

McPHERSON EYE RESEARCH INSTITUTE

2023
ANNUAL REPORT

2024
CALENDAR



From the Director



DEAR FRIENDS OF THE MCPHERSON ERI,

As 2023 ends, we are once again in an enviable but challenging position to choose which research highlights and images to share with you. As the Institute has grown in size and impact, so has the number of breakthroughs our researchers report annually. Our members develop, test, and optimize new technologies—gene editing, stem cells & regenerative medicine, artificial intelligence, data visualization, advanced imaging methods, and many others—which have improved the outlook for individuals with a host of blinding disorders.

In the next few pages, you'll read about projects to develop new therapies for inherited retinal diseases of childhood and for age-related macular degeneration (AMD). In 2023, the former effort garnered a \$29 million federal grant from the National Institutes of Health, while the latter received a tremendous boost with the establishment of the Trout AMD Project, along with continued major support from philanthropists like the Smiths and the Van Vreedes. As important as these efforts are, they remain a sample of the extensive work performed by McPherson ERI researchers, who also seek treatments and cures for glaucoma, diabetic retinopathy, inflammatory and infectious diseases, ocular injuries, and many other conditions that rob people of their sight.

Our namesake, Dr. Alice R. McPherson, looked forward to this annual report and calendar, and we enjoyed unveiling the theme and cover art to her every year. (This year, it depicts the Institute's resolve to repair the macula, the most important "piece" of the retina.) However, Dr. McPherson cared about results, not flash. Therefore, it was the research advancements that drew her close

attention. As one of the world's premier retina surgeons—and the first woman retina surgeon in the world—she was on the forefront of developing many of the techniques we use today to save or restore vision. But there were always conditions that could not be treated using existing procedures and medicines, and that is where her—and our—commitment to research was forged. Dr. McPherson passed away last January in Houston at the age of 96, and while her absence remains palpable, we are grateful for the many years of guidance and support that she cheerfully gave us.

I'm grateful beyond words for your interest in the McPherson ERI, and in the dedicated and cutting-edge work of our more than 200 members. We know that many who receive this calendar are personally affected by vision loss, and that knowledge drives us to look for new and better ways to help—just as Dr. McPherson did every day of her inspiring life.

David M. Gamm MD, PhD

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

Targeting A M D

Age-related macular degeneration (AMD) research at the McPherson ERI

When will we have better treatment choices for AMD? It is one of the most frequent questions that our researchers and clinician-researchers hear, not only from patients, but also from friends and family. The reason for this is two-fold. First, AMD is very common (~11 million people have it in the United States), and it will only become more prevalent as the population ages, with the number of affected individuals projected to double by 2050. Second, available treatments are currently limited or nonexistent. Anti-VEGF injections in the eye can temporarily slow or stop the proliferation of abnormal blood vessels for individuals with the "wet" form of AMD. While this treatment has certainly

Jeremy Rogers PHD

Principal Investigator, Ophthalmology and Visual Sciences Director, Wisconsin Advanced Imaging of Visual Systems (WAIVS) Laboratory



Tracking AMD

Advances in capturing and analyzing information about AMD are an important part of the McPherson ERI's research portfolio for this disease. McPherson ERI scientists do this by using advanced imaging tools, data handling methods, and artificial intelligence algorithms, often developing them in-house, with broad applications to other eye and systemic diseases as well.

Jeremy Rogers, a renowned optical engineer, directs the Wisconsin Advanced Imaging of Visual Systems (WAIVS) Laboratory at UW-Madison. The mission of Dr. Rogers and WAIVS is to capture the world's most detailed and accurate images of the living human retina (and other eye structures), which can then be used to understand disease processes and to evaluate the effects of new treatments. Using recent modifications of a remarkable tool called an Adaptive Optics Scanning Light Ophthalmoscope (AOSLO) (which Dr. Rogers builds from scratch), Rogers' lab can now capture and analyze images of individual retinal cells in living human patients faster than ever before. Dr. Rogers is aiming this powerful tool at AMD, which he hopes will unlock many of its secrets. Since humans are the only creatures on earth to get AMD, and studying humans requires a safe and noninvasive method to peer into their retinas, AOSLO promises to be the key. Data received thus far is allowing Rogers to build further advances into his system and to make it more compact so that it can be more easily incorporated into clinics.

Amitha Domalpally is working to take cutting-edge analytical tools for AMD beyond the clinic and into the home. Her focus is developing artificial intelligence (AI) methods in combination with hand-held screening tools to monitor retinal changes that occur in dry and wet AMD. Having this technology in the home (for example, homes in remote, rural areas) will help identify the need for further evaluation and possible treatment in real time, which will in turn improve health care access and utilization. Remarkably, AI-based diagnostic tools are now being developed for use with cell phone cameras, which would allow patients to monitor their own personalized treatment needs wherever they roam (assuming their cell service is good!).

helped thousands of people preserve or restore some of their sight, the blood vessels aren't the cause of AMD—they are a byproduct of a slow underlying process that continues unabated even if the injections are successful. That slow process is called "dry" AMD, which, in its most severe form, is called geographic atrophy. Recently, a new type of eye injection was shown to slow the formation of geographic atrophy, but no improvement in the vision of treated patients has been found thus far. And it is also important to know that areas of the retina already destroyed by AMD cannot be revived by these types of injections. So, while scientists are beginning to find cracks in AMD's previously impenetrable armor, much work is left to be done.

It probably comes as little surprise, then, that AMD research has been a major focus of the McPherson Eye Research Institute since its inception. Recently, our efforts have been greatly augmented with the establishment of the Trout AMD Project, the Pat and Jay Smith Macular Degeneration Treatment Innovation Program, and a dedicated AMD grant program supported by Lynn & Roger Van Vreede and the Robert A. Brandt Macular Degeneration Fund. These programs support our existing AMD researchers, attract new ones, and help to develop ideas, technologies, and therapeutic strategies to better understand and combat this disease. In the end, our goal is the same as yours—to find effective new treatments for an insidious blinding condition that threatens us all.

Below you will read about some of the ways our researchers are working to turn the tide on AMD by pooling our knowledge and resources and putting them into action.



Causes of AMD and Preventative Treatments

Understanding the cause of a disease is essential for developing effective treatments. Conversely, trying to devise therapies for diseases we know little about is like throwing darts with the lights off—you may get lucky and hit the target, but you are more likely to hit a random wall or your friend in the corner. Unfortunately, modern science is still in the dark about why certain people get AMD and others do not. Certainly, a person's genetics is a very big factor, as are environmental exposures (most prominently, smoking) and, undoubtedly, other issues we aren't aware of yet. These McPherson ERI scientists are working to fill these knowledge gaps and improve our basic understanding of AMD.

Dr. Nader Sheibani and Dr. Akihiro Ikeda both investigate AMD on the cellular level, where problems related to the disease begin. Their work and that of other cell and molecular biologists uses the information they obtain to repurpose or create new, targeted drugs to counteract the defective processes set in motion by AMD.

Aki Ikeda's work focuses on the "age-related" aspect of AMD. Have you ever wondered why age-dependent diseases occur when we get older? Although this may sound like a circular question (because they are age-dependent diseases, Einstein...), we really don't know why some cells and tissues—retina included—that aren't subject to mechanical "wear and tear" deteriorate over time. The Ikeda Lab made an important connection between aging and cell dysfunction with their investigation into a gene, *Tmem135*, which codes for a protein that promotes energy production within mitochondria, also known as



Akihiro Ikeda DVM, PHD



the "powerhouses" of the cell. Cells without properly functioning TMEM135 protein have a reduced capacity to process lipids (fats) into energy, which leads to the buildup of waste products called drusen, a key feature of AMD. In addition to being used to discover drugs that can slow or stop AMD, Dr. Ikeda's work may improve our ability to predict whether a person will get the disease and how severe it will become.

