

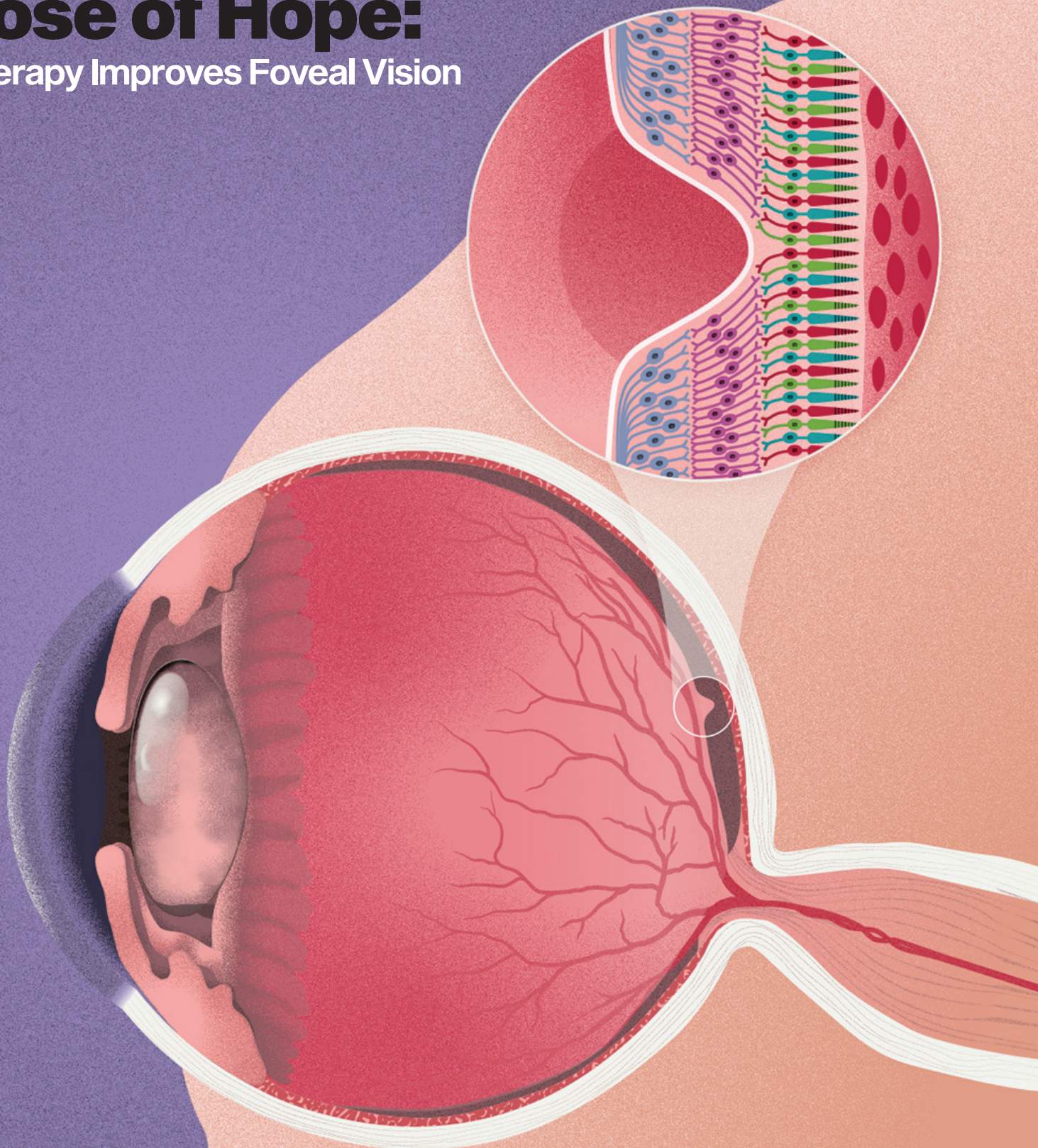
scheie vision



Penn Medicine

Department of Ophthalmology

A Dose of Hope: RNA Therapy Improves Foveal Vision



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Cover: The foveal retina in patients with Leber congenital amaurosis due to biallelic *CEP290* mutations retains near normal numbers of cone photoreceptor cells that cannot detect normal levels of light. A single intravitreal injection of RNA therapy provides substantial and long-lasting vision improvement originating from foveal cones. Graphic by ProQR Therapeutics.

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A MESSAGE FROM THE CHAIR

As many of you may know, I will be stepping down from my role as Chairman of the Department of Ophthalmology on June 30, 2022, as my second six-year term comes to an end.

The past 12 years have been filled with progress and change. I am so proud of the achievements of our faculty, staff, alumni, and trainees. Truthfully, as I sit down to write this column, I do not know where to start, as there are simply too many accomplishments, special moments, and relationships to acknowledge. I will do my best to choose among these highlights, knowing that it likely will not scratch the surface of all that our teams have accomplished this past decade.

Since 2010, our faculty has grown from 24 to 66 inspiring individuals. The Department now offers 17 subspecialties and sees more than 130,000 patient visits each year. We have four Master Clinicians and four Advisory Deans, representing 20% of our clinical faculty. In a recent climate survey across UPenn, ophthalmology faculty ranked #1 and staff ranked #2 in job satisfaction among the 19 departments surveyed. These numbers, though impressive, do not fully capture the generosity, compassion, and bravery of our faculty members and trainees. When the COVID-19 pandemic struck in March 2020, many of these individuals were the very first to volunteer in triage tents and testing sites. As a team, our Department was able to serve our community, maintain our research and education missions, provide urgent and emergent patient care from March through June of 2020, and reach and exceed pre-COVID outpatient and surgical volumes by the fall of 2020.

With respect to our research mission, the Department has become one of the top two recipients of National Eye Institute funding nationwide for the past five years. We have also developed strong and consistent sources of non-traditional funding (foundation, non-profit, corporate), which account for roughly 60% of additional research awards each year. Since 2010, we have raised more than \$40M in philanthropy. Our faculty consistently publish in high-impact journals such as *Nature*, *Nature Medicine*, *Nature Genetics*, *Lancet*, *New England Journal of Medicine*, and *PNAS*. We have built strong ties with the vision scientist community at UPenn, which includes 116 primary investigators and their lab members, including our ophthalmology department faculty.



We enjoy frequent collaborations, joint grants, publications, and weekly seminar series with these brilliant individuals who span many schools at UPenn.

The educational mission remains a core focus of our Department. The residency program,

which receives more than 600 applications for five positions each year, consistently matches with diverse, competitive, and compassionate individuals. The program has significantly increased surgical volume for residents (88% increase since 2010 for average number of cataract surgeries per resident), along with participation in many other subspecialty surgeries. The number of grants/trials per alumnus ranks in the top 1% of programs nationwide, suggesting that the Department is training academic leaders of the future. Third-year residents consistently secure first- or second-choice fellowships. Engagement with medical students at the Perelman School of Medicine is also robust, with up to 10% or more of the graduating class pursuing residencies in ophthalmology each year. I am always proud (and not surprised) to see the very high School of Medicine teaching evaluations that our faculty members receive each year. Honors such as Pearl Awards, the Leonard Tow Humanism in Medicine Award, the Penn Medicine Dean's Award, and honorary induction of faculty into Alpha Omega Alpha are certainly well-deserved.

Our faculty, staff, and trainees travel throughout Philadelphia and across the globe to care for underserved populations. Programs such as Penn Sight Savers and Puentes de Salud, staffed by volunteer physicians, residents, and medical students, provide comprehensive ophthalmic care to patients who are often uninsured and undocumented. Our faculty also lead many screening events across Philadelphia, providing free glaucoma screenings, glasses giveaways, and low vision device giveaways with training on the use of these life-altering tools. At every opportunity, we seek to help patients obtain insurance, provide referrals for follow-up treatment, and screen for systemic disease with ocular manifestations. The Penn Center for Low Vision Rehabilitation's Vision Loss Support Group, founded in 2017, has now provided support and training to dozens of patients with visual impairments that can no longer be improved through medical or surgical means. In the past decade, our faculty have also travelled to more than 30 countries to provide eye care to desperately at-risk and underserved populations internationally.

These accomplishments truly reflect the talent, compassion, and hard work of our faculty, staff, and trainees. However, when I consider my time at Scheie, it is not only these achievements that come to mind, but also the smaller moments, the relationships, and the laughter that I remember so fondly. I remember celebrating the ribbon cutting ceremony after years of renovations at Scheie were completed in 2014. I loved dancing at the Rittenhouse Hotel with so many of you at our

alumni events each year. I looked forward to getting to know the new residents every July, and to giving lectures to the medical students on genetics. I am grateful for the patience of the staff who tried to teach me to line dance at our winter holiday parties. I enjoyed watching the speakers, singers, and dancers at our annual African American History Month Celebration each winter. Of course, some memories are not as pleasant to recount, such as the time that I got stuck in an elevator between floors (and had to crawl out) on the day of my very first faculty meeting. I will miss so many big and small moments.

However, I am excited to share that the next phase of my career will also be at UPenn. For the past decade, I have led a large genetics study on glaucoma in African ancestry individuals. We received an \$11.25M R01 grant in 2014, and just recently received a \$6.6M renewal of this grant for the next five years. This study has grown in ways that I never could have imagined. More than 10,200 individuals in Philadelphia have now enrolled in our cohort, with full genetic information, including genome-wide association study data, whole-exome data, and now whole-genome data, with the ability to re-contact our participants. This rich dataset presents a new opportunity to study the genetics of glaucoma and other diseases that overaffect African ancestry individuals, yet remain understudied.

I am now in the process of launching a new Center at the Perelman School of Medicine to meet this need. The mission of this Center will be to elucidate the genetics of diseases that overaffect African ancestry individuals and to develop targeted diagnostic and therapeutic options for these individuals. We will continue to form close partnerships with researchers investigating these complex genetic diseases. Industry collaborations will help to bring genetic findings from bench to bedside, with several companies expressing interest in working together. We will also prioritize the close partnerships formed with Black community leaders in Philadelphia to address health disparities, provide free disease screenings, and spread awareness about our findings as they continue to develop.

I am so grateful to the colleagues, alumni, trainees, patients, and friends who have made these 12 years at Scheie the most rewarding of my life. I am looking forward to welcoming the new Chairman, continuing to support the Department, and embarking on this new phase of my career.

I wish you and your families a happy and healthy holiday.

Joan O'Brien, MD

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 Perelman School of Medicine
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Eydie Miller-Ellis, MD



TACKLING DISPARITIES IN GLAUCOMA AND IN HEALTHCARE

By Rebecca Salowe

Eydie Miller-Ellis, MD, Vice Chair for Faculty Affairs and Vice Chair for Diversity, Equity, and Inclusion (DEI) at the Scheie Eye Institute, was recently featured in an in-depth article about healthcare disparities in the American Academy of Ophthalmology's *EyeNet* magazine. In this article, Dr. Miller discusses how racial disparities play out in the care of glaucoma patients and provides insight into how to overcome these barriers.

A SILENT DISEASE

Glaucoma is a blinding eye disease that disproportionately affects individuals of African descent. African ancestry individuals are five to six times more likely to be affected by primary open-angle glaucoma (POAG), the most common form of the disease, and up to 15 times more likely to experience vision loss from the disease than European Americans. Furthermore, glaucoma is a familial disease, so vision loss early in life can affect multiple family members, possibly leading to adverse economic and health outcomes in these individuals.

