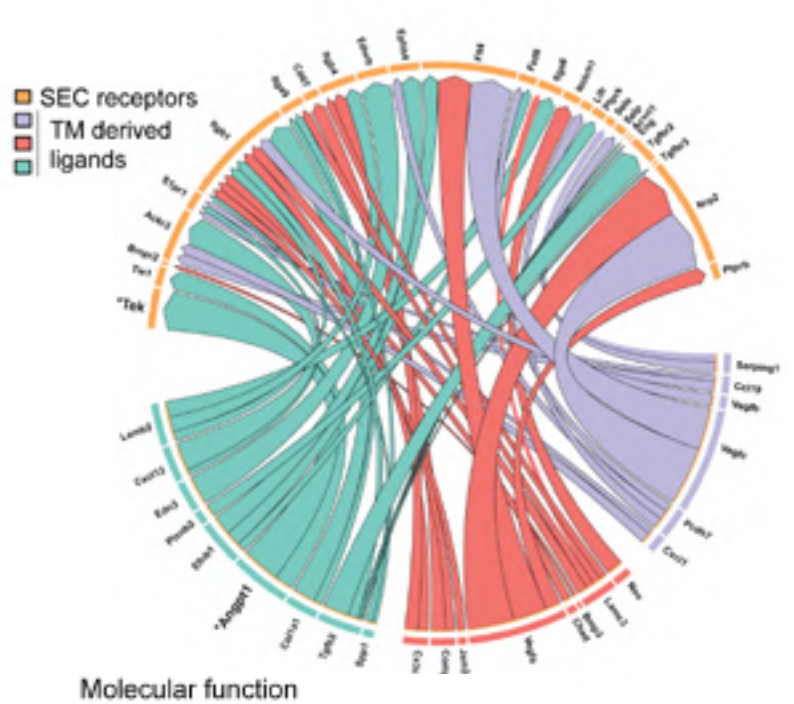
Stephen Tsang, MD, PhD Laboratory

Our clinical services offer unparalleled diagnostic and therapeutic options, including expert genetic diagnosis, genetic counseling, electrophysiology services, and clinical trials. Our experts include Irene Maumenee, MD, recognized as one of the founders of the field of ophthalmic genetics; Stephen Tsang, MD, PhD, a world leader in inherited retinal disorders research; Scott Brodie, MD, PhD, an expert in electrophysiology and its interpretation; and Aliaa Abdelhakim, MD, PhD, one of a handful of physicians across the nation who is dual boarded in both ophthalmology and clinical genetics. The service is also supported by Megan Soucy, MS, CGC, our genetics counselor who focuses solely on eye genetics and inheritance. Our team is unrivaled in its collective expertise and care.

Aliaa H. Abdelhakim, MD, PhD

Aliaa H. Abdelhakim, MD, PhD

04 Complex Inheritance + Applied Genetics



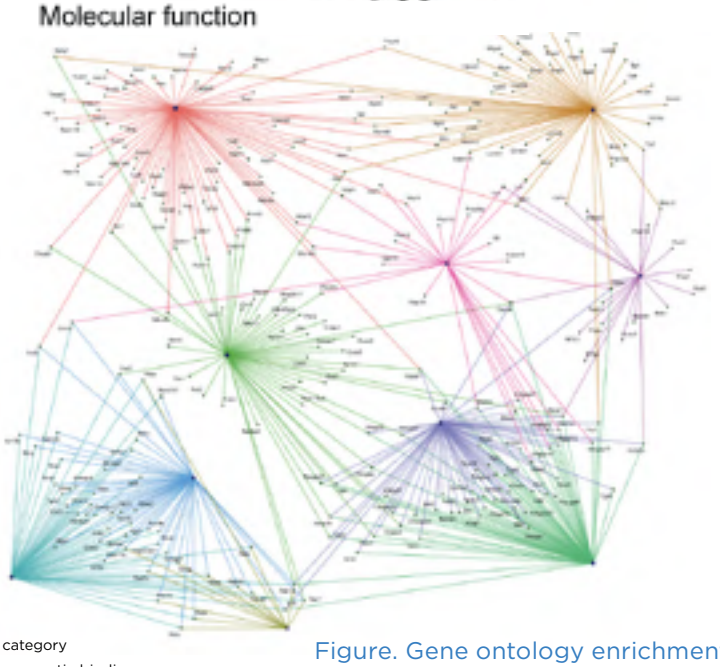


Figure. Gene ontology enrichment analysis of single-cell-resolution data highlights key molecular pathways active in Schlemm's canal endothelial cells (SECs). Net plot shows interaction between individual genes of enriched molecular pathways in SECs, identifying networks of genes and molecular pathways for IOP regulation. *Adapted from Balasubramanian et al., 2024 eLife.*

GENOMIC & MOLECULAR INTERCONNECTIONS IN HEALTH AND DISEASE

Figure. Predicted ligand-target analysis identifies signaling interactions between the trabecular meshwork (TM) and Schlemm's canal (SC). This highlights the crucial role of TM-derived molecules in controlling the development, maintenance, and function of the SC. *Adapted from Balasubramanian et al., 2024 eLife.*

Simon John, PhD, uses applied genetics and genomics to uncover the molecular and metabolic mechanisms driving glaucoma, a leading cause of blindness. Dr. John pioneered the use of mouse models to study this disease, including the now widely used DBA/2J model and the first method to measure intraocular pressure (IOP) in mice. More recently, his team developed models with mutations in Lmx1b, a key human glaucoma gene, to more directly replicate human glaucoma. Using these genetic models, his lab applies advanced genetic, molecular, and metabolic techniques to identify disease mechanism, focusing on early events leading to IOP elevation and retinal ganglion cell death.

A central aspect of Dr. John's research is understanding how the trabecular meshwork and Schlemm's canal—tissues responsible for regulating IOP—develop and function. His team has identified various genes and processes that cause dysfunction in these tissues and recently revealed a comprehensive list of critical molecular signals between these tissues, a list that informs efforts to develop new treatments. Dr. John is also advancing gene therapy approaches aimed at improving treatment precision and safety, offering new promise for more effective glaucoma interventions.

Simon John, PhD

EXAMPLES OF INHERITED RETINAL DISORDERS

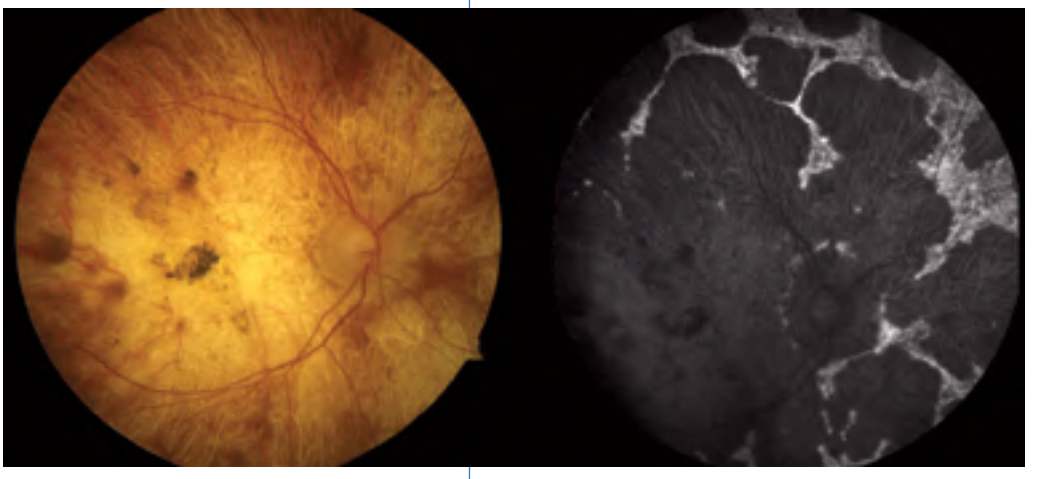


Figure. Color fundus image of right eye with Stargardt disease group 3

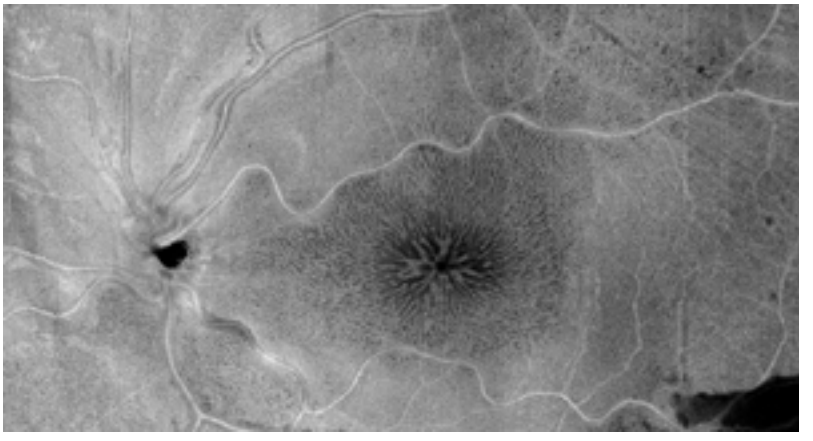


Figure. Fundus autofluorescence image of a patient with X-linked retinoschisis (XLRS), demonstrating characteristic foveoschisis with spoke-like radiating folds. The patient harbors a pathogenic variant in the RS1 gene. We are actively recruiting genetically confirmed XLRS patients for participation in precision AAV.SPR gene therapy trial.

There are many examples of inherited retinal disorders that can lead to severe vision loss, such as Stargardt disease and X-linked retinoschisis. Stargardt disease is a genetic eye disorder that causes progressive vision loss, typically beginning in childhood or adolescence. It primarily affects the macula, the central part of the retina responsible for sharp, straight-ahead vision. Symptoms usually include blurry central vision, difficulty seeing in low light, and slow adaptation to changes in lighting.

The condition is most often inherited in an autosomal recessive pattern, and results from mutations in the ABCA4 gene that lead to the buildup of toxic substances in the retina, a discovery made by Rando Allikmets, PhD. Precision therapies addressing the biochemical basis of Stargardt disease have subsequently been developed by Konstantin Petrukhin, PhD, and Janet Sparrow, PhD. Ongoing research is exploring gene therapy and other treatments to slow progression. This fundus photograph was taken from a Stargardt group 3 patient currently receiving care at the Applied Genetics Clinic.

Stephen H. Tsang, MD, PhD

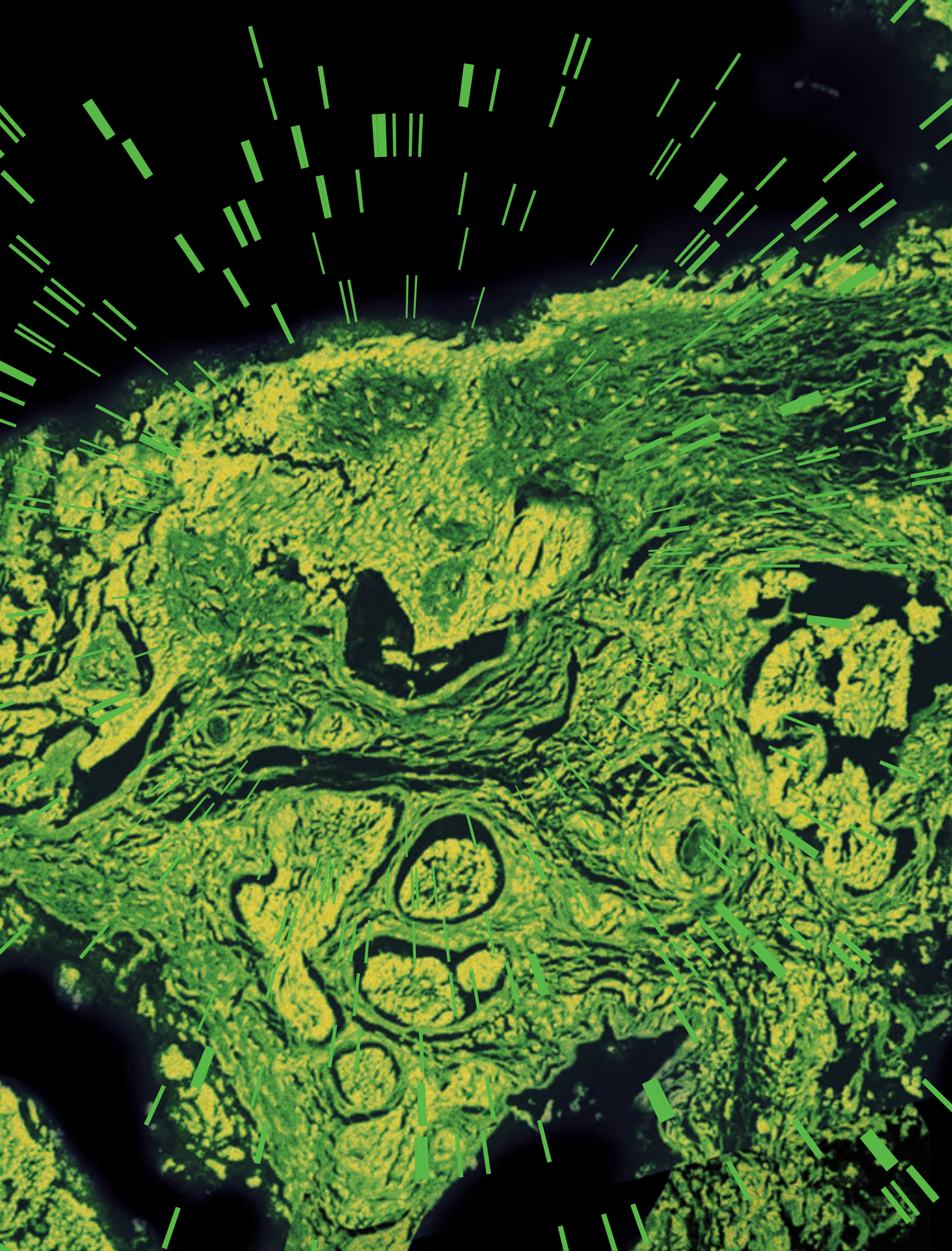
05

Clinical + Translational Science

"Translational science, the moving of scientific discoveries to medical care, has driven the extraordinary advances in clinical ophthalmology that have brought unprecedented benefit to our patients."

Stephen L. Trokel, MD

Professor, Harkness Eye Institute



05 Clinical + Translational Science

Clinical and translational ophthalmology at Columbia University's Edward S. Harkness Eye Institute plays a critical role in advancing the diagnosis, treatment, and prevention of eye diseases. By bridging the gap between laboratory research and patient care, the institute fosters innovations that lead to real-world improvements in vision health. Columbia's rich academic environment and access to cutting-edge resources allow clinician-scientists to collaborate across disciplines, ensuring that discoveries in molecular biology, genetics, and imaging are rapidly translated into new therapies and technologies for patients.

The Harkness Eye Institute stands out for its commitment to addressing both common and rare ophthalmic conditions through rigorous clinical trials and translational research.

From age-related macular degeneration to inherited retinal diseases, departmental researchers are developing targeted interventions that personalize treatment and improve outcomes. The synergy between clinical excellence and scientific inquiry ensures that patients receive the most advanced and evidence-based care while simultaneously contributing to the advancement of ophthalmology as a field.

Moreover, our clinical and translation research programs play pivotal roles in training the next generation of ophthalmologists and vision scientists. Through its integrated clinical and research programs, medical students, residents, and postdoctoral fellows gain hands-on experience in both patient care and innovative research. This dual focus cultivates a culture of inquiry and excellence, reinforcing Columbia's position as a global leader in vision science and patient-centered care. The Edward S. Harkness Eye Institute remains a cornerstone of ophthalmic innovation, dedicated to transforming scientific discoveries into life-changing outcomes for patients around the world.

Overleaf:
Histopathologic image of eyelid basal cell carcinoma.
Lora Glass, MD
Alejandro Gru, MD

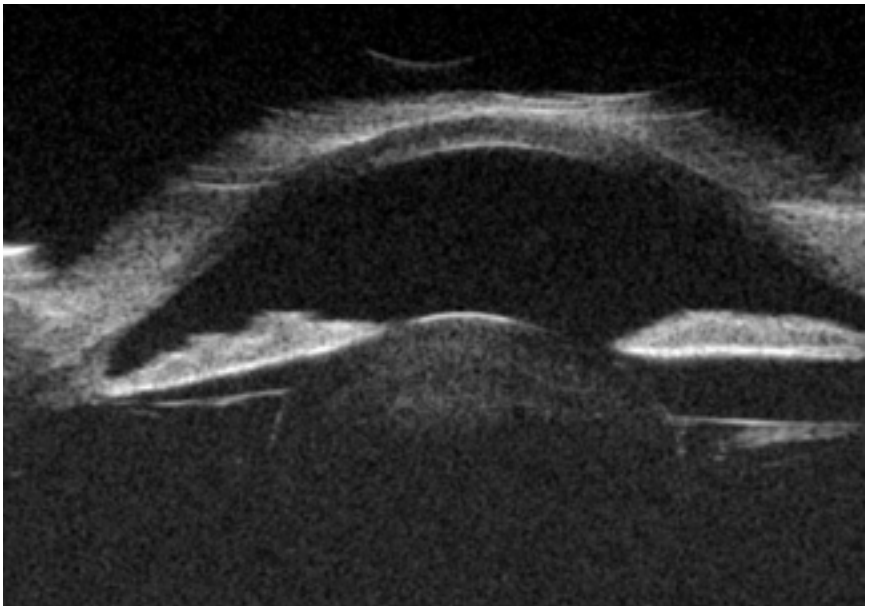


Figure. Ultrasound biomicroscopy (UBM) image of Marfan syndrome suspect. Lens is displaced and rounded. (Ronald Silverman, PhD)

Marfan syndrome (MFS) is a genetic connective tissue disorder whose cardinal features involve the musculoskeletal, cardiac, and ocular systems. With a relatively common worldwide incidence of 1 in 3,000 to 5,000, this disease affects men and women equally and occurs in all races and ethnic groups. Early diagnosis of these patients is critical due to the high mortality rate from cardiovascular complications, including aortic aneurysm and dissection. The Ghent diagnostic criteria for MFS have been refined over the last four decades and include a pathogenic mutation of the FBN1 gene on chromosome 15. Clinical manifestations of the disease vary significantly, with musculoskeletal features often raising the suspicion of MFS. Ocular manifestations of this disease include lens dislocation, which is seen in only 65% of patients but when found in combination with aortic disease is considered diagnostic for MFS.