Nader Sheibani's lab is looking into the role of mast cells in AMD. Mast cells are a type of immune cell that can migrate into the retina and contribute to chronic inflammation, which is now known to occur in AMD. Dr. Sheibani is investigating mechanisms that lead to the activation of mast cells in the retina, which should uncover ways to reduce or eliminate subsequent inflammatory damage. The Sheibani Lab is also studying how changes in the outer layers of the retina can lead to abnormal growth of blood vessels, a defining characteristic of wet AMD. By examining these early events, he hopes to stop these rogue blood vessels from causing problems in the first place.

As mentioned above, AMD has many risk factors in addition to older age, including genetics (variants in genes involved in the immune system, metabolism, and tissue structure) and certain lifestyle choices (unhealthy diet and cigarette smoking). Combining these risk factors increases the likelihood not only of getting AMD, but also of getting a more severe form.

Developing treatments for severe AMD

As AMD progresses, it destroys multiple levels of the retina—first the RPE cells that nourish the photoreceptor cells, and then the photoreceptors (cones and rods) themselves. When this happens, recovery of these cells is not an option, nor can they regenerate on their own. Replacement of the cells, however, is possible with a technology invented and championed at UW-Madison—human pluripotent stem cells. Induced pluripotent stem cells (iPS cells) are a particular type of adult stem cell, which **Dr. David Gamm's lab** has used to invent methods to produce unlimited quantities of RPE and photoreceptor cells. They are now using these cells to devise therapies for late-stage AMD and other retinal degenerative diseases.

The road from discovery to clinical trials is long and at times bumpy and unpredictable. Dr. Gamm, over the course of almost a decade, modified his stem cell protocols to generate tissue-like structures known as retinal organoids. In the last few years, his lab has collaborated with other McPherson ERI scientists to find better ways to deliver the cells under the retina in a safe and effective manner. Chief among these collaborators have been Dr. Shaoqin (Sarah) Gong and Dr. Zhenqiang (Jack) Ma, whose expertise in biomedical and computer engineering, respectively, allowed them to create biodegradable microscaffolds capable of capturing and precisely placing the stem cell-derived RPE and photoreceptor layers in the subretinal space. The Gamm Lab also worked with MERI researchers Drs. Raunak Sinha, Tim Gomez, and Xinyu Zhao (Department of Neuroscience) to test how well their lab-grown photoreceptors function. Each of these tests indicated that the prospective replacement cells have the intrinsic capacity to perform at levels akin to their counterparts in living retinas.

Before any new therapeutic gets to the clinic, it must first be formally tested in clinical trials. To that end, **Dr. Michael Altaweel** has spent the past three years developing effective surgical techniques to replace photoreceptors in the retina. The delicate procedure involves creating room in the subretinal space with a small amount of fluid, followed by gently inserting the cell implant, taking care to avoid additional damage to the diseased retina. Surgical tests on non-human subjects have proven the safety of the technique. The first surgery to implant iPS cell-derived RPE cells on a scaffold was performed at the National Institutes of Health under the direction of Dr. Kapil Bharti, who gave the inaugural Sandra Lemke Trout Lecture in Appleton in September 2023. Dr. Altaweel is working closely with Dr. Gamm and Dr. Bharti to go further down this road, with great hope for transformative results for AMD and other vision disorders.

Freya Mowat

BVSC, PHD, DECVO, DACVO, MRCVS

Assistant Professor, Surgical Sciences, School of Veterinary Medicine



Dr. Freya Mowat is currently performing a research study on AMD risk factors and how their cumulative action contributes to disease severity. Over the next 3 years, her lab will study the individual and combined effects of aging, metabolism, and high dietary glucose using a new mouse model that mirrors the exposures and genetics that lead to AMD in humans. Mowat predicts that the combination of all three risk factors will yield the closest laboratory representation of the human disease available thus far, which she will then use to define the pathobiological pathways that cause AMD. Once these pathways are better defined, Mowat and others will be better able to develop methods to counteract them.

Dr. Mowat—a veterinary ophthalmologist who focuses on human and animal aging and hereditary disorders—has moved full force into AMD research in recent years. Funded by the BrightFocus Foundation's New Investigator Award for Macular Degeneration Research, her lab's efforts will create a powerful platform upon which to study AMD and to create strategies to delay its onset or reduce its severity.





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

"My lab engineers innovative biomaterials for various biomedical applications including gene therapy, immunotherapy, and antimicrobials. The RRF Edwin & Dorothy Gamewell Professorship helps my laboratory to fight blindness by developing non-viral nanocarriers for safe and efficacious gene therapy, as well as 3D microstructured biodegradable and biocompatible polymeric scaffolds for photoreceptor and retinal pigment epithelium cell therapy."

Melissa Skala PHD

Biomedical Engineering and Morgridge Institute for Research RRF Daniel M. Albert Chair

"My lab develops imaging methods to sense chemical changes in the retina. Our goal is to use these technologies for early diagnosis of retinal disease and to monitor treatment to ensure the best outcomes for patients. We have used the RRF Daniel M. Albert Chair's support to test these technologies in animals and patients to determine whether these new methods have the sensitivity to impact clinical care."

Kris Saha PHD

Biomedical Engineering * RRF Kathryn & Latimer Murfee Chair

"The Saha lab engineers new gene therapies that can modify the DNA code of retinal cells. We are working with MERI-supported clinicians and biologists to test these strategies in clinical trials. Recent work has focused on developing novel nanoparticles that could be injected into the sub-retinal space to treat inherited retinal disorders."

RETINA RESEARCH FOUNDATION

CHAIRS AND PROFESSORSHIPS

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."

Mrinalini Hoon PHD

Ophthalmology and Visual Sciences

"Our recent research has uncovered a new form of 'plasticity' in the mammalian retinal circuit. With the support of the RRF Rebecca Meyer Brown Professorship, we discovered that visual signals early in development play critical roles to establish inner retinal synapses, and that light acts as a reversible modifier of these synapses such that adaptability or 'plasticity' is retained well into adulthood. This form of plasticity could be harnessed for correcting retinal circuit dysfunction prevalent in disease."

David Gamm MD, PHD

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

"Support from the RRF Emmett A. Humble Distinquished Directorship fuels my lab's efforts to refine methods to generate photoreceptors from human stem cell-derived retinal organoids for use in cell replacement therapies. Individuals with late-stage inherited retinal degenerations (such as retinitis pigmentosa, Stargardt disease, and Usher syndrome) go blind because their photoreceptors die. Therefore, this past year we developed ways to produce and isolate the photoreceptors that are most important for human vision—the red and green cones—and showed that they can reach out and make new connections with other retinal cells once they are removed from their organoid environment. This is an important step in our overall goal to reverse the effects of retinal degenerative diseases that destroy photoreceptors."

Bikash Pattnaik PHD

Pediatrics * RRF M. D. Matthews Research Professor

"Channelopathies are a group of conditions characterized by nonfunctional ion channels, which are integral to normal cell function. Exciting breakthroughs in my lab's research on channelopathies, supported by the RRF M. D. Matthews Research Professorship, have illuminated a path towards potential treatment for some forms of childhood blindness. After unraveling the disease mechanisms due to gene mutations, advanced gene editing and precision medicine permitted tailored treatments using patient iPSC cells and animal models to restore normal ion channel function. This provides hope for those affected by channelopathies beyond blindness."