Dr. Miller became interested in pursuing glaucoma as a specialty almost three decades ago. Not only does glaucoma run in her family, but she also noticed repeatedly that certain glaucoma patients were falling through the cracks of the healthcare system. Early care is critical for glaucoma patients, as vision loss from the disease cannot be reversed with current treatments.

“Glaucoma is the number one cause of preventable blindness, disproportionately affecting individuals of African descent—and glaucoma runs in my family,” said Dr.

Miller. “I thought glaucoma was where I could make the biggest difference.”

Thirty years later, glaucoma treatments have improved, but many disparities persist or have even worsened, both in glaucoma and in other diseases.

WHY CERTAIN DISPARITIES PERSIST

Many health disparities can be traced back to difficulties with access to care and the reality that many medical facilities in low-income neighborhoods are under-resourced. Additionally, for glaucoma patients, treatment compliance is essential to slowing vision loss. However, individuals who are economically disadvantaged typically have a hierarchy of concerns, including securing food and shelter. A visit to the ophthalmologist, or a purchase of eye drops, may be difficult to prioritize given other concerns.

Dr. Miller emphasizes the importance of patient health literacy and education when discussing treatment options with patients. For example, she has found that most patients are visual learners, so she often writes down treatment directions for patients as a reference. She also takes into account all possible factors when determining a treatment plan. For example, early intervention with a laser or surgery can help to mitigate the long-term challenges associated with eye drops.

Diversity of the physician workforce is another important factor to consider. As of 2015, only 2.5% of

ophthalmologists were Black. Racially concordant medical interactions have been shown to improve relationships, health information exchange, and treatment planning. Better pipelines for under-represented minorities to enter ophthalmology (and other medical specialties) are essential; they also provide role models for younger students of color.

Dr. Miller co-directs a program for under-represented students, residents, and fellows called the Rabb-Venable Excellence in Ophthalmology Research Program, with the National Medical Association. The goal of this program is to increase the number of under-represented minorities in ophthalmology residencies and in academic medicine. The Department contacts graduating fellows from this program about open faculty positions.

RESEARCH IS NOT IMMUNE

Disparities in glaucoma stretch beyond clinical care and into the realm of research. Despite African ancestry individuals being overaffected by glaucoma, the majority of glaucoma studies to date have focused on individuals of European or Asian descent. Many of these findings have little or unknown implications in African ancestry individuals.

This is a global problem across all of medicine: as of 2019, only 2% of participants in genome-wide association studies were of African descent. Polygenic risk scores, as another example, have primarily been tested in European

“While diversity, health disparities, and inclusion have been discussed for years, the events of 2020 have put these issues at the forefront,” said Dr. Miller. “We are finally seeing a real commitment from the government, health providers, and insurers to move these initiatives forward—working on inclusion in bench research and clinical trials while addressing disparities in healthcare.”

Americans, as the studies used to generate the scores were conducted in European Americans. This cyclical problem ultimately affects those least studied, as it impedes the translation of genetic results into clinical care, limiting diagnostic and therapeutic applications.

However, there has been some positive momentum in glaucoma research in recent years. Several large studies are now examining this disease in individuals of African descent, including the Genetics of Glaucoma in People of African Descent Consortium and International Glaucoma Genetics Consortium. The Primary Open-Angle African American Glaucoma Genetics (POAAGG) study, conducted here at the Scheie Eye Institute, has recruited more than 10,200 African ancestry individuals to its cohort. These studies will help to elucidate the genetics of glaucoma in the most affected individuals.

“Ultimately, we hope to find better ways to diagnose glaucoma at earlier stages, slowing or preventing vision loss,” said Dr. Miller, who is a Co-Investigator on the POAAGG study. “We also aim to develop more targeted treatments for the different subtypes of glaucoma.”

SCHEIE EYE INSTITUTE’S COMMITMENT

Glaucoma is just one disease that exemplifies the disparities that persist in healthcare. The Scheie Eye Institute is fully committed to tangible action to eradicate these disparities, both in glaucoma and more broadly. In her role as Vice Chair of Faculty Affairs and Vice Chair for DEI, Dr. Miller has led conversations and initiatives to take steps towards meeting this commitment. These actions have been consistently guided by the diverse voices of the Scheie community.

The Department supported implicit bias training for all faculty and staff, which is designed to make individuals aware of their implicit biases, provide tools to adjust automatic patterns of thinking, and ultimately help to eliminate any discriminatory behaviors. 100% of employees completed this training.

In 2020, Dr. Miller shared an anonymous survey with the Department, where faculty and staff could discuss any experiences of discrimination and racism in the workplace and in healthcare. The survey also asked for feedback and suggestions on how to open a dialogue.

“Approximately 50% of the Department responded to the survey,” said Dr. Miller. “While it was good to learn that most had not experienced discrimination, there were also reports of microaggressions and communication challenges. To address these issues, the Scheie DEI Committee has been formed.”

A forum was also facilitated by Dr. Miller, Paul Tapino, MD (Scheie Residency Program Director), and Enny Oyeniran, MD (recently graduated Scheie resident) to discuss findings and suggestions from the survey and to encourage further dialogue and feedback.

The Scheie DEI Committee includes representatives from faculty, staff, and administration who can express concerns and perspectives from all areas of the Department.

“Our goal is to improve our work environment by treating each other with respect and compassion, and to encourage an environment that is physically and emotionally safe,” said Dr. Miller. “Social restrictions resulting from COVID have put up barriers that have made it difficult to maintain morale and get to know new employees. Our goal is to break down barriers, encourage collaboration and tolerance, and provide a forum for difficult and important conversations.”

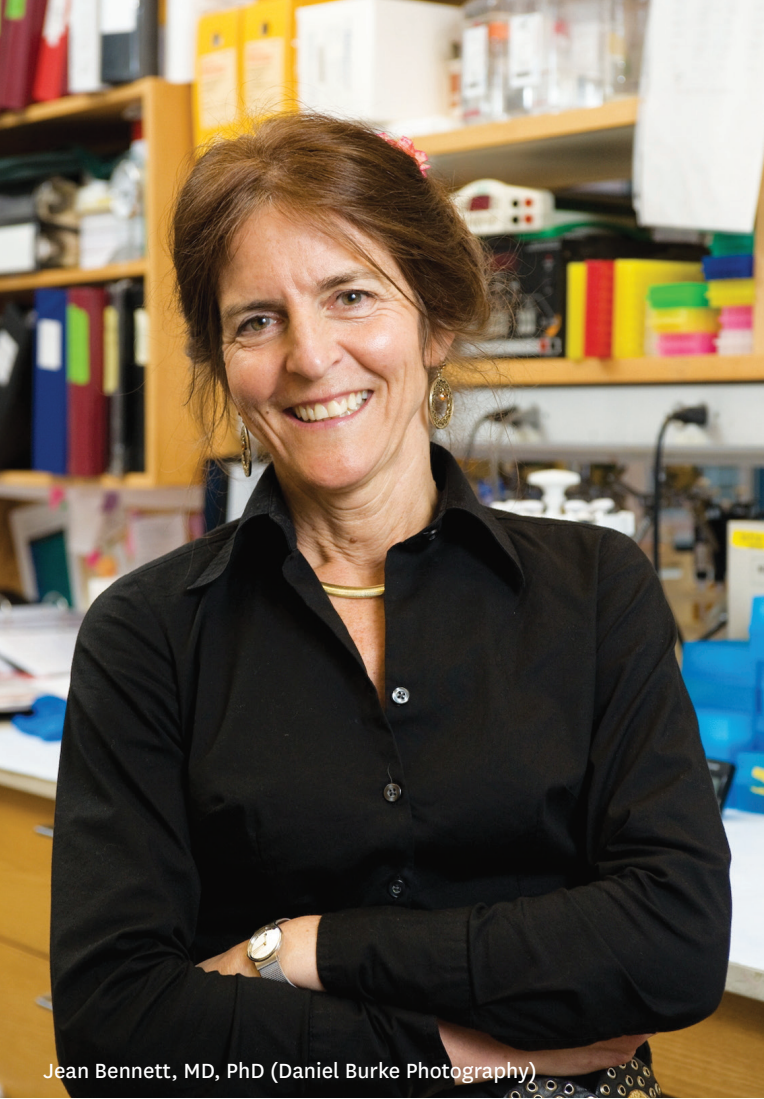
Presentations by experts in DEI, as well as sessions on anti-Asian violence and public safety, were scheduled for eight Grand Rounds in the past year. Examples of topics covered include “Misrepresenting Race: The Role of Medical Schools in Propagating Physician Bias,” “Achieving Health Equity in Ophthalmology,” and “Eradicating Systemic Racism and Microaggressions in Academic Medicine.”

The Department will continue (and expand where possible) other conversations, initiatives, and events that promote diversity. For example, a Black History Month celebration has been hosted by staff members and supported by the Department for almost ten years. This half-day event, which features singers, dancers, and speakers from the Philadelphia community, is open to all faculty, staff, and community members.

For faculty recruitments, the Department will continue to invest in outreach to diverse ophthalmology groups throughout the world, in order to make connections and discover new talent. The Department also seeks to recruit under-represented minorities for work-study positions, summer research internships, writing opportunities, and clinical shadowing experiences. These students are often offered full-time positions after college graduation as scribes, clinical research coordinators, or laboratory scientists, where they can receive mentorship and acquire the publications and experience needed to gain admission into outstanding medical or graduate schools.

The Chairman of the Ophthalmology Department, Joan O’Brien, MD, is fully supportive of these efforts. She is an active member of the CPUP Committee on Anti-Racism.

“While diversity, health disparities, and inclusion have been discussed for years, the events of 2020 have put these issues at the forefront,” said Dr. Miller. “We are finally seeing a real commitment from the government, health providers, and insurers to move these initiatives forward—working on inclusion in bench research and clinical trials while addressing disparities in healthcare. If we as a society can address issues facing the most disadvantaged of people, it will help everyone. Diverse ideas make organizations better. We need to keep moving forward.” ■



Jean Bennett, MD, PhD (Daniel Burke Photography)

From the Developers of Luxturna: **Opus Genetics**

By Isabel Di Rosa

In October 2021, Scheie Eye Institute researchers Dr. Jean Bennett and Mr. Junwei Sun launched a new biotech startup called Opus Genetics, which aims to discover new treatments for rare blinding conditions. Dr. Bennett and colleagues previously developed Luxturna, the novel gene therapy that has

treated vision loss in patients with a form of Leber congenital amaurosis (LCA) caused by mutations in the *RPE65* gene. Dr. Bennett and Mr. Sun have teamed up with Dr. Eric Pierce, Professor of Ophthalmology at Harvard Medical School and Massachusetts Eye and Ear Infirmary, to launch this new company.

Opus Genetics' \$19 million in seed funding is provided by the Foundation Fighting Blindness' Retinal Degeneration Fund, as well as the Manning Family Foundation and Bios Partners. Other founding members of Opus include Dr. Ben Yerxa, Dr. Rusty Kelley, Mr. Jason D. Menzo, and Mr. Peter Ginsberg, all of whom have senior positions at the Foundation Fighting Blindness.

Building upon Dr. Bennett and Mr. Sun's prior research and the expertise of the other founders, Opus Genetics has an initial goal of investigating potential gene therapies to treat variations of LCA. The gene therapies (namely, OPGx-001 and OPGx-002) would work by targeting genetic mutations in the *LCA5* and *LCA13* genes. If successful, these therapies could restore sight in patients with these forms of congenital blindness.

Opus Genetics coins itself as a patient-first company. "We are selecting some of the most neglected forms of inherited blindness that big pharma traditionally would not touch because they are extraordinarily rare," Dr. Bennett explained. "These are devastating diseases, and we want to help the patients and their families. The patients are an integral part of Opus Genetics - in fact, they helped found this company."