The foundational science for ultrasound biomicroscopy (UBM) in ophthalmology, an imaging technique used worldwide, was largely developed by Columbia faculty members D. Jackson Coleman, MD, and Ronald Silverman, PhD. This technique and direct examination by skilled clinicians allow the ocular findings to help categorize the various phenotypes (appearances) of MFS in the eye. For example, lens findings fall into four distinct phenotypes:

1. Congenital lens dislocation and microspherophakia as seen in neonatal Marfan syndrome, the most severe variant.

2. Development of myopia around ages 4-7 years, followed by progressive lens luxation into the vitreous cavity during the teenage years.

3. Development of myopia around ages 4-7 years without obvious lens dislocation, followed by slowly progressive lens dislocation superiorly and then decades of stabilization.

4. No evidence of lens dislocation on slit-lamp evaluation.

Our multidisciplinary team's objective is the early recognition of abnormalities in the lens-zonular complex not visible on slit-lamp evaluation. Using imaging modalities such as ultrasound biomicroscopy, we have been quantifying lens curvature in different meridians, which we believe may predict lens dislocation. Our hypothesis is that measurable parameters of the lens-zonule complex are correlated with aortic disease progression and therefore may be useful indicators of mortality risk in MFS.

Marfan Syndrome Team:
Lisa Park, MD
Ronald H. Silverman, PhD
Suzanne Daly, RN
Irene H. Maumenee, MD
Megan Soucy, MS, CGC
David Engel, MD
Aliaa H. Abdelhakim, MD, PhD
Caroline O'Connor, MPH

05 Clinical + Translational Science

NEW DIAGNOSTIC INSIGHTS WITH ULTRASOUND

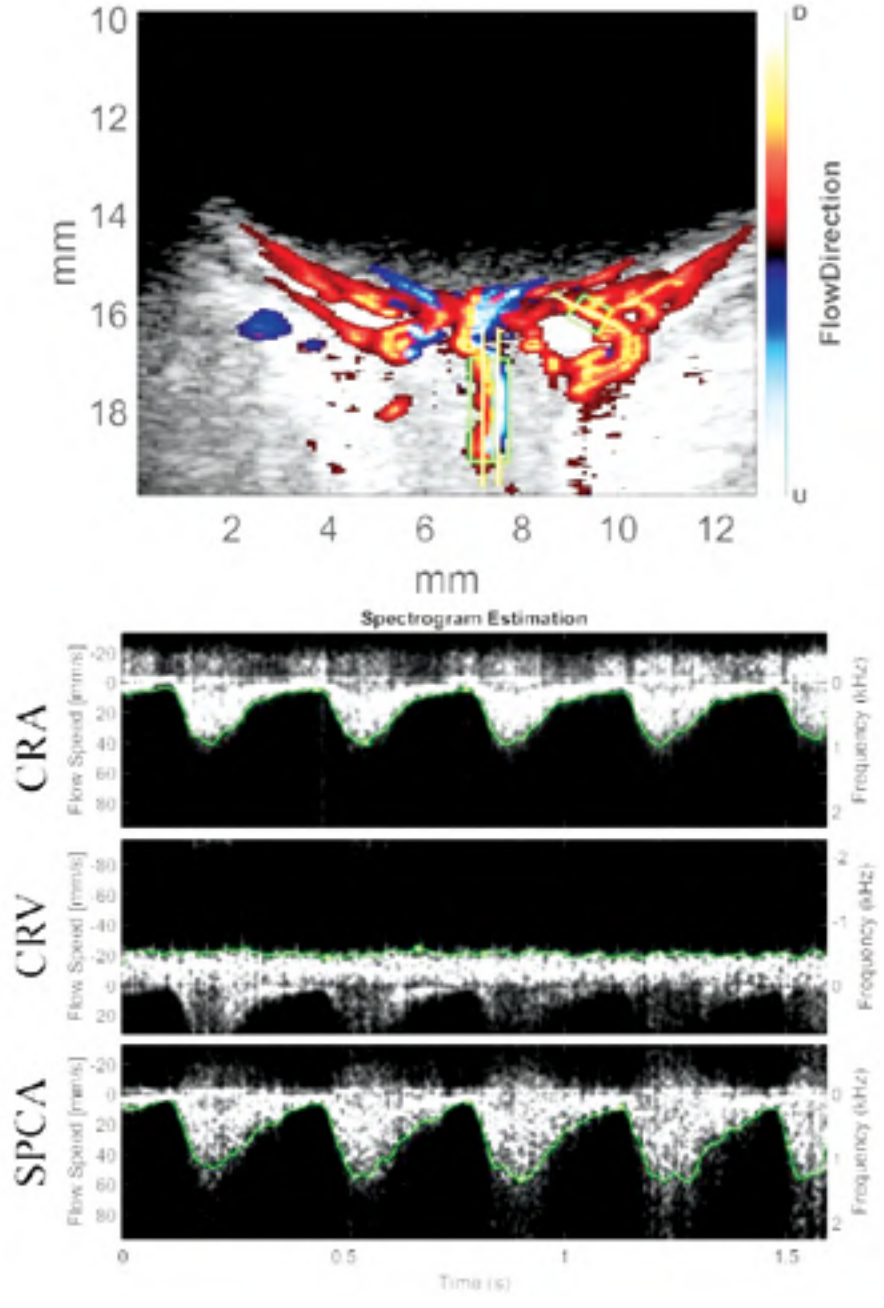


Figure. Plane-wave color-flow Doppler image of flow in the central retinal artery (CRA) and vein (CRV) and a short posterior ciliary artery (SPCA) of a preterm, low-birthweight neonate. Spectrograms depict pulsatile flow over 1.5 seconds.

The Silverman Lab is focused on the use of ultrasound in the eye. Dr. Silverman and his colleagues have developed a system for ultrafast imaging that enables display and measurement of blood flow in the orbital vessels supplying the retina and choroid. We conducted preclinical studies of blood flow in ocular hypertension and clinical studies of ocular blood flow in women affected by preeclampsia and preterm neonates at risk for retinopathy of prematurity and correlated our findings with optical coherence tomography angiography (in preeclampsia) and with RetCam images in retinopathy of prematurity. In the latter case, we analyzed retinal patterns quantitatively and found them to correlate with arterial flow velocity and with indirect-ophthalmoscopy classification as pre-plus disease. We have analyzed ultrasound biomicroscopy images of Marfan syndrome subjects and demonstrated significant associations between lens thickness and anterior radius of curvature with confirmation of Marfan genotype (mutations in the FBN1 gene) and with history of aorta repair surgery. In addition, we are participating in an NIH-sponsored study of acoustic backscatter in the vitreous and its correlation with contrast sensitivity, for which we are developing a system for 3D imaging of the eye.

Ronald H. Silverman, PhD

COLUMBIA'S OPHTHALMOLOGY CLINICAL TRIAL UNIT (CTU) PROVIDES NEW OPTIONS FOR PATIENTS

Figure. The Manhattan Vision Screening and Follow-Up Study (NYC-SIGHT), a five-year randomized clinical trial funded by the CDC, screened 708 residents living in New York City affordable housing developments, referring 428 for an in-office eye exam, including 26.6% with glaucoma. The study has received national attention and shown that patient navigators improve attendance to in-office eye exams following screening programs.

Established in 2014 through the generosity of the late Mike Nichols, the Department of Ophthalmology Clinical Trial Unit participates in numerous clinical trials involving novel therapeutic and diagnostic methods for various eye diseases, including glaucoma, inherited retina diseases, retinoblastoma and melanoma, cornea abnormalities, and thyroid eye disease. Clinical trials speed the application of novel therapies and basic science findings to the clinical realm. The benefits of being enrolled in a clinical trial include extensive monitoring and ocular testing during the trial, which can last from a few months up to five years if long-term follow-up is required. Clinical trials often provide patients with access to therapies that are otherwise inaccessible. Most importantly, clinical trials move the field forward and provide clinicians with answers and patients with options. The Clinical Trial Unit is co-directed by Dr. Lisa A. Hark and Dr. Marzhan Atakulova, who oversee seven full-time study coordinators, including Ioannis Michalopoulos, Maribel Rodriguez, Edylin Ma Bautista, Sokleab Em, Patricia Lemberg, Desiree Torres, and Stefania Maruri.

Lisa A. Hark, PhD, MBA

05 Clinical + Translational Science

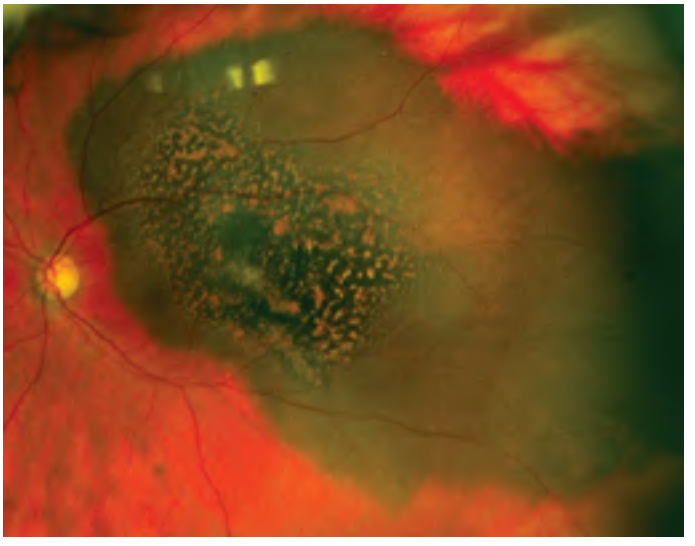


Figure. Fundus photography of a large, diffuse choroidal melanoma in a 77-year-old male. Gene expression profiling was performed prior to definitive treatment to assess metastatic risk.

Ocular oncology has a rich history, dating back to its founding in New York by Dr. Algernon Reese and Dr. Robert Ellsworth at the Harkness Eye Institute. After decades of absence, the service was revitalized under the leadership of Dr. Brian Marr. Over the past seven years, Dr. Marr has transformed the division, establishing it as one of the premier ocular oncology centers in the tristate area. Today, ocular oncology is experiencing a new era of progress, driven by breakthroughs in cancer physiology, genetics, and treatment options. Clinical trials targeting ocular tumors are expanding, offering new hope to patients. Recently, the field saw the first FDA-approved systemic treatments for metastatic uveal melanoma, while the introduction of gene expression profiling has revolutionized how we assess metastatic risk in uveal melanoma patients. This allows for tailored monitoring and treatment plans, with an emphasis on developing novel, targeted therapies. The division is also pioneering advancements in both neoadjuvant and adjuvant therapies for uveal melanoma and various other ophthalmic tumors. These innovations are expanding the scope of treatments available to patients, offering a more personalized and effective approach to care.

OCULAR ONCOLOGY DIVISION SPEEDS TREATMENTS TO THOSE IN NEED

Figure. Slit-lamp photograph of uveal melanoma involving the ciliary body. Treatment included plaque brachytherapy with Iodine-125.

Columbia's Ophthalmic Oncology Division is at the forefront of these developments, providing state-of-the-art diagnostics and individualized care for patients with complex ophthalmic tumors of the eyelid, globe, and orbit. Dr. Brian Marr, one of the most experienced leaders in ocular oncology, collaborates closely with a multidisciplinary team that includes radiation oncologists, medical oncologists, interventional radiologists, and surgical subspecialists to deliver comprehensive, bespoke care.

Research is integral to the division's mission, and we are currently leading two pioneering clinical trials. AURA is a Phase III multicenter trial investigating a novel therapy using viral nanoparticle conjugates and laser to treat small uveal melanomas or indeterminate lesions. This innovative treatment offers a vision-sparing, early intervention option for patients.

IDEAYA is a multicenter Phase II trial examining the use of Daroversertib, a systemic protein kinase C inhibitor, as a neoadjuvant treatment for uveal melanoma.

Brian P. Marr, MD and ***Lauren B. Yeager, MD***

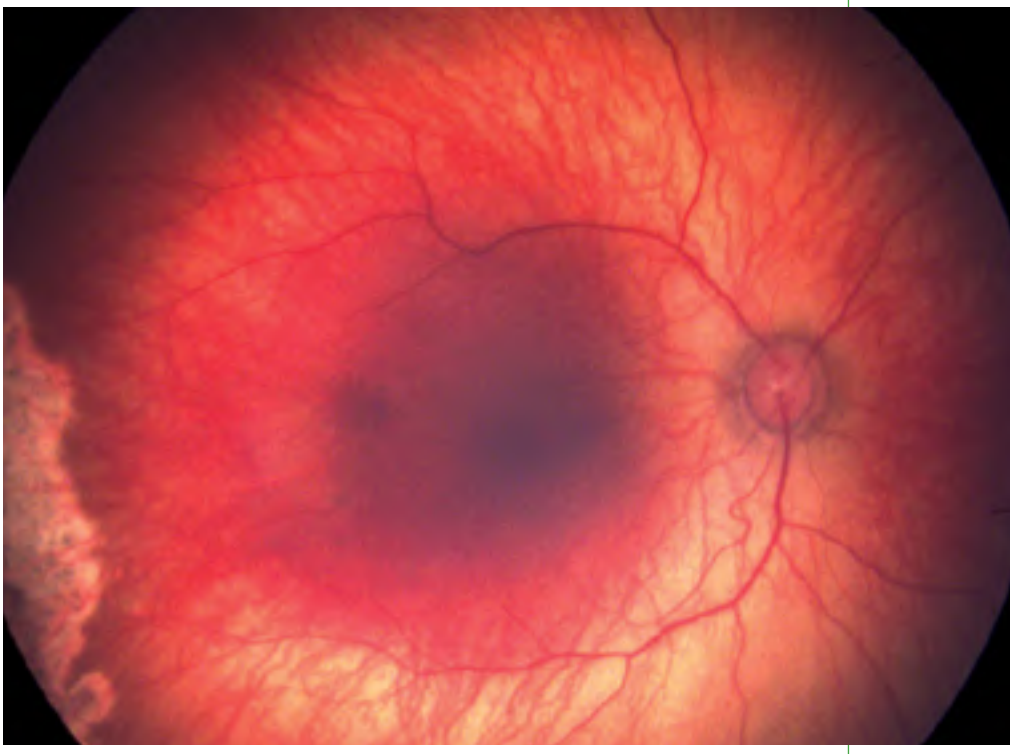


Figure. Successfully treated newborn infant's retina (white area on left) after laser treatment for ROP.

Retinopathy of prematurity (ROP) can cause blindness in severely premature babies by causing intractable retinal detachments that result from derangements in normal retinal vascular development. When performed on a timely basis, laser treatment or anti-VEGF therapy can save a neonate's retina from detaching and thereby preserve vision for a lifetime. Working with the Silverman Lab, we discovered a robust connection between ROP stage or severity and measured planar Doppler ultrasound flow characteristics in ocular vascular structures in neonates. The goal is to reduce the need for dilated fundus exams in fragile neonates and to improve the prognostication of critical ROP. One of the current lines of investigation involves the use of objective retinal image analysis for enhancing the accuracy of the predictive model for the purpose of increasing its clinical utility.

Jason D. Horowitz, MD

05 Clinical + Translational Science

APPLYING CLINICAL SCIENCE TO THE REGIONS AROUND THE EYE

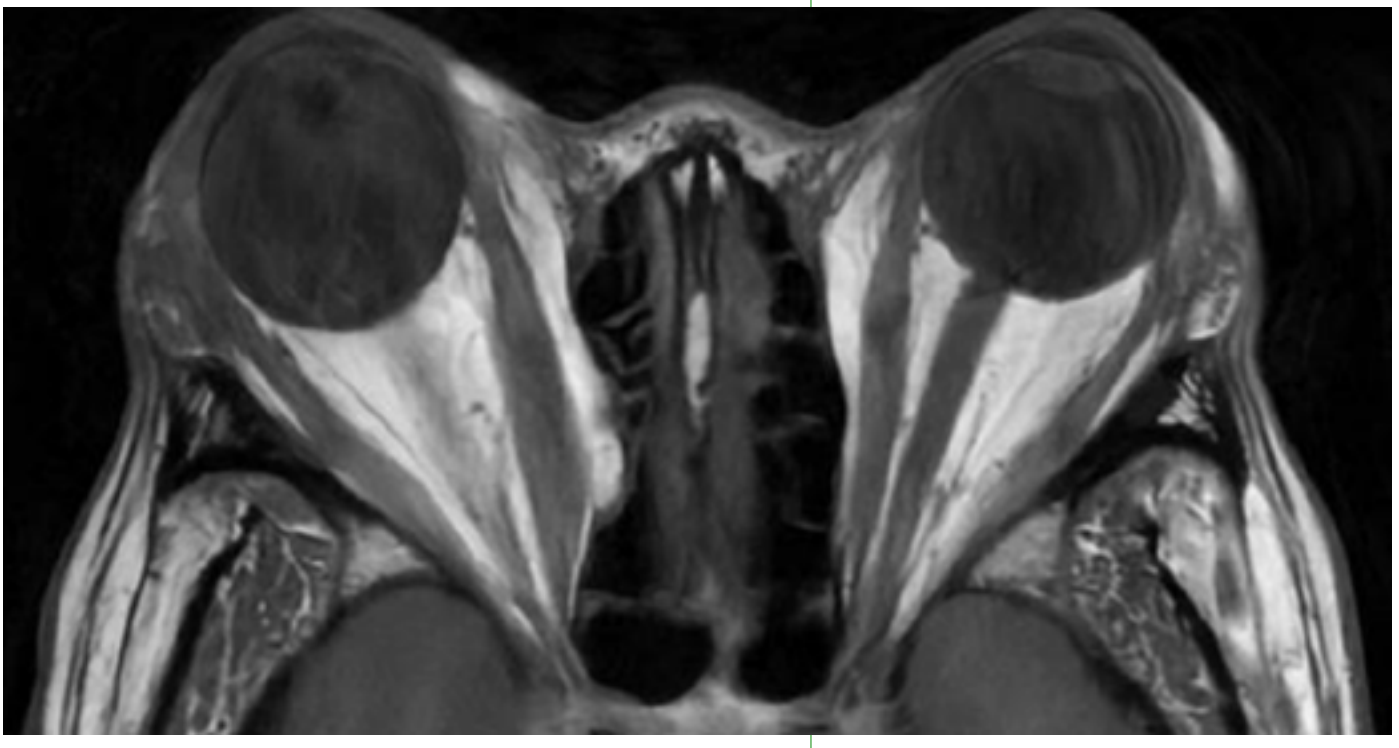


Figure. MRI scan of the orbits showing a patient with severe thyroid eye disease, manifesting as both extraocular muscle enlargement and proptosis, or bulging, of the eyes.

