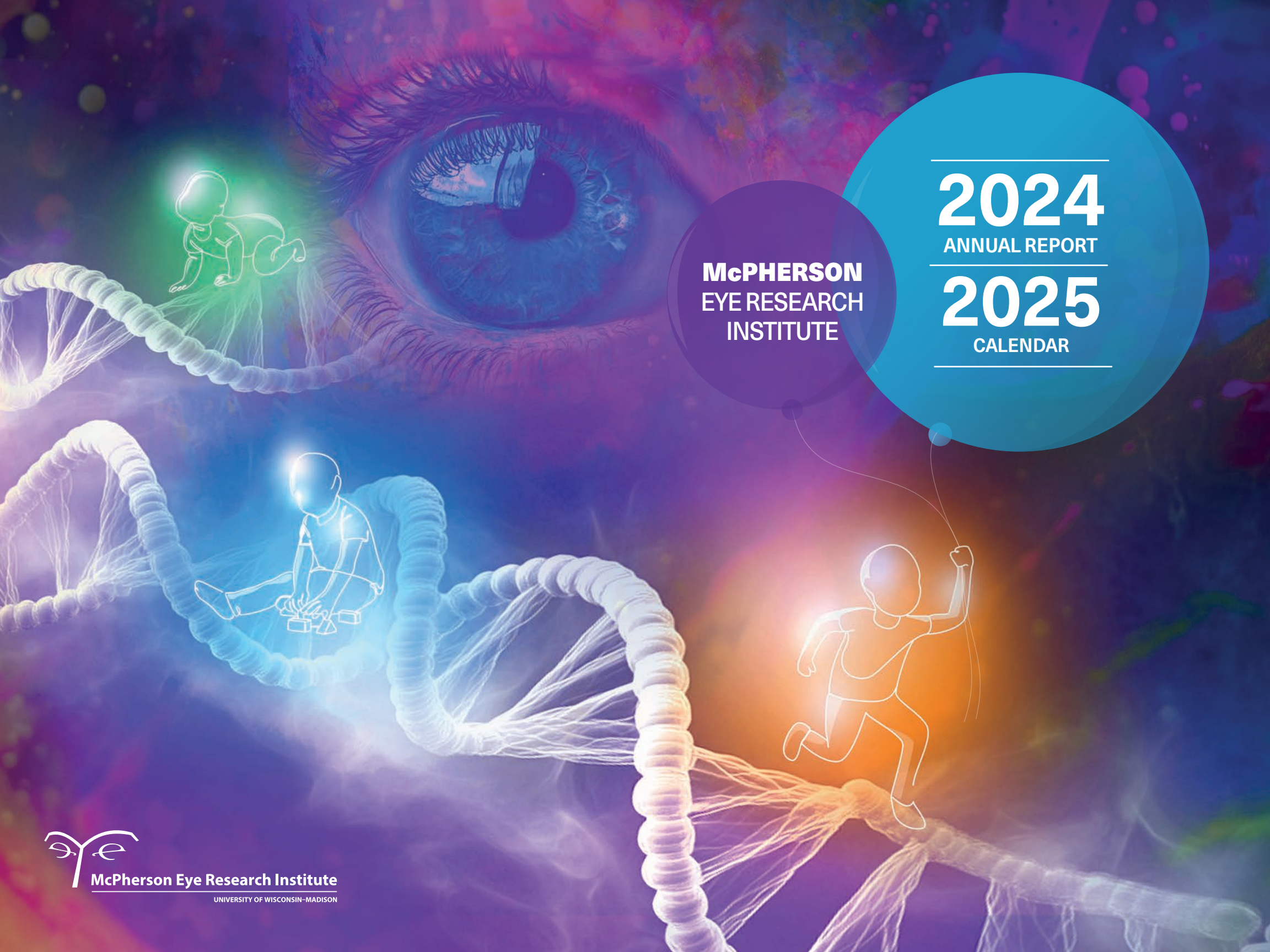




McPHERSON
EYE RESEARCH
INSTITUTE

2024

ANNUAL REPORT

2025

CALENDAR



McPherson Eye Research Institute

UNIVERSITY OF WISCONSIN-MADISON

From the Director

Dear Friends of the McPherson ERI,

2025 is a milestone year for the McPherson Eye Research Institute—our 20th anniversary. The concept of the Institute, born from the friendship and foresight of Dr. Daniel Albert and Dr. Alice McPherson, was revolutionary from the beginning. While traditional academic eye research institutes are largely confined to a single building or department and a handful of scientists, the McPherson ERI was designed to be limitless in its reach and impact. How? By taking advantage of one of the greatest qualities of UW-Madison—the willingness of its researchers and clinicians to work together to share ideas and resources in order to solve tough problems.

McPherson ERI started in 2005, eager to spearhead new collaborations and projects that bring the brightest scientists together irrespective of physical location,

departmental ties, or previous research focus. In the 20 years that followed, the Institute has grown to nearly 200 members across 9 different schools and 52 departments at UW-Madison. In addition, we have welcomed associate members at 5 other Wisconsin institutions and have supported over 100 talented students who will continue our mission to eradicate blinding conditions. The Institute's role doesn't stop after we recruit a promising new scientist, either. We also provide critical funds to start and finish projects that increase knowledge and translate into tomorrow's therapies. And we are committed to communicating our accomplishments to the people for whom the McPherson ERI was created—you.

In this year's calendar, we highlight our members whose research focuses on children. Losing sight at any age is devastating, but vision loss at a young age can have an especially profound and far-reaching impact. As a pediatric ophthalmologist myself, I often break the news to a family that their child has a currently untreatable blinding condition. Such situations drive my

laboratory's efforts to develop stem cell-based therapies to replace cells lost to retinal degenerative diseases. They also give me the opportunity to witness the courage, creativity, and brilliance of kids and families challenged by vision impairment. Other McPherson ERI researchers highlighted in this calendar have their own stories, but all of us are motivated to safeguard the vision of children.

We are grateful to those of you who have helped us out in our first twenty years, and look forward to working with you, and sharing our results, going forward. Thank you.



David M. Gamm, MD, PhD

RRF Emmett A. Humble Distinguished Director
Professor, Department of Ophthalmology
and Visual Sciences
Sandra Lemke Trout Chair in Eye Research



The Eyes of a Child

We are taught about the five senses in elementary school, although by the time we learn their names, we are already adept at using them to interpret the world. Loss or diminishment in any of these senses when young can seem catastrophic, a restriction in our growing knowledge of our surroundings. And surveys reveal that sight is the sense that is most valued—and its loss most feared—by people throughout the lifespan.

Our researchers know well the importance of preserving vision in young people. Work in their labs is aimed at understanding how the visual system develops, how to maximize its potential, and how to combat diseases and conditions that threaten to take it away. In the next few pages, we highlight a variety of research efforts that have a pediatric focus, starting with diseases that affect newborns and infants. You'll also read about inherited retinal diseases that manifest later in childhood or in young adults, and about one of many McPherson ERI members investigating how children perceive the visual world.

Diseases of Infancy

Retinopathy of Prematurity

Retinopathy of Prematurity (ROP) is the major cause of vision impairment in babies born prematurely, and the risk of ROP increases in tandem with the degree of prematurity. ROP occurs when the developing blood vessels in a baby's retina temporarily stop growing due to higher oxygen levels than what is present in the uterus. Such oxygen levels are needed for lung, brain, and other organ development, so it creates a 'Catch-22' for doctors and families. Eventually, the retinal blood vessels start growing again in response to molecules, or signals, released by the distant areas of the retina that find themselves lacking an adequate blood supply. Sometimes, these signals cause the growth of abnormal blood vessels that, if left untreated, result in retinal stretching or detachment, followed by scar formation and vision loss. Although we know that oxygen plays a major role in the process leading to ROP, the complete mechanism remains unknown. Without such knowledge, our treatment options—which have thankfully become more powerful in recent years—still remain limited. A group of McPherson ERI researchers, including **Drs. Ismail Zaitoun, Chris Sorenson, and Nader Sheibani**, are investigating the factors responsible for the developing retina's sensitivity to varying oxygen levels.

Dr. Sheibani focuses on the specific cellular pathways that go awry and drive the growth of abnormal blood vessels. His lab, which studies the proteins in retinal cells that normally inhibit blood vessel growth, has identified short regions of these proteins, called peptides, that are suitable as therapeutics. In their current model of ROP, these peptides reduced the growth of abnormal blood vessels and preserved retinal structure and function. The Sheibani lab is also investigating whether vitamin D may have a role in the prevention or treatment of ROP, although additional studies are needed to determine its risk-benefit ratio.



Retinopathy of prematurity in a mouse model retina, above right, compared with a normal retina, below left. Image courtesy of the Sheibani Lab.

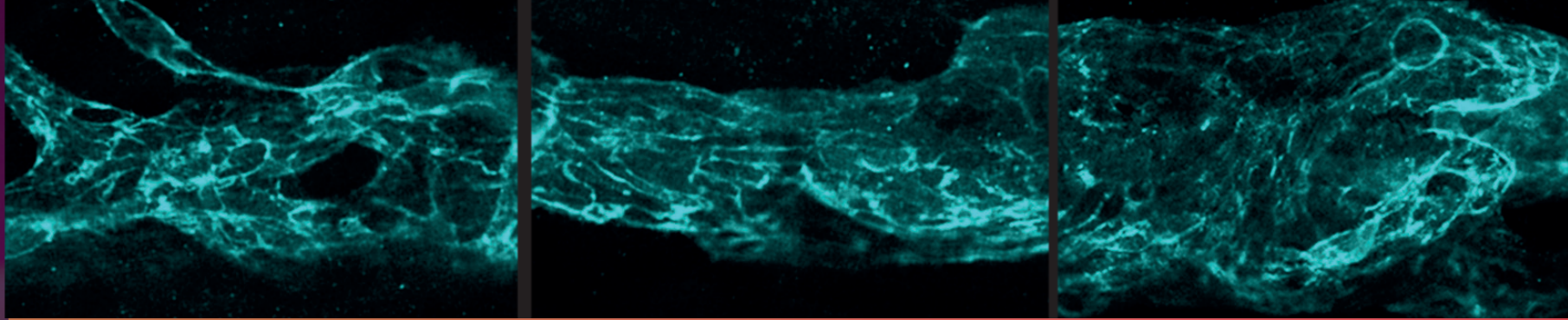
Proteins that control cell death are also a possible target for combatting ROP. Dr. Sorenson was the first scientist to show that a cell death protein by itself can drive abnormal blood vessel development in a mouse model of ROP. Mice that are completely deficient in the production of this protein are protected from the growth of aberrant vessels. However, Drs. Zaitoun and Sorenson also determined that locally eliminating this protein in particular cells that form retinal blood vessels could not prevent their abnormal growth (nature has a way of being more complicated than we like). Undaunted, Dr. Zaitoun was recently awarded a multimillion dollar grant by the National Institutes of Health to better understand how to harness their findings to create a safer and more effective ROP treatment.



Primary Congenital Glaucoma

Glaucoma is most often thought of as a disease of aging, but it can occur at any age. Pediatric ophthalmologist **Dr. Terri Young** and human molecular geneticist **Dr. Stuart Tompson** are investigating primary congenital glaucoma (PCG), a severe ocular disorder that can affect infants from birth. The disease is caused by impaired function of the eye's main fluid drainage tissues, which is composed of a sieve-like cover (trabecular meshwork) that leads into a large vessel (Schlemm's canal) connecting to the systemic blood circulatory system. In kids without a fully functional drainage system, eye pressure builds up, leading to enlargement of the eye, cloudiness of the cornea, and severe damage to the optic nerve and retina, which in turn can result in permanent vision impairment, blindness, or even loss of the eye.

Currently, the only treatment for PCG is surgical, which is challenging and often requires multiple operations. Unfortunately, a significant proportion of children with PCG do not respond adequately to these interventions. Drs. Young and Tompson investigate the genetic and molecular causes of PCG with the goal of developing non-surgical interventions that could halt PCG early in its development.



Schlemm's canal at 3 different stages of development (7, 14, and 28 days). Image courtesy of Stuart Tompson, PhD.

The molecular causes of PCG are largely unknown, but one-quarter of cases can be attributed to mutations in four genes important for outflow pathway development. By sequencing the genomes of affected children, Drs. Young and Tompson identified two of these genes, TEK and ANGPT1, which are crucial for the formation of Schlemm's canal—the main outflow conduit of the eye. Current research is aimed at delivering normal copies of these genes to young outflow tissues with the goal of at least partially rescuing drainage function and associated vision loss.

Dr. Tompson's recent research has used new sequencing approaches to identify the cell types and molecular pathways actively involved in the normal development of outflow tissues in a rodent model. His study successfully profiled approximately 30,000 genes in 10,000 developing trabecular meshwork cells and 600 developing Schlemm's canal cells. This data will help researchers discover new mechanisms underlying unsolved cases of PCG, which will hopefully enable development of more effective treatments for these children and young adults. In

addition, findings from this research may reveal biological pathways important for maintaining normal eye fluid drainage throughout life. Promise is already being shown for the TEK-ANGPT1 pathway, which researchers are currently targeting to treat late-onset forms of glaucoma.