MONROE & SANDRATROUT CHAIRS

The three Chairs endowed by McPherson ERI Advisory Board members and philanthropists 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.

Michael Altaweel MD

Ophthalmology and Visual Sciences Monroe E. Trout, Jr Chair in Eye Research

"I am fortunate to be able to use the **Monroe E. Trout**Chair in Vision Research as part of a team that is dedicated to the surgical delivery of stem cell-derived photoreceptors to the sub-retinal space. Our team has refined the process over the past three years as we move towards upcoming clinical trials for both inherited retinal diseases and age-related macular degeneration."

David Gamm MD. PHD

Ophthalmology and Visual Sciences \$\%\$ Sandra Lemke Trout Chair in Eye Research

"In the past year, my support from the Sandra Lemke Trout Chair in Eye Research has allowed my lab to test whether a custom-designed biodegradable microscaffold can deliver both retinal pigmented epithelial (RPE) cells and photoreceptors to the subretinal space in an organized, controlled fashion. Blinding disorders like age-related macular degeneration (AMD) result in the loss of both of these critical cell types, and thus it is critical to devise ways to replace them. To advance this work as quickly as possible, our lab works closely with other McPherson ERI labs headed by Drs. Sarah Gong and Jack Ma, and also Dr. Kapil Bharti's lab at the National Eye Institute."

Akihiro Ikeda DVM, PHD

Medical Genetics 蒙 Timothy William Trout Chair in Eye Research

"Support from the Timothy William Trout Chair in Eye Research has allowed my lab to study the function of TMEM135, a protein involved in retinal aging. Over-expression of the Tmem135 gene results in abnormal appearance and degeneration of retinal pigment epithelium (RPE) cells, the severity of which is determined by genetic makeup. Importantly, we have found a candidate gene that may determine the severity of these RPE abnormalities. This gene has a role in how cells process lipids, which could affect the survival of RPE cells. We were also able to discover that the actions of a cell's mitochondria are critical for the maintenance of the photoreceptor cell and its metabolic activity. Finally, based on our findings in mouse models, we are on our way to analyze lipid profiles of human age-related macular degeneration (AMD) patients to identify specific lipid profiles associated with AMD."

DAVID & NANCY WALSH FAMILY

PROFESSORSHIP IN VISION RESEARCH

Raunak Sinha PHD

Neuroscience

"The David and Nancy Walsh Family Professorship has enabled us to figure out how the cone photoreceptors, which mediate daylight vision, are functionally specialized in the central part of the primate retina, the fovea, compared to the rest of the primate retina. In particular, we have determined how photoreceptor adaptation to light levels is distinct in the foveal cones compared to peripheral cones. The Walsh professorship has also allowed us to further understand how cone photoreceptors regenerate their photopigment in the human stem cell-derived retina, which provides interesting insights into human cone physiology."

FEATURED RESEARCHERS

Haley Vlach PHD

Associate Professor, Educational Psychology, UW-Madison

Haley Vlach's Learning, Cognition, & Development (LCD) Lab 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. The LCD Lab has sought to understand this process. In particular, Dr. Vlach's work identifies where children look while learning, and how these eye movements are associated with significant cognitive milestones, such as learning language and other new concepts. In her studies, children are presented with several types of learning experiences, such as reading a storybook. Eye tracking technology—specifically, a Tobii X3-120 eye tracker—is used to measure where children look during these learning experiences. Researchers then determine if where a child looks predicts their success on a learning assessment; for instance, whether they learn new words from the storybook.

The results of the LCD Lab's work have highlighted the important role that children's eye movements play in their learning. Dr. Vlach's research has shown that sustained visual attention is important in learning language, particularly while an object is being verbally named. However, pausing

and looking away from the object can also facilitate a child's ability to recall information from memory. Thus, it may be possible to improve and/or accelerate higher-order cognition in children by optimizing the timing and sequence of a

visual learning exercise.

Left, children's eye movements are tracked using laptop learning tools and an eye tracker in Dr. Haley Vlach's lab.



Director of Emerging Animal Models, and Ophthalmology Program Lead at Fauna Bio, Inc.

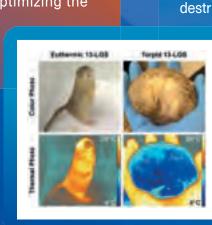
Many animals have evolved adaptations to avoid the worst diseases that affect humans. Ben Sajdak and his colleagues at the biotech company Fauna Bio have identified more than 65 mammalian species with disease resistance potential (and many more species when reptiles, amphibians, birds, and invertebrates are added in). The premise behind Dr. Sajdak's research and the company's work is that these adaptive differences can potentially be used to treat human disease. By comparing and contrasting the biological makeups of disease-resistant and disease-susceptible organisms, it is possible to tap into protective mechanisms that have already evolved in nature in order to find solutions for the greatest human health challenges.

The 13-lined ground squirrel provides an excellent example of Dr. Sadjak's work. Hibernating mammals like this squirrel can power down in cold weather to a physiological state called "torpor," which includes suppression of activity through decreased metabolism and temperature. The squirrel's heart rate goes from three hundred beats per minute to only three beats per minute during torpor. The animal also packs on fat in the fall prior to going completely without food or water for six months. In the process of avoiding the coldest seasons in Wisconsin, it emerges in spring having shed half its body weight but otherwise unscathed from a half-year "life pause."

So how does this line of investigation benefit people with vision-threatening conditions? During these states of torpor, 13-lined ground squirrels seemingly lose all senses, including sight. Their photoreceptors look unhealthy and disorganized, and they lose specialized structures called outer segments that are required to initiate vision. However, rather than being on the path to destruction, their photoreceptors are simply lying dormant, waiting for warmer

weather to recover full function. Perhaps most remarkably, the structural and functional recovery seen in the retinas of awakening 13-lined ground squirrels takes only a few hours. Dr. Sajdak and his colleagues are now investigating whether biological principles underlying this natural process can be used to recover vision in diseases like retinitis pigmentosa and Stargardt disease.

Left, non-thermal (normal) images (top row) of the 13-lined ground squirrel in both euthermic and torpid states, contrasted with thermal images (bottom row) of the squirrel in the same states. Thermal imaging highlights the squirrel's greatly lowered body temperature. Image courtesy of Ben Sajdak and Fauna Bio.



Yea-Seul Kim PHD

Assistant Professor, Computer Sciences, UW-Madison

As society becomes increasingly data-driven, people encounter numerical estimates on a daily basis. For example, news media regularly cover the unemployment rate to signal the pace of job growth or poll results to predict an election outcome, often using visualizations to summarize the data more efficiently. Indeed, the practice of communicating data—whether it be medical, scientific, social, economic, etc.—largely depends on visual representations in the form of charts, diagrams, and myriad other illustrations. While these visuals can be incredibly effective in conveying information to sighted individuals, they inadvertently create barriers for individuals with visual impairments, limiting their access to critical data and thus their ability to make independent, informed decisions.

Yea-Seul Kim's research aims to advance accessibility and inclusivity in data-driven content and data visualization. Her primary focus is on empowering individuals with visual impairments, particularly those who are blind or have low vision (BLV). Dr. Kim employs various user-centered methodologies to achieve these goals, through research projects like automatically generating personalized data facts by learning BLV users' informational needs, generating automated explanations for unfamiliar chart types BLV users have never experienced, and developing question-answering systems for data visualizations. Dr. Kim's recent work has investigated how low-vision individuals respond to online data images, which has informed her designs for a personalized tool that converts that data to a more accessible, less visually demanding format.