The ophthalmic plastic and reconstructive surgery division oversees pathology related to oculofacial, nasolacrimal, and orbital anatomy, including congenital, traumatic, neoplastic, inflammatory/rheumatologic, and age-related disease processes. The division, led by Dr. Lora Glass, provides care through the ColumbiaDoctors faculty practice and the NewYork-Presbyterian Hospital Ambulatory Care Network system, with a focus on individualized surgical and therapeutic care.

Current investigative efforts focus on thyroid eye disease and dermatologic periocular disease. The division is excited to serve as a clinical site for pharmaceutical trials in thyroid eye disease, which epitomize the "bench to bedside" progress of translational care. It is also working to help define the possible role of artificial intelligence in thyroid eye disease care. Finally, the division has also helped define and emphasize the cross-collaboration necessary for appropriate allergic dermatitis care.

Lora R. Dagi Glass, MD

PEDIATRIC CORNEAL SERVICE HANDLES BOTH COMMON AND RARE DISORDERS

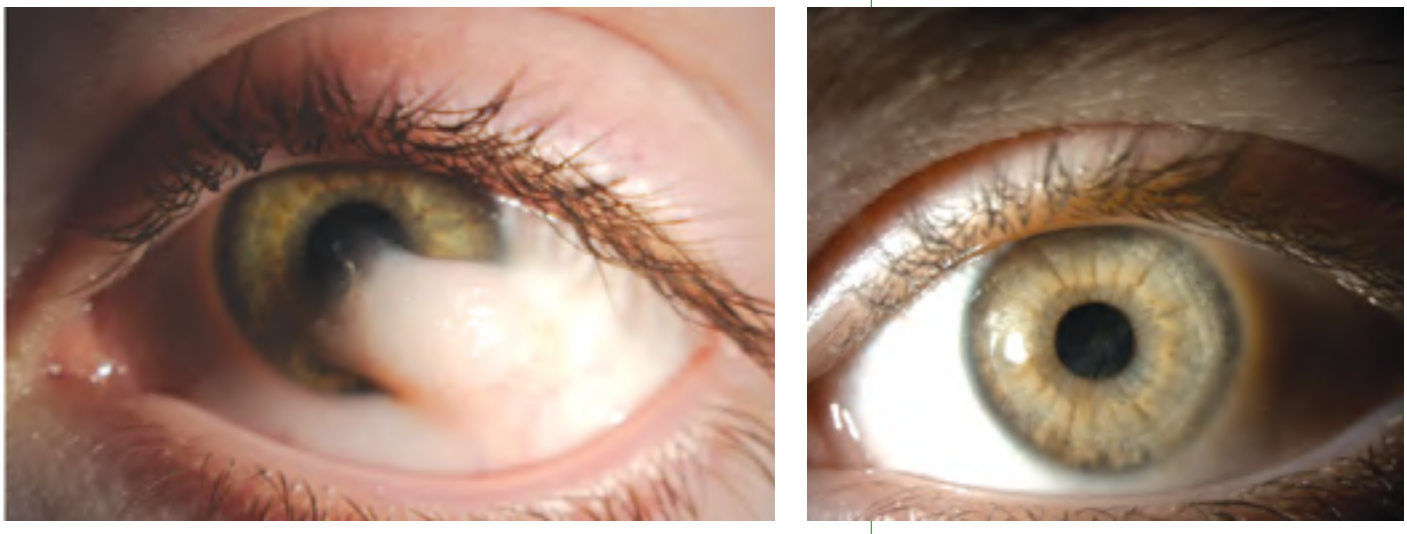


Figure. Superficial limbal dermoid (choriostoma) prior to (left) and following (right) surgical excision via partial keratectomy and amniotic membrane placement.

Corneal conditions present differently in children, and as one of the only pediatric corneal practices in the country, we conduct several studies looking at associations and pathogenesis of ocular conditions to provide better treatments. Under the direction of Dr. Danielle Trief, and in close collaboration with the departmental pediatric division under the direction of Dr. Steven Rosenberg, this subspecialty service has increased exponentially in recent years. We also collaborate with the departments of pediatric allergy and pulmonology at the Children's Hospital of New York to screen, for example, children with allergies that are associated with keratoconus, a corneal condition that is more prevalent in children with atopy. In addition, the service is presently investigating the effects of inflammatory markers in the tear film and their role in corneal scarring/neovascularization.

An example of a rare disorder that the Columbia Pediatric Service is equipped to address is limbal dermoids (see image). Limbal dermoids are benign congenital tumors that consist of normal tissue in an abnormal spot. On the eye, limbal dermoids can contain fat, hair or even bone and teeth elements. If they are large enough, they can block the visual axis, leading to vision loss. Surgical excision is indicated for comfort and cosmesis, as well as vision restoration. For superficial lesions, a keratectomy paired with amniotic membrane placement can be performed. For deeper or full-thickness dermoids, a keratoplasty (corneal transplant) may be necessary.

Danielle Trief, MD, MSc and
Steven E. Rosenberg, MD

05 Clinical + Translational Science

NOVEL RETINAL FINDINGS WITH HIGH-RESOLUTION IMAGING

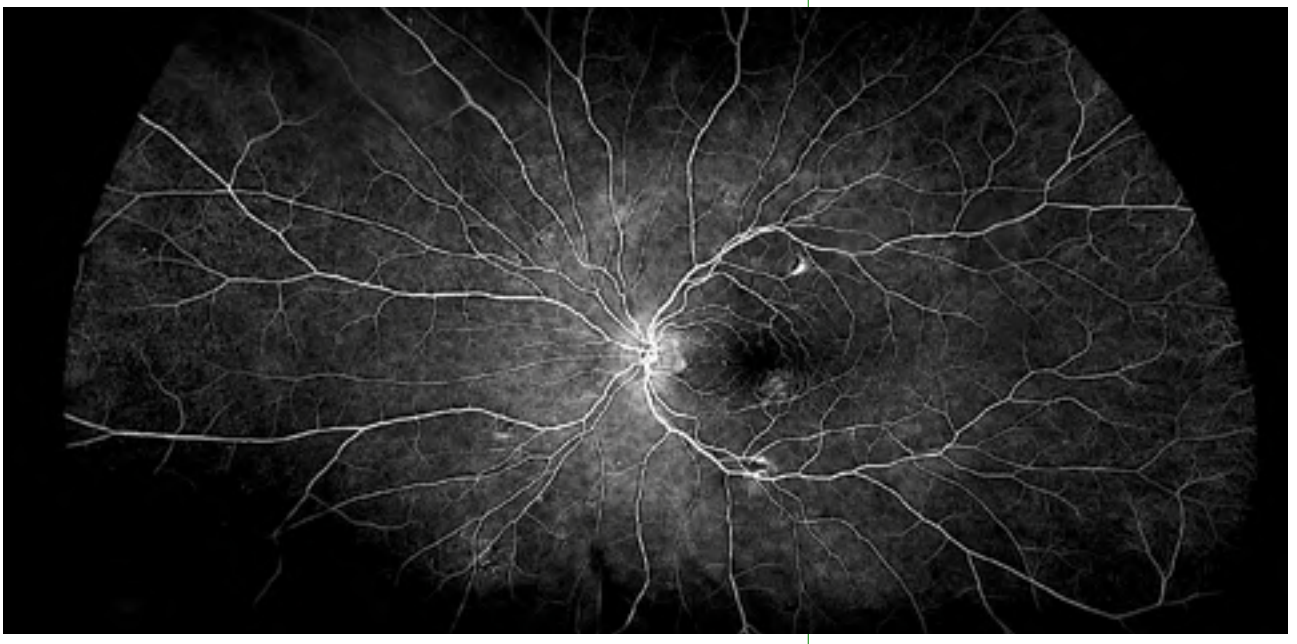


Figure: Ultra-widefield fluorescein angiography demonstrating retinal vascular anomalies in a patient with CREST syndrome. In addition to venous dilation and retinal aneurysms, there are peripheral arteriovenous anastomoses that are similar to changes seen elsewhere in the body.

In addition to being the Jean Sheng Vice Chair of Education, Dr. Royce Chen leads an active research program focused on educational innovation, imaging and surgical approaches in retina and uveitis, and applications of artificial intelligence. For example, during the peak of the COVID-19 pandemic, his group produced an important early study that described the impact of masking measures on 2,306 residents from 24 specialties in the New York metropolitan area. One notable finding: Ophthalmology was one of the highest-risk specialties for COVID-19 transmission.

More recently, his group has been collaborating with Dr. Kaveri Thakoor to identify novel approaches to ophthalmic imaging education, incorporating artificial intelligence and eye-gaze tracking to accelerate the learning process for trainees. In an increasingly imaging-dominated field, expertise in image interpretation is critically important for diagnosis and clinical decision-making in complicated patients.

Royce W. S. Chen, MD

COMBATING GLAUCOMA WITH NUTRITIONAL SUPPLEMENTS

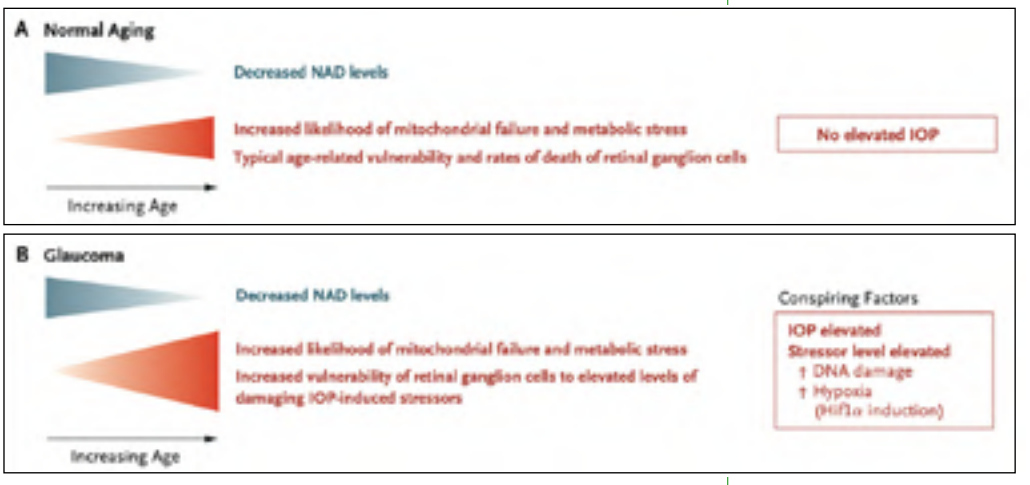
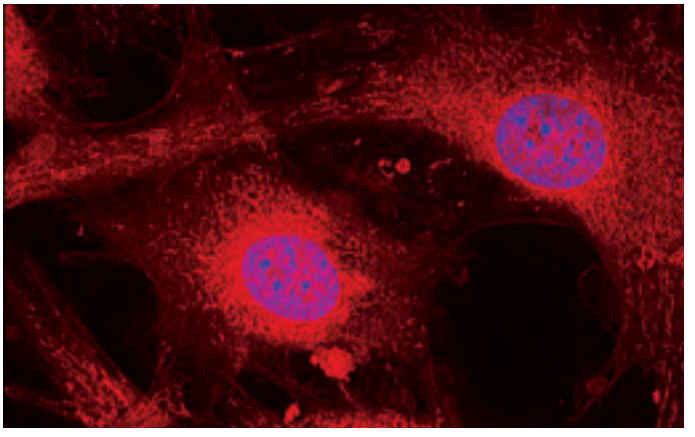


Figure. Supplementing levels of Nicotinamide (NAD) may protect the optic nerve in glaucoma patients. (Adapted from *Nicking Glaucoma with Nicotinamide?*, Liebmann, JM and Cioffi, GA. 2017, *New England Journal of Medicine, 376 (21) p. 2079.*



Mitochondrial resilience treatments are further investigated using cell culture models, enabling direct assessment via indicator stains. MitoTracker Red, a red-fluorescent dye, accumulates in active mitochondria, reflecting their function and structure. Shown: cells from glaucoma-prone Lmx1b mutant mice with mitochondria (red) and nuclei (blue). Top: untreated. Bottom: Vitamin B3-treated—enhanced red fluorescence indicates improved mitochondrial function. (Image courtesy of Juliette Buffault)

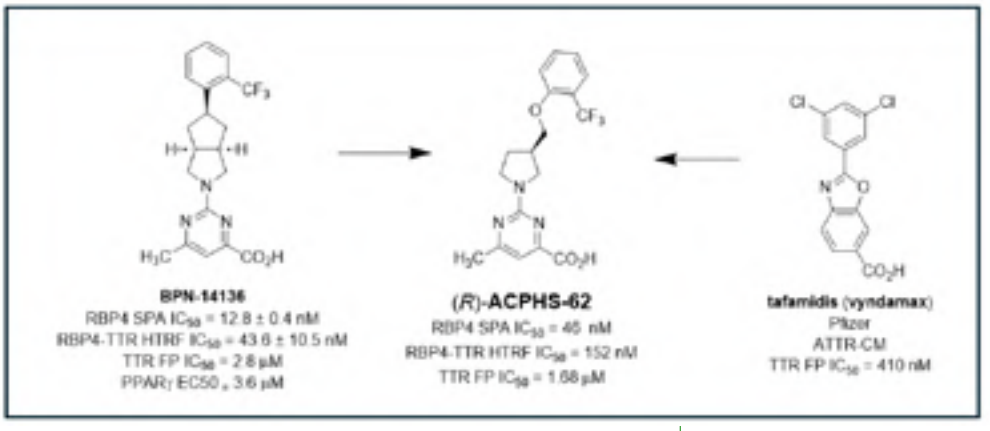
Glaucoma is the most common neurodegenerative disease and the leading cause of irreversible blindness globally, with a projected worldwide prevalence expected to affect 111.8 million people by 2040. While conventional intraocular pressure (IOP)-lowering therapy for glaucoma can effectively slow or halt the disease, many patients continue to experience optic nerve damage and visual field loss even when IOP reduction has been substantial. There is a strong unmet need for neuroprotective, IOP-independent agents that can both slow retinal ganglion cell damage and potentially heal damaged retinal ganglion cells.

Recent research has identified altered metabolic processes as a critical factor in the death of nerve cells in glaucoma. Supplementation with oral nicotinamide, a form of vitamin B3, to support metabolism has been found to protect 93% of eyes in glaucoma mouse models. Following laboratory studies, data from pilot human clinical studies, including a Phase 2 randomized controlled trial at Columbia University's Department of Ophthalmology, have provided encouraging results for the role of nicotinamide and pyruvate in glaucoma. Under the direction of Dr. Shukla, an ongoing 20-month Phase 3 clinical trial with 188 participants at Columbia University is evaluating the efficacy of long-term nicotinamide and pyruvate supplementation in slowing glaucoma progression and providing neuroprotection. Our groundbreaking trial has refined and validated novel structural and functional biomarkers that can reliably measure the effectiveness of neuroprotective therapies in glaucoma patients, laying the foundation for future clinical trials to accelerate the development of neuroprotective therapies that could transform the management of glaucoma and improve outcomes for patients worldwide.

Aakriti Garg Shukla, MD, MSc

05 Clinical + Translational Science

NEXT-GENERATION TREATMENTS FOR EYE DISEASES



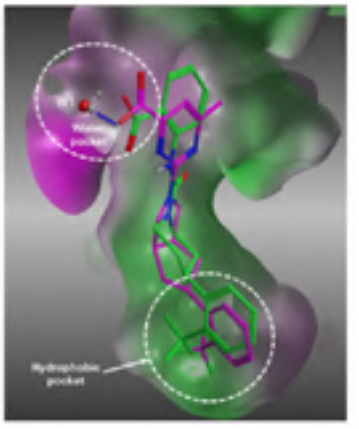


Figure: Identification of (R)-ACPHS-62, a balanced bispecific RBP4-TTR ligand intended for the treatment of dry AMD in older individuals, who commonly exhibit an age-related predisposition to cardiomyopathy associated with misfolding and aggregation of wild-type transthyretin.

The Petrukhin Lab focuses on drug discovery and development for ophthalmic disease. Tinlarebant, an oral drug developed in his lab, is currently in Phase 3 clinical trials for Stargardt disease and dry age-related macular degeneration (AMD).

Dr. Petrukhin also leads three NIH-funded projects focused on advancing therapies for Stargardt disease, dry AMD, and exfoliation glaucoma. One project supports the development of a bispecific RBP4/TTR ligand through Investigational New Drug (IND) filing with the Food and Drug Administration. Another focuses on discovering novel RPE65 modulators that can safely and effectively lower levels of the membrane-bound cellular waste lipofuscin, which plays a significant role in retinal degenerative diseases. The third project aims to develop a topical therapy for exfoliation glaucoma that targets the lysosomal pathway to limit production of exfoliation material while also reducing intraocular pressure by inhibiting aqueous humor formation. In addition, a project funded by the Thome Foundation is evaluating a small-molecule therapy for dry AMD that enhances autophagic and phagocytic clearance of misfolded proteins and aggregates in retinal pigment epithelial (RPE) cells, aiming to prevent pathogenic deposits such as sub-RPE drusen and reticular pseudo-drusen.