Looking to Learn

Dr. Haley Vlach's research examines how children's visual attention supports their thinking and learning. Infants and children enter the world with only basic perceptual capacities, which are used as building blocks for later learning. Dr. Vlach's Learning, Cognition, & Development (LCD) Lab studies the way that children view new information, and how those patterns of viewing support higher-order cognition.

In particular, Dr. Vlach's work identifies where children look while learning, and how these eye movements contribute to the achievement of cognitive milestones, such as learning language and new concepts. Studies in the LCD Lab present children with several types of learning experiences, such as reading a storybook.

Eye tracking technology—specifically, a Tobii X3-120 eye tracker—is used to record where children look during these learning experiences. Researchers then determine if the child's approach to visually surveying new information predicts their success on a learning assessment; for instance, whether they learned new words while reading a storybook.

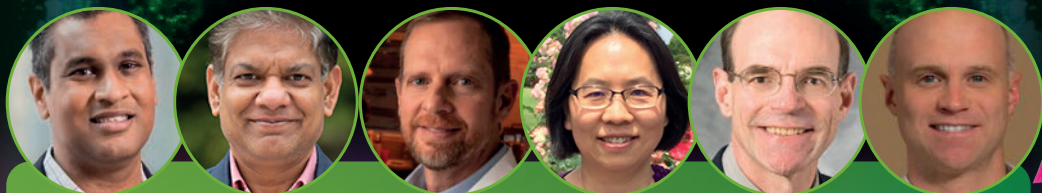
The results of the LCD Lab's work have highlighted the important role that children's eye movements play in their learning. The research shows that sustained visual attention can support learning; for example, looking at objects that are being named increases the ability of the child to learn the word associated with that object. Thereafter, looking away from the named object can



Eyetracking Storybook, image courtesy of Haley Vlach, PhD.

facilitate child's ability to recall that information from memory. That is, both looking—and looking away—are important perceptual processes that support children's higher-order cognition.

Children's Visual Attention & Cognition



Genetic Diseases of the Retina

Vision loss in childhood or teenage years can be the result of one of many rare genetic mutations that cause progressive retinal degeneration. These mutations come in a wide variety of types, and the resulting inherited retinal diseases (IRDs) have different names: retinitis pigmentosa (RP), cone-rod dystrophy, Usher syndrome, Stargardt disease, Leber congenital amaurosis (LCA), Best disease, choroideremia, etc. McPherson ERI researchers are working to develop treatment strategies for these diseases that will correct the underlying genetic causes before retinal cells degenerate (through gene therapies) or replace the cells once they are lost (using stem cells).

In recent years, gene editing (or “repair”) has offered great promise for permanently fixing IRD mutations and halting vision loss in its tracks. Gene editing is still in its infancy, but a large and dedicated group of McPherson ERI researchers has shown using multiple model systems that it can correct mutations in at least two types of IRDs—LCA and Best disease. The group, which includes **Drs. Kris Saha, Bikash Pattnaik, David Gamm, Sarah Gong, Mike Nork, and William Murphy**, received a 5-year, \$29 million NIH grant in 2023 to advance this technology and develop treatments for affected individuals.

The long path leading to this effort included the Gamm Lab’s creation of human retina “in a dish” (2009), followed

by collaborative work between the Gamm, Saha, and Pattnaik labs to develop the first human stem cell-derived model of Best disease (2013). Shortly thereafter (2015), the Pattnaik Lab invented a new method of studying the genetic basis of a rare form of LCA (LCA16). These early achievements opened the door for the Gamm and Pattnaik Labs to work with Kris Saha, a world-leading gene editing expert, to devise an approach to repair the gene mutations in Best disease and LCA16. In 2020, this group used gene editing to fully correct Best disease mutations in retinal stem cell models, and in 2023, a similar method was used to repair a gene mutation that caused the disease LCA16. In the latter case, the gene editor was delivered using nanoparticles developed by the Gong Lab—a true coalescence of UW-Madison McPherson ERI know-how and teamwork! In the next five years, these researchers will take steps to bring these therapies to the clinic.

But what can be done in late stages of disease once retinal cells have deteriorated? David Gamm’s lab has worked to answer that question for over 20 years. His lab is dedicated to using induced pluripotent stem cells (iPSCs) to generate authentic human photoreceptors and retinal pigment epithelium (RPE) cells with potential

The components of gene editing, illustration by Adam Steinberg. Nanocapsule image courtesy of Sarah Gong, PhD. Gamm Lab retinal organoid image, courtesy of the Gamm Lab.



to replace those that are lost from disease or injury. Human iPSCs are created by reprogramming a person’s own blood or skin cells to a very primitive state, at which point they can be coaxed into producing any other type of human cell, including those found in the retina.

Over the past ten years, the Gamm lab has worked to convert their breakthroughs to a product that can be used to treat people. To do so required help from some big-time friends, including OpSis Therapeutics and Fujifilm-Cellular Dynamics Inc. (Madison, WI), FUJIFILM (Tokyo, Japan), BlueRock Therapeutics (Boston, MA), and Bayer AG (Germany). This past summer, after years of work that culminated in a 12,000-page Investigational New Drug (IND) application, the FDA approved their request to initiate the first-ever clinical trial for a human photoreceptor replacement therapy, which is scheduled to begin in 2025. The trial is designed to see if the approach is safe and effective in a broad range of IRDs. Additional clinical trials, including those designed to replace both photoreceptors and RPE cells in diseases that cause macular degeneration, are also in the works.

RETINA RESEARCH FOUNDATION

CHAIRS AND PROFESSORSHIPS

Bikash Pattnaik PHD, MPHIL

Pediatrics 🌟 RRF Daniel M. Albert Chair



"Our ongoing work was formerly supported by the **RRF M.D. Matthews Research Professorship** and is now supported by the **RRF Daniel M. Albert Chair**; both have had a significant impact on our research, including allowing us to develop new mouse models of photoreceptor ion channel mutations that cause blindness. Since we demonstrated positive outcomes in treating RPE-specific channelopathies such as Leber Congenital Amaurosis, our goal has been to target photoreceptor cells from the same subretinal space delivery. Current work includes translating our research outcome applications to channelopathies that affect other conditions in addition to blindness."



David Gamm MD, PHD

Ophthalmology and Visual Sciences
🌟 RRF Emmett A. Humble Distinguished Directorship

"The **RRF Emmett A. Humble Distinguished Directorship** has continuously supported my lab's efforts to generate photoreceptors (rods and cones) from human stem cell-derived retinal organoids for use in cell replacement therapies. This past year, in close collaboration with multiple industry partners, we obtained FDA approval to proceed with a clinical trial aimed at replacing degenerated photoreceptors in patients with these conditions. It is our hope and plan that the trial will begin in 2025. While this is a major milestone, we continue to work to improve the technology on multiple fronts with the assistance of this important source of funding."

Endowed positions funded by the Retina Research Foundation, founded by Dr. Alice McPherson in 1969, have been essential to the McPherson ERI's work since its beginning.

Timothy Gomez PHD

Neuroscience
🌟 RRF M. D. Matthews Research Professor



"My laboratory is focused on understanding in detail the cellular and molecular mechanisms that promote the development of human photoreceptor axons, and how these axons extend toward their targets and form synapses. We recently described for the first time how human photoreceptors naturally lose the ability to extend axons with age. We hope to exploit this natural switch to identify target genes that could be over-expressed to enhance photoreceptor axon extension. With the help of the **RRF M.D. Matthews Professorship**, our goal is to improve the integration of transplanted stem cell-derived photoreceptors into patients with degenerative disorders."



Mrinalini Hoon PHD

Ophthalmology and Visual Sciences
🌟 RRF Rebecca Meyer Brown Professor

"Through the support of the **RRF Rebecca Meyer Brown Professorship**, our research is expanding our understanding of the molecular and activity-dependent mechanisms that regulate information processing in the mammalian retina. Retinal neurons communicate at junctions of contact called synapses. Efficient formation and function of retinal synapses underlies visual information processing, and our research is uncovering new cues that regulate the establishment and maintenance of functional retinal synapses. This information can be harnessed for reinstating visual function in a diseased retina."

Kevin Eliceiri PHD

Director/LOCI, Morgridge Institute for Research
🌟 RRF Walter H. Helmerich Research Chair



"My research interests involve the development of computational imaging approaches to study the role of the cellular microenvironment in wound healing processes such as those that occur in the eye. The **RRF Walter H. Helmerich Research Chair** supports the development of novel optical imaging methods for investigating dynamic cellular interactions, and the development of deep learning approaches for image analysis."



Krishanu Saha PHD

Biomedical Engineering 🌟 RRF Kathryn and Latimer Murfee Chair

"In 2024, we made significant strides in the CRISPR Vision Program with the support of the **RRF Kathryn and Latimer Murfee Chair**. We focused on developing injectable drugs for Best disease and Leber congenital amaurosis, supported by the NIH. Our collaborative efforts have yielded promising data in animal models and human tissue models, and we aim to submit an investigational drug application to the FDA by 2028. New projects this year include testing the nonviral base editing strategies for additional pathogenic mutations that cause inherited retinal diseases affecting the retinal pigment epithelium."



Sarah Gong PHD

Ophthalmology and Visual Sciences and Wisconsin Institute for Discovery 🌟 RRF Edwin and Dorothy Gamewell Professor

"The Gong Laboratory specializes in engineering innovative biomaterials for gene therapy, cell therapy and immunotherapy. In 2024, with support from the **RRF Edwin and Dorothy Gamewell Professorship**, we focused on combating blindness through two main approaches: Developing lipid nanoparticles for ocular genome editing therapy and creating honeycomb-shaped 3D microstructured scaffolds for photoreceptor and retinal pigment epithelium cell therapy."

MONROE AND SANDRA TROUT CHAIRS

The three Chairs endowed by McPherson ERI friends Monroe and Sandra Trout are at the forefront of bringing new therapies for age-related macular degeneration to the clinic as part of the Trout AMD Project. They will soon be joined by a fourth Chair, the Monroe E. Trout Jr Chair in Eye Research.



David Gamm MD, PhD

Ophthalmology and Visual Sciences

☼ Sandra Lemke Trout Chair in Eye Research

“While photoreceptor replacement alone may be sufficient to improve vision in patients with retinitis pigmentosa and related diseases, many macular conditions (such as AMD, Stargardt disease, Best disease, and choroideremia) may require replacement of both photoreceptors and retinal pigmented epithelium (RPE) cells. In the past year, support from the **Sandra Lemke Trout Chair in Eye Research** has allowed my lab to work on strategies to deliver both RPE cells and photoreceptors to the subretinal space. To advance this work, our lab works closely with other MERI labs headed by Drs. Sarah Gong and Jack Ma, as well as Dr. Kapil Bharti's lab at the National Eye Institute.”

Akihiro Ikeda DVM, PhD

Medical Genetics

☼ Timothy William Trout Chair in Eye Research

“Support from the **Timothy William Trout Chair in Eye Research** has been instrumental in advancing the work of my lab, which focuses on the relationship between metabolic regulation of the retina and the aging process, as well as its link to age-related diseases. A key aspect of our research involves using a mouse model with accelerated retinal aging. Recent studies from our lab have shown that supplementation of docosahexaenoic acid (DHA) in these mice can alleviate age-related retinal issues, including inflammation and degeneration. We have also initiated a new line of research focusing on changes in mitochondrial structure and function. Regulation of mitochondrial dynamics is critical for the healthy aging of retinal cells.”

Michael Altaweel MD, FASRS

Ophthalmology and Visual Sciences

☼ Monroe E. Trout Chair in Eye Research

“**The Monroe E. Trout Chair in Eye Research** has supported the development of a surgical program at MERI to deliver stem cell-derived photoreceptors (developed by Dr. Gamm and his team) into the subretinal space. Our successful surgery in preliminary models has contributed to FDA approval of a first in human clinical trial where I will conduct this surgery at the University of Wisconsin Hospital. There is a tremendous opportunity to advance the care of our patients. The Chair has enabled the acquisition of surgical equipment and resources to continue development of our techniques in an outstanding team environment.”

DAVID AND NANCY WALSH FAMILY

PROFESSORSHIP IN VISION RESEARCH



Raunak Sinha PhD

Neuroscience



“The **David and Nancy Walsh Family Professorship** has supported our efforts to understand how the way in which cone photoreceptors function in the centermost part of the primate retina, the fovea—responsible for high-acuity vision—is specialized and distinct from cone function in the rest of the primate retina. This work also serves as a benchmark for our collaborative efforts on evaluating the functional authenticity of photoreceptors in human stem cell-derived retinas for cell replacement therapy and modeling retinal diseases in a dish.”