Shyam S. Chaurasia MSC, PHD

Associate Professor, Ophthalmology & Visual Sciences, Medical College of Wisconsin

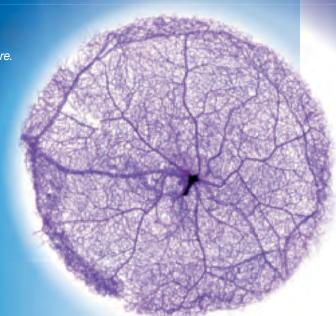
Shyam Chaurasia focuses on two pernicious diseases that spur abnormal blood vessel growth—diabetic retinopathy and retinopathy of prematurity. Dr. Chaurasia's Ocular Immunology and Angiogenesis Lab focuses on basic and translational research aimed at identifying and validating new biomarkers and targets for next generation precision therapeutics for these diseases.

The Chaurasia lab employs state-of-the-art 2D and 3D ocular imaging methods to perform long-term animal studies *in vivo*. To better study these diseases, the lab has developed several ocular animal disease models, including a pig model of diabetic retinopathy and a rodent model of retinopathy of prematurity. Their long-term goal is to identify early key factors that cause metabolic dysfunction and eventually damage neuronal and vascular cells.

The lab's recent noteworthy discovery of myeloid-associated S100A9 protein in the retina has opened a new therapeutic window for managing retinal vascular diseases by modulating the innate immune system. Dr. Chaurasia's immediate goals are to advance understanding of the role of inflammation in diabetic eye diseases, unveil molecular signaling pathways that contribute to retinal degenerative diseases, and develop new nanomedicine-based tools and therapeutics to counteract eye injuries.

Right, mouse retina digested with trypsin to depict retinal microvasculature. Image courtesy of the Chaurasia Lab.

Left, methods to make web data tables more accessible to blind and low vision users are developed in Yea-Seul Kim's lab. Image courtesy of the Kim Lab.



AMD & RP Pilot Grants

In late 2022, MERI instituted a new pilot grant program to support promising research programs on a larger scale than in past years. The awards were supported by Roger and Lynn Van Vreede, of Appleton, WI, (two \$50,000 awards, one each for research on age-related macular degeneration and retinitis pigmentosa) and the Robert A. Brandt Macular Degeneration Fund (for a \$50,000 AMD grant).

This generous funding supported the following projects:



AMD Award: Akihiro Ikeda, DVM, PhD, Lipidomic Analysis of Age-related Macular **Degeneration Patients**



AMD Award: Sushmita Roy, PhD. High-Resolution Characterization of Photoreceptor Populations in Cell-Based Therapy



RP Award: Mrinalini Hoon, PhD, Understanding How Connections Between Inner Retinal Neurons are Altered During Retinitis Pigmentosa

MERI is grateful to the Van Vreedes and the Robert A. Brandt Macular Degeneration Fund for their support.

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



The third annual David G. Walsh Graduate Student Support Initiative award was given to Freya Mowat, BVsc, PhD, DECVO, DACVO, MRCVS to support the work of PhD candidate Michele Salzman. Michele's thesis focuses on The Effects of Cadmium Exposure on the Retina in Outbred and Laboratory Animal Species. The \$12,000 GSSI grant is financed by the David G. Walsh Research Fellowship Endowment.

MCPHERSON ERI

RESEARCH **AWARDS**

2022-2023

Kenzi Valentyn Vision Research Grants



Due to their dedication, we were able to award five \$7500 Kenzi Valentyn Vision Research Grants, an all-time high, in late 2022:



David Barnett, MD, a postdoctoral fellow in Surgery, mentored by Michelle Ciucci, PhD and Freya Mowat, BVSc, PhD



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Mason Shipley, a graduate student in the Cellular and Molecular Pathology Program. mentored by Donna Neumann, PhD



Praveen Susaimanickam, PhD, a postdoctoral researcher in the Gamm Lab, mentored by David Gamm, MD, PhD



Serena Wisner, a graduate student in the Neuroscience Training Program. mentored by Mrinalini Hoon, PhD



Ruosen "Alex" Xie, PhD, a postdoctoral researcher in Ophthalmology and Visual Sciences, mentored by Shaogin "Sarah" Gong, PhD

Walsh Research Travel **Awards**



In 2023, Walsh Research Travel Awards were given to:

Kristina Chern, a graduate student in Cell Biology, Neurobiology & Anatomy at Medical College of Wisconsin (Daniel Lipinski, MSc. DPhil, mentor)

Kim Edwards, a graduate student in the Cellular & Molecular Pathology Training Program (David Gamm, MD, PhD, mentor)

Ru Wang, a graduate student in Computer Sciences (Yuhang Zhao, PhD, mentor)

Mason Shipley, a graduate student in the Cellular and Molecular Pathology Program

Andrew Miller, PhD, a postdoctoral researcher in Neuroscience (Raunak Sinha, PhD, mentor)



Distinguished Paper Awards

In early 2023, the McPherson ERI instituted the **Distinguished Paper Award** to recognize trainee members who are the first author or co-first author on papers of note. Inaugural award recipients were Kristina Chern (graduate student, Cell Biology, Neurobiology, and Anatomy, MCW); Ray Doudlah (graduate student, Neuroscience); Vishnu Lokhande (graduate student, Computer Sciences); Steven MayerI (graduate student, Ophthalmology and Visual Sciences); Philip Myzk (graduate student, Ophthalmology and Visual Sciences); and Aindrila Saha (graduate student, Neuroscience).



The McPherson ERI distributed additional student and trainee awards in 2022-2023, including:

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 two SMPH students in 2023: Asha Jain (Roomasa Channa, MD, mentor) and Katriel Williams (Cat Burkat, MD, FACS, mentor).

The McPherson ERI supported two Hilldale Undergraduate Awards in 2023. 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. Haoshen Zhai (mentor, Raunak Sinha, PhD, Neuroscience), and Melina Meuller (mentor, Karen Schloss, PhD, Psychology) were the recipients of this year's awards.

5 McPherson ERI trainees received support to attend the StoryForm Science Course, developed by Holly Kerby and Adam Steinberg, in Summer 2023.

Visiting Scholars were once again hosted by the McPherson ERI in 2023, following a COVID hiatus.

Recipients of these \$3000 grants were:

Visiting Scholar Awards

Gillian McLellan, BVMS, DACVO, DECVO, PhD, Surgical Sciences (SVM) and Ophthalmology & Visual Sciences (SMPH), who hosted Rebecca Sappington, PhD (Ophthalmology, Wake Forrest University School of Medicine)

Kristen Pickett, PhD & Andrea Mason, PhD, Kinesiology, and Kevin Ponto, PhD, Design Studies and WID, who hosted Jan Hondzinski, PhD (Kinesiology, Louisiana State University)

Robert F. Cooper, PhD, Joint Department of Biomedical **Engineering at Marguette University and Medical** College of Wisconsin/Ophthalmology, who hosted Ramkumar Sabesan, PhD (Ophthalmology, University of Washington)

Grant Summit Program

Nader Sheibani, PhD, was awarded a \$10,000 GSP Award in 2023 for his project, Regulation of mast cell homeostasis and pathogenesis of dry AMD by thrombospondin-1.