Konstantin Petrukhin, PhD

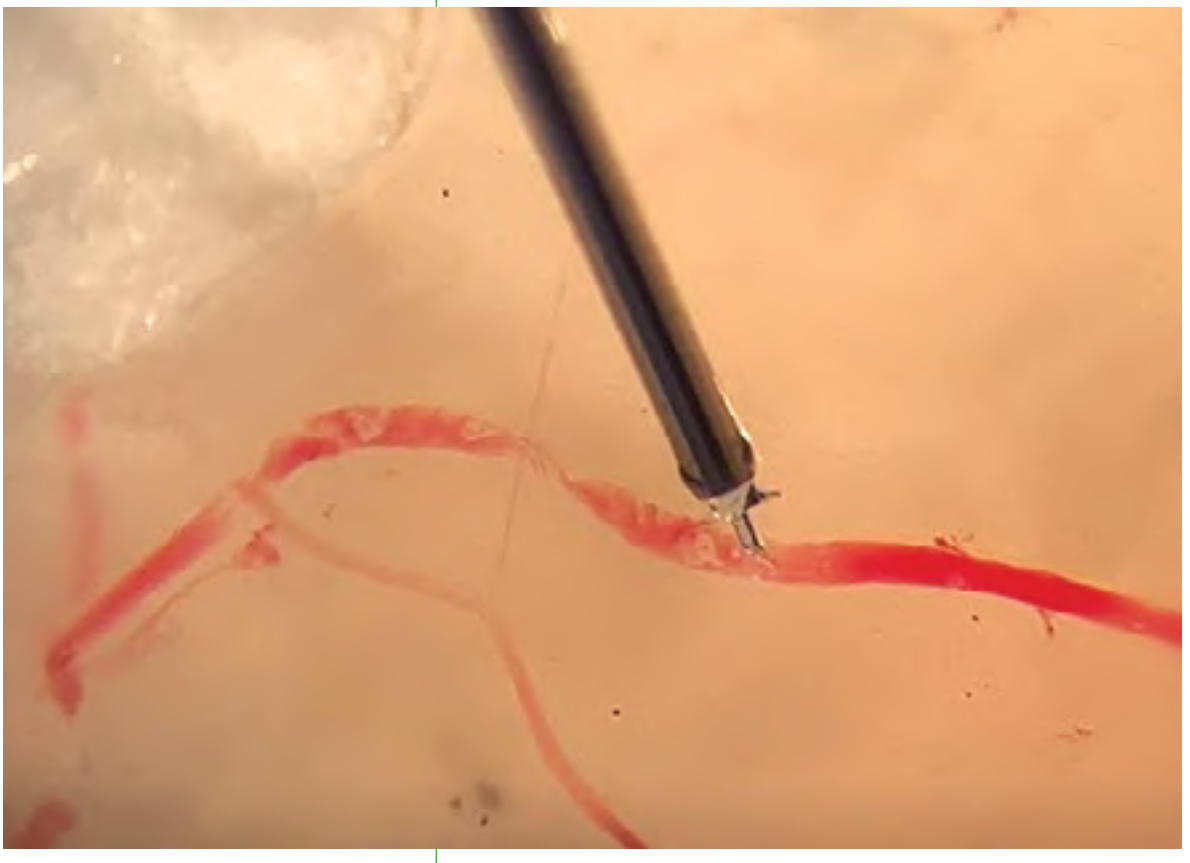


Figure. Cannulation of a retinal vessel using a microneedle.

Building on a proud tradition of retinal surgical innovation started by Dr. Stanley Chang, the retinal division continues to push the field forward. In a collaboration with bioengineers from the Columbia School of Engineering, a retinal microneedle for canalizing the retinal vessels has been developed. This needle may open a new field in our profession by enabling the direct cannulation of micro vessels in the eye without damaging the vessels. This technology may allow surgical intervention for retinal endovascular pathologies, such as retinal arteriole and vein occlusions. This microneedle may also be useful for the subretinal gene treatment, aspiration of subretinal perfluorocarbon liquid droplets, and intraarterial chemotherapy. Collaborations across the many departments and schools at Columbia University is a hallmark of the innovation in the Department of Ophthalmology.

Tongalp H. Tezel, MD

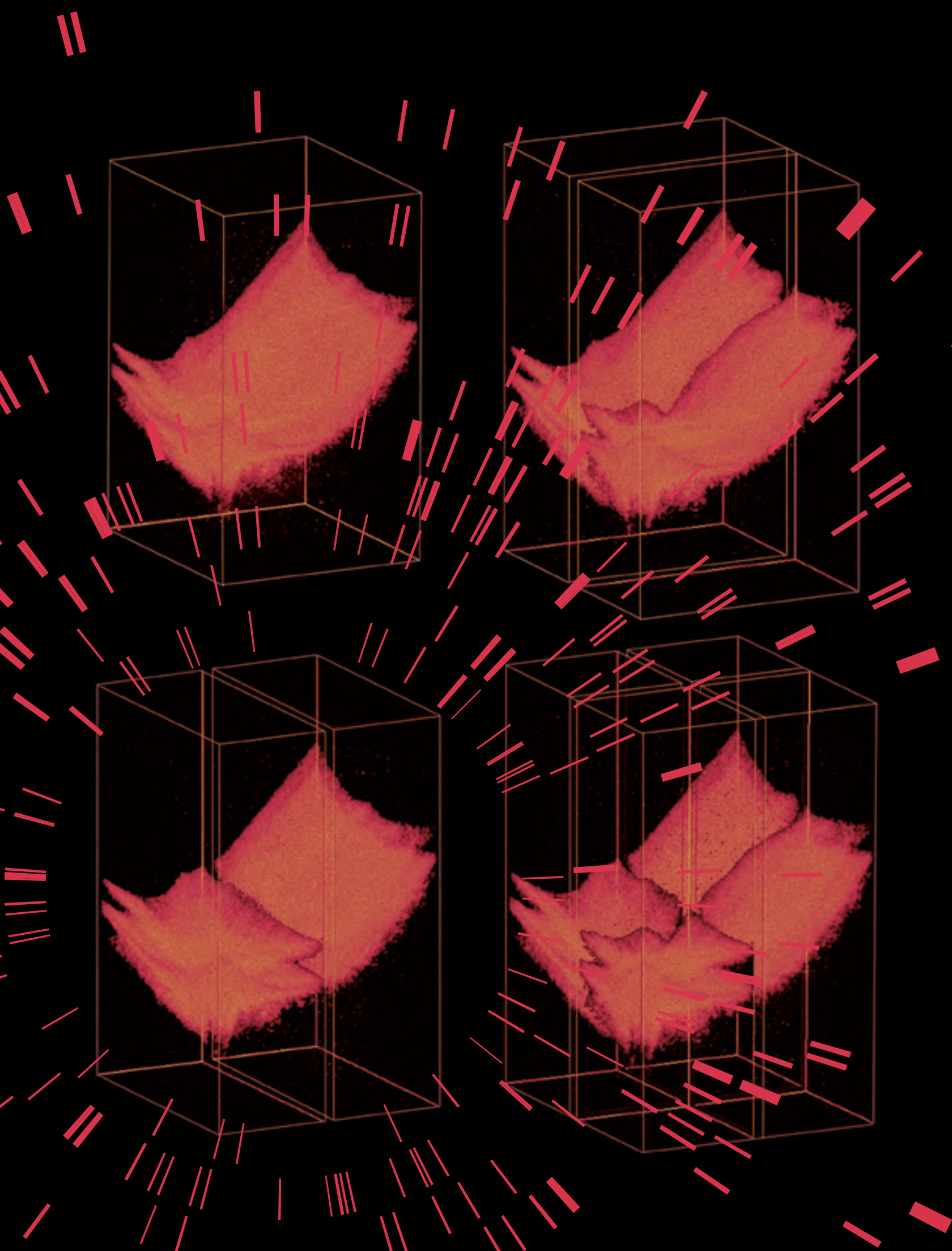
06

Data Science, Bioinformatics + Artificial Intelligence

"Artificial intelligence is emerging as a transformative force, unveiling insights across entire populations, generating precise hypotheses for individual disease mechanisms, and empowering care teams by distilling complex data into accessible, actionable knowledge."

Noémie Elhadad, PhD

Chair, Columbia Department of Biomedical Informatics



06 Data Science, Bioinformatics + Artificial Intelligence

At the Department of Ophthalmology, the convergence of data science, bioinformatics, and artificial intelligence (AI) is revolutionizing vision sciences, transforming vast datasets into actionable insights that enhance patient care. From genomic sequencing to high-resolution imaging, the sheer volume and complexity of ophthalmic data demand sophisticated analytical tools.

By harnessing the power of computational methods, we can decipher the vast, intricate datasets generated by modern medicine, thus revolutionizing our understanding of biological systems. Data science provides the tools to manage, analyze, and visualize these complex datasets, while bioinformatics applies these tools to biological questions, unveiling patterns in genomics, proteomics, and metabolomics.

AI algorithms can sift through these intricate patterns, identifying subtle biomarkers for diseases like glaucoma and macular degeneration that may elude the human eye. Machine learning models, trained on extensive patient records, can predict disease progression, personalize treatment strategies, and even automate routine diagnostic tasks, ultimately improving the precision and efficiency of clinical workflows. This interdisciplinary approach not only accelerates research but also paves the way for preventative and personalized medicine, shifting the paradigm from reactive treatment to proactive vision preservation.

The transformative potential of this interdisciplinary field is evident in its applications across diverse domains in our department. Bioinformatics plays a crucial role in deciphering the genetic underpinnings of ocular diseases, revealing the intricate interplay between genes, environment, and disease phenotypes. By integrating genomic data with clinical information, our researchers can pinpoint specific genetic variants associated with inherited retinal dystrophies and other vision-threatening conditions. This understanding facilitates the development of targeted gene therapies and personalized treatment plans, offering hope for previously untreatable conditions. Moreover, computational tools in bioinformatics have enabled our analysis of protein interactions and signaling pathways, providing valuable insights into disease mechanisms and identifying potential drug targets. Deep learning algorithms, trained on vast repositories of retinal images, can detect subtle abnormalities indicative of diabetic retinopathy, age-related macular degeneration, and other retinal diseases with remarkable accuracy. This technology not only enhances the efficiency of screening programs but also enables early detection, crucial for preventing irreversible vision loss. Furthermore, AI-powered tools can automate the segmentation and quantification of ocular structures from optical coherence tomography (OCT) scans, providing objective and reproducible measurements for disease monitoring and treatment evaluation. This integration of AI into clinical practice empowers ophthalmologists with powerful decision-support tools, leading to more precise diagnoses, personalized treatment strategies, and ultimately, improved patient outcomes.

This chapter delves into the cutting-edge methodologies and applications that define the intersection of data science, bioinformatics, and AI at the Department of Ophthalmology. We explore how these disciplines are converging to address some of the most pressing challenges in biology and medicine, from unraveling the complexities of the human genome to developing intelligent systems for drug discovery. The ability to model complex biological systems computationally at our department has accelerated the pace of discovery, bridging the gap between basic research and clinical application.

C. Gustavo De Moraes, MD, PhD, MPH

Overleaf:
Image of 3-D volumes derived from OCT images of patients with various ocular disorders. Kaveri Thakoor, PhD

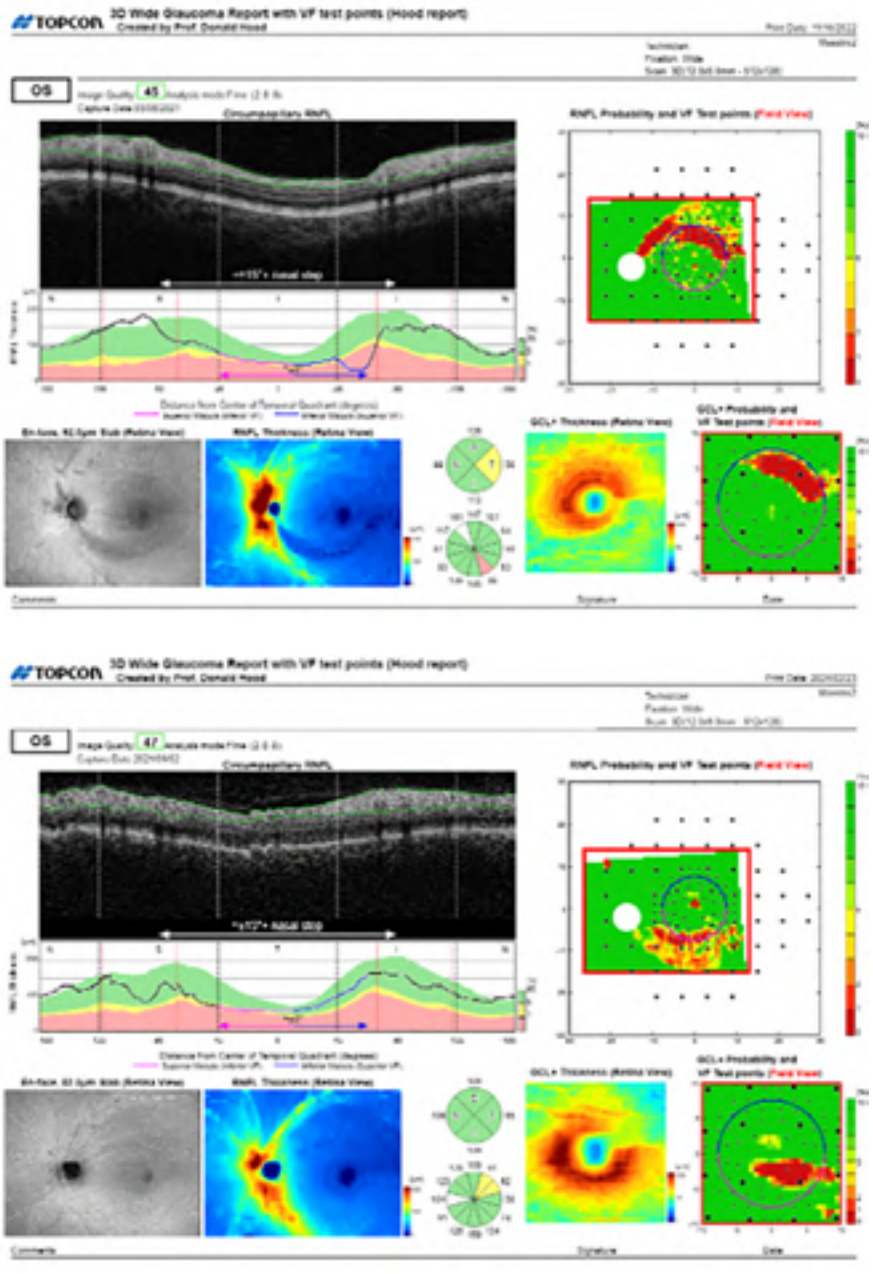


Figure. These two examples, one with inferior (upper panel), the other with superior (lower panel) glaucomatous damage, were successfully detected by the H-T index while the Global cpRNFL metric missed them.

Over the past two decades, there has been an explosion of novel imaging techniques used to examine the eye with greater and greater resolution. Optical coherence tomography (OCT) has become an essential test for diagnosing and monitoring glaucoma, as well as many other ocular disorders. However, there is disagreement on how best to interpret OCT results. Clinicians often rely solely on single summary metrics, but these are prone to false positives and false negatives. The Hood-Tsamis laboratory has focused on applying data analysis techniques to better interpret these extremely large imaging data sets. We recently developed the Hood-Tsamis (H-T) index, a logistic regression modeling metric based on six variables that account for known patterns of damage to the OCT macular ganglion cell layer (GCL+) and cpRNFL. The H-T index showed superior performance, especially in eyes with localized damage affecting the foveal region. The new metric outperforms other conventional OCT metrics for detecting glaucomatous damage, showing the potential to improve accuracy in referrals to glaucoma clinics and in glaucoma definitions for clinical trials. The individual variables of this model could also aid in clinical diagnosis.

Donald Hood, PhD and
Emmanouil Tsamis, PhD

06 Data Science, Bioinformatics + Artificial Intelligence

ARTIFICIAL INTELLIGENCE FOR VISION SCIENCE (AI4VS) LAB

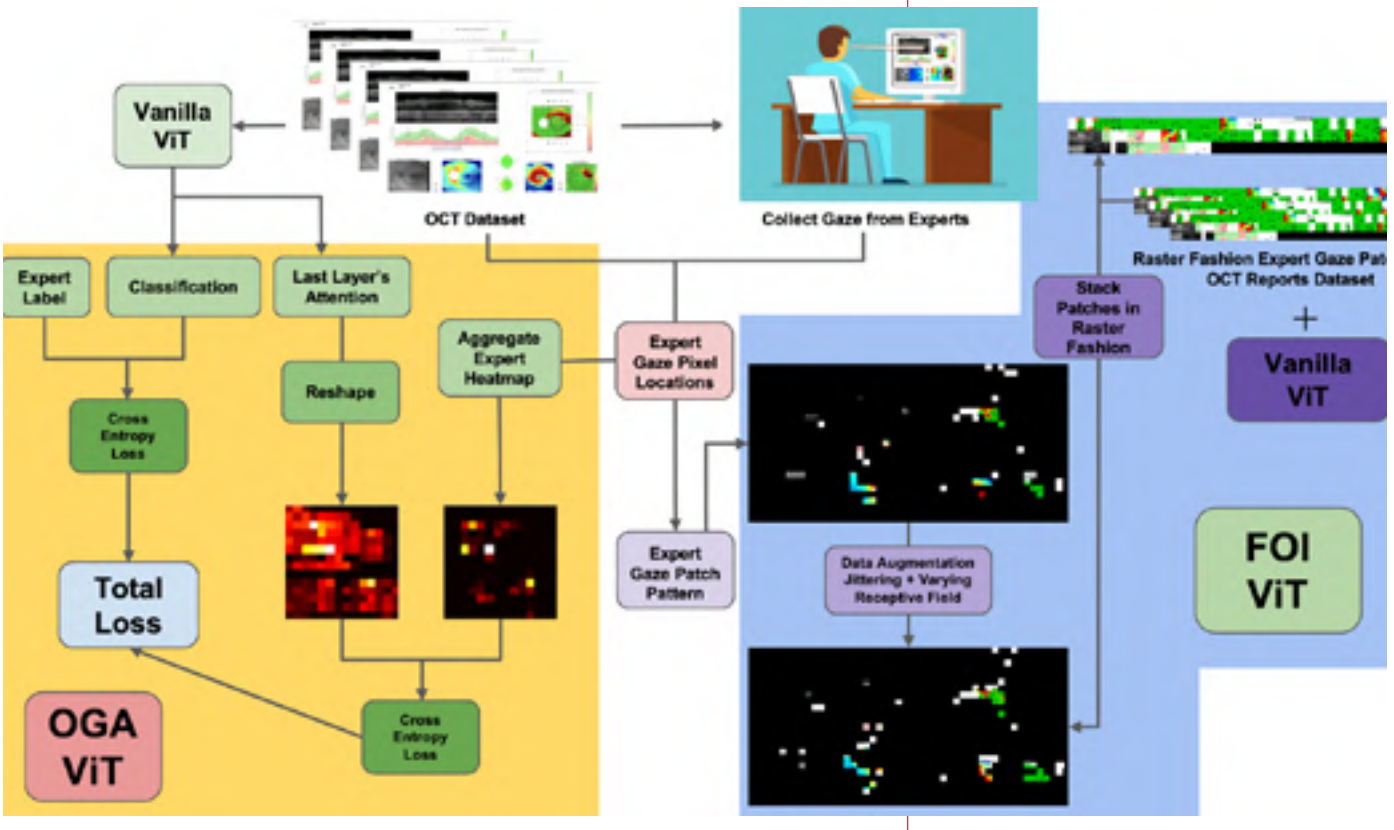


Figure. Flow chart showing distinctions between FOI and OGA ViT algorithms innovated. FOI ViT does not modify the main ViT architecture and only modifies the input image, which is composed only of the raster-stacked patches fixated by the expert ophthalmologist in the order in which the patches were fixated (blue background, right panel of figure). In contrast, OGA ViT modifies the ViT loss function to include a term representing the alignment between the ViT's self-attention and aggregated expert eye-movement attention (yellow background, left panel of figure).