Filiz Yesilkoy PHD

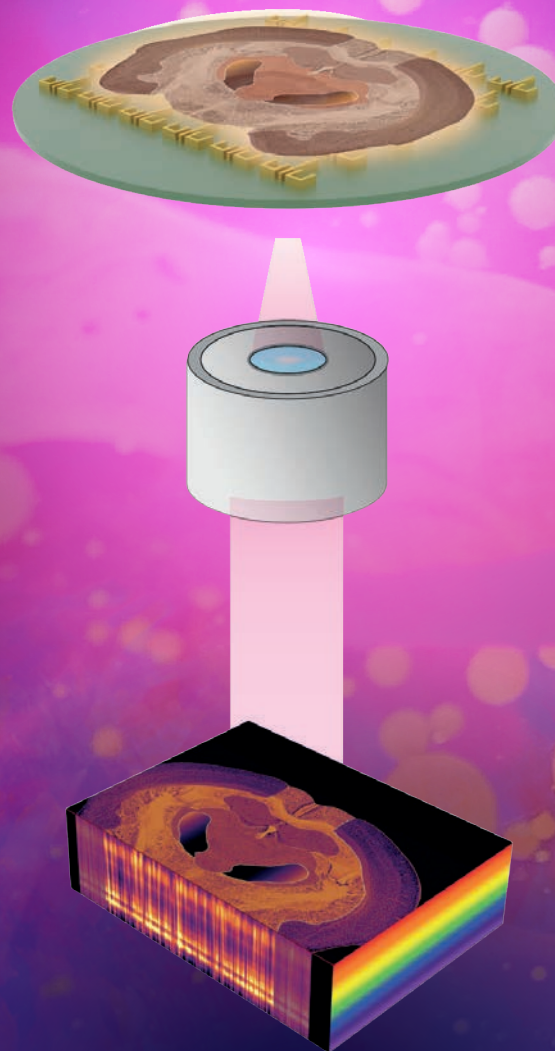
Assistant Professor 🌱 Biomedical Engineering

Research in biomedical sciences often depends on the quality of imaging techniques, which have improved dramatically in recent years. Optical microscopy, for instance, is essential in most efforts to enhance understanding of disease and to develop new diagnostic methods and effective treatments. Advancements in fluorescence microscopy—which can be used to visualize individual cells, parts of cells, or even proteins that are involved in eye disease—have led to numerous scientific and medical breakthroughs. However, such imaging methods are limited when molecular tools (called labels, or probes) capable of homing in on target cells and proteins do not exist. In this situation, the underlying disease process becomes effectively “invisible.”

Fortunately, light interacts with molecules in various interesting ways, allowing us to measure the composition of biological samples based on these intrinsic light-matter interactions, without the need for labels. **Dr. Filiz Yesilkoy's** research focuses on infrared spectrochemical imaging—a label-free optical microscopy technique that can identify the vibration frequencies in molecules' bonds, similar to those of guitar strings.

In their recent work, Dr. Yesilkoy's team developed a process that combines the strengths of different optical imaging techniques with machine learning to investigate chemical and structural changes in tissue samples. Importantly, the imaging modalities developed by Dr. Yesilkoy's group can detect protein degeneration and accumulation of damaged proteins in tissues, which occur in numerous retinal diseases including AMD. Going forward, Dr. Yesilkoy is eager to apply these imaging methods to disease-specific studies, including research on neural and retinal degenerative diseases.

FEATURED RESEARCHERS



Above: Hyperspectral mid-infrared imaging of murine brain sections (at the top) helps characterize the chemical composition of tissues without the need for labeling with dye molecules. Image courtesy of Filiz Yesilkoy, PhD.



Natascha Merten PHD, MS

Assistant Professor
🌱 Population Health Sciences
and Medicine (Geriatrics & Gerontology)

Dr. Natascha Merten, a psychologist (MS) and epidemiologist (PhD) by training, is interested in understanding the processes of human brain aging. As the Principal Investigator of the Beaver Dam Offspring Study-Neurocognitive Aging Study (BOSS-NCAS), a large cohort study on aging funded by the National Institutes of Health, she has an extraordinary resource for her work. The BOSS-NCAS aims to study both cognitive and sensory changes, including vision and hearing loss. Through this effort, scientists will investigate whether blood tests can be used to understand who is at risk for developing particular age-related changes in neurological and visual function.

Dr. Merten's lab uses a holistic approach by investigating general aging processes that affect multiple aspects of brain aging and dementia, with a focus on vision, hearing, and smell. Her team considers a wide range of risk factors for Alzheimer disease to identify common pathways of neurodegeneration and brain aging. She also investigates early biomarkers of aging to identify individuals at greater risk for other health conditions.

Prevention is an important goal—perhaps the most important goal—and Dr. Merten's team is searching for modifiable risk factors of brain aging with a primary focus on lifestyle and behavior, such as active learning, regular exercise, and smoking cessation. Understanding how such factors contribute to normal and abnormal aging is a powerful means to inform prevention and treatment strategies that might benefit a wide range of blinding diseases.



Akhilesh Jaiswal PHD, MS

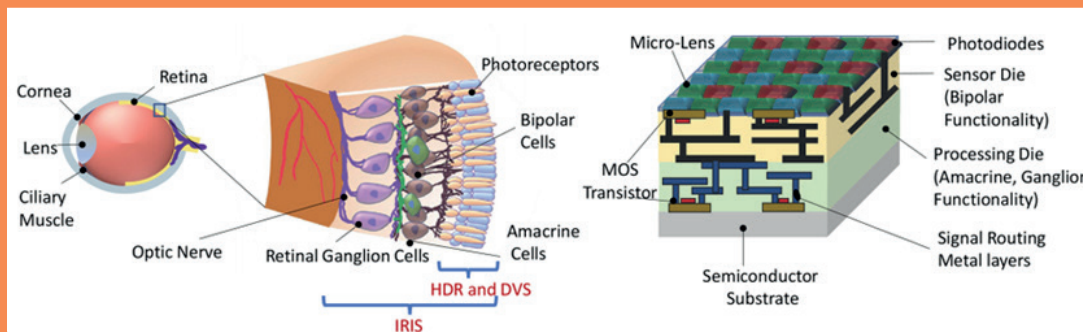
Assistant Professor 🌐 Electrical and Computer Engineering

The retina is an incredible instrument for image data collection, far superior to the tools currently used to compile computer vision. **Dr. Akhilesh Jaiswal's** work aims to close the gap by using lessons from the retina to develop a new type of retina-inspired sensor for computer vision.

Today's computer vision relies exclusively on light intensity-based pixel data collected through state-of-the-art image sensors. However, in almost all cases, appropriate context for the pixels is missing (or are extremely vague) with respect to the “real-world events” being captured by the sensor. Thus, the onus of processing is put on intelligent machine learning algorithms to pre-process, extract appropriate context, and make intelligent decisions based on light intensity-based pixel data. Unfortunately, there are numerous limitations in this computer vision pipeline that

increase the time required to make critical decisions. Computers are only as fast as the processing time of the machine learning algorithms—and the process itself is energy-hungry.

In contrast, the biological retina provides dozens of feature-selective computations that involve object trajectory, velocity, shape, and orientation with an emphasis on approaching threats. The visual cortex receives precise feature data from the retina that is heavily geared toward quick processing and maneuverability (for example, avoiding an oncoming bus). Dr. Jaiswal is developing a new family of retina-inspired sensors called IRIS (Integrated Retinal functionality in CMOS Image Sensors) that will introduce a new frontier in vision-based decision-making that provides real-world context to the pixels that computers rely on to “see”.



Using the structure of the retina as a model, Dr. Akhilesh Jaiswal's lab aims to create a new generation of sensors to improve computer vision. Image courtesy of the Jaiswal lab.



Pallavi Tiwari PHD

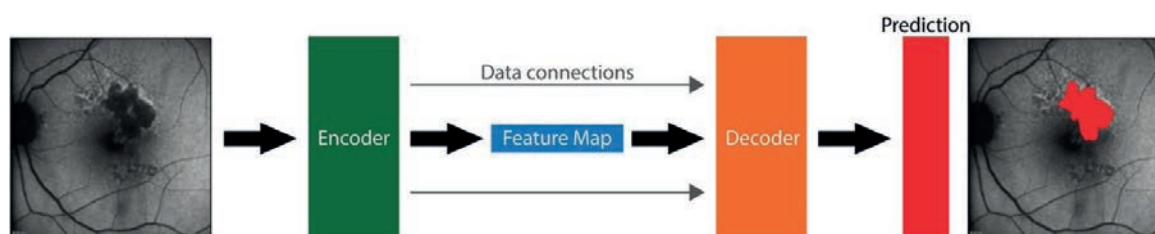
Assistant Professor 🌐 Radiology, Biomedical Engineering, and Medical Physics

Pallavi Tiwari's Integrated Diagnostics and Analytics (IDiA) Lab has been breaking new ground in precision medicine through their work in computational imaging and AI to predict patient treatment responses in cancer and neurological conditions, including vision threatening diseases. The strength of Dr. Tiwari's group lies in their ability to create unique AI tools that capture biologically relevant and clinically intuitive data from routinely acquired radiographic imaging (MRI, CT, PET).

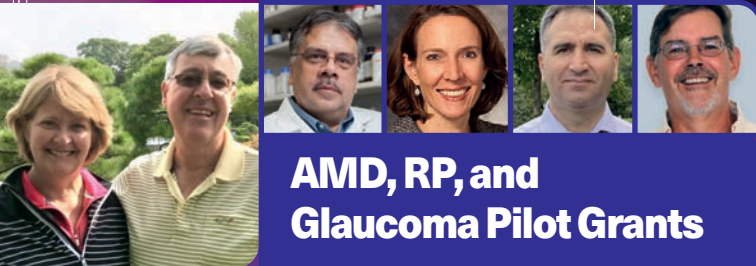
The IDiA Lab has several goals. One is to develop AI approaches that discern patterns in images that are not evident to an expert radiologic reader by extracting basic patterns (“primitives”) from routine imaging. The Lab also establishes associations between radiologic features and different molecular and pathological aspects of disease to obtain important new insights into their causes and cures. Dr. Tiwari's ultimate goal is to enable advances in personalized medicine through AI to improve diagnosis, prognosis prediction, and treatment response assessment.

However, AI is only effective if it is built and utilized correctly. Dr. Tiwari is currently collaborating with the A-EYE Research Unit to investigate the utility of an AI that identifies subtle changes in retinal images that are below the level of detection of a human observer. Their team recently published results from their first effort, which examined the performance of different AI programs in assessing the presence and progression of geographic atrophy (a severe form of dry AMD) in retinal images of AMD patients. The study showed that not all AI is created equal; rather, the choice of AI program significantly impacted its ultimate performance.

Dr. Pallavi Tiwari's lab uses AI to detect and predict areas of geographic atrophy. Image courtesy of the Tiwari lab.



McPHERSON ERI RESEARCH AWARDS 2023-2024



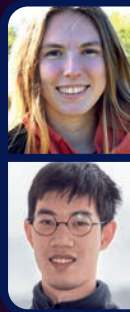
AMD, RP, and Glaucoma Pilot Grants

McPherson ERI's pilot grant program was supported by several generous donors in 2023-2024, including Roger and Lynn Van Vreede, of Appleton, the Robert A. Brandt Macular Degeneration Fund, and an anonymous donor. In future years, these pilot grants (along with the Expanding Our Vision Award) will be folded into our new **Grant Accelerator Program (GAP)**.

2023 AMD, RP, and Glaucoma Awards were given to these projects:

- ☀ **AMD Award:** Nader Sheibani, PhD, *Caffeine and Mitigation of Angioinflammatory and Fibrotic Processes in Exudative AMD*
- ☀ **AMD Award:** Ismail Zaitoun, PhD, *Undesirable Outcomes of Wound Healing in Exudative AMD*
- ☀ **RP Award:** Kimberly Stepien, MD, *Comparison of Clarus and Optos Ultrawide Field Imaging for Retinitis Pigmentosa (COCO – RP)*
- ☀ **Glaucoma and Optic Neuropathies Award:** Robert Nickells, PhD, *Measuring and mapping mitochondria in retinal ganglion cells*

MERI is grateful to the donors who have made these large-scale grants possible.



David G. Walsh Graduate Student Support Initiative (GSSI) Award

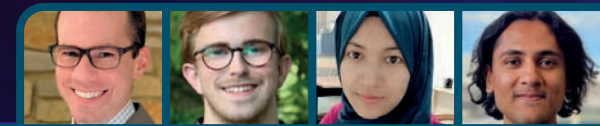
In the fourth year of support for the **David G. Walsh Graduate Student Support Initiative**, two \$12,000 tuition support awards were funded. Gillian McLellan, BVMS, PhD, was funded to support the work of graduate student **Virginia Mathu**, on *Disease Mechanisms at the Intersection of Glaucoma and Alzheimer's disease*. Ari Rosenberg, PhD, was funded to support graduate student **Zikang "John" Zhu**, who is working on *Causal Contributions of Parieto-Occipital Cortex to 3D Visual Perception*.