Bilge Mutlu, PhD, (Computer Sciences) was awarded the 2023 Expanding Our Vision Award (\$10,000) for his project, Designing Interfaces to Enhance the Experience of Remote Vision through Robotic Cameras. Dr Mutlu's project abstract notes that "existing interfaces for controlling robotic cameras lack usability. The purpose of our project is to develop more effective and accessible interfaces for remote vision experiences through robotic cameras, with a focus on enabling mobility-impaired older adults to participate in activities in remote spaces that would be otherwise inaccessible to them."

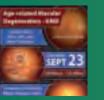
McPherson ERI Lectures, 2023



11th Annual McPherson Lecture, May 2023

Patricia D'Amore, PhD, MBA, Charles L. Schepens Professor of Ophthalmology at Harvard University. Dr. D'Amore spoke on Ocular Angiogenesis: Biology, Pathology, and Translation.

Sandra Lemke Trout Lecture, September 2023



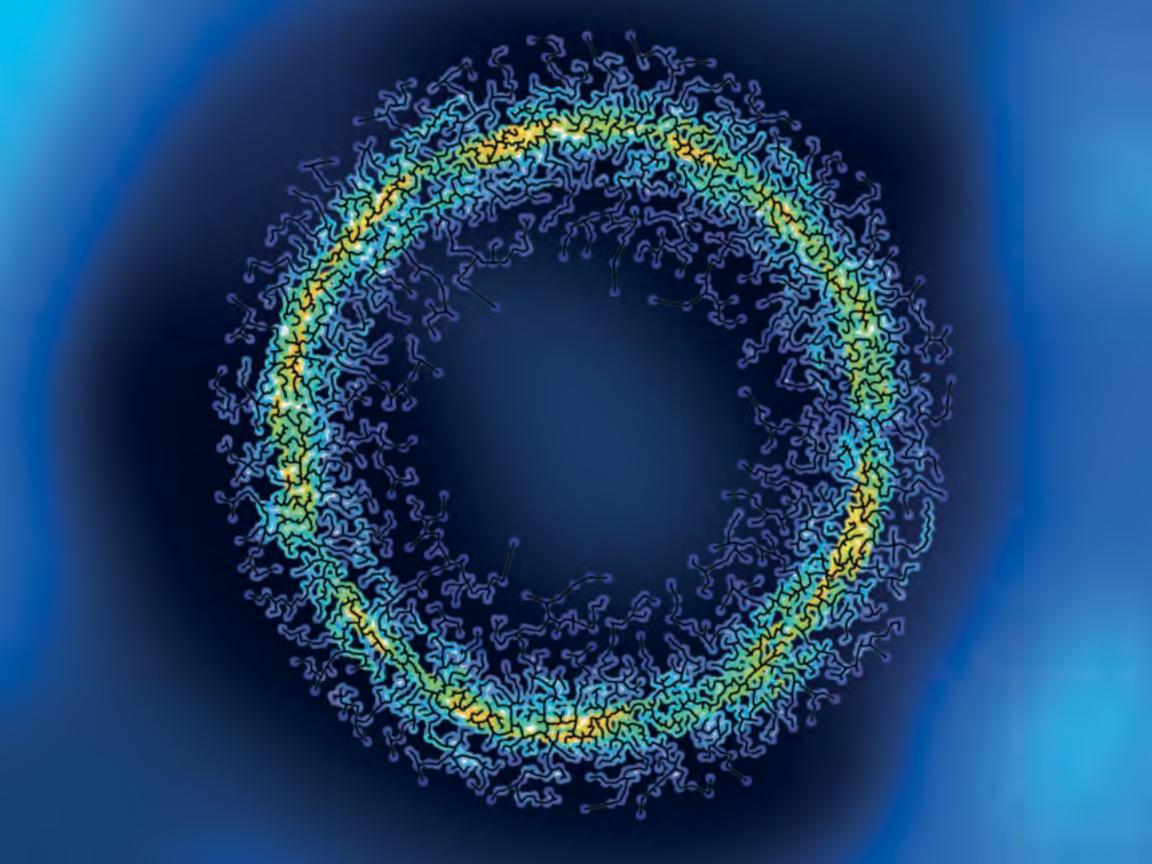
Kapil Bharti, PhD, Scientific Director and Senior Investigator at the National Eye Institute, gave the inaugural Sandra Lemke Trout **Lecture** as part of a larger symposium on age-related macular degeneration held in Appleton, WI. The event, which kicked off the Trout AMD Project, drew almost 200 people to the Lawrence University campus. Dr. Bharti spoke on A Cell Therapy Clinical Trial for AMD: Replacement Eye Tissue Made from Patients' Stem Cells.



Daniel M. Albert Lecture, October 2023

The inaugural **Daniel M. Albert Lecture** took place in Madison on October 26th. The Albert Lecture was endowed by Dr. Alice McPherson in honor of the distinguished career of Daniel Albert, the McPherson ERI's Founding Director. Dr. David Gamm presented this first Albert Lecture, speaking on Overcoming Challenges to Photoreceptor Cell Replacement.

15th Annual Vision Science Lecture, November 2023 Mary Peterson, PhD (Cognition Science Program, University of Arizona), delivered the McPherson ERI's 15th Annual Vision Science Lecture—Visual Ambiguity: Is It Really Rare?—to an appreciative audience following the Institute's annual poster session.