Large pharmaceutical companies are less likely to research rare diseases because of the low profit margin; treatments for common diseases can generate much greater revenue. Opus Genetics will help fill the gap in research on LCA, and hopefully result in targeted treatment options. ■

“We are selecting some of the most neglected forms of inherited blindness that big pharma traditionally would not touch because they are extraordinarily rare.”



From left to right: Panteleimon Rompolas, MBA, PhD; Olivia Farrelly; Vivian Lee, MD.

COLLABORATION WITH DERMATOLOGY elucidates stem cell behavior in cornea

By Rebecca Salowe

A recent collaboration between the ophthalmology and dermatology departments at the University of Pennsylvania revealed new knowledge about the localization and function of stem cells in the cornea. This study, led by Panteleimon Rompolas, MBA, PhD, Assistant Professor of Dermatology, with collaborator Vivian Lee, MD, Assistant Professor of Ophthalmology, was published in *Cell Stem Cell*.

The cornea, which is the transparent layer forming the front of the eye, can easily become scratched or injured. Though initially painful, these injuries—which typically affect a layer called the corneal epithelium—are able to heal remarkably quickly. “This replenishment and regeneration after injury is made possible by stem cells, which are residents in these tissues,” said Dr. Rompolas. “Stem cells not only replace cells as they naturally die off,

but are also activated in settings such as wound healing.”

Like many skin diseases, corneal diseases are often characterized by abnormal cell proliferation and differentiation, which are the inherent roles of stem cells. Thus, it is essential to understand how stem cells support these activities in a healthy cornea—and what conditions can cause their activity to go awry, leading to disease.

Dr. Rompolas previously investigated a similar question in skin, publishing a paper in *Nature* describing the biological behavior of cutaneous stem cells in vivo. “Given the similarities between the skin and eye epithelia, in terms of barrier function and histological organization, curiosity about corneal stem cells naturally arose between our groups,” he said.

Revelation of this unique organization of corneal stem cells provides us with the understanding that not all stem cells have the same function or capacity.”

“Another motivating factor in our partnership was the long tradition of collaboration between dermatology and ophthalmology here at Penn,” added Dr. Lee. “In fact, the existence of corneal stem cells was first discovered by the current Chairman of Dermatology, Dr. George Cotzarelis.”

The main goal of this collaboration was to capture stem cell dynamics during corneal maintenance and regeneration. To investigate this question, Drs. Lee and Rompolas used a cutting-edge imaging technology called two-photon microscopy to monitor the activity of corneal stem cells in intact eyes of live mice.

“Two photon microscopy is ideal for imaging cells in intact live organs, such as the cornea,” explained Dr. Rompolas. “The cornea is thin and relatively transparent, so detailed images of individual cells can be obtained and their activities captured in real-time, even when imaging the eye of a live, breathing mouse.”

The study identified and characterized two distinct compartments of stem cells in the cornea. The team was the first to discover these two compartments of functionally diverse stem cell populations, which have unique roles in repairing and replenishing the corneal epithelium. These two compartments are defined as outer and inner limbal stem cells. While inner limbal cells help to support corneal homeostasis, outer limbal cells are more involved in corneal regeneration after injury.

“Revelation of this unique organization of corneal stem cells provides us with the understanding that not all stem cells have the same function or capacity,” said Dr. Lee.

“An assumption that there is one homogenous population of stem cells, instead of two, could lead to indeterminate

conclusions,” added Dr. Rompolas. “However, by now knowing that there are two populations, a more precise approach to study the individual populations separately could lead to robust data.”

One unexpected finding from the study was that when corneal cells underwent terminal differentiation, they had an unconventional, “centrifugal” 3D trajectory. “This behavior appears to be fundamentally different to all other stratified epithelia, but its functional significance remains to be determined,” said Dr. Rompolas.

These results have important implications for treating corneal diseases. Ocular trauma and diseases of the cornea are major causes of blindness worldwide. However, the main treatment methods of corneal grafts and transplants are limited by the lack of resources globally, such as surgical expertise and donor tissue. Additionally, corneal transplants can be met with complications such as rejection and infection.

Because ocular surface diseases predominantly manifest through abnormal stem cell proliferation and/or differentiation, the findings of this study are key to understanding how stem cells coordinate and interact with their surrounding microenvironment to support tissue homeostasis. “Now armed with that knowledge, more informed therapeutic strategies can be developed for the variety of conditions that stem cells can treat,” said Dr. Lee.

“By understanding the mechanisms that regulate stem cells, one can harness this information to investigate new therapies, such as tissue regeneration,” added Dr. Rompolas. ■

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cosmetic corner *with* dr. sonul mehta



Sonul Mehta, MD

Sonul Mehta, MD is an oculoplastic surgeon in the Department of Ophthalmology and Director of the Oculoplastic Surgery Service. She specializes in cosmetic and reconstructive surgery around the eyes, and has a special interest in aging-related changes of the eyes and midface, skin cancers of the eyelids, and inflammatory conditions of the eyelids.

REJUVENATION OF THE EYES: POST-COVID GLOW-UP

In this Q&A, Dr. Mehta discusses what to consider for periorcular rejuvenation this winter and a post-COVID glow-up. It has been an exhausting and stressful two years with the pandemic and the lockdown, and now with masks, there is greater focus on the eyes. Below, Dr. Mehta describes what patients can do to help refresh and rejuvenate their eyes.

Q

The dreaded under-eye **dark circles**...what causes them?

Dr. Mehta: There are a number of reasons why you can have dark circles around the eyes. Two main causes are hyperpigmentation of the skin and fat prolapse (bags under the eyes) as we get older. We start to see the shadowing of blood vessels of the fat pads under the thinning periorcular skin.

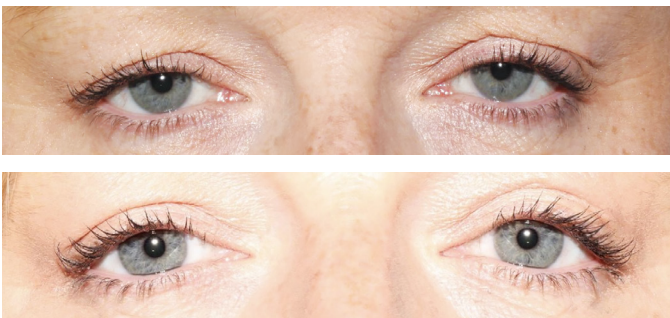
Q

What can patients do to treat this hyperpigmentation?

Dr. Mehta: A proper evaluation is essential to determine the cause of the hyperpigmentation. There are a number of reasons why we can get periocular hyperpigmentation. Two common causes of hyperpigmentation of the facial skin are melasma and post-inflammatory hyperpigmentation (PIH). Melasma is characterized by patchy pigmentation of the skin that can be caused by genetics or aggravated by factors such as UV exposure and hormones. PIH is hyperpigmentation that results from inflammation or trauma to the skin. Prevention is key. Topical sunscreen, even in the winter months, is a must. There are other topical agents, including serums, antioxidants, and creams, that can be added to your skincare routine to prevent worsening and reverse hyperpigmentation depending on the cause. Which agent or combination of agents is best to use depends on the patient's skin type and the cause of the hyperpigmentation. There are lasers that can be used to help with this as well.

Q

What treatments are available for saggy or droopy eyelids?



(top) Before the upper lid ptosis repair and blepharoplasty.
(bottom) After the upper lid ptosis repair and blepharoplasty.

Dr. Mehta: There are multiple causes of droopy, saggy, or baggy eyelids. The first step to treatment is to determine the cause of the droop—is it an eyelid muscle issue, fat prolapse, excess eyelid skin, or droopy eyebrows causing the saggy eyelid? Oftentimes, we have to do surgery to either tighten the muscle in the eyelid, called a ptosis repair, or do a blepharoplasty to remove the excess skin and fat that has come forward in the upper or lower eyelids as we age. This can make someone appear less tired and more refreshed, and can decrease the shadowing of the blood vessels, thereby improving the dark circles. Above, you will see one of my patients that had upper lid ptosis repair and blepharoplasty to help improve her drooping eyelids.

Q

Do you offer non-surgical treatments for this?

Dr. Mehta: Yes, botox and fillers can also be used around the eyes for periocular rejuvenation to help improve wrinkles and hollowing, and to lift the brows.

Q

What are some takeaway points for our readers?

Dr. Mehta: A comprehensive and thorough evaluation of the eyes, skin, and structures of the eyelids is an important first step in refreshing the appearance of your eyes. The eyes, eyelids, and eyebrows are an intricate and dynamic area balancing function, aesthetics, and expression. Secondly, every patient is different. For some, a topical skincare regimen is needed, while others may need non-surgical treatments such as botox, fillers, or lasers. And for others, surgical treatments are necessary, or a combination of the above is suggested. It is essential to examine and review a patient's skin type, eye health, and structural changes, and to understand what the goals of treatment are, in order to determine the best personalized management for a patient's periocular aging changes, without compromising function or facial expression. It is a blend between art and science, with the mission of helping others function and feel better about themselves, and which is why I love what I do! ■



Michael Granato, PhD

dr. granato investigates

SPONTANEOUS OPTIC NERVE REGENERATION IN ZEBRAFISH

By Rebecca Salowe

Michael Granato, PhD, Professor of Cell and Developmental Biology, is conducting groundbreaking research on spontaneous regeneration of the optic nerve. A vision scientist at the University of Pennsylvania, he has received two R01 grants from the National Eye Institute to investigate this poorly understood topic.

In mammals, the central nervous system (CNS) has a minimal capacity for regeneration. The CNS includes the retina and the optic nerve, which is made up of axons from retinal ganglion cells (RGCs). These axons extend from the retina to the brain and associated glia. When the optic nerve becomes damaged in diseases such as glaucoma, the injury can lead to irreversible vision loss and blindness due to the limited capacity of the optic nerve for regeneration.

Amphibians and fish, on the other hand, have a remarkable capacity for optic nerve regeneration following injury. As a result, these animals are often used as model systems to study injury to the CNS. “Zebrafish in particular are a productive model for spontaneous spinal cord regeneration, as well as optic nerve regeneration,” said Dr. Granato.

There are many unanswered questions about regeneration. Models such as zebrafish can be used to understand how

optic nerve axons and surrounding glia interact during optic nerve regeneration. For example, how are immune and glia cells summoned to the injury site, and how do they provide guidance to regenerate RGCs?

Prior research in this area has uncovered several intrinsic neural signaling pathways that boost axonal growth of injured RGCs and suppress cell death. However, this growth is frequently characterized by axonal misguidance and limited functional regeneration.