Kenzi Valentyn Vision Research Grants

Kenzi Valentyn Vision Research Grants are named in honor of a courageous young woman who fought a long battle with Kearns-Sayre syndrome before passing away in 2017. Late 2023 marked the 7th round of Kenzi Valentyn Awards, and grants of \$7,500 were given to five outstanding projects:

- ☀ **Theodore Bucci**, a graduate student in Neuroscience, mentored by **Raunak Sinha, PhD**
- ☀ **Bikalpa Ghimire**, also a graduate student in Neuroscience, mentored by **Xin Huang, PhD**
- ☀ **Jake Khoussine**, a PhD/MD student in Ophthalmology and Visual Sciences, mentored by **Mrinalini Hoon, PhD**, and **Jeremy Rogers, PhD**
- ☀ **Michele Salzman**, a graduate student in Surgical Sciences in the School of Veterinary Medicine, mentored by **Freya Mowat, BVSc, PhD, DECVO, DACVO, MRCVS**
- ☀ **Tania Sharmin**, a graduate student in Ophthalmology and Visual Sciences, who also received a Walsh Travel Award (above right), mentored by **Colleen McDowell, PhD**



Walsh Research Travel Awards

Walsh Research Travel Awards, given each semester and supported by the David G. Walsh Research Fellowship Endowment, allow trainee researchers to present their findings and connect with other researchers at conferences—an essential aspect of career development. In 2024, Walsh Research Travel Awards were given to **David Barnett, MD** (Ophthalmology and Visual Sciences), **Carter Sifferman** (Computer Sciences), **Tania Sharmin** (Ophthalmology and Visual Sciences), and **Tanuj Kumar** (Electrical and Chemical Engineering).

Student and Trainee Awards

- ☀ **Dan & Ellie Albert Student Vision Research Awards**, supporting a summer vision research project for an SMPH student through the Shapiro Summer Internship Program, were given to four students in 2024, a record! Recipients were **Parabjhot Singh** (Curtis Brandt, PhD, mentor); **Elaine Botros** (Amitha Domalpally, MD, mentor); **Britney Naolhu** (Mihai Mititelu, MD, mentor); and **Carol Wann** (Suzanne Van Landingham, MD, mentor).
- ☀ **Hilldale Undergraduate Awards went to four students in 2024:** **Alex Huang** (Computer Science), **Rainy Jin** (Psychology), **Ngawang Namru** (Neuroscience), and **Mckenzie Schmidt** (Neuroscience). These awards, with \$3000 given to the student and \$1000 to the student's mentor, allow undergraduates to obtain valuable experience early in their careers.
- ☀ **5 McPherson ERI trainees—Celia Bisbach, PhD, Miral Abdalaziz, Lauren Sarko, Purnima Gogol, PhD, and Lauren Kresser—**received support to attend the StoryForm Science Course, developed by Holly Kerby and Adam Steinberg, in Summer 2024.

Distinguished Paper Awards

In early 2024, the McPherson ERI awarded the second round of **Distinguished Paper Awards** to recognize trainee members who are the first author or co-first author on papers of note. Award recipients this year were **Meha Kabra, PhD** (postdoc, Pediatrics); **Michael Landowski, PhD** (postdoc, Medical Genetics); **Allison Ludwig** (dual DVM/PhD Resident, Comparative Biosciences, SVM); **Kazuya Oikawa, PhD** (postdoc, Ophthalmology and Visual Sciences); and **Melissa Schoenlein** (graduate student, Psychology). Links to their papers are at vision.wisc.edu/funding_opportunities/distinguished-paper-awards/recipients.

Special Interest Group Lunches

McPherson ERI launched a new award program in 2024, the **Special Interest Group Lunch** program, designed to promote focused discussion and bring together researchers across campus. **Karen Schloss, PhD**, is the first recipient of SIG Lunch support, for a group that will discuss information visualization and visual communication.



Grant Summit Program

Two Grant Summit Program Awards were given in 2024, for \$10,000 each, to **Akihiro Ikeda, DVM, PhD**, and **Colleen McDowell, PhD**. These awards support revision and resubmission of well-scored grant applications that (in many cases) need only a small amount of revision to receive major funding. Dr. Ikeda received a 4-year grant from NIH totaling over \$1.5 million for his GSP-funded submission; Dr. McDowell's R21 grant from the NIH in 2024 followed on a previous Grant Summit Program Award.



Grant Accelerator Program (GAP)

The new **Grant Accelerator Program (GAP)** provides seed funding at a larger scale than the Institute has awarded in the past, thanks to an outstanding gift from the Estate of Dr. Alice McPherson, as well as generous support from the Van Vreede McPherson ERI Greatest Needs Fund and the Robert A. Brandt Macular Degeneration Fund. GAP Awards will support innovative research that advances knowledge of the visual system in health or disease, and/or applies such knowledge to augment, protect, or restore vision or the visual experience.

In early 2025, MERI will announce the recipients of seven \$50,000 GAP awards to support vision research at UW-Madison.

Visiting Scholar Awards

Visiting Scholar Awards underwrite multi-day working visits from distinguished scholars who are hosted by McPherson ERI researchers. Two \$3000 awards were made in 2024, to **Natascha Merten, PhD** (Population Health Sciences and Medicine), who hosted **Willa Brenowitz, PhD, MPH** (Epidemiology, Kaiser Permanente Center for Health Research), and to **Leandro Teixeira, DVM, MS, DACVP** (COPLOW Director, SVM) and **Richard Dubielzig, DVM** (COPLOW Founding Director, SVM), who hosted **Kelsey Jenkins, PhD** (Earth and Planetary Sciences, Yale University).

MCPHERSON ERI LECTURES, 2024

12th Annual Alice McPherson Lecture

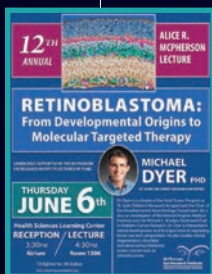
June 2024

Michael Dyer, PhD, (St. Jude's Children's Research Hospital) presented the annual lecture honoring the McPherson ERI's co-founder, Dr. Alice McPherson. Dr. Dyer spoke on *Retinoblastoma: From Developmental Origins to Molecular Targeted Therapy*.

2nd Annual Sandra Lemke Trout Lecture

September 2024

Goldis Malek, PhD, FARVO, FAOPT, (Duke Eye Center, Duke University), gave the 2nd Annual Sandra Lemke Trout Lecture, part of the Trout AMD Project. Dr. Malek spoke on *Potential Therapeutics for Age-related Macular Degeneration: The Nuclear Option*.



16th Annual Vision Science Symposium

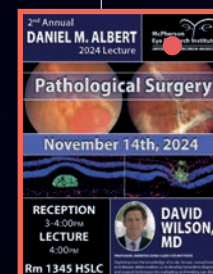
October 2024

Sönke Johnsen, PhD (Biology, Duke University), spoke as part of the annual Vision Science Symposium, which also included the Institute's annual poster session. Dr. Johnsen's talk was titled, *How Our Cognitive and Sensory Biases Affect Our Study of Vision: Three Tales from the Sea*.

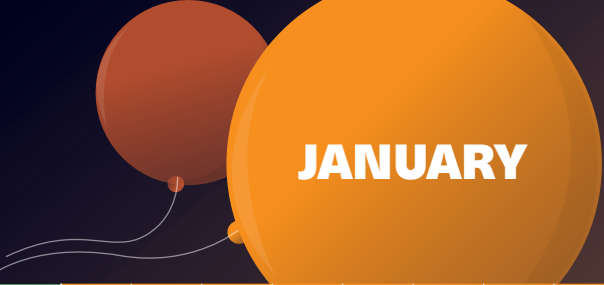
2nd Annual Daniel M. Albert Lecture

November 2024

The Daniel M. Albert Lecture took place in Madison on November 14th. **Dr. David Wilson, MD** (Emeritus Professor, OHSU-Casey Eye Institute) spoke on *Pathological Surgery*.







Phantom of the Arctic: Unlike most owls, the Snowy Owl (*Bubo scandiacus*) is not primarily a nocturnal hunter, which is not surprising, as these owls live most of their lives in arctic regions with 24 hours of daylight for much of the year. In winter, some Snowy Owls migrate south into the fields of Canada and the northern United States. Occasionally, one will even be seen in Madison, Wisconsin. This shot was taken near Toronto in a farmer's field, on a bright but frigid winter morning, by Emeritus Professor Paul Ludden, PhD. The photo was displayed in the 2024 exhibit *Birds' Eye Views*, in the McPherson ERI's Mandelbaum & Albert Family Vision Gallery.

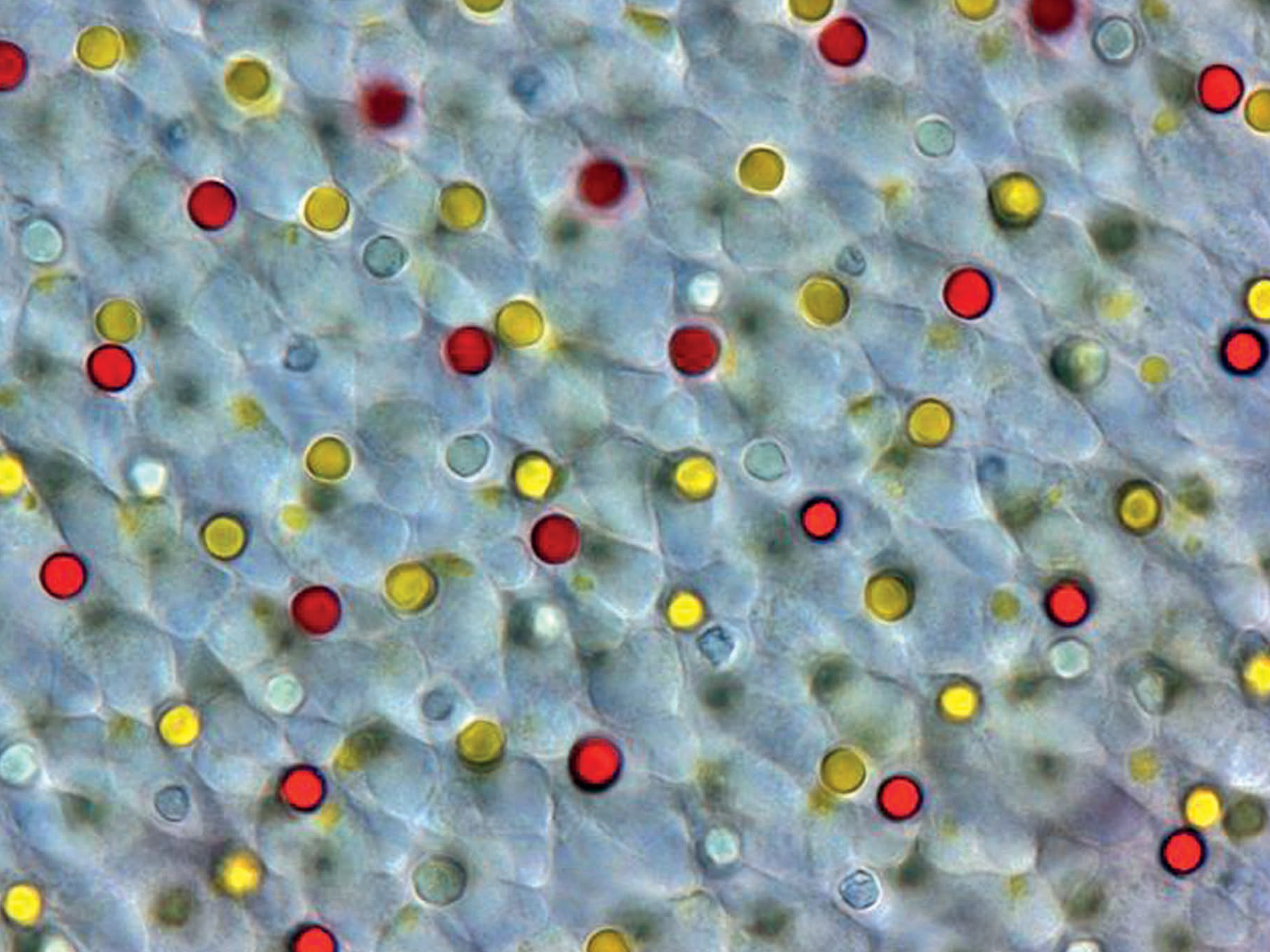
• IMAGE COURTESY OF PAUL LUDDEN, PHD.