The Artificial Intelligence for Vision Science (AI4VS) Lab, under the direction of Kavi Thakoor, PhD, is bringing 21st-century data science and artificial intelligence into Columbia Ophthalmology. For example, AI4VS is pioneering the integration of medical domain-expert eye tracking as a paradigm-shifting avenue for training AI systems in order to make them more interpretable, accurate, and computationally efficient, both in the ophthalmic clinic and in ophthalmic education. In particular, we utilize medical-expert gaze data to augment state-of-the-art vision transformer (ViT) architectures. Typically, image patches are encoded in the ViT based on their position in the image (e.g., left to right, top to bottom). However, to enable eye-tracking–informed AI, we use eye fixation locations to encode image patches, giving more importance to image patches viewed first or viewed longer/more often. Our fixation-order-informed (FOI) ViT replaces image-structure derived positional embeddings with those learned from the clinician participant's eye movement trajectory to improve downstream glaucoma classification. We are also developing an ophthalmologist gaze augmented (OGA) ViT, which adds an "attention-alignment score" that encourages the ViT's self-attention to "learn" the expert's fixation attention during training. By blending regions from clinician fixations with areas that the ViT pinpoints as important, we aim to bridge existing medical prior knowledge with novel AI-based insights, generating suggestions for clinicians while improving performance for deep learning models.

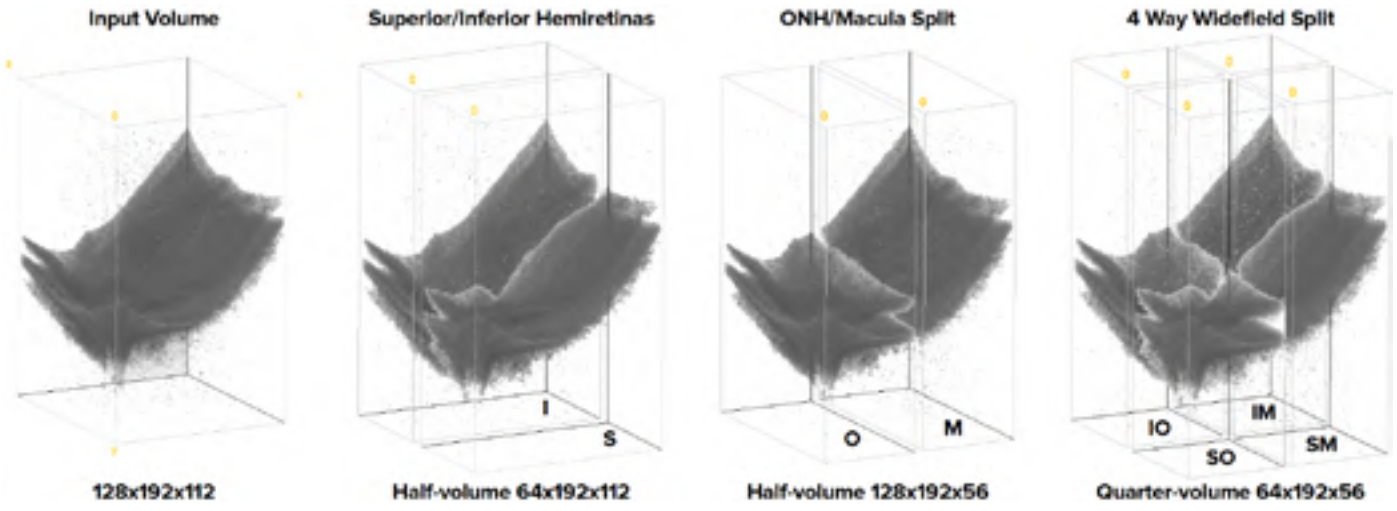


Figure. An example of how we split an OCT volume along different axes to separate the anatomy in the volume. Hemiretina attention uses inferior (I) and superior (S) hemiretinas. Neuron/axon attention is computed using the ONH (O) and macula (M). Hemiretina with neuron/axon attention is computed using the inferior ONH (IO), inferior macula (IM), superior ONH (SO), and superior macula (SM).

In addition, AI4VS is using 3D OCT images to discover novel retinal anatomies in ophthalmic disease and enhancing our diagnostic abilities. For example, glaucoma, one of the top causes of irreversible blindness worldwide, is characterized by thinning of the axons of the ganglion cells that make up the retinal nerve fiber layer (RNFL), which forms the optic nerve that carries visual information from the retina to the rest of the brain. Traditionally, ophthalmologists rely on 2D optical coherence tomography (OCT) reports derived from raw 3D OCT volumes to assess the thickness of the RNFL, but this approach can lead to ambiguity, especially in cases of atypical ocular anatomy or imaging artifacts. Although raw 3D OCT data provides a more comprehensive view of the retina, its complexity and time-intensive analysis present significant hurdles to its practical use.

By leveraging long-range, targeted anatomical relationships between retinal regions in 3D OCT volumes using AI attention mechanisms combined with novel Channel Attention REpresentation (CARE) visualization techniques, we aim to uncover novel correlations between retinal regions that may play a role in the pathophysiology of glaucoma and other ophthalmic disease. Our research will also enable scalable adoption of AI across diverse clinical settings by advancing fundamental model interpretability approaches.
We trained and evaluated our models across four configurations; attention models split the feature volume during training and compute cross-attention between corresponding sub-volumes. Across all datasets, attention-based models significantly outperformed the baseline (no-attention) models.

Kaveri A. Thakoor, PhD

06 Data Science, Bioinformatics + Artificial Intelligence

COMPUTERIZED CELL IDENTIFICATION IN RETINAL DISEASE MODELS

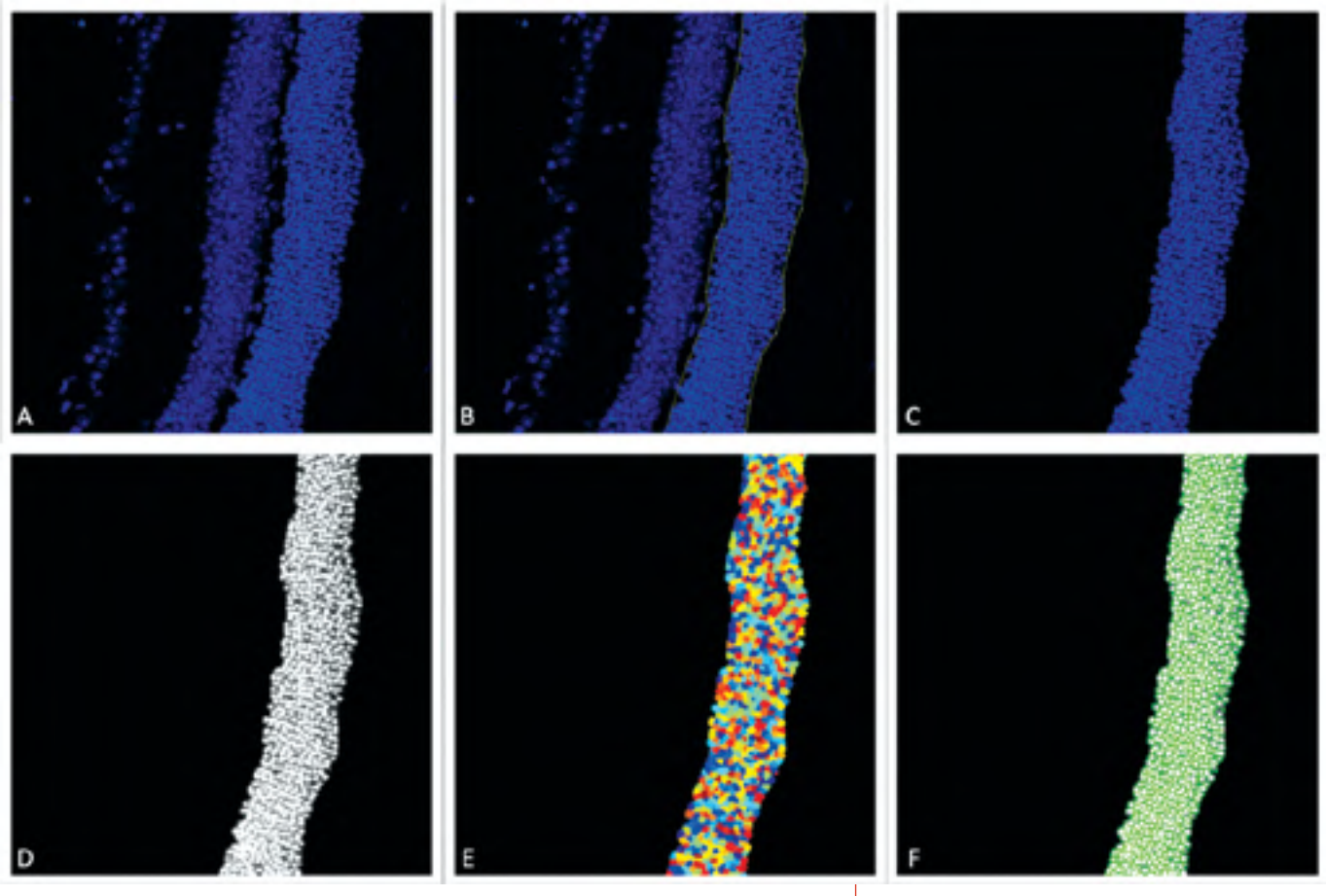


Figure. Automated delineation of the cell borders and computerized cell-counting revealed increased photoreceptor cell death in tissue-specific retinal pigment epithelium hemoglobin (RPE-Hb) knockout animal model.

The Tezel Lab previously described the local production of hemoglobin in the outer retina. Expression of hemoglobin in the outer retina suggests that it plays a role in carrying oxygen to photoreceptor cells, which are known to consume the highest amount of oxygen in the body. We are investigating the impact of deranged retinal pigment epithelium hemoglobin (RPE-Hb) production with age in the pathogenesis of age-related macular degeneration using a RPE-Hb conditional knockout animal model. Our earliest findings reveal that silencing hemoglobin production in the retina causes accelerated loss of photoreceptor cells, similar to age-related macular degeneration. Therapeutic strategies to restore RPE-Hb production may open new avenues for treating age-related macular degeneration.

Tongalp H. Tezel, MD

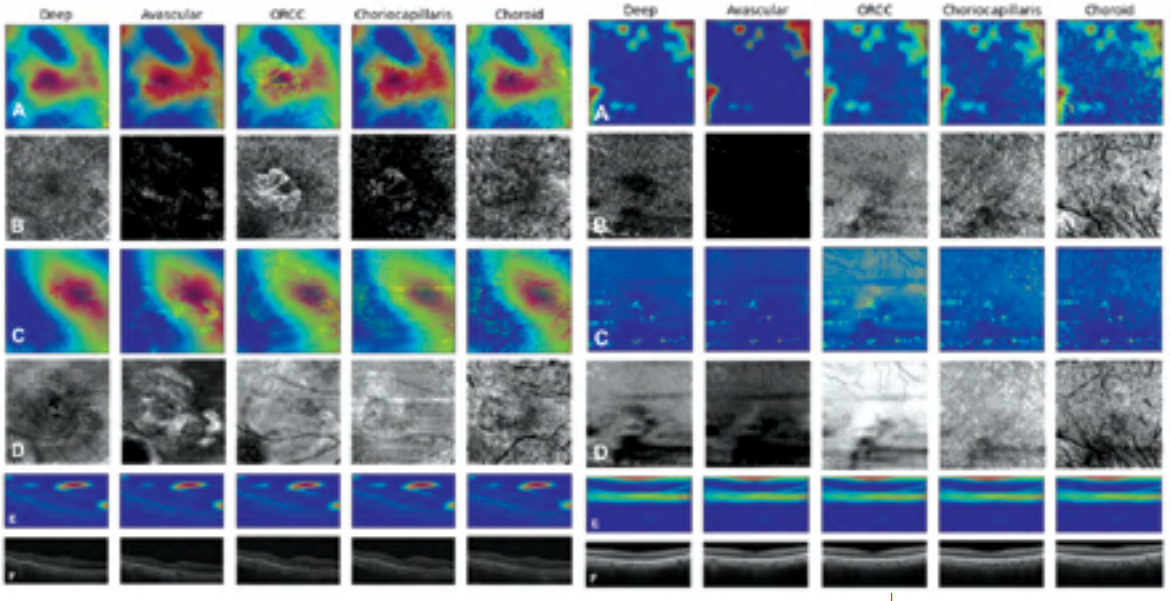


Figure. A deep learning system to distinguish late stages of AMD. Grad-CAMs of false positive (row A) with corresponding structural OCT images in row B. Bright dots in row A may be artifacts, misconstrued by the convolutional neural network as drusen, suggesting the model has learned the importance of drusen for AMD. Bottom: Grad-CAMs of true positive neovascular AMD patients; rows A, C, and E show Grad-CAMS, while corresponding original OCTA, OCT structure, and 5-line b-scan layers are shown in Rows B, D, and F. The model has detected patterns consistent with CNV, shown by the highlighted red/yellow regions in the Grad-CAMs. (Adapted from Thakoor, K.A., Yao, J., Bordbar, D., Moussa, O., Lin, W., Sajda, P. and Chen, R.W., 2022. *A multimodal deep learning system to distinguish late stages of AMD and to compare expert vs. AI ocular biomarkers. Scientific Reports,* 12(1), p. 2585.)

The Artificial Intelligence for Vision Science (AI4VS) Lab collaborates with every clinical division to accelerate the development of potential applications into clinical medicine. One example is the collaboration between Kaveri Thakoor, PhD, and Royce Chen, MD, leveraging AI and deep learning (DL) to speed the identification of patients most likely to benefit from new anti-VEGF therapies for age-related macular degeneration (AMD), a leading cause of blindness that impacts millions of people worldwide. It is estimated that more than 14% of middle-aged and older adults will have AMD within the next 15 years.

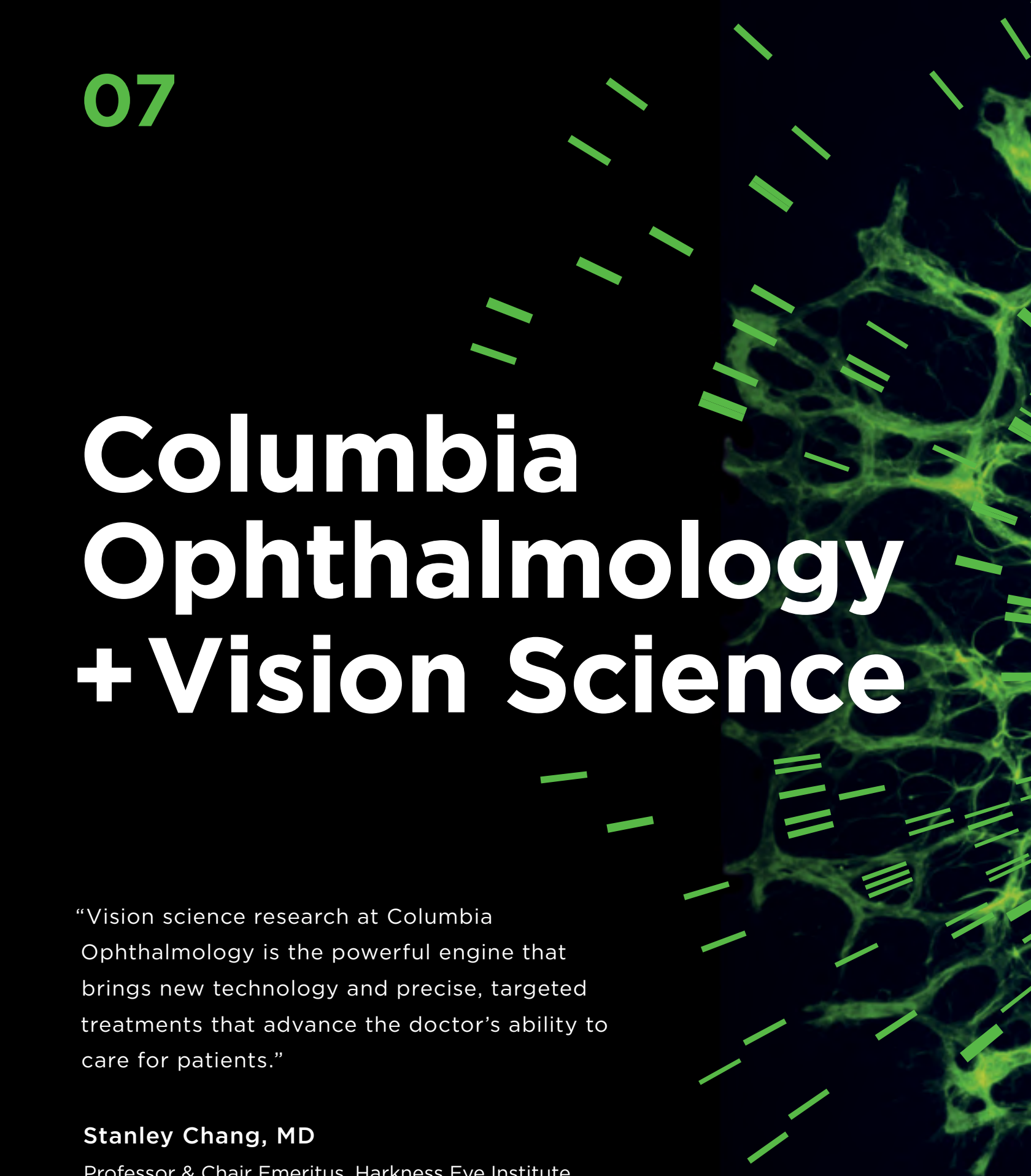
Choroidal neovascularization (CNV) is a key feature of progression to neovascular or "wet" AMD (NV AMD), a late stage of the disease that can rapidly lead to blindness if left untreated. Optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA) have become critical noninvasive imaging modalities for assessment of features (such as intraretinal, IRF, and subretinal fluid, SRF) to measure disease progression and response to treatment.