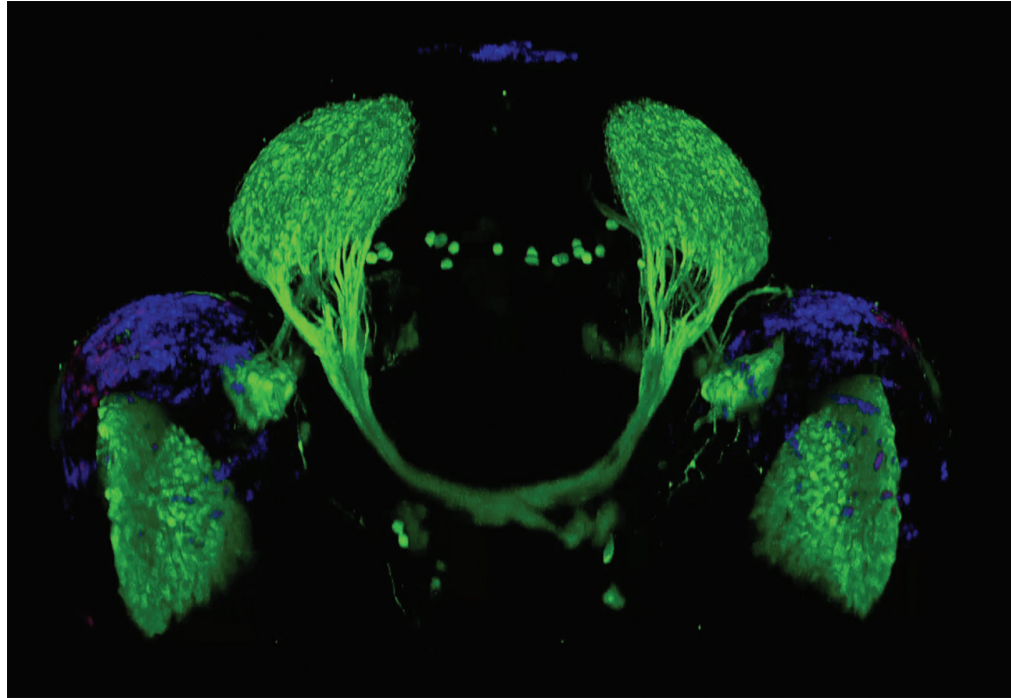
This limitation spurred Dr. Granato’s interest in studying how guidance cues and underlying cellular mechanisms play a role in optic nerve regeneration.

“Which extrinsic cues and guidance pathways ensure correct RGC guidance during regeneration is unclear,” said Dr. Granato. “Identifying these cues, and the underlying cellular mechanisms, appears paramount to achieving functional optic nerve regeneration.”

A large reason for these gaps in knowledge is due to challenges in live cell imaging in mammals. Dr. Granato sought to fill this void by investigating the cellular and molecular pathways of spontaneous optic nerve regeneration in larval zebrafish. He received an R01 grant

This research has implications for many human diseases that damage the optic nerve, such as hereditary optic neuropathies and glaucoma.

A transgenic line that labels the retinal ganglion cells in the retina (lateral clusters) and the axons in the optic nerve leading up to the optic tectum.



from the National Eye Institute in 2014 for this project, which was recently renewed for a second five-year period, extending to 2024.

Dr. Granato specifically investigates larval zebrafish, as they have a functional visual system yet still maintain optical transparency. His laboratory was among the first to develop larval zebrafish as a model for optic nerve regeneration. The research team established a powerful assay to transect the optic nerve in larval zebrafish and monitor the regeneration of axons.

“We found that RGC axonal regeneration is rapid, as re-growing axons enter the optic tectum by 48 hours post transection, independent of RGC cell death or proliferation,” said Dr. Granato.

The team also performed a candidate gene screen and a small molecule screen to investigate which genes are involved in this spontaneous regeneration. The genetic screen identified mutants in two genes that are critical for guidance of injured RGC axons.

“Combined, our preliminary data support the hypothesis that these two genes participate in a molecular pathway that selectively provides extrinsic guidance to regenerating RGC

axons, likely by surrounding glia,” explained Dr. Granato.

The renewal grant will use live cell imaging to elucidate the cellular interplay between regenerating RGC axons and glia cells. This will be the first time that these interactions are observed in their native environment in a vertebrate system.

“This proposal will also determine the cellular and molecular mechanisms by which the two genes we identified ensure proper regenerative guidance in vivo,” said Dr. Granato. “Additionally, mutations in the human counterpart of one of these genes leads to glaucoma and irreversible optic nerve degeneration. Thus, the proposed experiments will identify the mode of action of a glaucoma-causing disease gene.”

This research has implications for many human diseases that damage the optic nerve, such as hereditary optic neuropathies and glaucoma. It will allow for specific hypotheses of optic nerve regeneration that can be applied to restoration of human vision in the future.

“The results from this proposal on spontaneous optic nerve regeneration will provide answers to fundamental questions of optic nerve regeneration across the board, including in mammals,” said Dr. Granato. ■



RESEARCHERS RECEIVE GRANT

TO TEST DIABETES DRUG EFFECTIVENESS AS GLAUCOMA THERAPY

By Alexandra Brodin

In February 2021, Qi Cui, MD, PhD received the \$50K Glaucoma Research Foundation (GRF) Shaffer Grant for Innovative Glaucoma Research. Her project, titled “Evaluating the Glucagon-like Peptide 1 Receptor (GLP-1R) as a Therapeutic Target in Glaucoma,” will help to determine the translational potential of a well-known diabetes drug to treat glaucoma. Dr. Cui is an Assistant Professor of Ophthalmology specializing in glaucoma at the Scheie Eye Institute. Her project is one of nine selected by the GRF to receive the Shaffer Grant this year.

Glaucoma, a complex group of eye diseases, is the leading cause of irreversible blindness worldwide. It is characterized by damage to the optic nerve resulting from the death of retinal ganglion cells (RGCs), often due to high intraocular pressure (IOP). Many of the underlying mechanisms of glaucoma, including genetic susceptibility, are not fully understood. In addition, the standard treatment of lowering IOP is not effective in a subset of patients, whose glaucoma may continue to progress even after reaching normal IOP levels.

Dr. Cui and her team previously found that a class of medications known as GLP-1 receptor agonists had a neuroprotective effect in mouse models of glaucoma, effectively reducing RGC death. They hypothesized that NLY01, a novel GLP-1 receptor agonist, which is a drug class used to treat type 2 diabetes that was recently approved to help with weight loss, may be protective against RGC death.

For this project, Dr. Cui’s team plans to test the protectiveness of NLY01 in a different mouse model

of glaucoma to determine if NLY01 offers longitudinal protection. In collaboration with Brian VanderBeek, MD, MPH, MSCE, a retina specialist at Scheie, she will also retrospectively evaluate existing data on patients who have taken this drug for type 2 diabetes to see if they have experienced neuroprotective effects.

Another aim of Dr. Cui’s grant is to test whether these drugs exert their effect by dampening the activity of myeloid cells in the brain and the retina. “We think the microglia and macrophages within the retina work to convert astrocytes, an important class of support cells within the central nervous system, into a form that can be toxic to ganglion cells,” explained Dr. Cui.

Of note, glaucoma shares similarities with other types of neurodegenerative conditions, such as Alzheimer’s and Parkinson’s disease. Research shows that the type of neuroinflammation observed in mouse models of glaucoma also occurs in mouse models and human eyes of individuals with these other conditions. NLY01 is currently in clinical trials to treat Alzheimer’s and Parkinson’s, as it appears to reduce neuroinflammation.

“One reason that we are excited about this project is that it has considerable translational potential,” said Dr. Cui. “This is a class of medication that is already in use clinically, and its safety data has been collected for over 15 years.”

Considering the complex nature of glaucoma, as well as the potential for severe, irreversible vision loss, advancing novel therapies for this disease is paramount. Dr. Cui’s grant shows great promise for translating existing medications to help prevent RGC death and blindness due to glaucoma. ■

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DEPARTMENT RECEIVES

\$1M Grant for Renovated Resident Wet Lab

By Kristen Mulvihill

The Department of Ophthalmology recently received a \$1 million grant from the Benjamin & Mary Siddons Measey Foundation to renovate and expand the department's existing ophthalmic surgery training laboratory.

The new program will encompass both a wet lab and simulator training facility to allow medical students, residents, and fellows to learn and master techniques used in the operating room. With renovated

This gift ... will significantly propel our mission to train the next generation of world-class ophthalmic surgeons.”

space and up-to-date equipment, the lab will allow ophthalmology trainees to safely and efficiently practice basic and advanced surgical techniques.

Given the complex nature of most ophthalmic procedures, the newly equipped lab will augment medical student, resident, and fellow surgical training, and promote a collaborative learning environment.

The project will be led by Victoria Addis, MD, Assistant Professor of Ophthalmology and Associate Program Director for the Residency Program, and Christina Moon, MD, Assistant Professor of Clinical Ophthalmology.



Ophthalmology residents in the Department's current wet lab.

“This gift from the Measey Foundation will enable us to update, expand, and equip our wet lab training facility with state-of-the-art technologies, and will significantly propel our mission to train the next generation of world-class ophthalmic surgeons,” explained Dr. Addis.

The Benjamin & Mary Siddons Measey Foundation was founded in 1957 by William Maul Measey, a Philadelphia-based lawyer and philanthropist. The Foundation supports medical education in the Philadelphia area, funding various scholarships and fellowships. The foundation also provides support to cutting-edge programs at medical schools throughout the city. ■



Samuel G. Jacobson, MD, PhD



Artur V. Cideciyan, PhD

RNA therapy

reverses blindness in patient after one dose

By Rebecca Salowe

In a recent publication in *Nature Medicine*, Scheie researchers showed that a patient with a genetic form of childhood blindness gained vision that lasted for more than one year after receiving a single injection of an experimental RNA therapy. This study was led by Artur V. Cideciyan, PhD and Samuel G. Jacobson, MD, PhD, Professors of Ophthalmology and co-Directors of the Center for Hereditary Retinal Degenerations.

The patient was a participant of a larger international clinical trial for patients with Leber congenital amaurosis due to a *CEP290* mutation, which is a commonly implicated genetic cause for this disease. Patients with this mutation typically have severe visual impairment that begins in infancy.

Patients in the clinical trial received an intravitreal injection of an antisense oligonucleotide called seprofarsen. This short RNA molecule is designed to correct the commonly

occurring *CEP290* mutation. A prior study, also led by Drs. Cideciyan and Jacobson and published in *Nature Medicine*, showed that repeated injections of seprofarsen every three months resulted in consistent vision gains in 10 patients.

The 11th patient—featured in this most recent publication—received only one injection of seprofarsen. The patient decided to forgo the quarterly maintenance doses to avoid potential adverse effects, but allowed for continued monitoring.

“Sepofarsen half-life within the non-foveal retina was previously estimated to be two months based on animal studies,” said Dr. Cideciyan. “Our work showed that this second-generation antisense oligonucleotide remains active in human foveal cone photoreceptors for more than 15 months and continues to provide improved vision throughout this period.”

Before treatment, the patient had reduced visual acuity, limited visual fields, and no night vision. Fifteen months after the single injection, the patient maintained large improvements in vision, which were characterized by more than a dozen measurements of visual function and retinal structure.

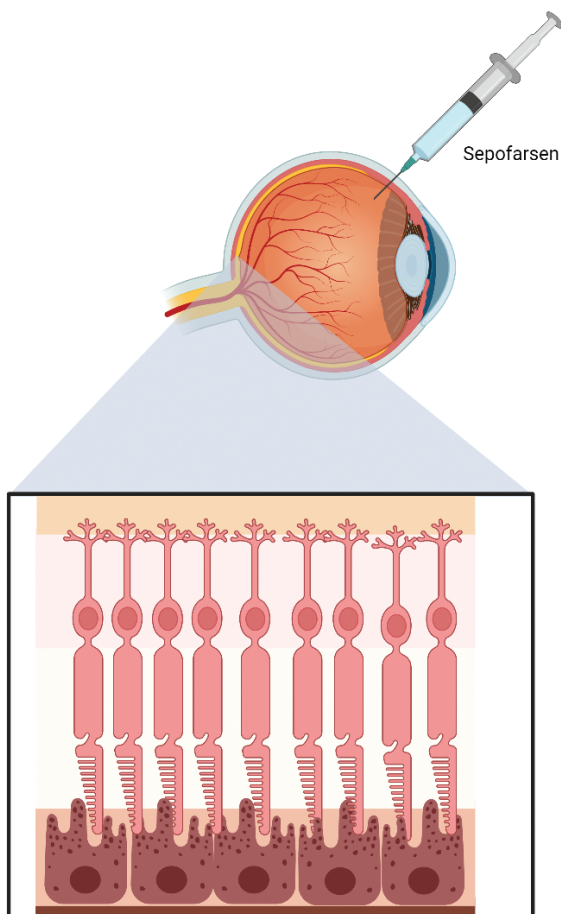
“Peak vision improvement occurred near three months after the injection,” explained Dr. Cideciyan. “Most impressive were co-occurrence of subjective measures, such as acuity and visual fields, with objective changes, such as pupil responses and retinal structural improvements, confirming without a doubt the biological effect in foveal cones.”