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									CHINESE NEW YEAR											

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FEBRUARY

Bird retinas contain oil droplets positioned in front of their short cone outer segments, an unusual feature. Any light that makes it to the outer segment must pass through an oil droplet. In this image of a retinal flat mount of a bird retina, the oil droplets are seen as multicolored circles. They serve three functions: They direct any light that makes it to that level into only one photoreceptor, they filter out harmful ultraviolet light, and the color of the droplet matches the appropriate color function for that particular photoreceptor. This is one of many reasons that birds have marvelous color vision. • **IMAGE COURTESY OF CHRISTOPHER MURPHY, DVM, PHD, DACVO.**

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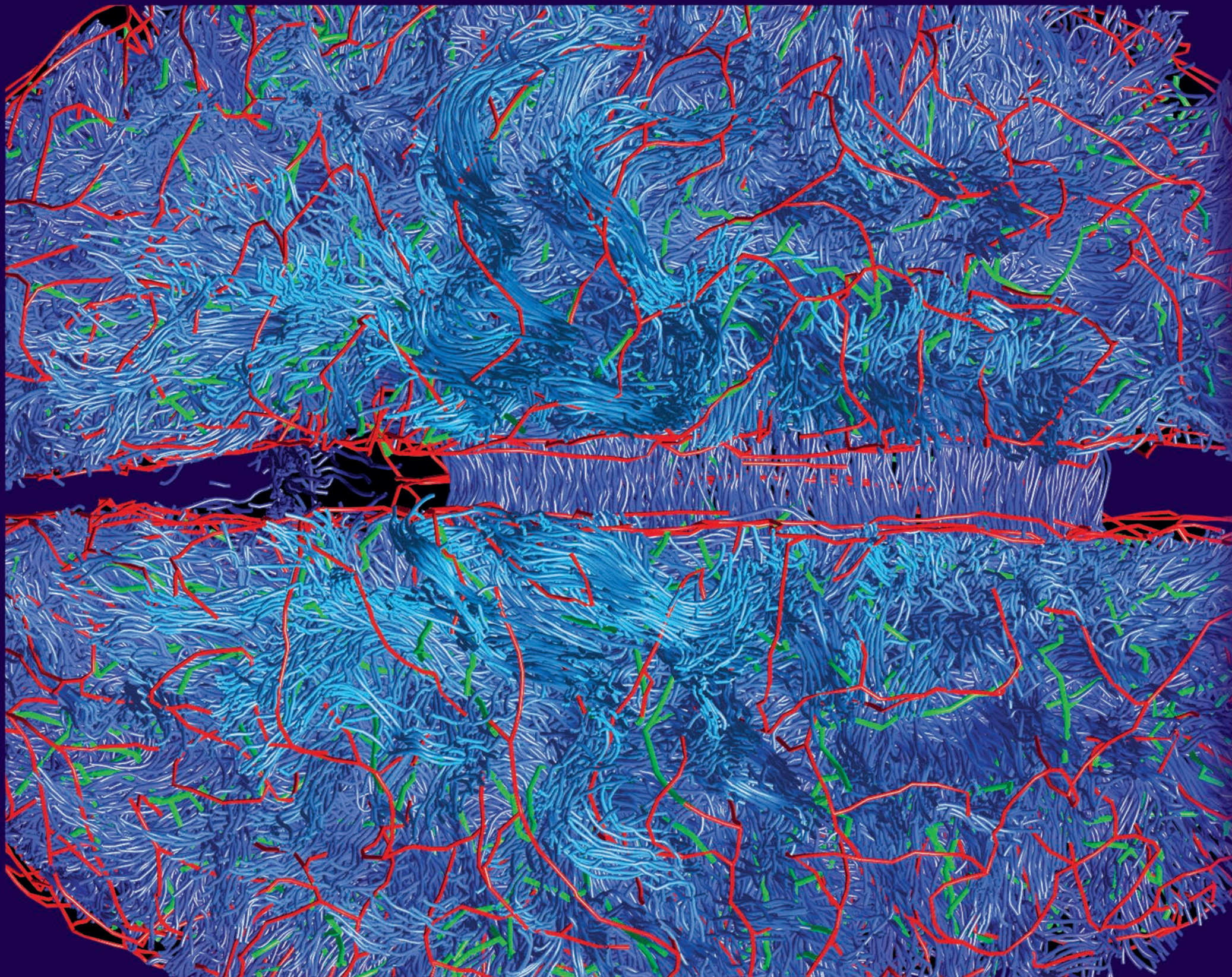
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GROUNDHOG DAY

VALENTINE'S DAY

PRESIDENTS' DAY

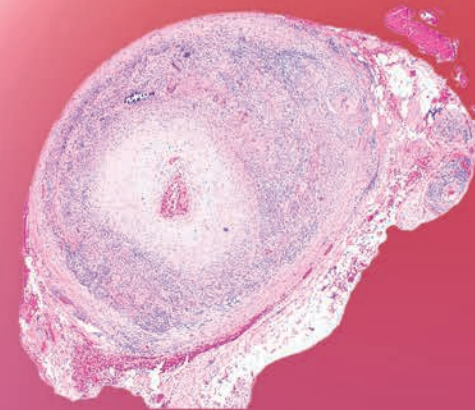
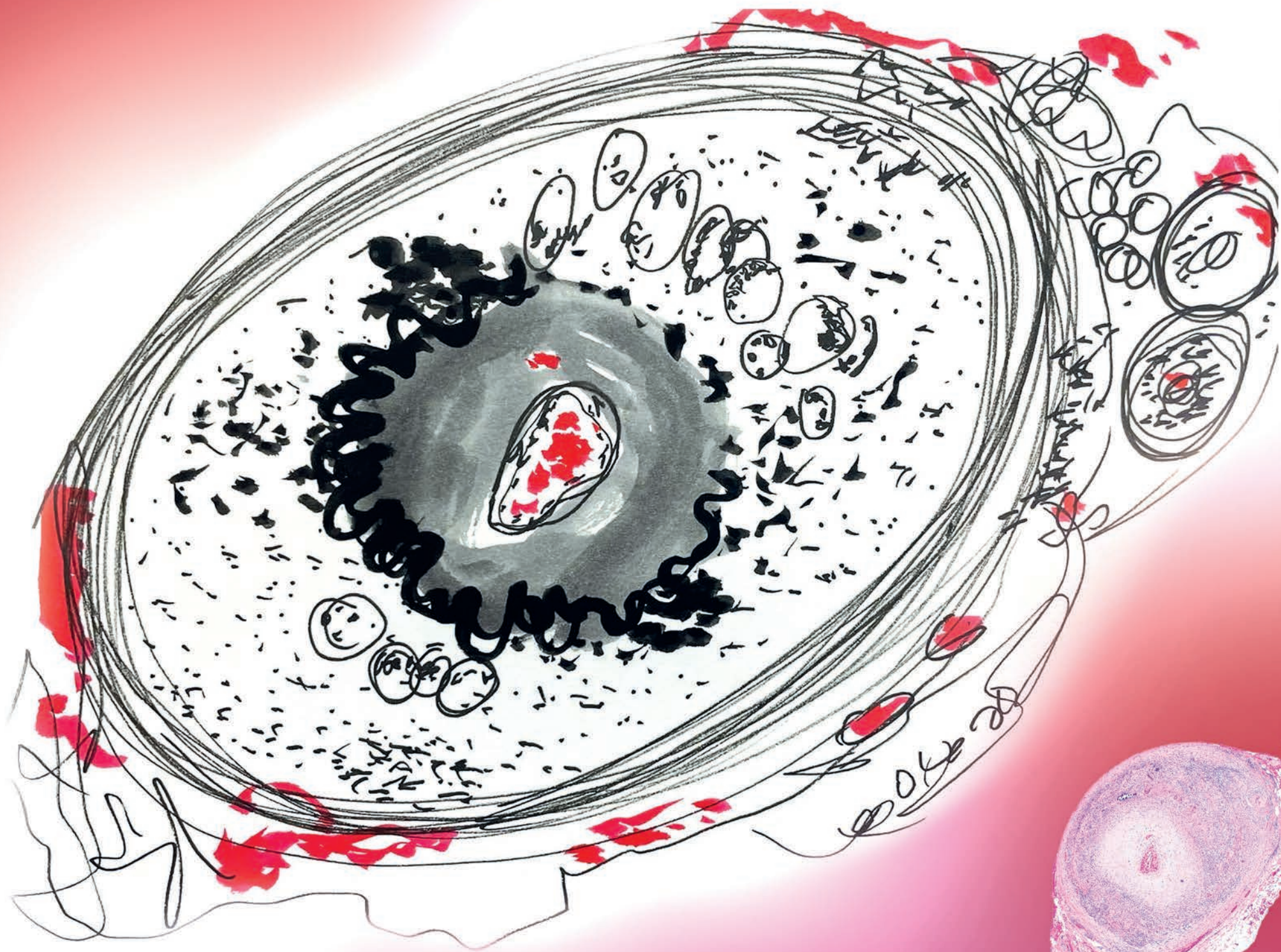
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The remarkable brain image above displays a structural brain network reconstructed from diffusion magnetic resonance imaging data from the Human Connectome Project (HCP). Red lines trace the gyral (ridge) regions, while green lines trace the sulcal (valley) regions of the brain's cortical folds. Li Shen, PhD (University of Pennsylvania) assisted with image processing (tractography). The visualization pipeline is based on methods developed by Moo Chung from UW-Madison's Department of Biostatistics and Medical Informatics. • **IMAGE COURTESY OF MOO CHUNG, PHD.**

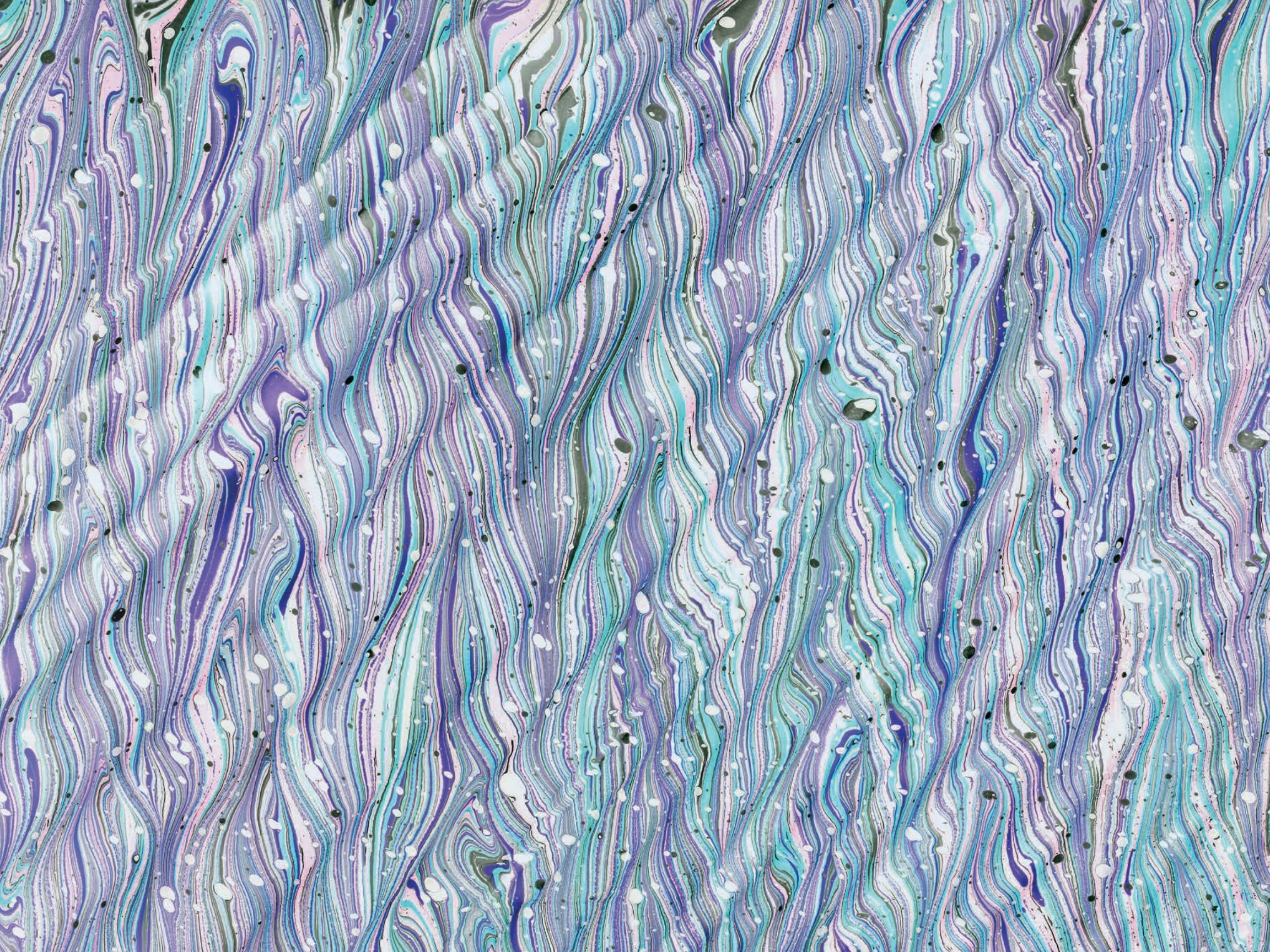
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APRIL

Two versions of a temporal artery with abundant chronic inflammation and other signs of temporal arteritis. The larger ink on paper drawing is a graphic representation of the H&E-stained slide image (insert). Dr. Hilary Highfield, the artist (and Director of Neuropathology at the Norton Neuroscience Institute), uses her artwork to highlight pertinent histologic findings. Her work will be featured in an upcoming second edition of an eye pathology casebook by Drs. Daniel Albert (the Founding Director of the McPherson ERI) and Hillary Stiefel. • **IMAGES COURTESY OF HILARY HIGHFIELD, MD, PHD.**