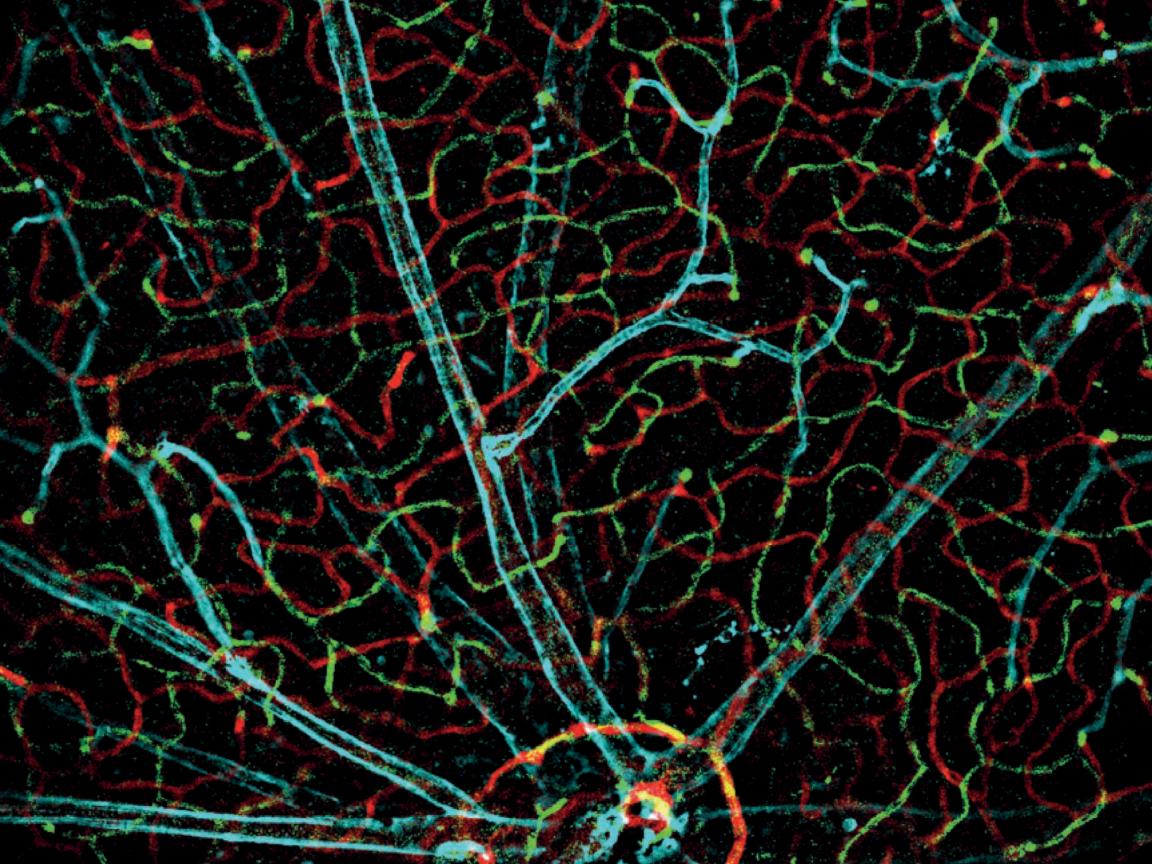
JANUARY

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The functional network of the human brain at rest is derived from MRI scans by calculating correlations across 5,000 brain regions. Due to its complexity, the network is difficult to visualize in three dimensions. Thus, scientists map the network onto the Poincaré disk, a specialized type of geometrical model. They then look to find the most economical way to connect the points of the model by an approach known as the minimum spanning tree (MST), which captures the overall geometric structure of the resting brain network. The observed structural interactions can be modeled as a Turing pattern which models patterns in nature, in this case reminiscent of zebra stripes. • IMAGE COURTESY OF MOO CHUNG, PHD.

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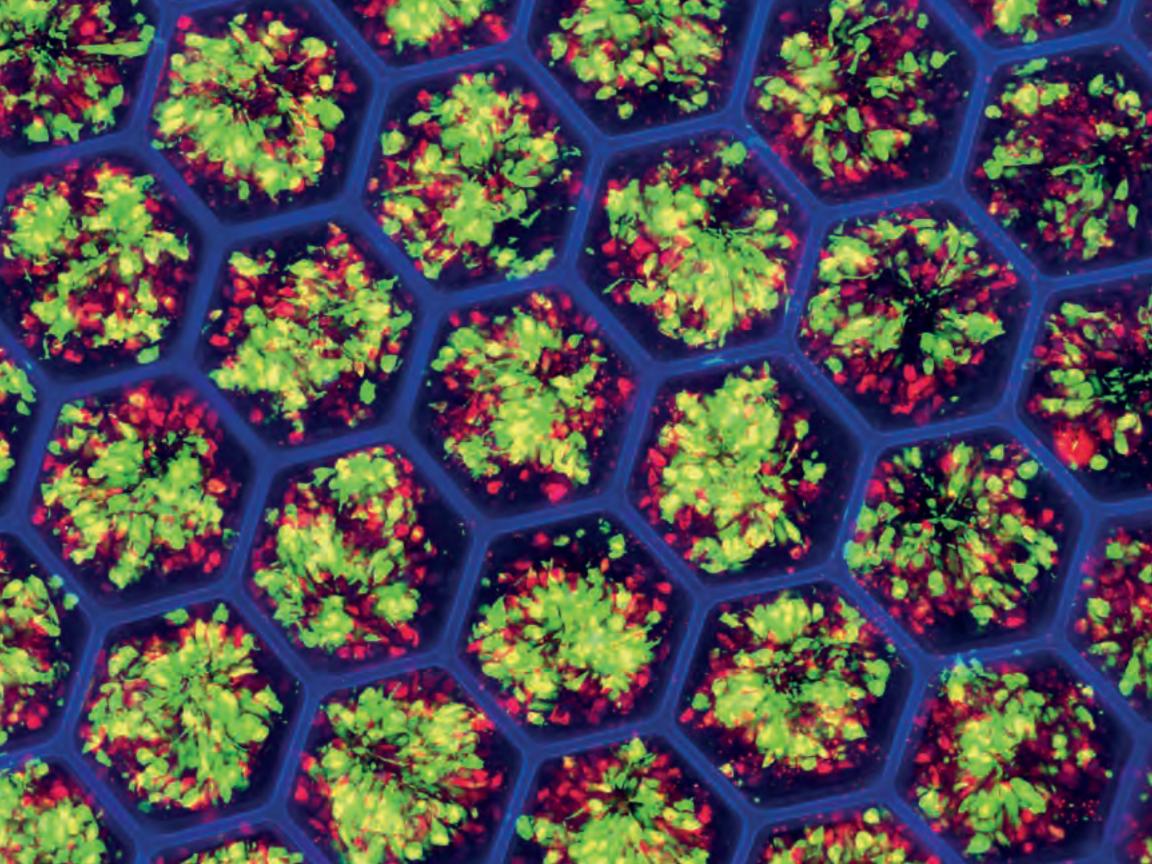




FEBRUARY

The inner retina has three layers of blood vessels—captured in this image of mouse retinal microvasculature—which provide nutrient and waste exchange. Each of these layers have been assigned a different color—cyan (the superficial layer), green (the intermediate layer), and red (the deep layer). Abnormalities detected in these vessels can indicate problems in the retina. The Ocular Immunology and Angiogenesis Lab at the Medical College of Wisconsin studies these retinal vessels to find new management strategies for combating devastating retinal diseases. • IMAGE COURTESY OF SHERMAINE W. Y. LOW, WAYLON ALVARADO, & SHYAM S. CHAURASIA, MSC, PHD.

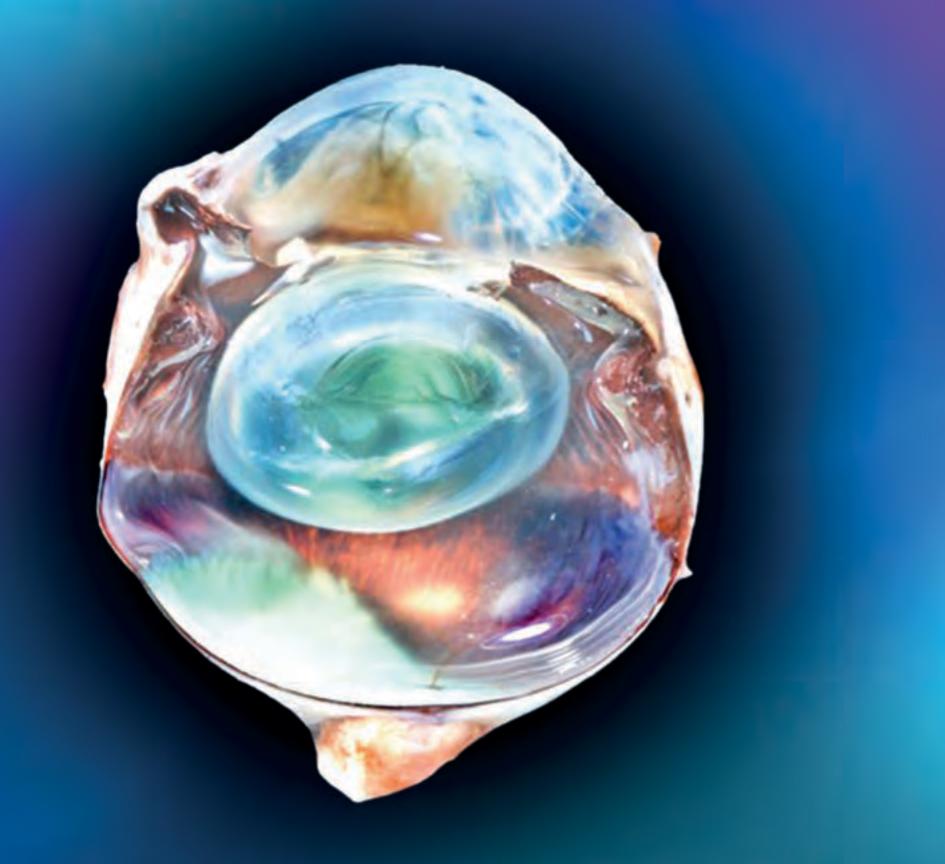
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MARCH

Stem cell-derived photoreceptors grown in the Gamm Lab are seeded in honeycomb-patterned scaffolds. Recoverin and CRX photoreceptor proteins are labeled in green and red, respectively. The versatility of these scaffolds, developed and manufactured by Shaoqin (Sarah) Gong, PhD, and Zhenqiang (Jack) Ma, PhD, can accelerate retinal cell transplantation efforts in patients with retinal degenerative diseases. • PHOTO BY AGUSTIN LUZ MADRIGAL, PHD, AND JIAHE JIN.