The durability of effect is believed to be a result of increased levels of normal CEP290 protein, as well as the slow natural rate of degradation of this protein. The molecule is small enough to enter the cell nucleus, but is not cleared away quickly, so it remains effective for a long duration.

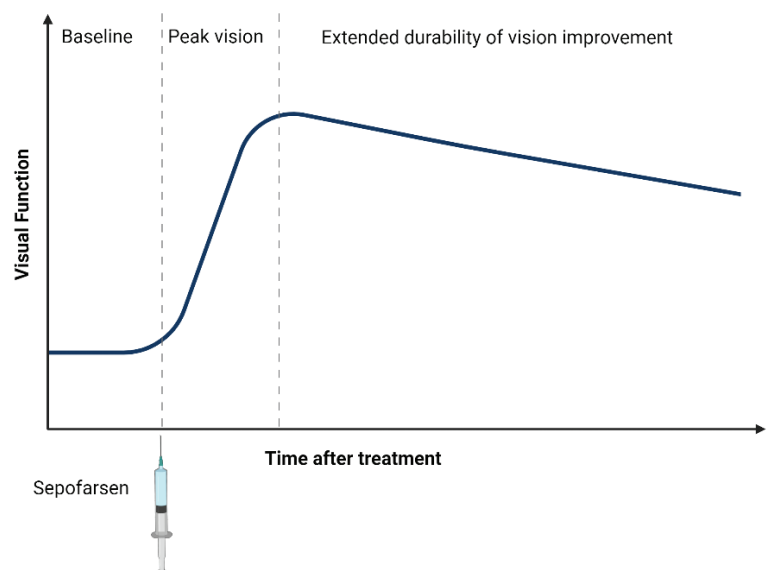
“This work represents an exciting direction for RNA antisense therapy,” said Dr. Jacobson. “The unexpected stability of vision improvements noted in the patient prompts reconsideration of dosing schedules for seprofarsen, as well as other cilium-targeted therapies directed to the fovea.”

Additionally, antisense oligonucleotide therapy has the potential to treat many other monogenic diseases. In ophthalmology, a number of clinical trials using antisense oligonucleotides for genetic defects are now in progress. Gene editing is another promising approach in this area, and the relative merits of each intervention for different diseases and patients can now be compared.

The research team included Wills Eye Hospital surgeon Allen C. Ho, MD, and Scheie researchers Alexandra V. Garafalo, Alejandro J. Roman, Alexander Sumaroka, Arun K. Krishnan, and Malgorzata Swider. ■



Treatment of *CEP290*-LCA foveal cones



Schematic for the treatment of foveal cone photoreceptors with RNA anti-sense oligonucleotide seprofarsen. A single intravitreal injection was performed into the eye of a patient with LCA due to biallelic *CEP290* mutations. Visual function at foveal cone photoreceptors improved slowly to a substantial peak near three months after the injection. Vision improvement remained well above baseline at the latest time point measured 15 months after the single injection. Created with BioRender.com.

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Cideciyan AV, Jacobson SG, Drack AV, Ho AC, Charng J, Garafalo AV, Roman AJ, Sumaroka A, Han IC, Hochstedler MD, Pfeifer WL, Sohn EH, Taiel M, Schwartz MR, Biasutto P, Wit W, Cheetham ME, Adamson P, Rodman DM, Platenburg G, Tome MD, Balikova I, Nerinckx F, Zeytjnd J, Van Cauwenbergh C, Leroy BP, Russell SR (2019) Effect of an intravitreal antisense oligonucleotide on vision in Leber congenital amaurosis due to a photoreceptor cilium defect. *Nat Med* 25(2):225-228.

how the vision loss support group

assisted a penn medicine employee

By Kristen Mulvihill

The Penn Center for Low Vision Rehabilitation's Vision Loss Support Group has been serving members of the Philadelphia community since 2017, offering support to individuals with visual impairments that can no longer be improved through medical or surgical means. The group provides an opportunity for members to share their experiences and learn about available resources.

One of these members, John Skokowski, Jr., is a Penn Medicine employee. John serves as the Senior Patient Care Manager at the Penn Medicine Autism Clinic. He was diagnosed with a genetic retinal degenerative disease called myopic degeneration and has been legally blind and color blind for the past 20 years. A leading cause of legal blindness, myopic degeneration is a severe form of nearsightedness that damages the retina.

John began to lose his vision during adolescence and was forced to stop driving around the age of 21. Despite this debilitating disease, John persevered. He received his graduate degree from the University of Pennsylvania in psychological services, and went on to obtain his school counseling certificate. Before joining Penn Medicine in 2019, John worked for a non-profit agency that provided school-based behavioral support programs for students in kindergarten through eighth grade.

On the last Tuesday of each month, John attends the Vision Loss Support Group, led by Ranjoo Prasad, OD, Director of the Penn Center for Low Vision Rehabilitation, and Sheri Grand Drossner, a Clinical Research Coordinator at



the Scheie Eye Institute. "It's always helpful to hear different people's perspectives in the group," he said. "Even though we're all kind of dealing with the same thing, everyone has a different background and a different way of handling things."

The support group has connected John to various resources that have helped him to navigate his daily life, including a range of visual assistive devices. John uses software such as ZoomText, which magnifies the text on his phone and reads messages aloud. He also uses a handheld digital, electronic magnifier to help locate numbers on documents such as his state identification card and his Penn Medicine identification card. Though he has been managing his vision loss for more than 20 years, John always learns something new from the support group.

"One of the group members helps a lot with distributing and disseminating some of the information and resources that are out there that other members might not know about, like participation groups, survey groups, and other ways to get involved," he explained.

John maintains a positive mindset and stays focused on what he can accomplish rather than his limitations. Despite being legally blind, John continues to lead a healthy lifestyle and exercises regularly. He holds a fifth degree black belt in Tae Kwon Do and a sixth degree black belt in Sin Moo Hapkido, a type of Korean martial arts. He has been training and teaching these disciplines since 1993.

"It's always easier to rationalize excuses for what you can't do, but when you find solutions for problems that allow you to do what you can and want to do, life becomes much more rewarding and satisfying," said John. "While yes, I do have limitations related to legal blindness, I am also strong, capable, intelligent, and competent. Having a visual impairment is only one aspect of who I am and not the only defining characteristic of John Skokowski, Jr.!" ■

Vision Loss Support Group meetings are held on the last Tuesday of each month from 3-4PM. Due to the pandemic, meetings are temporarily being held virtually. Interested patients can contact Sheri at [215.662.8177](tel:215.662.8177) for more information.

RESEARCHERS DISCOVER NEW APPROACH FOR OCULAR DRUG DELIVERY

By Kristen Mulvihill

Physicians often use topical treatments such as eye drops to deliver drugs to the eye. While this is typically the most practical approach, a substance in tears can interfere with the drug delivery system (DDS) and drug absorption process.

DDS refers to the engineered technologies involved in transporting a therapeutic compound to its target site. A lipoplex is a common form of DDS found in ophthalmic medications. Considered the most effective DDS, lipoplexes serve many functions, including in gene therapy and chemotherapy.

Mucin, the deepest layer of the tear film, typically protects the eye. However, when mucin is exposed to certain molecules such as a lipoplex, it binds to the molecule and prevents the treatment from targeting the appropriate cells. When mucin binds to the lipoplex, only a minor fraction of the drug is efficiently absorbed and retained in the eye.

A team of researchers, including Mina Massaro-Giordano, MD, dry eye specialist at Scheie and Co-Director of the Penn Dry Eye and Ocular Surface Center, explored the interaction between lipoplexes and mucin to address this limitation and find a more effective method of ophthalmic drug delivery. Dr. Massaro is part of an international, multi-institutional collaboration between the Sbarro Institute for Cancer Research and Molecular Medicine at Temple University, the University of Pennsylvania's Scheie Eye Institute, and several universities in Italy.

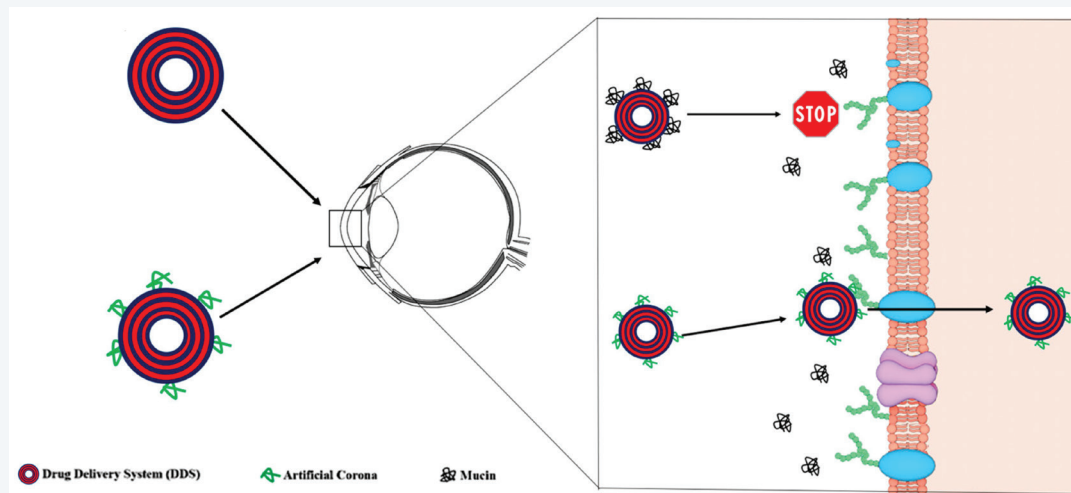
The researchers discovered that using an engineered, artificial protein coating (i.e. protein corona) to conceal the lipoplex improves ophthalmological drug uptake. The protein corona (PC) alters the physical and chemical properties of the DDS, providing an entirely new biological identity.

Specifically, researchers found that a coating comprised of a protein called fibronectin and a tripeptide of the amino acids valine, glycine, and aspartate was efficient in disguising the lipoplex and avoiding mucin interference. The artificial coronas were able to successfully reach and bind to the targeted tissue (i.e. corneal epithelial cells) for improved drug delivery and absorption.

“As a surface disease researcher and clinician, it is imperative to create drugs that will ‘sneak’ through the tear film and target the appropriate cells,” explained Dr. Massaro.

This study presents significant, novel opportunities for ocular drug delivery. The results have the potential to improve treatment options for a variety of ocular diseases and conditions.

“Dry eye is a very common problem and many novel molecules with diverse mechanisms are currently in clinical trials. However, these drugs will fail if delivery methods are not taken into consideration,” said Dr. Massaro. “Scientists must consider methods of ocular drug delivery in future research.” ■



When mucin binds to the drug delivery system, only a fraction of the drug is effectively absorbed and retained in the eye. Using an artificial protein corona to conceal the drug delivery system improves ocular drug uptake.