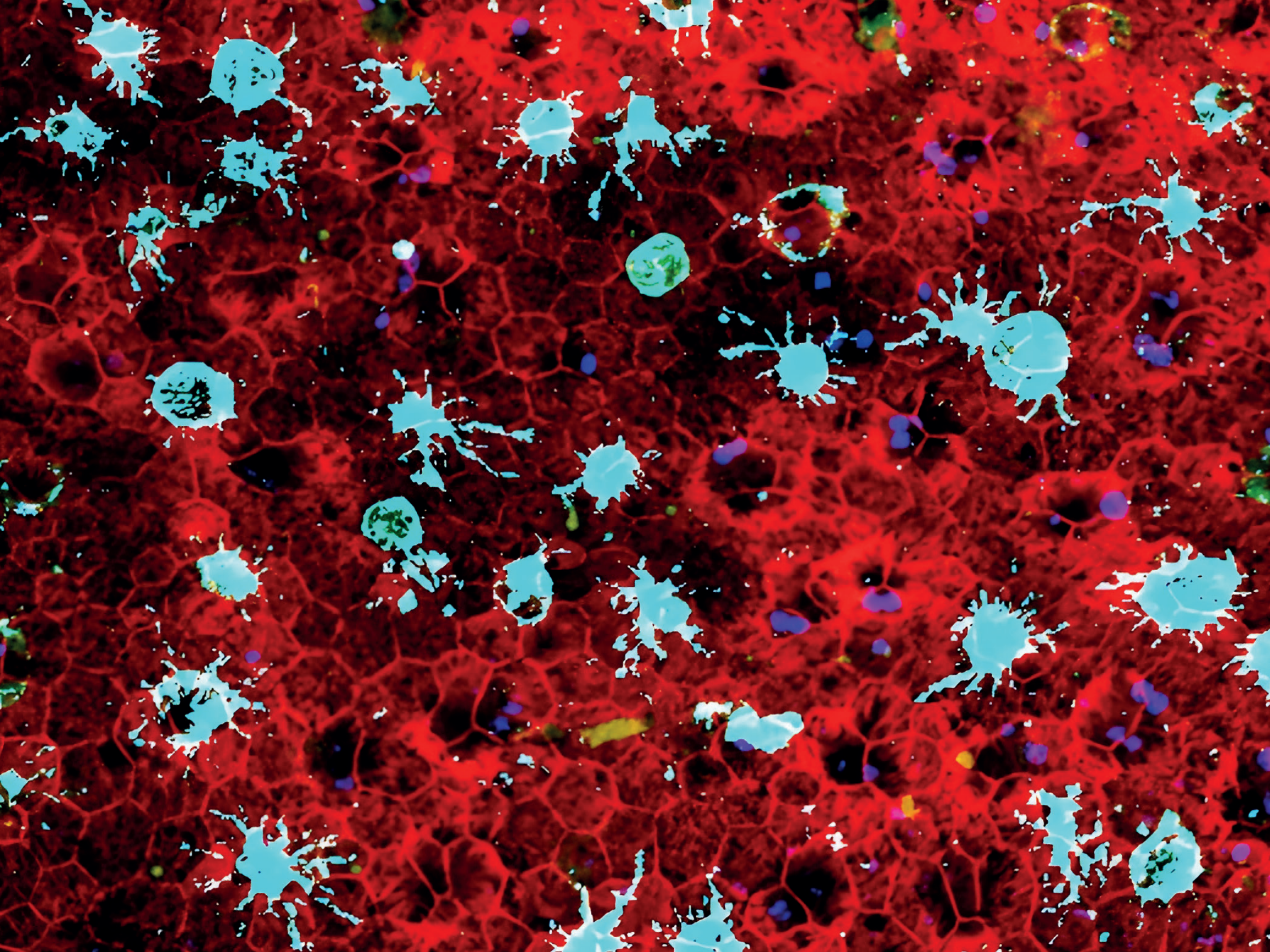
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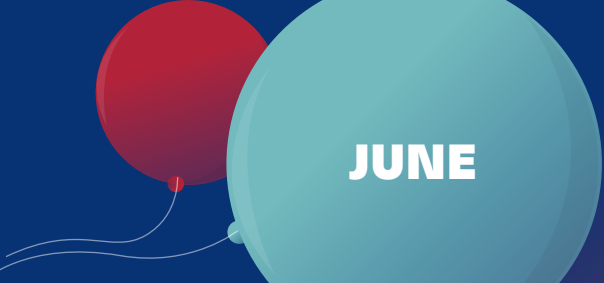




Researchers in UW-Madison's Applied Math, Engineering and Physics Laboratory study interactions at the interfaces of different liquids by making marbling art, in which complex patterns in paint floated on a water bath are transferred onto paper. This scanned paper sheet—combining patterns known as “Spanish wave” and “antique”—was made in the lab in 2023 during a study of how the bath’s viscosity affects the stability of the patterns in the floating paint. The image, by Yue Sun, PhD, was one of the winners of UW-Madison’s annual Cool Science Images Contest in 2024. • **IMAGE COURTESY OF YUE SUN, PHD.**

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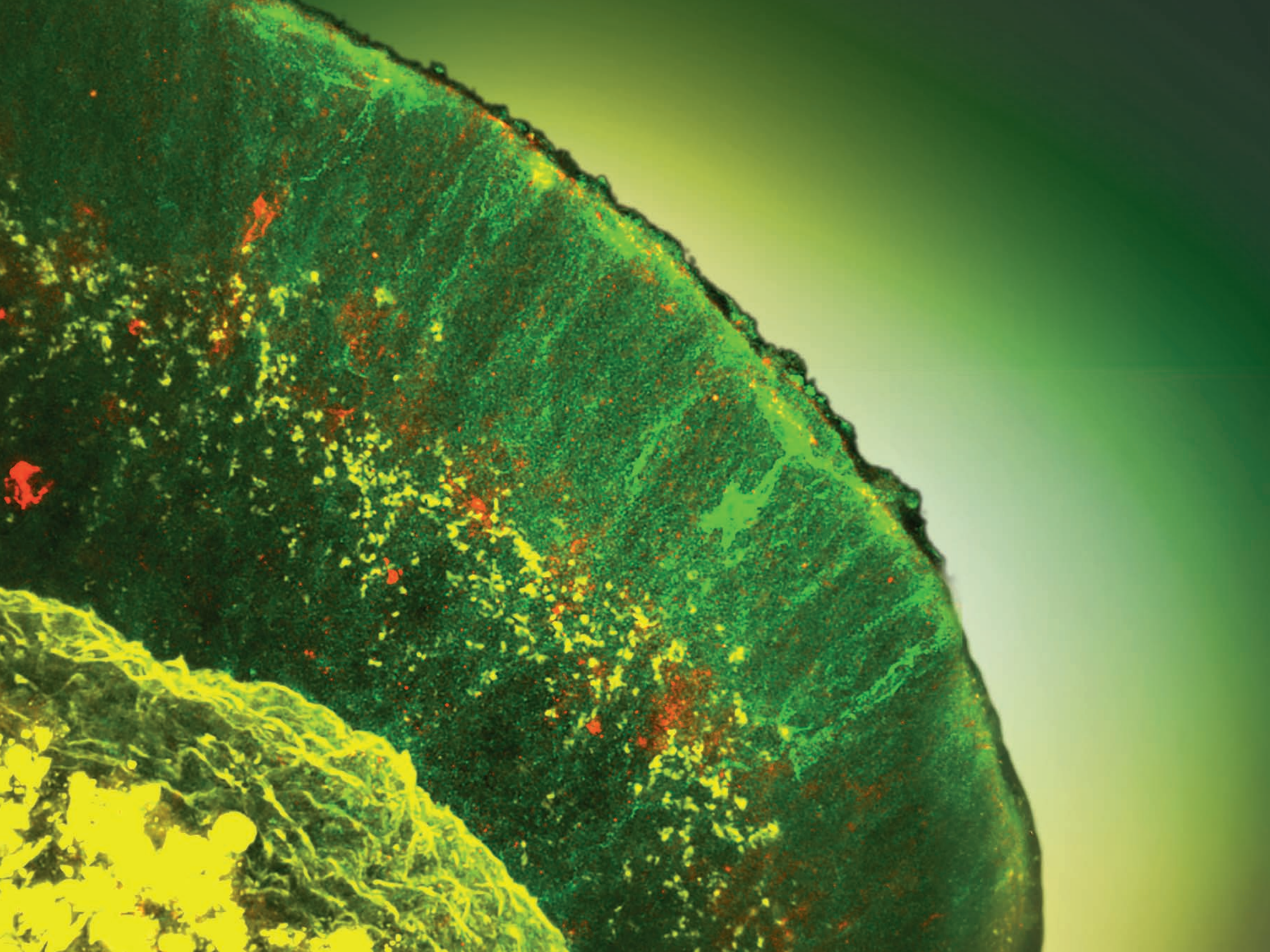
Inflammation is a hallmark of human AMD symptoms. A mouse mutant carrying a mutation in the *Tmem135* gene shows massive inflammation and other AMD-like symptoms, making it a good model to study AMD. This image, from Dr. Akihiro Ikeda's lab, shows the retinal pigment epithelial (RPE) layer of a mouse model of accelerated retinal aging. Red signals represent RPE cells with nucleus (blue), while cyan signals represent activated microglia (immune cells) in the subretinal space. • **IMAGE COURTESY OF THE IKEDA LAB.**

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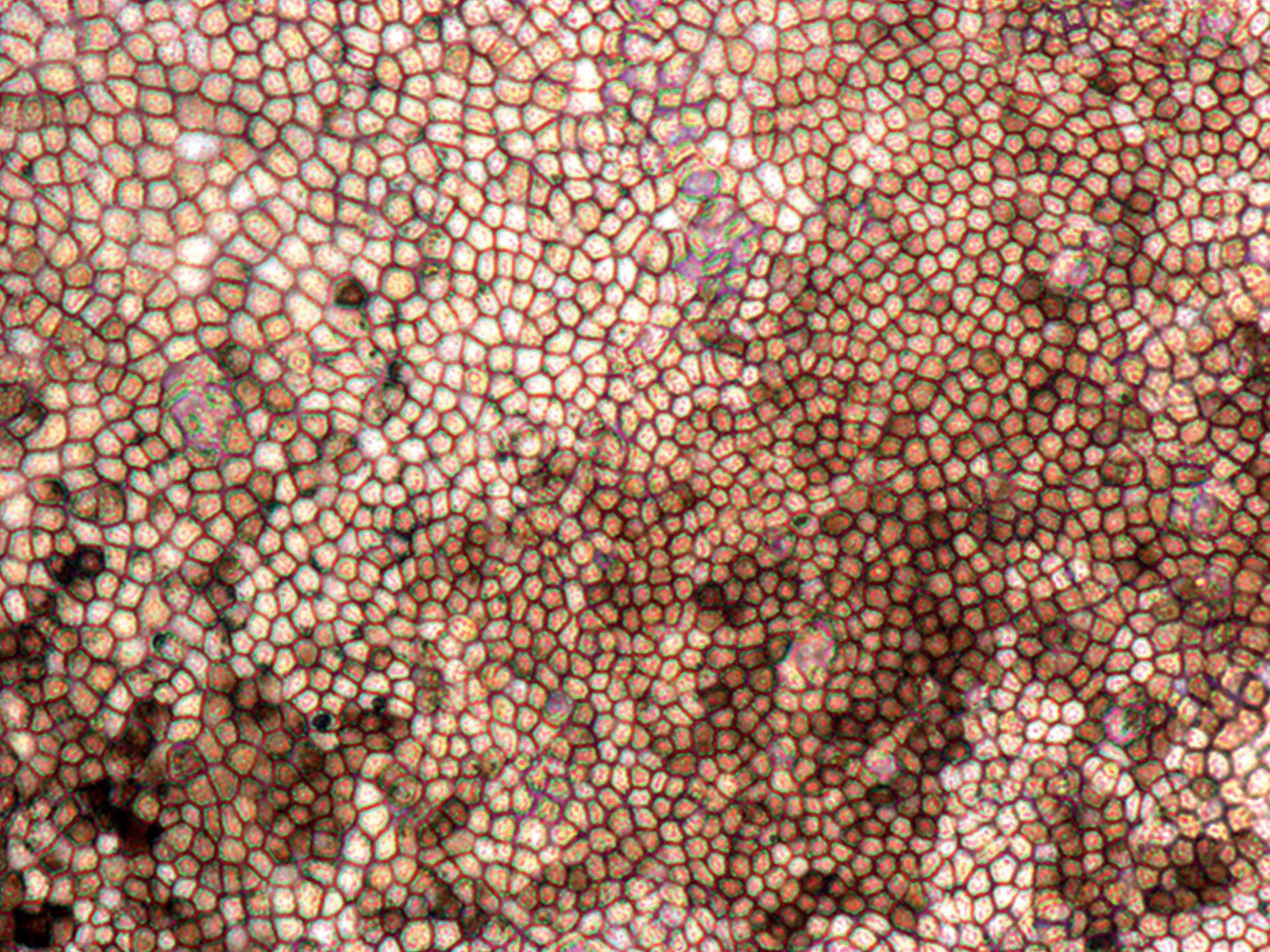
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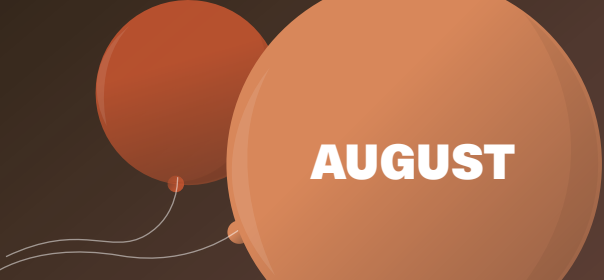




The image above shows a fluorescent microscope image of a human 3D retinal organoid generated from stem cells. This developing organoid, which mimics the naturally developing human retina, has been labeled for specific markers that may be involved in normal retinal circuit formation. Photoreceptors are labeled red, while a specific adhesion receptor is labeled green, and a secreted adhesion “matrix” protein is labeled yellow. • **IMAGE COURTESY OF TIM GOMEZ, PHD, AND MADISON DILLERUD.**