However, these imaging modalities generate a tremendous amount of volumetric data for each patient, with each volume potentially containing critical evidence for determining disease state. To expedite clinician workflow and expand the amount of data a single ophthalmologist can effectively parse, artificial intelligence (AI) can serve as a "teammate" in screening data volumes that unambiguously belong to specific disease classes. The AI4VS Lab developed a DL system that achieves multiclass detection of non-AMD vs. non-neovascular (NNV) AMD vs. NV AMD from a combination of OCTA, OCT structure, 2D b-scan flow images, and high-definition (HD) 5-line b-scan cubes. Multimodal data were used as input to 2D-3D convolutional neural networks (CNNs). Detection of AMD from OCTA data via CNNs has tremendous potential to expedite screening of early and late-stage AMD patients.

Kaveri A. Thakoor, PhD
and ***Royce W. S. Chen, MD***

07

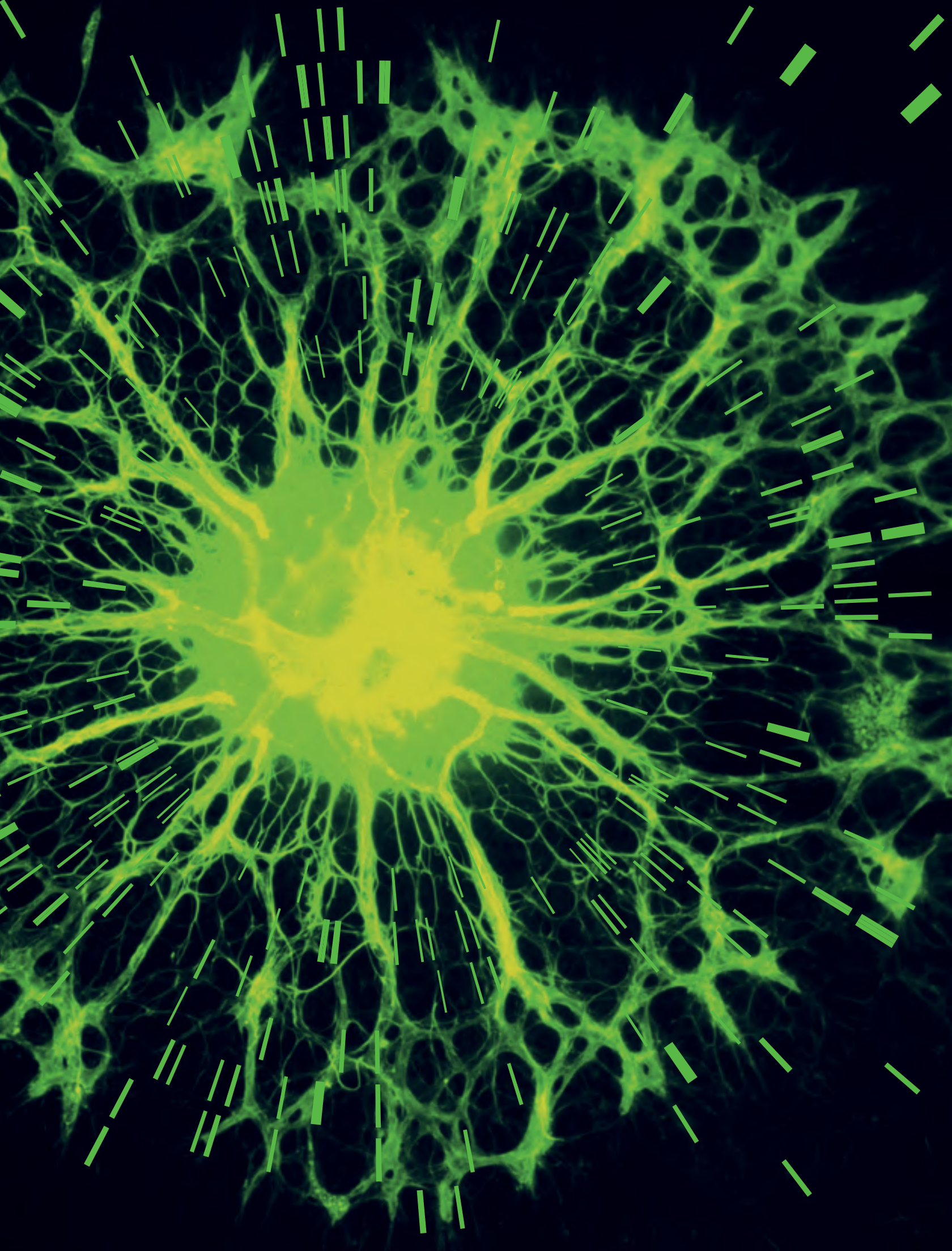
Columbia Ophthalmology + Vision Science



"Vision science research at Columbia Ophthalmology is the powerful engine that brings new technology and precise, targeted treatments that advance the doctor's ability to care for patients."

Stanley Chang, MD

Professor & Chair Emeritus, Harkness Eye Institute



07 Columbia Ophthalmology +Vision Science

Founded in 1866 by Dr. Cornelius Agnew, ophthalmology at the College of Physicians and Surgeons grew through the contributions of early leaders like Drs. Herman and Arnold Knapp. In 1933, the Harkness Eye Institute was established through the philanthropy of Edward S. Harkness, whose endowment continues to support its operations. From its earliest years, the Eye Institute played an important role in vision research and clinical care, shaped by faculty such as Drs. Zacharias Dische, Karl Meyer, Ludwig von Sallman, and George Smelser. Drs. Algernon Reese, Abraham Spector, Stephen Trokel, Max Forbes, Daniel Kirby, Francis L'Esperance, László Z. Bitó, John Flynn, and Stanley Chang contributed to developments in laser therapies, genetic eye disease research, glaucoma treatment, and retinal surgery. These efforts helped establish a reputation for innovation and clinical contributions in ophthalmology. Construction of a new Harkness Eye Institute, designed to provide the care and research environment of the future at Columbia University Irving Medical Center, is scheduled to be completed in 2028.

The 1990s brought new developments under the leadership of Dr. Stanley Chang, who expanded the Department's clinical and research faculty, created endowed professorships, and strengthened research.

Notable recruitments, including Drs. Rando Allikmets, Janet Sparrow, Ron Silverman, Stephen Tsang, James Auran, Daniel Casper, Sri Bearelly, Stephen Trokel, Vivienne Greenstein, and Kosta Petrukhin, helped grow the Department's clinical and research capacities. The formation of NewYork-Presbyterian Hospital in 1998 added further institutional support.

In 2012, Dr. George A. ("Jack") Cioffi became Chair and oversaw significant faculty growth, clinical expansion, and creation of new divisions in ocular oncology, ophthalmic genetics, and neuro-ophthalmology.

He recruited nationally and internationally renowned faculty, including Drs. Xin Zhang, Jeffrey Liebmann, D. Jackson Coleman, Irene Maumenee, Leejee Suh, Jeffrey Odel, Jason Horowitz, Tongalp Tezel, Brian Marr, Lisa Hark, George Florakis, and Simon John, as well as returning former trainees such as Drs. Royce Chen, Lora Dagi Glass, Aakriti Shukla, Ives (Tony) Valenzuela, Gabriel Rand, Vlad Diaconita, and Aliaa Abdelhakim, all of whom contributed to departmental growth and innovation. In recent years, exceptional talent continues to be added to the Columbia Ophthalmology team from across the globe to expand both the depth and breadth of expertise, with the addition of Drs. Danielle Trief, Lauren Yeager, Nan-Kai Wang, Sonali Talsania, Revathi Balasubramanian, Tarun Sharma, Qing Wang, Gustavo De Moraes, Lisa Park, Noga Harizman, Meital Ben Dov, Megan Soucy, Steven Rosenberg, Scott Brodie, Tingting Yang, Emmanouil Tsamis, Kaveri Thakoor, and Gülgün Tezel. The Department's growth and progress reflect its ongoing efforts to advance care and research in ophthalmology.

Overleaf: Postnatal day 5 retina stained with GFAP (green) for astrocytes and IB4 (yellow) for endothelial cells. Xin Zhang, PhD

VISION SCIENCE ACROSS COLUMBIA UNIVERSITY: ILLUMINATING THE PATHWAYS OF SIGHT

Tingting Yang, PhD, Laboratory

Columbia University stands at the forefront of vision science, uniting a dynamic cohort of researchers who decode the complexities of sight, from molecular mechanisms to cognitive perception. Pioneers like Dr. Carol A. Mason map the intricate choreography of visual system development, revealing how retinal neurons wire the brain, while Dr. Dritan Agalliu investigates neurovascular interactions critical for ocular health, uncovering links between blood-brain barrier integrity and vision disorders. Drs. Yasmine El-Shamayleh and Michael E. Goldberg bridge species, studying primate visual circuits to unravel how the brain transforms light into perception and action. This unique interdisciplinary synergy, spanning developmental biology, neurophysiology, and systems neuroscience, positions Columbia as a nexus for understanding vision's biological foundations and vulnerabilities.

At the intersection of innovation and inquiry, Columbia's vision scientists dissect both the microscopic and systemic drivers of sight. Dr. Erin L. Barnhart explores the mechanism of cellular organelles shaping neuronal responses, while Dr. Andrew Tomlinson leverages Drosophila genetics to decode conserved molecular pathways in eye development. Cognitive neuroscientists like Dr. Mariam Aly probe the interplay between memory and visual processing, revealing how prior experiences sculpt what we see. Meanwhile, Dr. Rafael Yuste pioneers cutting-edge neurotechnologies, imaging neuronal activity in real time to decode visual cortex dynamics. These efforts are complemented by Dr. Jian Yang's study of ion channels, which are crucial for converting light into electrical signals, and Dr. Filippo Mancia's structural insights into proteins implicated in vision loss. Together, they illuminate the full spectrum of visual function, from single molecules to conscious experience.

Translating discovery into impact, Columbia's researchers redefine therapeutic frontiers. Agalliu's work on neurovascular crosstalk informs treatments for diabetic retinopathy, while Mason, Barnhart, and Tomlinson's foundational studies on cellular morphogenesis offer blueprints for regenerative therapies, and Yuste's neuroengineering breakthroughs hint at future interventions for blindness. Clinical insights from El-Shamayleh and Goldberg refine strategies for restoring vision in neurodegenerative diseases, underscoring Columbia's commitment to merging basic science with patient-centered innovation. United by a mission to preserve and enhance sight, these collaborations exemplify how interdisciplinary vision science transforms lives—one discovery at a time.

Stephen Tsang, MD, PhD

07 Columbia Ophthalmology +Vision Science

Over the past decade, the Department of Ophthalmology has nearly doubled its residency size and surgical volumes while earning recognition as the top ophthalmology training program in New York City and among the top 20 nationally (Doximity Residency Navigator). One hundred percent of Columbia's Vagelos College of Physicians & Surgeons medical students who sought ophthalmology residency positions have matched into U.S. ophthalmology residencies, including Columbia, Massachusetts Eye and Ear Infirmary, Bascom Palmer Eye Institute, and University of California-San Francisco, compared with a national match rate of approximately 75%. This equates to more than three dozen trainees over the past decade. The Department established new fellowships in pediatric ophthalmology and ocular oncology, introduced an integrated internship program in 2021, and enhanced core didactics through daily Morning Report, a revised lecture series, and a monthlong Basic & Clinical Science Course. Surgical education innovations, including a structured cataract curriculum and risk-stratification systems, have lowered trainee complication rates to match faculty practice levels. Clinical training spans major hospitals, including NYP-Columbia, Harlem Hospital, and NYP Children's Hospital. These efforts position the Department to lead a new era of precision ophthalmology education at the future Harkness Eye Institute.

Vagelos Education Center

COLUMBIA EDUCATIONAL PROGRAMS

Lisa Park, MD, teaching in East Africa.

Resident Luke Oh, MD, on HelpMeSee simulator

In addition to innovations in surgical and clinical training, the Department has prioritized simulation and resident wellness. A brand-new resident wet-lab, featuring two operating microscopes (expanding to four), was completed in 2023, with a formalized monthly curriculum underway. Residents participate in diverse wet-lab experiences, from vitrectomy and glaucoma shunt labs to the "Suturing Olympics." The program also invests heavily in virtual simulation, with residents completing the 40-hour HelpMeSee™ simulation course, improving surgical readiness. Applicant interest has nearly doubled over the past decade, with applications rising from fewer than 400 to over 700 annually. Fellowship placement remains strong, with 90% of graduates pursuing additional training and over 75% holding academic appointments. These achievements reflect the Department's commitment to cultivating skilled, resilient, and academically engaged ophthalmology leaders.

CLINICAL EXPANSION THROUGHOUT THE REGION & BEYOND

Through strategic expansion and thoughtful recruitment, the Department of Ophthalmology has built a robust clinical program that serves both the local community and the wider region. The Department now offers comprehensive subspecialty services, including corneal surgery, pediatric ophthalmology, clinical genetics, oncology, and rare disease identification. The Department provides more than 110,000 patient visits per year, with over 80,000 originating within the Columbia Ophthalmology Faculty Practice. Our care teams see patients in midtown Manhattan, the Upper West Side, in Westchester county and on the Columbia University Irving Medical Center campus. In addition, the NewYork-Presbyterian Ambulatory Care Network Eye Clinic manages over 20,000 visits annually, offering accessible care to patients regardless of insurance status. Integration with NYPH ensures smooth coordination of referrals and follow-up care. Recently renovated interim space at the Vanderbilt Clinic provides improved access, supported by additional clinical and administrative staff. At Harlem Hospital, faculty and residents manage over 10,000 patient visits per year, with expanded services in retinal surgery and emergency ophthalmology. These developments reflect the Department's continued focus on strengthening care delivery, expanding access, and maintaining high standards across its clinical operations.

Robert Burch Family Eye Center

Harlem Hospital Center

NewYork-Presbyterian The One in Westchester

07 Columbia Ophthalmology +Vision Science

Administrative offices, Presbyterian Hospital building

"Building for success" at Columbia University's Edward S. Harkness Eye Institute reflects both a physical and metaphorical commitment to excellence in eye care, research, and education. The Department of Ophthalmology reflects this ethos through state-of-the-art facilities designed to support advanced clinical care, groundbreaking research, and interdisciplinary collaboration. These modern spaces provide the infrastructure necessary for high-level innovation and patient-centered service. The Department is also building for success by fostering a culture of intellectual rigor, mentorship, collegiality, and forward-thinking leadership. Through investment in talent development, pioneering research programs, and community engagement, Columbia Ophthalmology is constructing a resilient foundation that ensures sustained progress and global impact in vision science and ophthalmic care.

Research labs, Hammer Health Sciences Center

THE NEW HARKNESS EYE INSTITUTE

Columbia University's Department of Ophthalmology is embarking on a transformative journey with the construction of a new state-of-the-art facility designed by the esteemed architectural firm Studio Gang. To be called "The Beacon" and scheduled for completion by 2028, this modern building will double the Department's current space and feature new eye operating rooms, significantly enhancing the capacity for advanced ophthalmic care. The design emphasizes cutting-edge technology and patient-centered environments, aligning with the Department's commitment to delivering 21st-century eye care. The new facility will also serve as a hub for interdisciplinary collaboration, housing not only ophthalmology but related, highly specialized imaging suites. This integration fosters a multidisciplinary approach to research and treatment, encouraging innovations that span various fields of medicine. By bringing together diverse specialties under one roof, the building is poised to become a nexus for pioneering research and comprehensive patient care. These enhancements are designed to support the training of future ophthalmologists and vision scientists, ensuring that Columbia remains at the forefront of medical education. The new building represents a physical and symbolic commitment to excellence, embodying the Department's vision for a future where innovation, collaboration, and superior patient care converge.

The Harkness Eye Institute will be located in "The Beacon," opening in 2028.