References

Astarita C, Palchetti S, Massaro-Giordano M, Domenico MD, Petrillo F, Boffro S, Caracciolo G, Giordano A (2021) Artificial protein coronas enable controlled interaction with corneal epithelial cells: New opportunities for drug delivery. *Pharmaceutics* 13(867).

SCHEIE BY THE NUMBERS

FY2021*

59 CLINICAL & RESEARCH FACULTY



2,411 SURGERIES PERFORMED BY FACULTY



17 OPHTHALMIC SPECIALTIES



130,331 PATIENT VISITS



186 FACULTY PUBLICATIONS



A LEADER IN RESEARCH IMPACT



122 H-INDEX


100+ CLINICAL STUDIES IN PROGRESS



100% OF GRADUATING RESIDENTS PURSUE TOP FELLOWSHIP PROGRAMS



17 PENN MEDICAL STUDENTS MATCHED A TOP OPHTHALMOLOGY RESIDENCY PROGRAM IN PAST TWO YEARS



RESIDENCY PROGRAM RANKED **TOP 10** IN NATION FOR RESEARCH OUTPUT PER ALUMNUS



FACULTY HAVE TRAVELED TO **>30** COUNTRIES FOR CLINICAL SERVICE OVER LAST 5 YEARS

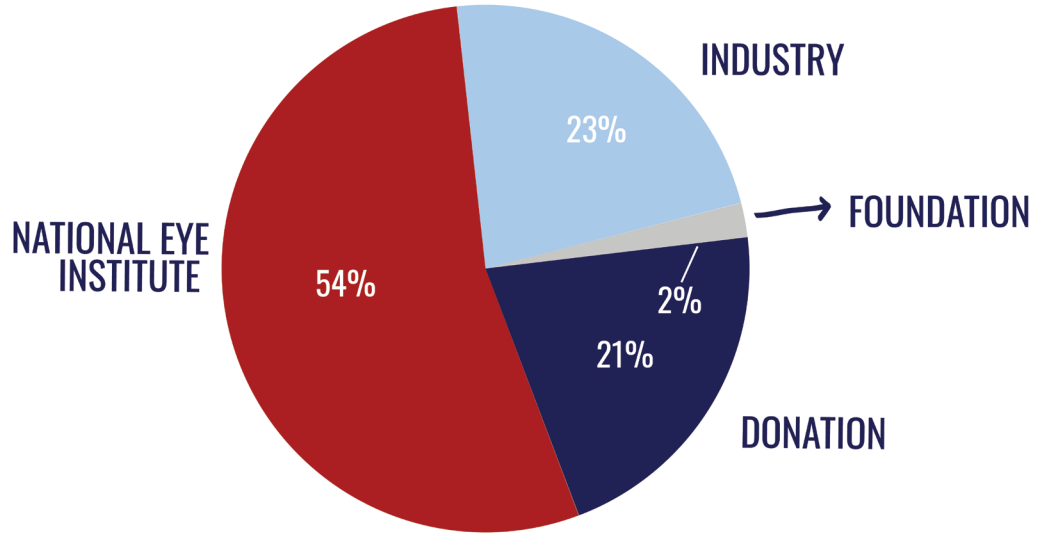


TOP 5

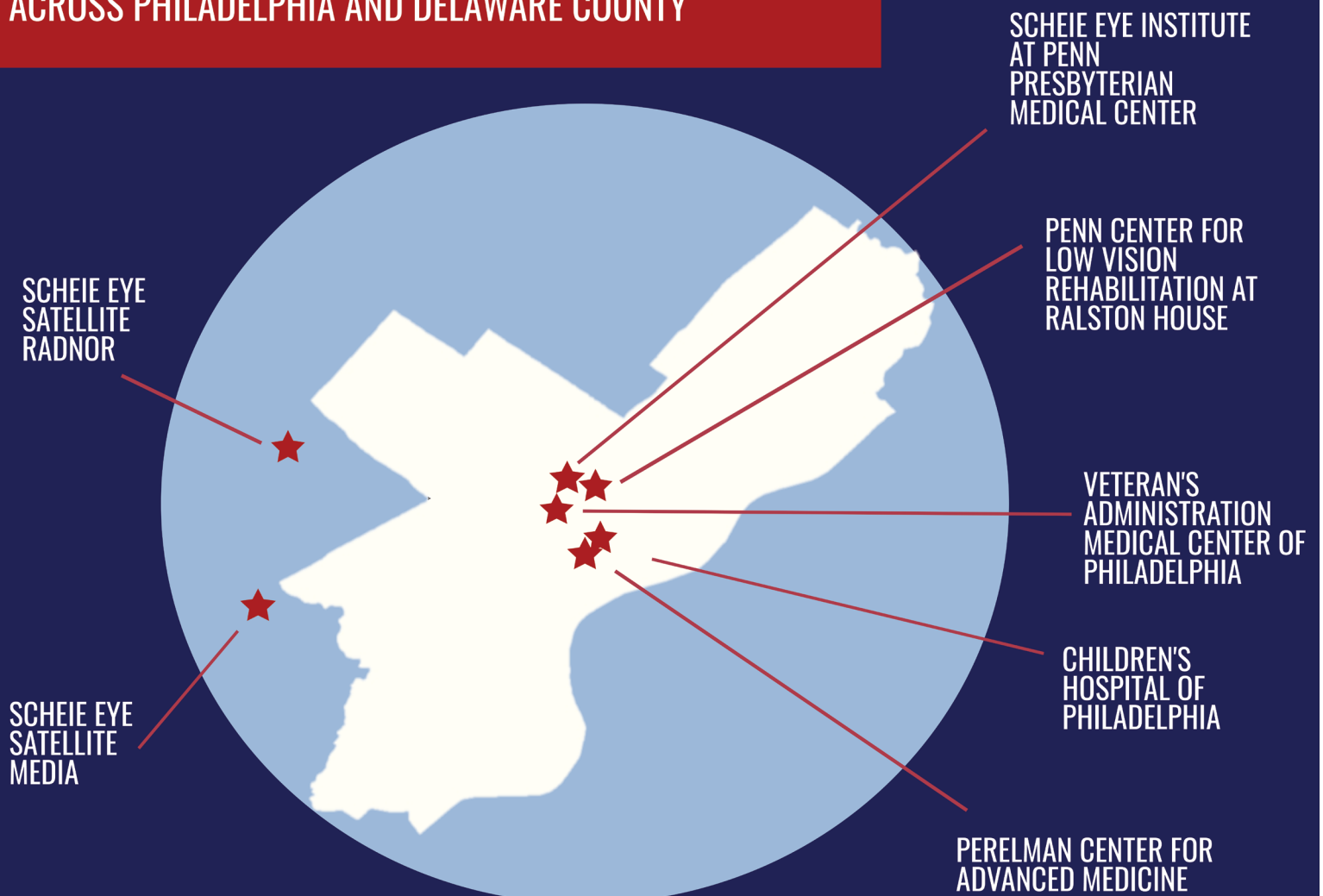
**IN THE NATION FOR
NATIONAL EYE INSTITUTE FUNDING**
of active projects

\$16,983,506

SOURCES OF EXTERNAL FUNDING FOR CLINICAL STUDIES



SCHEIE OFFERS EYE CARE IN SEVEN CLINICAL FACILITIES ACROSS PHILADELPHIA AND DELAWARE COUNTY



*July 1, 2020 - July 1, 2021

faculty updates

By Rebecca Salowe

New Leadership Positions

dr. gil binenbaum

APPOINTED NEW CHIEF OF DIVISION OF OPHTHALMOLOGY



Gil Binenbaum, MD, MSCE

“I have always felt fortunate to work at CHOP and with such exceptional, devoted colleagues,” said Dr. Binenbaum. “I am both excited and honored to help grow and support our group as Chief.”

Gil Binenbaum, MD, MSCE was appointed Chief of the Division of Ophthalmology at the Children’s Hospital of Philadelphia (CHOP) effective July 1, 2021.

Dr. Binenbaum graduated magna cum laude from the Wharton School at the University of Pennsylvania (UPenn). He then pursued his medical degree at the Perelman School of Medicine at UPenn and his ophthalmology residency at the Scheie Eye Institute. He completed his fellowship in pediatric ophthalmology at CHOP. Dr. Binenbaum also received a Master of Science in Clinical Epidemiology from UPenn.

Dr. Binenbaum began his career at CHOP as an attending surgeon in 2007. He also serves as an Associate Professor of Ophthalmology at the Perelman School of Medicine and as the Divisional Director of Research at CHOP. He was the inaugural recipient of the Richard Shafritz Endowed Chair in Pediatric Ophthalmology Research and, as of July 1, now holds the Mabel E. Leslie Endowed Chair of Pediatric Ophthalmology.

Dr. Binenbaum is widely known for his expertise in retinopathy of prematurity (ROP) and the ocular manifestations of child abuse. In addition to these areas, his clinical practice includes complex pediatric and adult strabismus, as well as general pediatric ophthalmology.

A true clinician–scientist, Dr. Binenbaum has greatly enhanced the diagnostic accuracy and treatment of ROP through his research. He serves as the Chair of a 45-hospital collaborative ROP research group, which seeks to develop a better way to predict which infants are at highest risk for developing ROP. The group successfully developed new screening criteria that could identify which babies require ROP examinations and possibly treatment, while sparing other infants resource-intensive and physically stressful retinal examinations.

Dr. Binenbaum has authored more than 300 peer-reviewed publications, abstracts, chapters, and editorials. In addition to his clinical and research responsibilities, he teaches and mentors medical students, residents, fellows, junior faculty, and subspecialists in other pediatric fields.

Dr. Binenbaum will be taking the place of Monte D. Mills, MD, who stepped down from his role as Chief after 21 years of exceptional service. Dr. Mills will remain a senior surgeon in the Division of Ophthalmology at CHOP, where he will continue his superb clinical, research, and educational work.

dr. maureen maguire

ELECTED PRESIDENT OF 2022 ARVO ANNUAL MEETING



Maureen Maguire, PhD

“I hope that we emerge from the pandemic years with a clearer view of what matters in our research,” said Dr. Maguire. “ARVO aims to facilitate the acceleration of the research of its members by providing platforms for sharing the best vision science and bringing committed vision researchers together.”

Maureen Maguire, PhD, FARVO, Emeritus Professor of Ophthalmology, was elected to serve as the President of the Association for Research in Vision and Ophthalmology (ARVO) in 2022.

Dr. Maguire served as the Carolyn F. Jones Professor of Ophthalmology and Director of the Center for Preventive Ophthalmology & Biostatistics until her retirement in July 2021, after 27 years of exceptional service. She will continue to work on several clinical trials and grants, as well as with the Jaeb Center for Health Research on multicenter clinical research projects.

ARVO is the largest eye and vision research organization in the world, with more than 11,000 members from over 75 countries. Founded in 1928, the organization’s mission is to advance vision research in order to prevent, treat, and cure ocular disorders.

Dr. Maguire has been an active member of ARVO throughout her career. She has served as a member of ARVO’s Annual Meeting Planning Committee, Advocacy Committee, and Mentorship Program; an organizer of educational courses in clinical research methods and biostatistics; and a reviewer and editorial board member for the ARVO journal, *Investigative Ophthalmology and Vision Science*. She has also presented her research at most Annual Meetings.