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AUGUST

Retinal pigment epithelium (RPE) is the site of dysfunction in many retinal disorders. Patient induced pluripotent stem cell-derived RPE (iPSC-RPE) cells provide a critical tool to understand retinal disease at cellular and molecular levels, and to perform preclinical therapeutic testing, more so when relevant animal models are not available. This image shows iPSC-RPE derived "in-a-dish" using methods established by the Gamm lab. These human iPSC-RPE disease models are paving the way for rapid and high-throughput testing of therapies for retinal diseases. • **IMAGE COURTESY OF THE GAMM LAB.**

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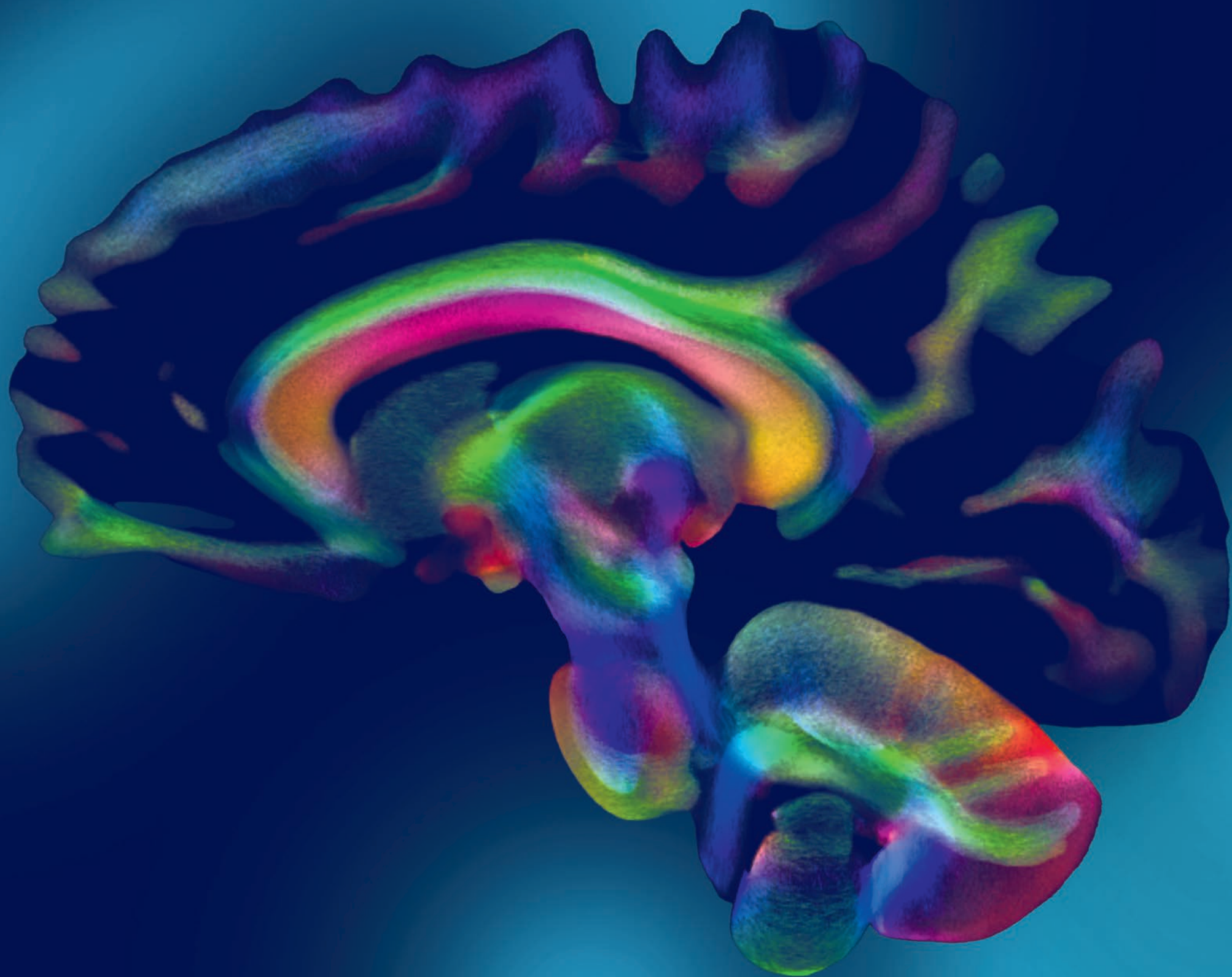
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SEPTEMBER

Shown here is a diffusion weighted imaging (DWI) photo of the brain's white matter tracts, with an RGB (red-green-blue) map overlaid. Red indicates white matter tracts that primarily go between the hemispheres (left/right). Green indicates white matter tracts that primarily go anterior/posterior (front of brain/back of brain). Blue indicates the tracts that primarily go superior/inferior (up/down). These images allow researchers to examine brainstem (and whole brain) connections in autistic and non-autistic individuals. • **IMAGE COURTESY OF OLIVIA SURGENT, PHD, TAKEN IN DR. BRITTANY TRAVERS' LAB.**

AUG	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN
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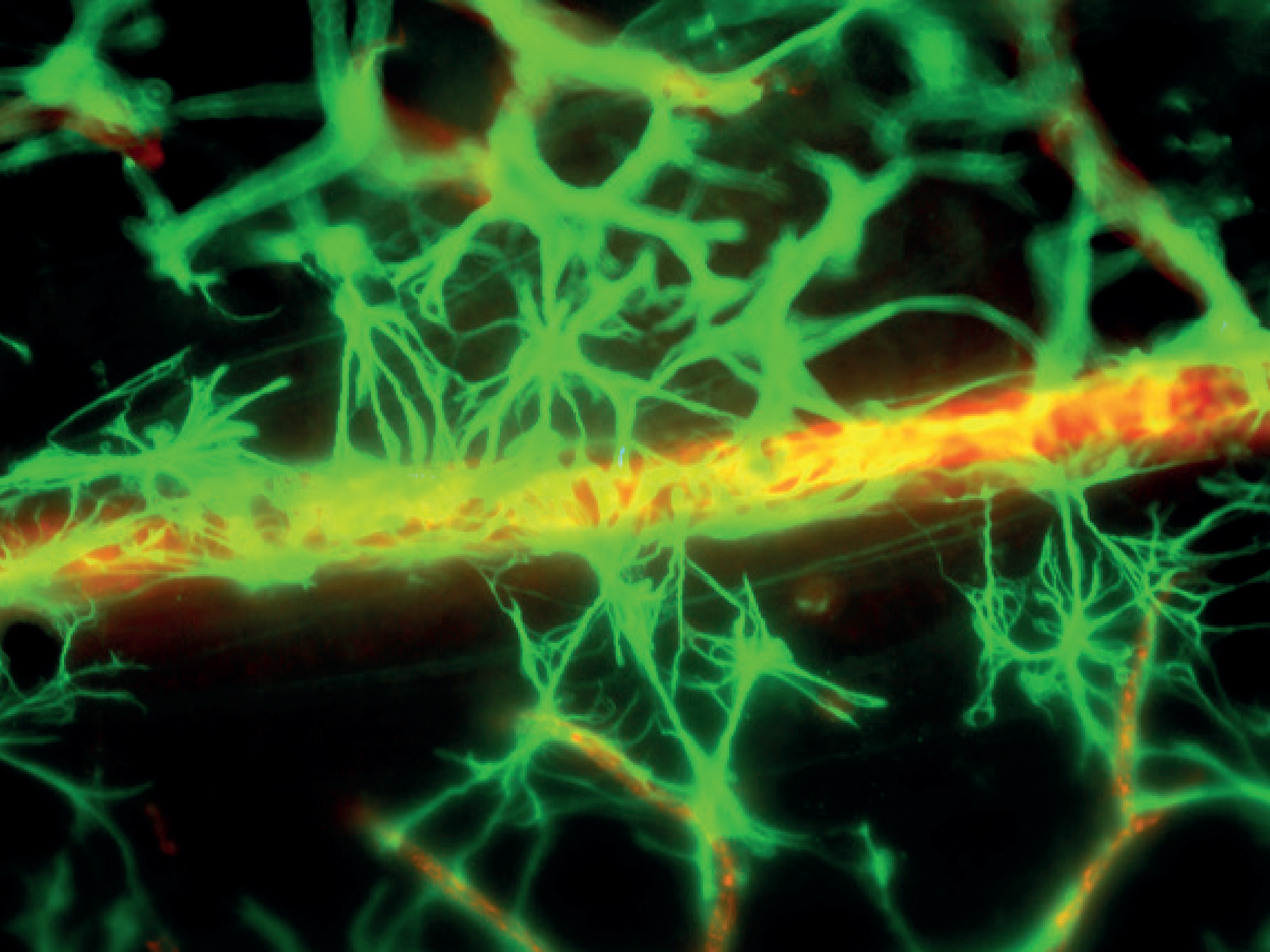
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		FIRST DAY OF FALL				
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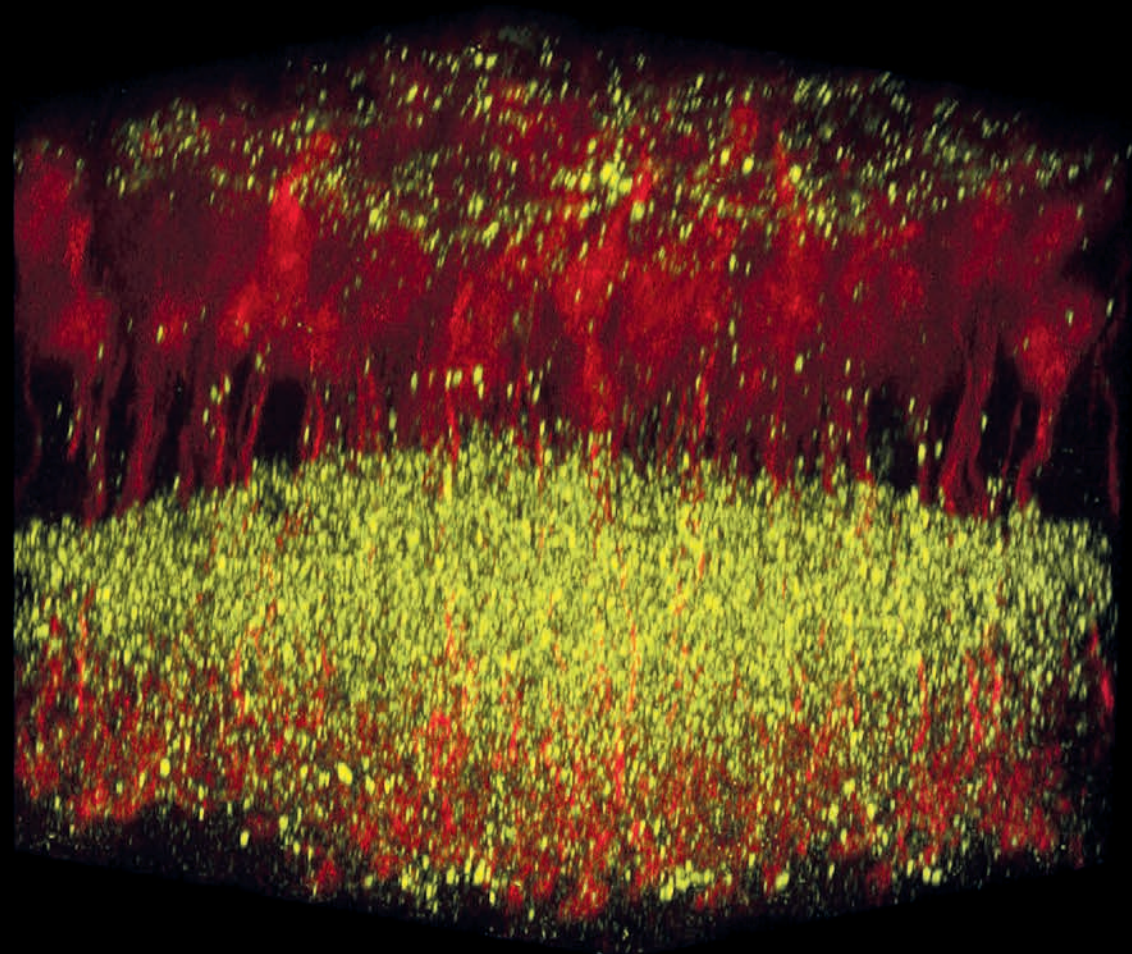
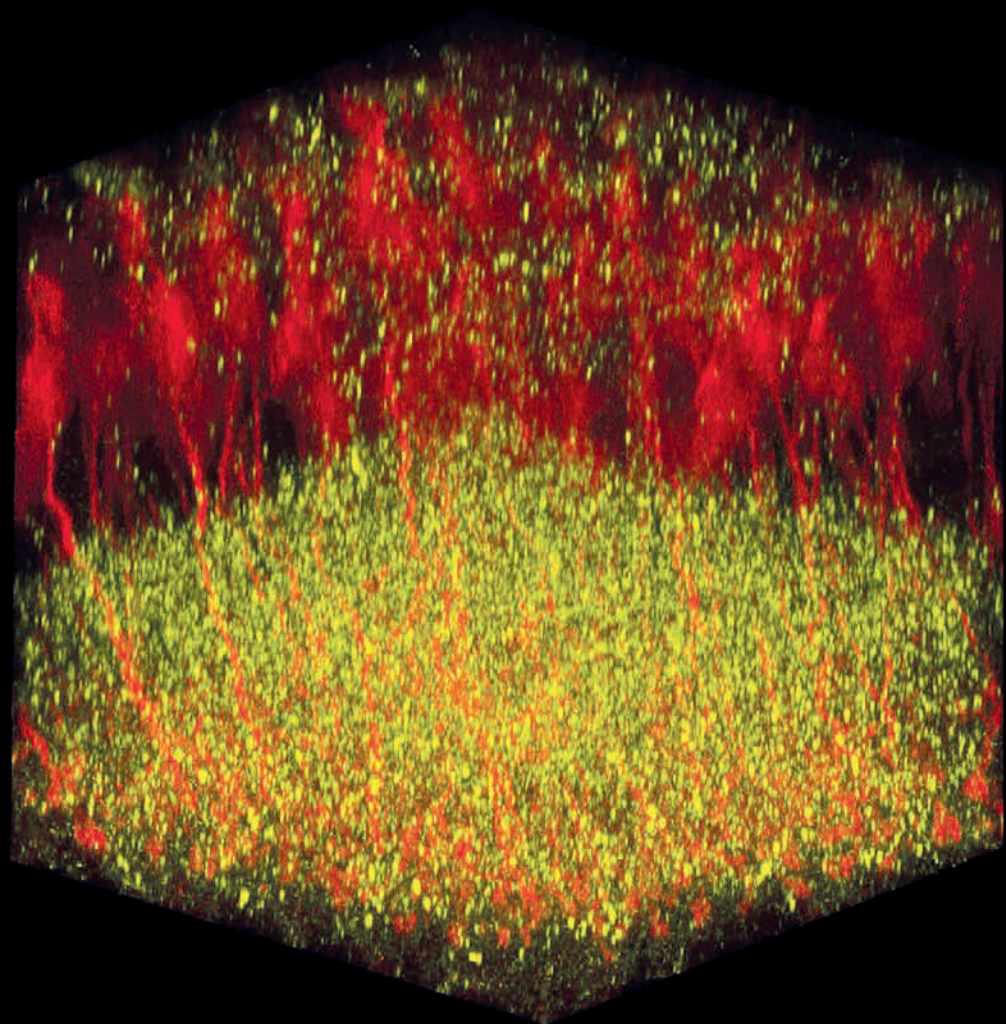