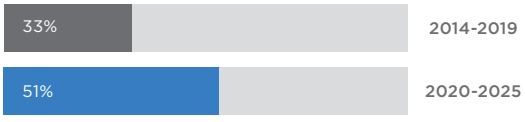
08 Department Data

40+ Ongoing Clinical Trials

300+ Abstracts & Publications in the last year

Top 10
NIH Funding

51%
Growth in Overall Departmental Budget
over 5 years



Federal Funding FY19
$10.4M

Federal Funding FY25
$11.5M

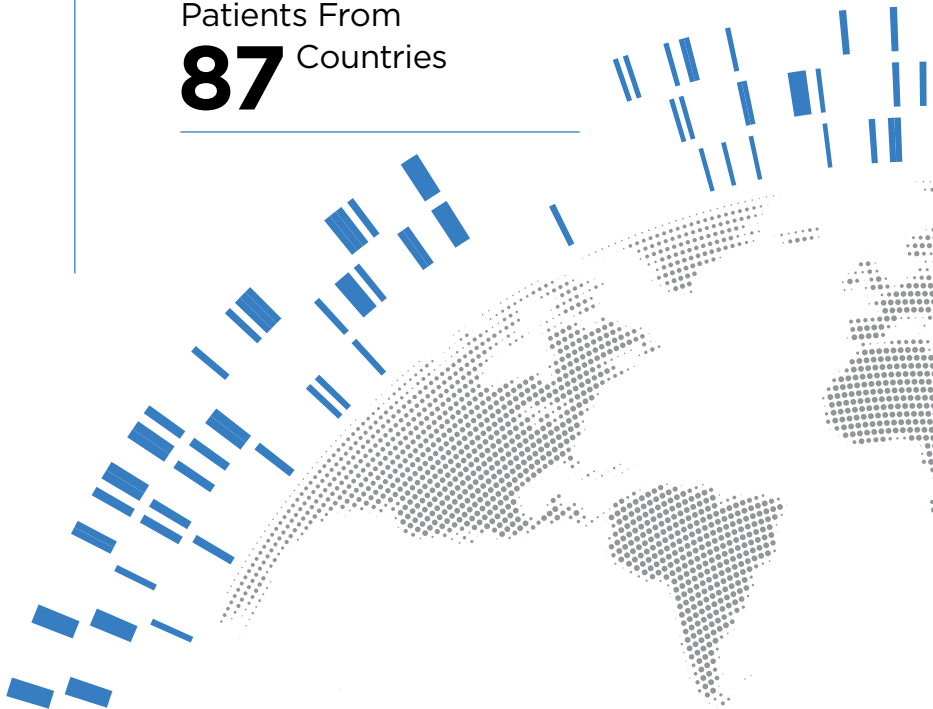
300+
Total Staff and Faculty

- **56** Full-Time Clinical & Research Faculty
- **16** Ophthalmology Residents
- **8** Clinical Fellows
- **15** Principal Investigators
- **10** Postdoctoral Fellows and Scientists

5,000+
Surgeries Annually

110,000+
Patient Visits Annually

Patients From
87 Countries



MAJOR FUNDED PROGRAMS

Basic and Clinical Science Course in Ophthalmology (BCSCO)

Jonas Vision Research Laboratory

Bernard and Shirlee Brown Glaucoma Research Laboratory

Foley Retina Research Fund

Kirby Fellowship

Robert Burch Family Eye Center

The Louis V. Gerstner Jr. Clinical Research Center in Vision at Columbia University

Stephen Ross Pediatric Eye Center

Florence and Herbert Irving Translational Vision Research Lab

Bernard and Shirlee Brown Glaucoma Initiative

Edith and Denton McKane Memorial Fund

Gloria and Louis Flanzer Vision Care Center

The Starr Foundation Retina Research Unit

Flanzer Eye Center

C.V. Starr Scholarship Fund

Gloria Cestone Young Faculty Development Fund

Jonas Children's Vision Care

Retinoblastoma Research Fund

Eye Surgery Fund

Kaplen Retina Research Fund

Stem Cell Transplantation Fund

Chang-Burch Scholars Fund

Frederick A. Jakobiec, MD, DSc Annual Research Prize

Myles Behrens, MD, Prize Fund

ENDOWED PROFESSORSHIPS

William and Donna Acquavella Professor – Rando L. Allikmets, PhD

Malcolm Aldrich Clinical Professor – George J. Florakis, MD

Malcolm Aldrich Research Professor – Xin Zhang, PhD

László Z. Bitó Professor – Stephen H. Tsang, MD, PhD

Shirlee and Bernard Brown Professor – Jeffrey M. Liebmann, MD

Robert L. Burch III Professor – Simon John, PhD

Chang Family Professor – Tongalp H. Tezel, MD

Anne S. Cohen Professor – Steven E. Rosenberg, MD

Jean and Richard Deems Professor – G.A. (Jack) Cioffi, MD

Anthony Donn Professor – Janet R. Sparrow, PhD

John Wilson Espy, MD, Professor – Brian P. Marr, MD

Edward S. Harkness Professor & Chair – G.A. (Jack) Cioffi, MD

Herbert and Florence Irving Professor – Vacant

D. H.-Kauffmann Jokl Family Professor – Jeffrey G. Odel, MD

Helen and Martin Kimmel Assistant Professor – Ives A. Valenzuela, MD

Leonard A. Lauder Associate Professor – Aakriti Garg Shukla, MD, MSc

Jean Sheng Associate Professor – Royce W.S. Chen, MD

Miranda Wong Tang Professor – Leejee H. Suh, MD

K.K. Tse and Ku Teh Ying Professor – Stanley Chang, MD

DIRECTORSHIP

A. Gerard DeVoe – B. Dobli Srinivasan Director of the Harkness Eye Clinic – Jason D. Horowitz, MD

ENDOWED FELLOWSHIPS

Foley Clinical Vitreoretinal Fellowship

Danny H.-Kauffmann Jokl, MD, International Vitreoretinal Fellowship

Danny H.-Kauffmann Jokl Neuro-Ophthalmology Fellowship

Mohapatra Pediatric Ophthalmology and Strabismus Fellowship

Jean and Kent Sheng Glaucoma Fellowship

ENDOWED LECTURESHIPS

Stanley Chang, MD Lectureship

Arthur Gerard DeVoe, MD Lectureship

Zacharias Dische, MD Lectureship

John H. Dunnington, MD Lectureship

John Flynn, MD Memorial Lectureship

Max Forbes, MD Lectureship

The Barbara and Donald Jonas Lectureship

Ulrich Ollendorff, MD Lectureship

David Pearce, MD Memorial Lectureship

George K. Smelser, MD Lectureship

Abraham Spector, MD Prize Lectureship

Florence Epstein Teicher Lectureship

Lori Zabar Lectureship

08 Department Data

PHILIP KNAPP MEMORIAL TEACHING AWARD

The Philip Knapp Memorial Teaching Award honors the legacy of Dr. Philip Knapp, a pioneering ophthalmologist and educator at Columbia University. Presented by the residents of the Edward S. Harkness Eye Institute, the award recognizes a faculty member for dedication and outstanding contributions to resident clinic and surgical education.

2024
Lisa Park, MD
Ives (Tony) Valenzuela, MD

2023
James D. Auran, MD
Roslyn Stahl, MD

2022
Lisa Park, MD

2021
Noga Harizman, MD

2020
Roslyn M. Stahl, MD

2019
Steven Brooks, MD

2018
James D. Auran, MD

2017
G. A. (Jack) Cioffi, MD
Roslyn M. Stahl, MD

2016
Steven Brooks, MD
John Henry Johnson, MD

2015
Bryan Winn, MD

2014
G. A. (Jack) Cioffi, MD
Roslyn M. Stahl, MD

2013
Michael Kazim, MD

2012
Howard Eggers, MD

2011
Jason D. Horowitz, MD

2010
Michael Chiang, MD

2009
Michael Weiss, MD

JOHN MARTIN WHEELER MEMORIAL TEACHING AWARD

The John Martin Wheeler Memorial Teaching Award honors the enduring legacy of Dr. Wheeler, the founding director of the Eye Institute and a pioneering educator who helped shape modern clinical practice. Presented by the residents of the Edward S. Harkness Eye Institute, this award is given to a faculty member who exemplifies Dr. Wheeler's commitment to resident teaching and ophthalmology.

2024
Tarun Sharma, MD
Jason D. Horowitz, MD

2023
Steven E. Rosenberg, MD
Michael Weiss, MD

2022
Tarun Sharma, MD

2021
Hanna Coleman, MD

2020
G. A. (Jack) Cioffi, MD

2019
Royce W. S. Chen, MD

2018
Jason D. Horowitz, MD

2017
Jason D. Horowitz, MD

2016
Hanna Coleman, MD

2015
Stanley Chang, MD

2014
Hermann D. Schubert, MD

2013
Jeffrey G. Odel, MD
Michael Weiss, MD

2012
Max Forbes, MD

2011
Bryan Winn, MD

2010
Roslyn M. Stahl, MD

2009
Amilia Schrier, MD

BOARD OF ADVISORS

William Acquavella
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Edward Enninful
Arthur Hershaft
Leslie Hinton
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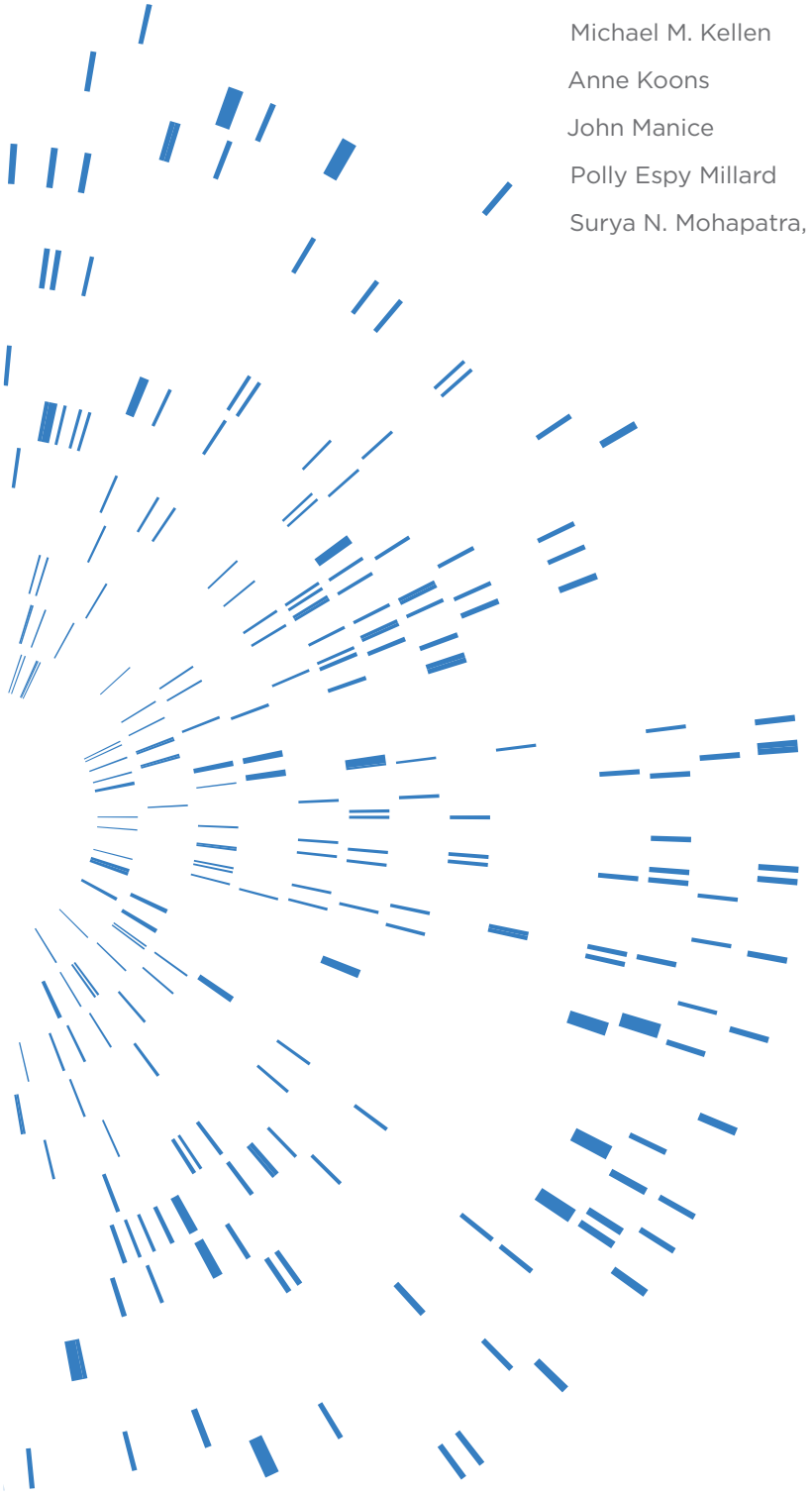
Anne Koons
John Manice
Polly Espy Millard
Surya N. Mohapatra, PhD
Alan Richard Morse, JD, PhD
Stephen Ollendorff
Jean Sheng
Frederick N. Sheppard
James Shinn
Adam Silver
Miranda Wong Tang
Stanley Zabar
Gregory Zaic
Sir Howard Stringer, Chair Emeritus
Louis V. Gerstner Jr., Chair Emeritus



IN MEMORIAM

Shirley R. Brown
Bernard A. Brown
Gloria Milstein Flanzer
Louis Flanzer
T.C. Hsu
Florence Irving
Herbert Irving
Helen L. Kimmel
Martin S. Kimmel
Henry A. Kissinger
Seymour Milstein
Bjørg Ollendorff
J. Dukes Wooters, Jr.

08 Department Data

DEPARTMENT FACULTY

CLINICAL FACULTY BY SUBSPECIALTY

Comprehensive Ophthalmology
Lisa Park, MD – Division Director
James D. Auran, MD

Cornea & Refractive Surgery
Leejee H. Suh, MD – Division Director
George H. Florakis, MD
Jerry Hsu, MD
Gabriel M. Rand, MD
Danielle Trief, MD, MSc

Glaucoma
Jeffrey M. Liebmann, MD – Division Director
G. A. (Jack) Cioffi, MD
Noga Harizman, MD
C. Gustavo De Moraes, MD, PhD, MPH
Aakriti Garg Shukla, MD, MSc
Roslyn M. Stahl, MD
Ives A. Valenzuela, MD
Qing Wang, MD, PhD

Neuro-Ophthalmology
Jeffrey G. Odel, MD – Division Director
Meital Ben Dov, MD

Pediatric Ophthalmology
Steven E. Rosenberg, MD – Division Director
Daphna Mezad-Koursh, MD
Sonali D. Talsania, MD
Lauren B. Yeager, MD

Ophthalmic Oncology
Brian P. Marr, MD – Division Director

Oculoplastic and Reconstructive Surgery
Lora R. Dagi Glass, MD – Division Director
Rupin N. Parikh, MD

Optometry and Contact Lens
Daniel Diamond, OD, FAAO
Sharon P. Keh, OD, FAAO
Alicia Jones, OD
Rebecca Rojas, OD, FAAO

Retina and Vitreoretinal Surgery
Tongalp H. Tezel, MD – Division Director
Aliaa H. Abdelhakim, MD, PhD
Srilaxmi Bearelly, MD, MHS
Scott E. Brodie, MD, PhD
Stanley Chang, MD
Royce W. S. Chen, MD
Vlad Diaconita, MD
Jason D. Horowitz, MD
Tarun Sharma, MD
Stephen H. Tsang, MD, PhD

Applied Genetics
Stephen H. Tsang, MD, PhD – Service Co-Director
Aliaa H. Abdelhakim, MD, PhD – Service Co-Director
Irene H. Maumenee, MD
Megan Soucy, MS, CGC

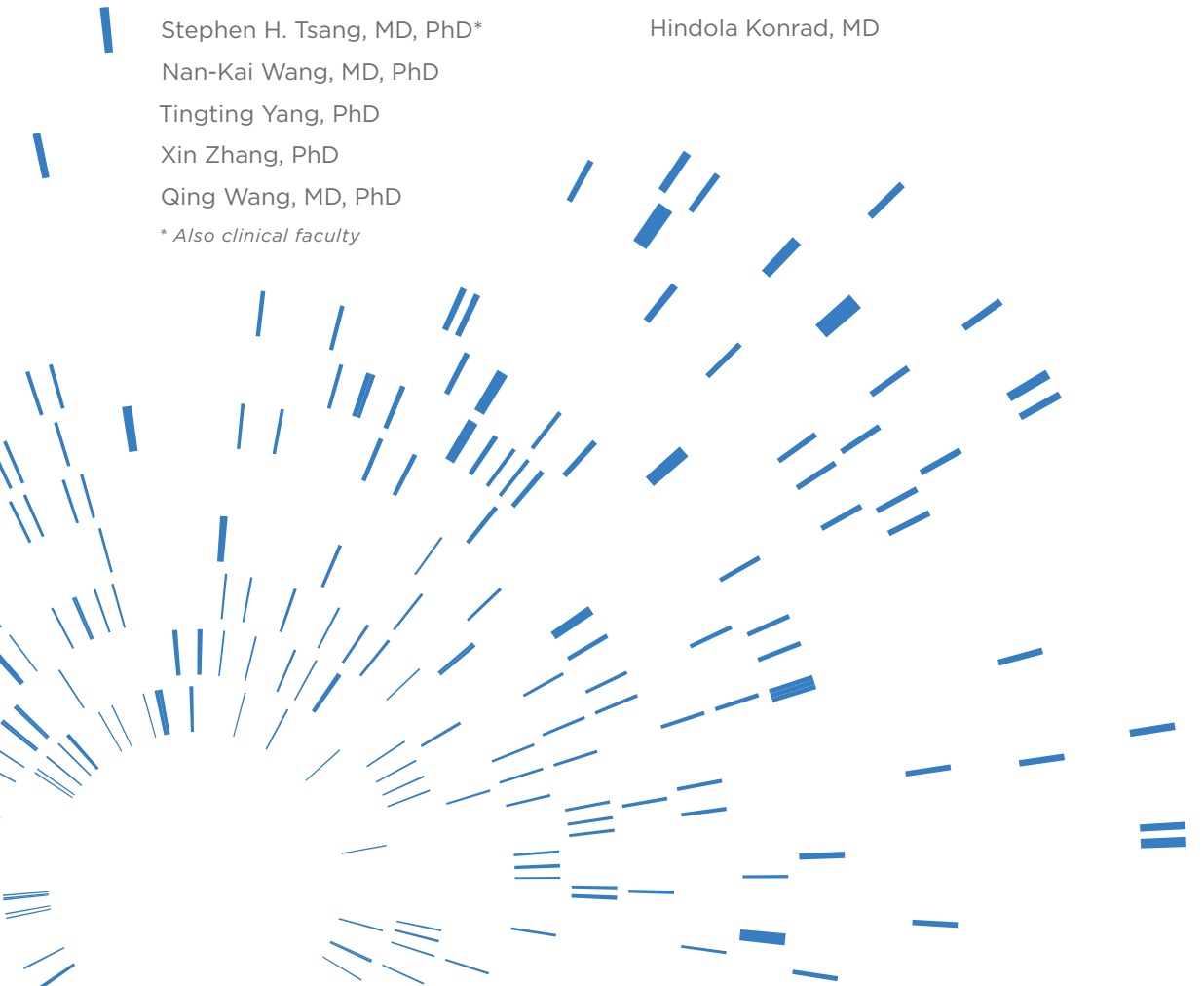
RESEARCH FACULTY

Rando L. Allikmets, PhD
Revathi Balasubramanian, PhD
Srilaxmi Bearelly, MD, MHS*
C. Gustavo De Moraes, MD, PhD, MPH*
Lisa A. Hark, PhD, MBA
Donald Hood, PhD
Simon John, PhD
Carol A. Mason, PhD
Irene H. Maumenee, MD
Takayuki Nagasaki, PhD
Konstantin Petrukhin, PhD
Lawrence S. Shapiro, PhD
Ronald H. Silverman, PhD
Janet R. Sparrow, PhD
Gülgün Tezel, MD
Tongalp H. Tezel, MD*
Kaveri A. Thakoor, PhD
Emmanouil Tsamis, PhD
Stephen H. Tsang, MD, PhD*
Nan-Kai Wang, MD, PhD
Tingting Yang, PhD
Xin Zhang, PhD
Qing Wang, MD, PhD

** Also clinical faculty*

TEACHING FACULTY

Alexandra Braunstein, MD
Robert Braunstein, MD
Daniel S. Casper, MD (Emeritus)
Donald J. Coleman, MD (Emeritus)
Hanna Coleman, MD
Arthur Cotliar, MD
Jeremy Cotliar, MD
Stephen Doro, MD
Nancy Fan-Paul, MD, MPH
Elliott Feinman, MD
Max Forbes, MD (Emeritus)
Pamela F. Gallin, MD
Gennifer Greebel, MD
Vivienne C. Greenstein, PhD (Emeritus)
Thomas E. Flynn, MD
Danny H.-Kauffmann Jokl, MD
Steven A. Kane, MD
Michael Kazim, MD
Hindola Konrad, MD
Paul Krawitz, MD
Martin Lederman, MD
Carolyn Lederman-Barotz, MD
Martin L. Leib, MD
Peter Libre, MD
Robert Lopez, MD
Eli Marcovici, MD
Peter Maris, Jr., MD
John C. Merriam, MD
Peter Michalos, MD
Alan Morse, JD, PhD
Louis Pizzarello, MD
Dan Reinstein, MD
Stephen L Trokel, MD
Hermann D. Schubert, MD
Michael Weiss, MD, PhD
Eric Wolf, MD
Lawrence Yanuzzi, MD



DEPARTMENTAL PAGES

01 Columbia Ophthalmology Department Overview

Highlights Columbia's commitment to innovate clinical care of eye disorders, advance knowledge in medicine through research, and train the next generation of clinicians and scientists.