As President, Dr. Maguire will serve as the Chair of the Board of Trustees and Executive Committee. For the 2022 Annual Meeting, she has chosen the theme “Accelerating Discovery through Team Science.” This theme recognizes the rapid progress in developing vaccines for COVID-19, as well as the importance of collaborative research. Throughout her career, Dr. Maguire led many multicenter clinical trials and observational studies where researchers from different disciplines worked together.

In 2020 and 2021, ARVO was held virtually due to the COVID-19 pandemic. In 2022, the meeting is expected to be held in Denver, Colorado from May 1 to May 5.

dr. César briceño

NAMED RHOADS HOUSE ADVISORY DEAN



César Briceño, MD

“This is one of the most rewarding aspects of being an educator,” said Dr. Briceño. “I enjoy helping our wonderful students to thrive and fulfill their dreams.”

César Briceño, MD, Associate Professor of Clinical Ophthalmology, was named an Advisory Dean of the Rhoads House at the Perelman School of Medicine (PSOM) in August 2020. Dr. Briceño is a specialist in ophthalmic plastic and reconstructive surgery at the Scheie Eye Institute.

The PSOM is divided into four main houses, including the Rhoads House. This division is intended to foster interaction between students in different classes and programs and to develop small communities within the medical school. Each House is led by an Advisory Dean.

Dr. Briceño leads the Rhoads House with Amy Pruitt, MD, who is the William N. Kelley Professor of Neurology at the University of Pennsylvania. In this role, they are responsible for mentorship, academic advising, career planning, and professional coaching of students.

Dr. Briceño is committed to medical student, resident, and fellow education. Among his many recognitions, he has received the Golden Apple Teaching Award for resident education and the Penn Medicine Dean’s Award for Excellence in Clinical Teaching. He also serves as an Advisory Dean at the PSOM. Much of his research centers on strategies to enhance medical student and resident education, especially in surgical settings.

Promotions

The following faculty members have received promotions in the past calendar year:



paul tapino, MD

Promoted to Professor of Clinical Ophthalmology.

dr. prithvi sankar

NAMED SENIOR ADVISOR TO THE GRADUATING MEDICAL SCHOOL CLASS



Prithvi Sankar, MD

“It is such an honor to work with the students at this stage of their careers,” said Dr. Sankar. “This final year is the culmination of all their hard work, and it is very special to share this ride with them. The students are incredible.”

Prithvi Sankar, MD, Professor of Clinical Ophthalmology at the University of Pennsylvania (UPenn), was named a Senior Advisor to the Graduating Class at the Perelman School of Medicine. Dr. Sankar is currently an Advisory Dean to the Perelman School of Medicine and serves as the Director of Medical Student Education for the Ophthalmology Department.

In this new role, which began on July 1, 2020, Dr. Sankar works with medical students in their final year to provide guidance on residency and career plans; in particular, Match requirements for residency. At the Class of 2021 Commencement Ceremony, he gave the introduction to the celebration of the class.

Dr. Sankar also teaches residents and glaucoma fellows at UPenn, and provides educational courses at national and international ophthalmology conferences. He has received many awards for his superb teaching and mentoring, such as the Leonard Tow Humanism in Medicine Award from the Gold Foundation, Penn Pearl Teaching Award, and Senior Achievement Award at the American Academy of Ophthalmology. In 2018, he was elected to the Academy of Master Clinicians.

In addition to the above educational roles, Dr. Sankar is a skilled glaucoma specialist and a Co-Investigator on a large glaucoma genetics study in African Americans.



thomasine gorry, MD, MGA
Promoted to Professor of Clinical Ophthalmology.



césar briceño, MD
Promoted to Associate Professor of Clinical Ophthalmology.

dear friends

Change is always inevitable. The seasons change on their own as the earth progresses along its annual orbit. In the business world, competitors always push the envelope to reinvent industries. The first computer in the world filled an entire building at Penn. Now it fits in your pocket and on your wrist. In my childhood, Woolworths and Kmart were the discount stores of choice until Walmart and Target took over and now dominate.

In medicine, many of the cancer therapies of today could only be dreamed of 30 years ago. Ophthalmology is no different. When I finished residency in 2000, optical coherence tomography was not being used clinically, intravitreal therapeutic injections for age-related macular degeneration had not been proposed, and multifocal lenses did not exist. Yet through research and hard work, science has made great strides.

This edition of the newsletter highlights the heavy lifting that has been done by Scheie scientists to create paradigm shifts in healthcare and vision restoration. Their research has led to change at the cellular level through gene therapy and other techniques. I always smile when I see this research grab headlines and receive recognition. This scientific collaborative effort shines a light on the hard work being done at the Scheie Eye Institute and should make us all proud to be part of a rich fabric of innovation and patient care.

Scott M. Goldstein, MD Res '00, Fel '02
President, Scheie Alumni Society



Scott M. Goldstein, MD
Pediatrics & Adult Oculo-Facial Plastic Surgeon
Tri-County Eye & Wills Eye Institute

SAVE the DATE

148th Anniversary Meeting of Department of Ophthalmology

50th Anniversary of the Scheie Eye Institute

CME-Accredited Conference

Saturday, April 9, 2022

7:30am - 4:30pm

Scheie Eye Institute, Kozart Auditorium, Breakfast and Lunch served

Inaugural Honored Alan M. Laties, MD Alumnus Lectureship: Joseph W. Sassani, MD, MHA
David M. Kozart Memorial Lecturer: Michael F. Chiang, MD (Director of the National Eye Institute)

7:00pm-10:30pm

Dinner and Dancing at The Rittenhouse Hotel

The above plans are subject to change depending on the course of the COVID-19 pandemic. Any changes will be communicated as soon as possible.

Meet Our Team

Comprehensive Ophthalmology

Charles Nichols, MD
Dwight Stambolian, MD, PhD
Paul Tapino, MD
Thomasine Gorry, MD, MGA
Allison Brucker, MD

Cornea

Stephen Orlin, MD
Christina Moon, MD
Michael Sulewski, MD

Dry Eye

Giacomina Massaro-Giordano, MD
Vatinee Bunya, MD, MSCE

Glaucoma

Eydie Miller-Ellis, MD
Prithvi Sankar, MD
Eve Higginbotham, SM, MD, ML
Victoria Addis, MD
Qi Cui, MD, PhD
Prathima Neerukonda Atluri, MD
Amanda Lehman, MD, MSc

Low Vision

Ranjoo Prasad, OD

Neuro-Ophthalmology

Madhura Tamhankar, MD
Kenneth Shindler, MD, PhD
Ahmara Ross, MD, PhD
Grant Liu, MD

Ocular Oncology

Joan O'Brien, MD

Ocular Pathology

Vivian Lee, MD

Oculoplastics

Sonul Mehta, MD
César Briceño, MD

Optometry

Alisha Fleming, OD
Stacey Cesarano, OD
Sara Bierwerth, OD, FAOO
Samantha Dougherty, OD
Shelley Cutler, OD, FAOO, Dipl, FSLs

Pediatric Ophthalmology (CHOP)

Gil Binenbaum, MD, MSCE
Monte Mills, MD
William Anninger, MD
William Katowitz, MD
Stefanie Davidson, MD
Robert Avery, DO, MSCE
Priyanka Kumar, MD
Karen Revere, MD
Anne Jensen, MD
Julia Reid, MD

Retina & Vitreous

Alexander Brucker, MD
Samuel Jacobson, MD, PhD
Albert Maguire, MD
Tomas Aleman, MD
Benjamin Kim, MD
Brian VanderBeek, MD, MPH, MSCE
Katherine Uyhazi, MD, PhD

Uveitis

Nirali Bhatt, MD

Research Faculty

Artur Cideciyan, PhD
Joshua Dunaief, MD, PhD
Gui-shuang Ying, MD, PhD
Jessica Morgan, PhD
Manzar Ashtari, PhD, DABR
Ebenezer Daniel, MBBS, MS, MPH, PhD
Venkata Ramana Murthy Chavali, PhD

Emeritus Faculty

Juan Grunwald, MD
Alan Laties, MD
James Katowitz, MD
Graham Quinn, MD, MSCE
Stuart Fine, MD
Edward Pugh, Jr., PhD
Maureen Maguire, PhD
Jean Bennett, MD, PhD
Richard Stone, MD
Brian Forbes, MD, PhD

2021-2022 Fellows

Adam M. Kruszewski, MD
(Neuro-Ophthalmology)
Alexander M. Solomon, MD
(Neuro-Ophthalmology)
Mohib U. Khan, MD
(Glaucoma)
Charles G. Miller, MD, PhD
(Retina)
Gabriela M. Lahaie Luna, MD
(Oculoplastics CHOP)
Jonathan C. Tsui, MD
(Retina)
Lana D. Verkuil, MD
(Pediatric Ophthalmology CHOP)
Tatiana S. Zanganeh, MD
(Pediatric Ophthalmology CHOP)

2021-2022 Residents

First Year Residents

Caroline W. Chung, MD
Devin C. Cohen, MD
Angela S. Gupta, MD, PhD
Tejus Pradeep, MD
Michael B. Wong, MD, MSc

Second Year Residents

Brian J. Nguyen, MD
Samantha L. Marek, MD
Tianyu Liu, MD
Tomas Andersen, MD, MPH
Vivian L. Qin, MD

Third Year Residents

Daniel J. Choi, MD
Dario Marangoni, MD, PhD
Diana H. Kim, MD
Jennifer B. Nadelmann, MD
Zujaja Tauqeer, MD, DPhil

Faculty Awards

(July 1, 2020 – Present)

Jean Bennett, MD, PhD

- Llura Liggett Gund Award, Foundation Fighting Blindness
- 2021 Distinguished Research Achievement Award, Harvard Medical School, Department of Ophthalmology
- 2021 Invited Kober Lecturer, American Association of Physicians
- 2021 Honorary Doctor of Science, Icahn School of Medicine at Mount Sinai, NY
- 2021 Invited Keynote Co-Speaker, The Jules Francois Lecture, International Society for Genetic Eye Disease and Retinoblastoma, Lausanne, Switzerland
- Invited Member (2021-2025), Yale University Council

César Briceño, MD

- 2021 Secretariat Award, American Academy of Ophthalmology
- 2021 Achievement Award, American Academy of Ophthalmology

Alexander Brucker, MD

- 2021 Philadelphia Magazine Top Doctor
- 2021 Castle Connolly Top Doctor

Vatinee Bunya, MD, MSCE

- Penn Center for Innovation's Fifth Annual Celebration of Innovation Patent Award

Qi Cui, MD, PhD

- 2021 Shaffer Grant for Innovative Glaucoma Research, Glaucoma Research Foundation

Stefanie Davidson, MD

- 2021 Philadelphia Magazine Top Doctor
- 2021 Castle Connolly Top Doctor

Joshua Dunaief, MD, PhD

- Appointed Chair, The Pathophysiology of Eye Disease (PED) Study Section, National Institutes of Health

William Katowitz, MD

- 2021 Philadelphia Magazine Top Doctor
- 2021 Castle Connolly Top Doctor

Grant Liu, MD

- 2021 Castle Connolly Top Doctor

Albert Maguire, MD

- 2021 Invited Keynote Co-Speaker, The Jules Francois Lecture, International Society for Genetic Eye Disease and Retinoblastoma, Lausanne, Switzerland

Maureen Maguire, PhD

- 2020 J. Donald M. Gass Lectureship Award Co-Recipient, The Retina Society
- 2021 Richard and Leonora Hill Distinguished Lecturer, College of

Optometry, The Ohio State University

- Elected President (June 2021-May 2022), Association for Research in Vision and Ophthalmology