OCTOBER

Tissues in the central nervous system have specialized cells that function to maintain a homeostatic environment. Astrocytes are one type of these cells, providing nutrients to the neurons and balancing the chemical environment they live in. This picture shows astrocytes (in green) in the mouse retina. They wrap processes around blood vessels to draw in the nutrients that are then passed on to other cells.

• IMAGE COURTESY OF ROBERT NICKELLS, PHD.

SEP	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	
SUNDAY				MONDAY				TUESDAY				WEDNESDAY				THURSDAY				FRIDAY				SATURDAY							
28				29				30				1				2				3				4							
																YOM KIPPUR															
5				6				7				8				9				10				11							
				SUKKOT BEGINS												WORLD SIGHT DAY															
12				13				14				15				16				17				18							
				COLUMBUS DAY												WHITE CANE SAFETY DAY															
				INDIGENOUS PEOPLE'S DAY																											
19				20				21				22				23				24				25							
				DIWALI																											
26				27				28				29				30				31				1							
																				HALLOWEEN											
NOV	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	
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NOVEMBER

Communication between nerve cells in the retina is regulated by a class of neurochemicals called GABA, which can inhibit and fine tune neuronal signaling. These images show cross-sectional volumes of a mammalian retina. On the left is a normal retina. On the right is a retina with a specific class of GABA receptors genetically removed to assess its role in retinal function. The second-order nerve cells in the retina, the bipolar cells, are labeled red, and the dense expression of these inhibitory GABA receptors is labeled yellow. Alteration in GABA receptor expression (right) resulting in inhibition in the retina occurs in blinding disorders. • **IMAGE COURTESY OF MRINALINI HOON, PHD.**

OCT	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI
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SUNDAY

MONDAY

TUESDAY

WEDNESDAY

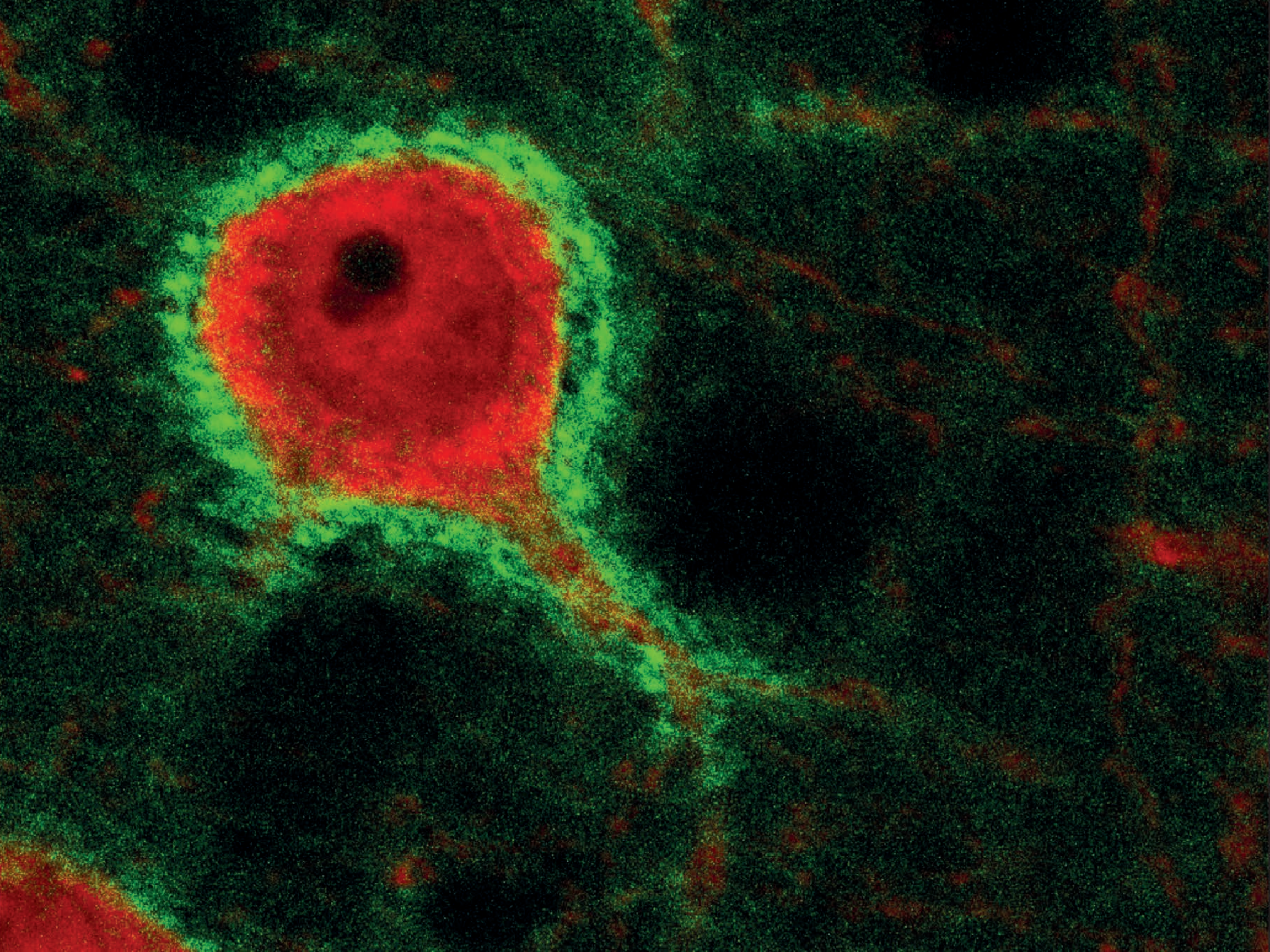
THURSDAY

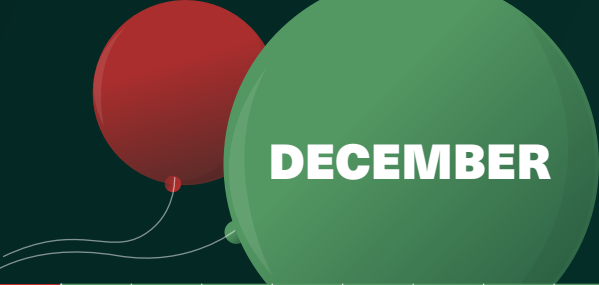
FRIDAY

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DAYLIGHT SAVING TIME ENDS		ELECTION DAY				
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		VETERANS DAY				
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30					THANKSGIVING	

DEC	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED
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Amblyopia becomes resistant to reversal with age, due in part to the formation of dense perineuronal nets (green) that enshroud inhibitory basket neurons (red) in the adult visual cortex (shown at 100X magnification). Betsy Quinlan’s lab (Department of Neuroscience) studies how degradation of these nets, by visual deprivation followed by light reintroduction, promotes the recovery of vision in experimental models of adult amblyopia. • **IMAGE COURTESY OF SACHIKO MURASE, PHD, AND BETSY QUINLAN, PHD.**

NOV	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN		
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SUNDAY			MONDAY			TUESDAY			WEDNESDAY			THURSDAY			FRIDAY			SATURDAY		
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JAN	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31

McPherson Eye Research Institute

2023-2024



McPherson ERI sadly notes the passing of two Honorary Advisory Board members in 2024. **Dr. Monroe Trout**, along with his wife Sandy, was a major benefactor of the Institute since 2013, driven by his desire to support transformative macular degeneration research. Dr. Trout passed away in March 2024. **Derilyn Cattellino** was a longtime supporter and Advisory Board member to the McPherson ERI, and a lively presence at Board meetings and events. Deri passed away in May 2024. Both will be greatly missed.

Advisory Board

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- ✿ **Kenneth Frazier** | *Director (retired)* | UW-Madison General Library System
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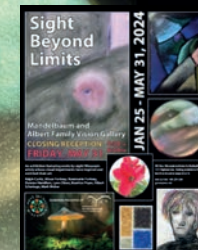
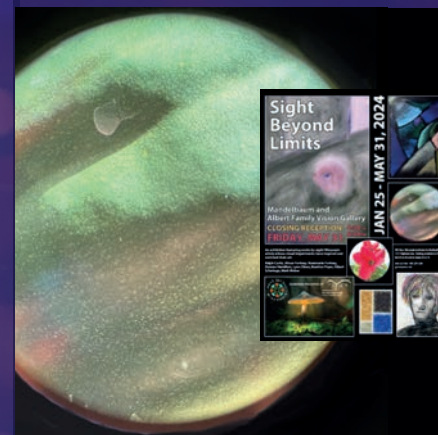
Cycle for Sight 2024 Raises the Bar Again!

Cycle for Sight 2024 raised more than \$72,000 through June 2024—an all-time high! Our Princeton Club spinning sessions on March 16th went very well and were followed by various team events outdoors through April. Kenzi's Team once again took the lead in fundraising, with other teams also excelling. 10,000, an all-time high for that amazing team! Teams that exercised elsewhere in April included med students from UW's School of Medicine and Public Health, the Isthmus Eye Care team, Delta Gamma, and multiple McPherson ERI labs. Bonus points to Dr. Karen Schloss's lab, which on a rainy day exercised by "hiking" through the Chazen Museum. We're very grateful that our major sponsors continue to support the event; thank you to Opsis Therapeutics, the Chippewa Valley Eye Clinic, and the Princeton Club. Cycle for Sight again supported vision research grants including the Kenzi Valentyn Vision Research Awards, and each year, we've been able to add additional research awards thanks to our fabulous teams and supporters.

You can continue to support Cycle for Sight at vision.wisc.edu/giving.

The Mandelbaum & Albert Family Vision Gallery

Installations in 2024



Sight Beyond Limits, an exhibition featuring works by eight Wisconsin artists whose visual impairments have inspired and enriched their art, in Spring 2024.

Rose Fortney, *Planet Squash*



Birds' Eye Views, which ran through the summer of 2024, explored avian life and vision through extraordinary images taken by four Madison-area photographers (Arlene Koziol, Paul Ludden, Rob Streiffer, and Tom Yin).

Arlene Koziol, *Eye to Eye (Roseate Spoonbills)*



Cool Science Images 2024 is showing in the gallery in Fall 2024 (through January 10th, 2025) and features the winners of UW-Madison's annual contest for the year's best science-related images.

Angie Tebon Oler, *human lung cells marked by light blue nuclei*, a Cool Science Images Contest winner in 2024

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TO THE FOLLOWING DONORS TO THE
McPHERSON EYE RESEARCH INSTITUTE

July 2023
to October
2024

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If you'd like to discuss what you can do to help our research, please contact Michael Chaim, chaim@wisc.edu, 608-320-9347.

Thank you for your help!

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