02 Ophthalmology Education

Outlines Columbia's residency, fellowship, and medical student programs.

03 Department History

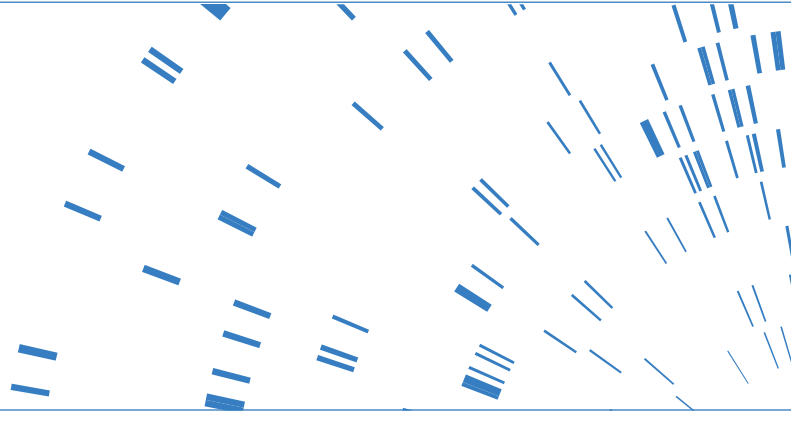
Traces our origins from the 1800s, highlighting pioneering faculty, facilities, and milestones that shaped Columbia's role in patient care and research.

04 Precision Ophthalmology

Describes Columbia's personalized medicine approach using genetics, imaging, and stem cell therapies to treat retinal degenerations and other complex eye conditions.

05 Viewpoint Newsletter

Viewpoint is the official publication that presents biannual updates on research advances, faculty achievements, clinical innovations, and other department news.

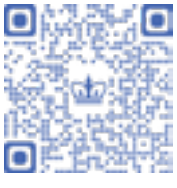


06 Our Faculty

Showcases over 50 faculty members, offering insights into their roles, research interests, patient services, and clinical expertise.

07 Ophthalmology Patient Care

Details the wide array of clinical services, ranging from simple eye examinations for vision correction to sophisticated diagnostics and treatments for all eye conditions by top specialists across Columbia's multiple eye centers.



08 Giving Opportunities

Describes ways to support research projects, new investigator recruitments, fellowships, and special funds that advance clinical innovation, education, and patient care in ophthalmology.

09 Vagelos College of Physicians & Surgeons

Provides comprehensive information on Columbia's medical school, including academic programs, research, and clinical departments.

10 Comprehensive Ophthalmology and Optometry Division

Columbia's optometrists and ophthalmologists provide comprehensive vision care through a wide range of diagnostic and screening services to treat general eye conditions.

11 Cornea & Refractive Surgery Division

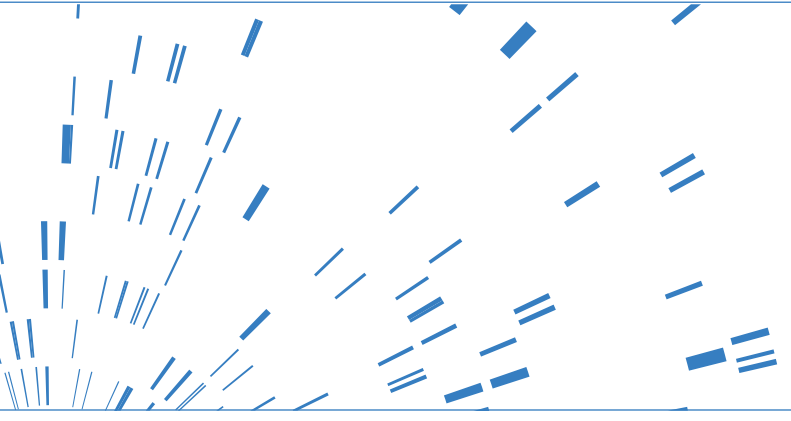
Cornea and External Disease specialists treat conditions such as corneal dystrophies, corneal infections, and refractive or visual problems with advanced medical and surgical care options.

12 Glaucoma Division

Columbia's glaucoma specialists are at the forefront of diagnosing, treating, preventing, and studying glaucoma to manage and slow the progression of this vision-threatening disease.

13 Neuro-Ophthalmology Division

Our Neuro-Ophthalmology specialists are experts in diagnosing and managing neurologic and systemic disorders that affect how the brain perceives vision and the complicated and intricate connections between the eyes and the brain.



14 Oculoplastic and Reconstructive Surgery Division

Meet the Oculoplastic surgeons who treat disorders involving the eyelids, tear drainage system, and orbit, providing both functional and cosmetic procedures to restore appearance and improve vision-related structures.

15 Ophthalmic Oncology Division

As a recognized center of excellence for rare and complex cancers, Columbia's Ophthalmic Oncology physicians diagnose and treat intraocular tumors using advanced therapies and multidisciplinary expertise while engaging in rigorous research.

16 Pediatric Ophthalmology Division

Our pediatric eye specialists are expertly trained to diagnose, monitor, and treat the complete range of pediatric eye conditions and adult strabismus.

17 Retina and Vitreoretinal Surgery Division

Our Vitreoretinal Specialists diagnose and treat macular degeneration, diabetic retinopathy, and other retinal diseases using the most advanced medical and surgical treatments.

18 Applied Genetics Service

Applied Genetics is an innovative program that takes an interdisciplinary approach to evaluate ophthalmic disorders of genetic origin using advanced testing, counseling, and personalized care.

RESEARCH LAB PAGES & PROFILES

19 Allikmets Lab

The Allikmets Lab aims to discover genetic defects underlying Mendelian and complex eye disorders, like Stargardt disease, to develop diagnostic tools and new approaches for gene-based therapies.

20 Balasubramanian Lab

The Balasubramanian Lab investigates Schlemm's canal and trabecular meshwork development to understand congenital glaucoma.

21 Clinical Trials

Lists active clinical studies that explore innovative treatments for glaucoma, macular degeneration, and corneal diseases, including gene therapy.

22 Community-Based Research

Improving vision care access for underserved communities using telehealth screenings and innovative outreach

23 G. Tezel Lab

The Gülgün Tezel Lab evaluates the complex disease of glaucoma, exploring cellular mechanisms of glaucomatous neurodegeneration and identifying new treatment targets.

24 Hood Lab

The Hood Lab studies the anatomical, behavioral, and physiological bases of visual processing in normal and diseased eyes, focusing on early detection and monitoring of glaucoma and retinal disorders.

25 John Lab

The John Lab studies glaucoma and neurodegenerative diseases using genetics, metabolism studies, and mouse models to provide new understanding of disease mechanisms and improve care.

26 Mason Lab

Dr. Mason studies how nerve cells in our eyes grow and connect to the brain, allowing us to see. Understanding these cells could lead to new therapies to restore vision to the blind.

27 Petrukhin Lab

Investigates the molecular mechanisms of retinal degeneration, particularly age-related macular degeneration (AMD), aiming to identify therapeutic targets and develop new treatments to preserve vision.

28 Silverman Lab

The Silverman Lab develops high-resolution imaging systems, high-intensity ultrasound, and photoacoustic technologies for diagnosing ocular diseases.

29 Sparrow Lab

The Sparrow Lab studies the causal link between the intracellular accumulation of lipofuscin fluorophores and retinal pigmented epithelial (RPE) cell death and explores therapies to reduce cellular damage.

30 T. Tezel Lab

The Tongalp Tezel Lab investigates retinal degenerative diseases, exploring molecular mechanisms, gene therapy for age-related macular degeneration, and novel techniques to preserve vision.

31 Thakoor Lab

The Thakoor Lab develops human-vision-inspired AI tools to augment and assist clinicians in accurate and fast detection of eye diseases.

32 Tsamis Lab

The Tsamis Lab focuses on enhancing glaucoma detection using technologies of optical coherence tomography (OCT) and perimetry (visual fields) for earlier, more accurate diagnosis.

33 Tsang Lab

The Tsang Lab focuses on genome engineering/CRISPR approaches to reprogramming metabolome in the retina and therapeutics to treat neurodegenerative disorders.

34 Wang Lab

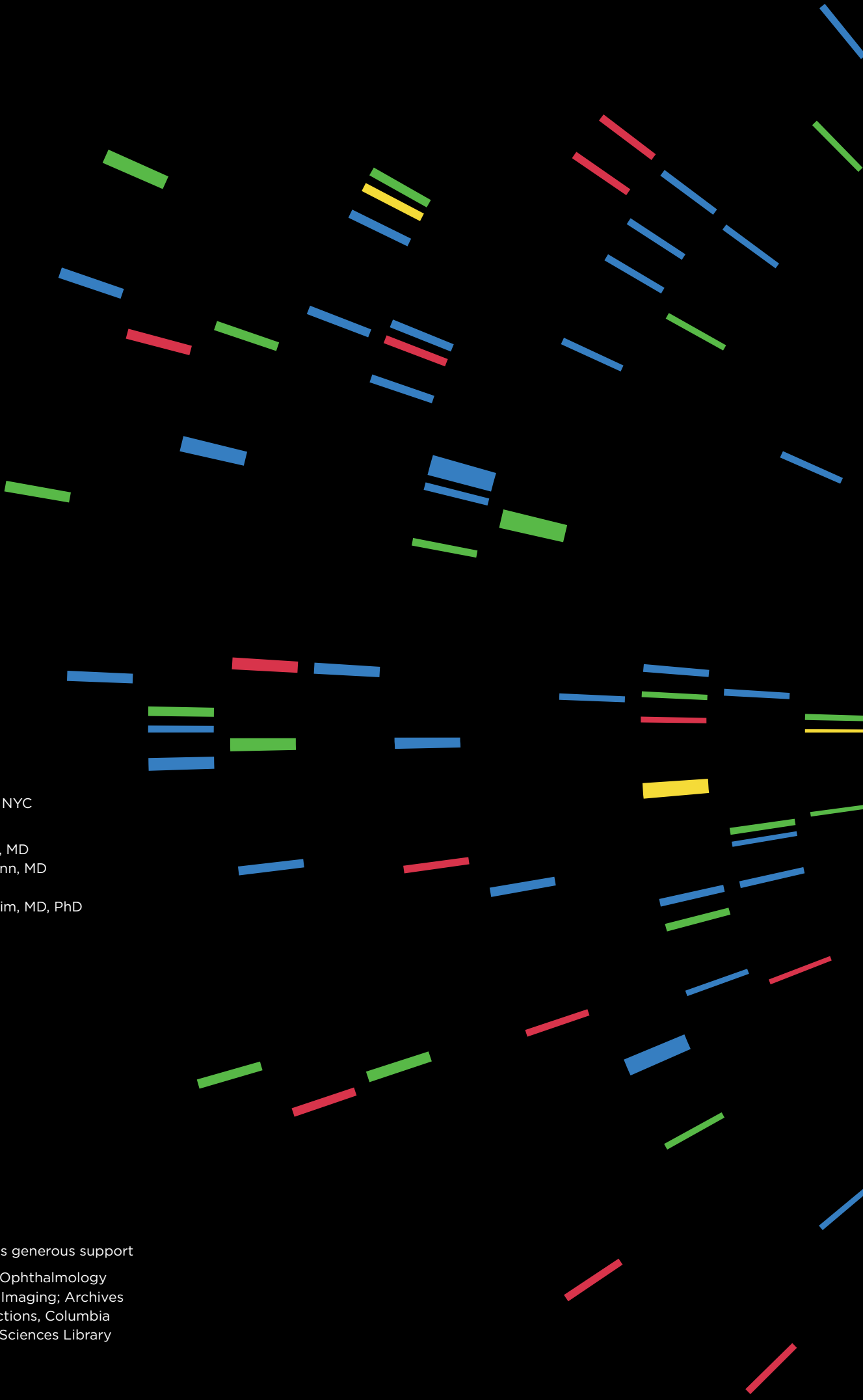
The Wang Lab studies mitochondrial function in retinal disease to develop therapies for retinitis pigmentosa and retinal ganglion cell (RGC) degeneration.

35 Yang Lab

The Yang Lab studies the structure, function, and regulation of ion channels in the eye as well as genetic mutations linked to retinal diseases such as Best disease.

36 Zhang Lab

The Zhang Lab investigates cell signaling during eye development to understand how congenital disorders develop and inspire future treatment for these diseases.



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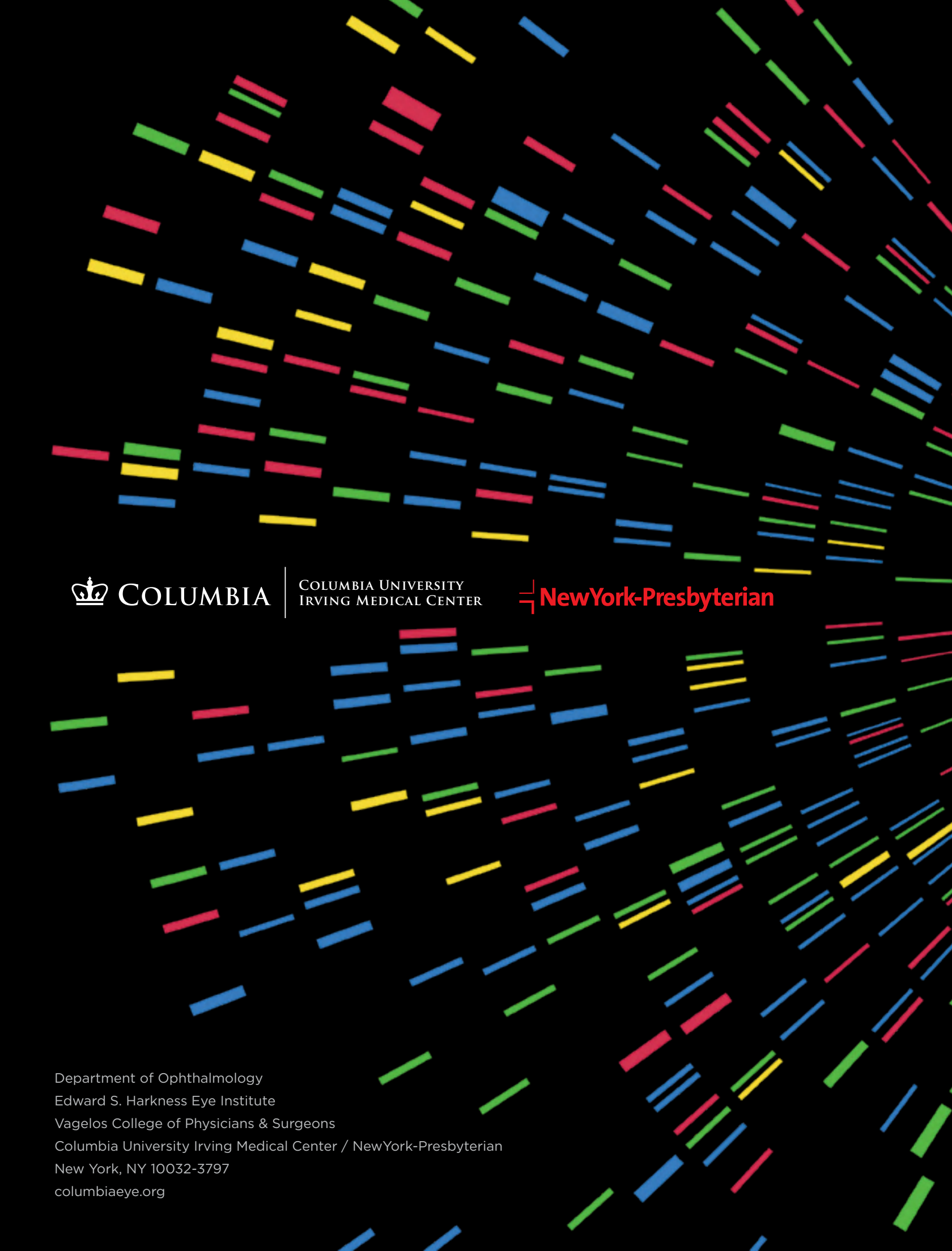

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NewYork-Presbyterian

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