Mina Massaro-Giordano, MD

- 2021 Italian American Spirit of Medicine Award
- 2021 Achievement Award, American Academy of Ophthalmology
- Penn Center for Innovation's Fifth Annual Celebration of Innovation Patent Award

Eydie Miller-Ellis, MD

- 2021 Philadelphia Magazine Top Doctor

Monte Mills, MD

- 2021 Castle Connolly Top Doctor
- 2021 Philadelphia Magazine Top Doctor

Joan O'Brien, MD

- 2021 Philadelphia Magazine Top Doctor
- 2021 Castle Connolly Top Doctor
- 2021 Castle Connolly America's Top Doctors in Cancer
- 2021 Castle Connolly Exceptional Women in Medicine

Stephen Orlin, MD

- 2021 Philadelphia Magazine Top Doctor
- 2021 Castle Connolly Top Doctor

Ahmara Ross, MD, PhD

- 2021 Emerging Leaders Award, Women in Ophthalmology

Michael Sulewski, MD

- 2021 Resident Surgical Teaching Award, Scheie Eye Institute

Madhura Tamhankar, MD

- 2021 Philadelphia Magazine Top Doctor
- 2021 Castle Connolly Top Doctor
- 2021 Castle Connolly Exceptional Women in Medicine

Katherine Uyhazi, MD, PhD

- 2020 Linda Pechenik Montague Investigator Award

Brian VanderBeek, MD, MPH, MSCE

- 2021 Secretariat Award, American Academy of Ophthalmology

Faculty Publications

(July 1, 2020 – July 1, 2021)

Adams-Chapman I, Watterberg KL, Nolen TL, Hirsch S, Cole CA, Cotten CM, Oh W, Poindexter BB, Zaterka-Baxter KM, Das A, Lacy CB, Scorsone AM, Duncan AF, DeMauro SB, Goldstein RF, Colaizy TT, Wilson-Costello DE, Purdy IB, Hintz SR, Heyne RJ, Myers GJ, Fuller J, Merhar S, Harmon HM, Peralta-Carcelen M, Kilbride HW, Maitre NL, Vohr BR, Natarajan G, Mintz-Hittner H, Quinn GE, Wallace DK, Olson RJ, Orge FH, Tsui I, Gaynon M, Hutchinson AK, He YG, Winter TW, Yang MB, Haider KM, Cogen MS, Hug D, Bremer DL, Donahue JP, Lucas WR, Phelps DL, Higgins RD, Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network (2021) **Neurodevelopmental outcome of preterm infants enrolled in myo-inositol randomized controlled trial.** *J Perinatol* 41(8):2072–2087.

Addis V, Chan L, Chen J, Goodyear K, Pistilli M, Salowe R, Lee R, Sankar P, Miller-Ellis E, Cui QN, Maguire MG, O'Brien J (2021) **Evaluation of the Cirrus High-Definition OCT Normative Database Probability Codes in a Black American Population.** *Ophthalmol Glaucoma* S2589-4196(21):00134-4.

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Ammar MJ, Carroll R, Kolomeyer A, Ying GS, Whitehead G, Brucker AJ, Kim BJ (2021) **Clinical Utility of Beta-D-Glucan Testing for Endogenous Fungal Chorioretinitis or Endophthalmitis.** *Retina* 41(2):431–437.

Ammar MJ, Kolomeyer AM, Bhatt N, Tamhankar MA, Mullen MT, Brucker AJ (2020) **Recurrent Branch Retinal Artery Occlusion from Susac Syndrome: Case Report and Review of Literature.** *Retin Cases Brief Rep* 14(4):315–320.

Amutah C, Greenidge K, Mante A, Muniyikwa M, Surya SL, Higginbotham E, Jones DS, Lavizzo-Mourey R, Roberts

D, Tsai J, Aysola J (2021) **Misrepresenting Race - The Role of Medical Schools in Propagating Physician Bias.** *N Engl J Med* 384(9):872-878.

Antoszyk AN, Glassman AR, Beaulieu WT, Jampol LM, Jhaveri CD, Punjabi OS, Salehi-Had H, Wells J.A., 3rd, Maguire MG, Stockdale CR, Martin DF, Sun JK, DRCR Retina Network (2020) **Effect of Intravitreal Aflibercept vs Vitrectomy with Panretinal Photocoagulation on Visual Acuity in Patients With Vitreous Hemorrhage From Proliferative Diabetic Retinopathy: A Randomized Clinical Trial.** *JAMA* 324(23):2383-2395.

Barbieri JS, Bunya VY, Massaro-Giordano M, Margolis DJ (2021) **Encounters and medication use for ocular surface disorders among patients treated with dupilumab: A cohort study.** *JAAD Int* 4:1-9.

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Chen X, Tai V, McGeehan B, Ying GS, Viehland C, Imperio R, Winter KP, Raynor W, Tran-Viet D, Mangalesh S, Maguire MG, Toth CA, BabySTEPS Group (2020) **Repeatability and Reproducibility of Axial and Lateral Measurements on Handheld Optical Coherence Tomography Systems Compared with Tabletop System.** *Transl Vis Sci Technol* 9(11):25.

Cheng QE, Quinn GE, Daniel E, Baumritter A, Smith E, Ying GS, e-ROP Cooperative Group (2020) **Progression from preplus to plus disease in the Telemedicine Approaches to Evaluating Acute-Phase Retinopathy of Prematurity (e-ROP) Study: incidence, timing, and predictors.** *J AAPOS* 24(6):354.e1-354.e6.

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Faculty In the News

Below is a selection of recent news stories featuring our ophthalmology faculty's research and clinical work.

September 22, 2021: Dr. Jean Bennett. **Penn Gene Therapy Spinout Taking on Rare Retinal Diseases Launches with \$19M in Seed Funding.** *Philadelphia Business Journal*: "A new gene therapy company attempting to commercialize the research of Penn Medicine's Dr. Jean Bennett launched Wednesday with \$19 million in seed capital."

September 20, 2021: Drs. Qi Cui and Brian VanderBeek. **Diabetes Medications Linked to Glaucoma Prevention.** *Science Daily*: "A popular class of diabetes medications called GLP-1R agonists (Trulicity and Rybelsus) may also protect against glaucoma in diabetic patients, according to a new study led by researchers in the Scheie Eye Institute at the University of Pennsylvania."

August 12, 2021: Dr. Vatiee Bunya. **Relief for Dry Eyes.** *Penn Today*: "Many of our patients have told us that it's the worst medical problem that they suffer from. Even though dry eye in itself won't cause you to completely lose your vision, it can really be debilitating."

August 8, 2021: Drs. Joan O'Brien, Eydie Miller-Ellis, and Ahmara Ross. **More Than 10,000 Black Philadelphians are Participating in a Penn Study to Understand Glaucoma.** *The Philadelphia Inquirer*: "Led by Joan O'Brien, professor of ophthalmology and director of Scheie, the Primary Open-Angle African American Glaucoma Genetics Study has recruited more than 10,000 Black Philadelphians for one of the largest genetic studies of the disease in this population."

August 6, 2021: Dr. Ahmara Ross. **Understanding Ocular Migraine: Symptoms, Diagnosis, and Treatment.** *SELF*: "What experts do know is that the same triggers that cause regular migraine attacks can prompt an ocular migraine as well."

July/August 2021: Dr. Artur Cideciyan. **Let's Talk About Gene Therapy for Inherited Retinal Diseases.** *Retina Today*: "The approval of the first gene

therapy in the United States has sparked significant interest in this patient population. What's next in the research pipeline?"

July 13, 2021: Dr. Joan O'Brien. **Recent PSOM Awards and Accolades.** *University of Pennsylvania Almanac*: "Joan O'Brien, chair of ophthalmology, and researchers at the Scheie Eye Institute were awarded a five-year, \$6.6 million National Eye Institute grant renewal to investigate genetic variants associated with primary open-angle glaucoma (POAG) in Black people."

June 16, 2021: Dr. Mina Massaro. **The Medicine in Eye Drops Needs a Disguise to Sneak Past Your Tears.** *Newsweek*: "As a dry eye specialist I see a myriad of patients with various surface disease issues, and in order to achieve an effective treatment, drugs need to reach the target tissue (i.e. the corneal epithelial cells)."

June 8, 2021: Dr. Vatiee Bunya. **How Novel Autoantibodies May Improve Screening Dry Eye Patients for Sjogren's Syndrome.** *Ophthalmology Times*: "Researchers seek to identify new serological biomarkers that could better characterize Sjogren's syndrome and overcome the limitations of traditional antibodies."

June 7, 2021: Dr. Grant Liu. **A Mysterious Condition Threatens Vision, Especially in Young Black and Hispanic Women.** *The Philadelphia Inquirer*: "A new study from Penn Medicine has found that [idiopathic intracranial hypertension (IIH)] is more common among Black and Hispanic women and that patients diagnosed with IIH were more likely than other ophthalmology patients to live in food swamps, or neighborhoods with abundant sources of junk food and fast food."

June 1, 2021: Dr. Eydie Miller-Ellis. **Tackling Health Care Disparities.** *EyeNet Magazine*: "While the genetic underpinnings of glaucoma continue to be studied, the relationship between socioeconomic status, ethnicity, access to eye care, and reduced quality of life also play a role in glaucoma development and disease severity."

April 1, 2021: Drs. Artur Cideciyan and Samuel Jacobson. **A Single Injection Reverses Blindness in Patient with Rare Genetic Disorder.** *Science Daily*: "Results of the case, detailed in a paper published today in *Nature Medicine*, show that the treatment led to marked changes at the fovea, the most important locus of human central vision."

March 30, 2021: Dr. Stephen Orlin. **Corneal Transplantation Experiences a Revolution.** *Ophthalmology Times*: "A revolution is afoot in corneal surgery. New, evolving procedures have bumped penetrating keratoplasty as the gold standard despite its high success rates."

March 3, 2021: Dr. Eydie Miller-Ellis. **Q&A Mentorship Key to Preparing Next Generation of Ophthalmologists.** *Healio*: "One welcome consequence of the COVID-19 pandemic is that people are seriously talking about health disparity and lack of access to care in communities of color, Eydie G. Miller-Ellis, MD told Healio/OSN."

January 11, 2021: Drs. Jean Bennett, Ahmara Ross, and Kenneth Shindler. **Gyroscope Therapeutics, UPenn to Develop Gene Therapies for Serious Eye Diseases.** *Ophthalmology Times*: "Investigators from the clinical-stage gene therapy company and the University's Penn Center for Advanced Retinal and Ocular Therapeutics (CAROT) will collaborate to analyze specific gene therapy targets for glaucoma, optic neuritis, and retinitis pigmentosa."

December 3, 2020: Drs. Jean Bennett and Albert Maguire. **These Scientists Set Out to End Blindness. Their Innovations Just Won Them \$3 Million.** *National Geographic*: "Bennett and her colleagues developed a groundbreaking treatment for Leber congenital amaurosis (LCA) that replaces the faulty gene that causes the [blinding] condition with a healthy one."

Note: This list includes a selection of news items published in 2020 and 2021. For a complete list, visit <https://www.pennmedicine.org/departments-and-centers/ophthalmology/about-us/news/faculty-in-the-news>.



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The Scheie Eye Institute is the Department of Ophthalmology at the University of Pennsylvania. Scheie has been a leader in the field of ophthalmic research, education, and patient care for 147 years. Many of our greatest advancements in vision-saving therapy have been made possible by donations from individuals and organizations.

Will you join the Scheie Eye Institute?

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