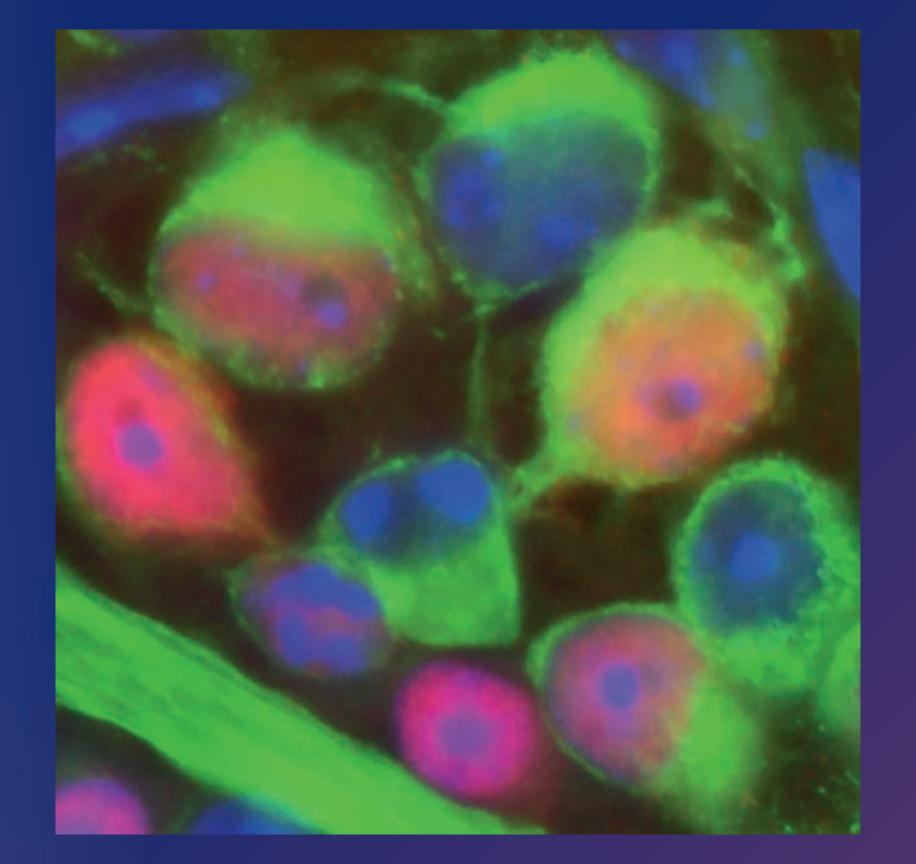
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APRIL

In the upper left side of this cat eye there is a small outpouching called a staphyloma. The medical history suggests that this defect is due to a scratch from another cat. The turquoise-colored area in the back of the eye is the tapetum lucidum. This reflective layer causes the eye to glow when you shine a light towards the eye in the dark. • IMAGE COURTESY OF THE COMPARATIVE OCULAR PATHOLOGY LABORATORY OF WISCONSIN (COPLOW).

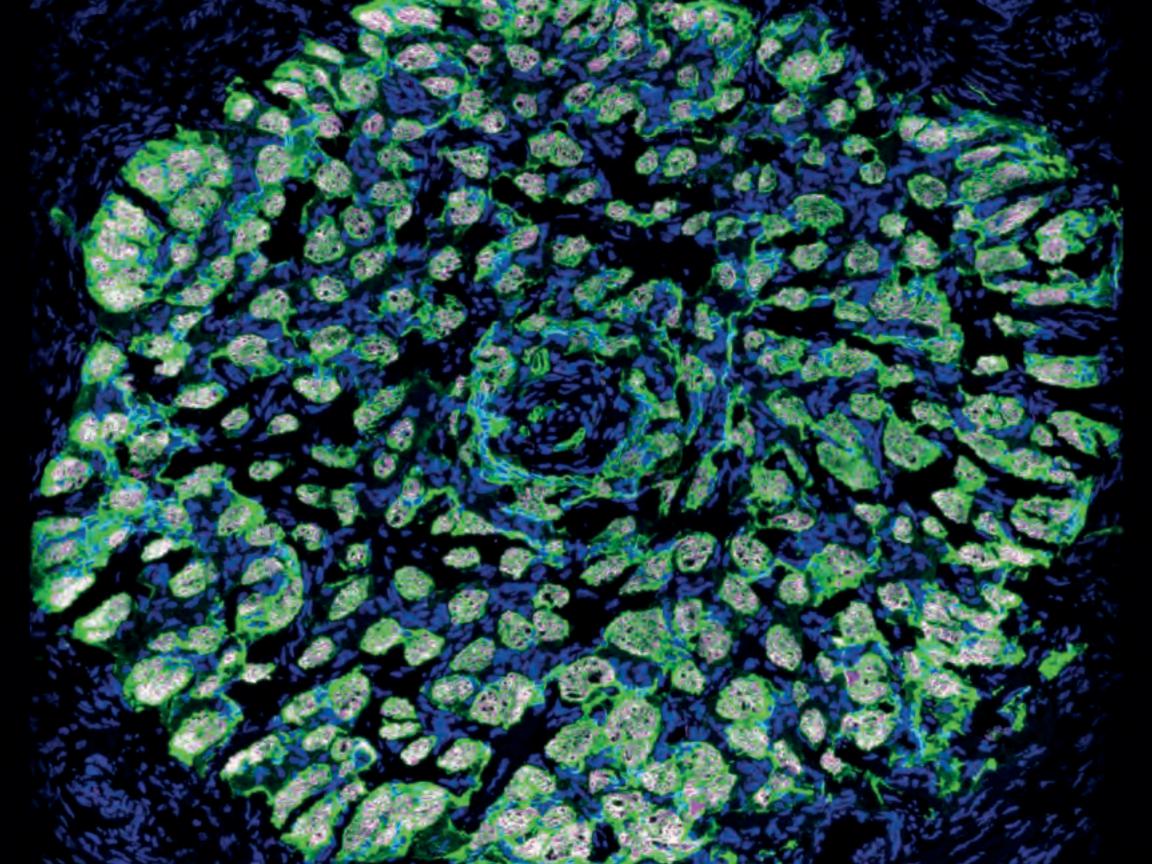
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A high magnification image of the surface of a mouse retina showing retinal ganglion cells (RGCs) which are stained for the cytoplasmic marker Tubulin (green). This retina was treated with a virus to introduce a gene called histone deacetylase 3 (HDAC3) which has been tagged with a red fluorescent protein. Studies indicate that HDAC3 participates in the process of RGC loss during glaucoma and the resultant acute damage to the optic nerve. In this experiment, the forced expression of HDAC3 in undamaged RGCs makes them more sensitive to pathology induced by optic nerve damage. The nuclei of retinal cells are stained blue. • IMAGE COURTESY OF THE NICKELLS LAB.

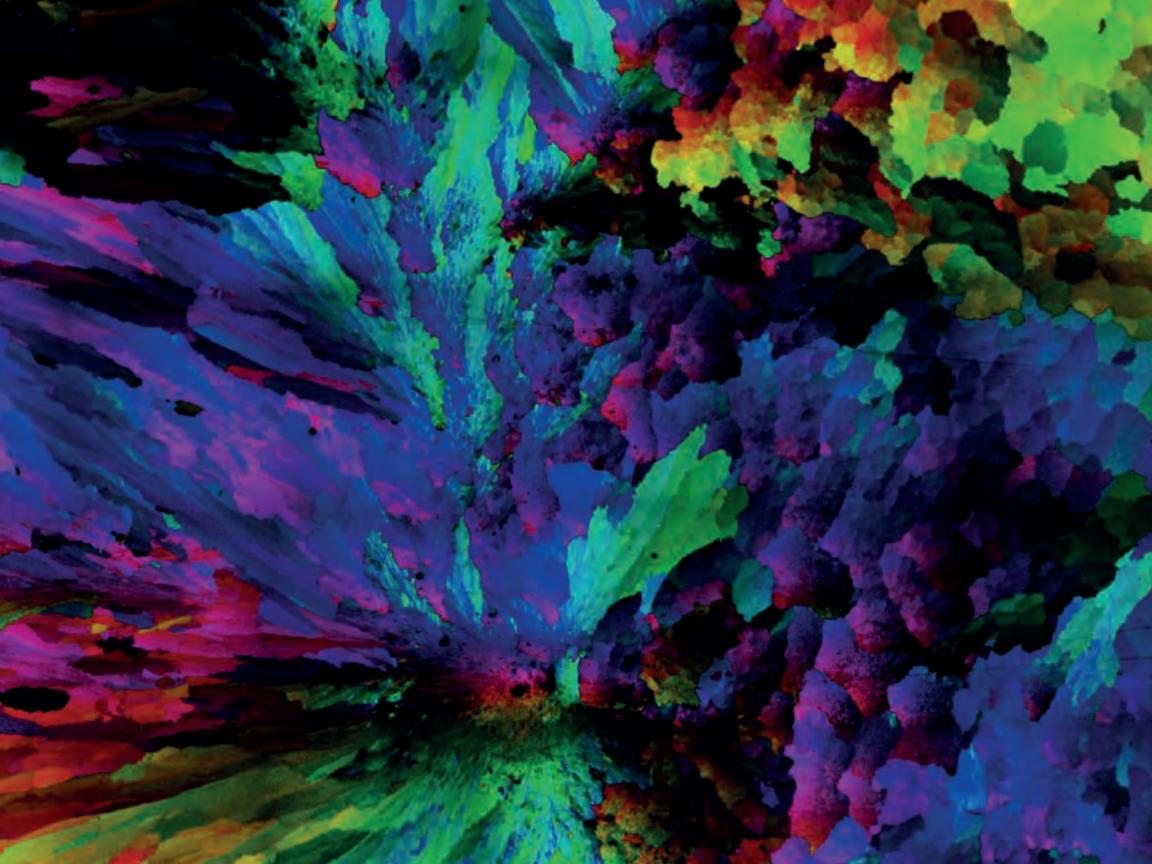
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This image highlights the intimate relationship between nerve fibers (pink) and nervous system supporting cells known as astrocytes (green) in the optic nerve. Their close association plays a critical role in maintaining the health of the optic nerve and in its response to blinding diseases such as glaucoma. Understanding cellular and molecular relationships between these cells in glaucoma is the focus of research efforts by Professor Gillian McLellan and her vision research lab. • IMAGE COURTESY OF KAZUYA OIKAWA, BVSC, PHD, MCLELLAN LAB.

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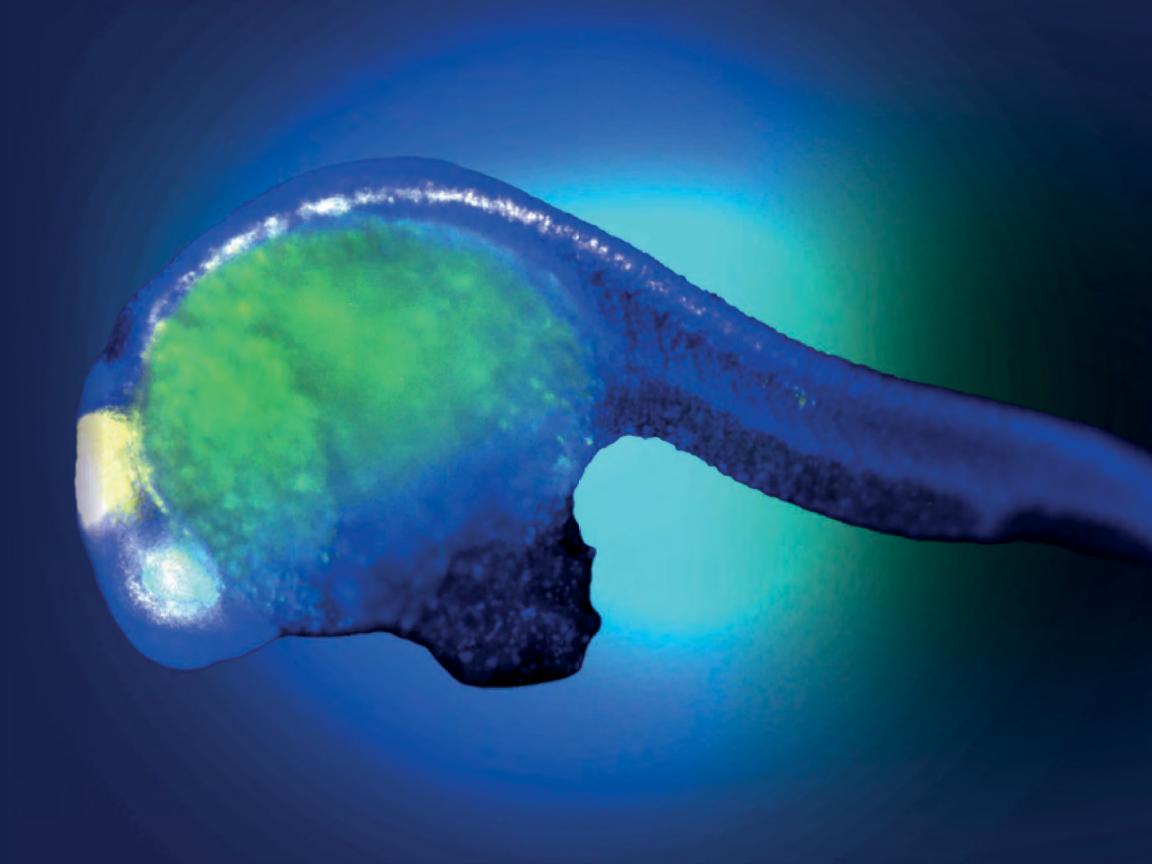




This striking image is a Polarization-dependent Imaging Contrast (PIC) map of a coral skeleton (Stylophora pistillata) from the Red Sea. The 2D image shows the aragonite (CaCO3) nanocrystal orientation in each pixel, so that color quantitatively corresponds to the orientation of the crystalline c-axis in 3D. The in-plane angle of the c-axis is displayed as hue, the off-plane as brightness in each image pixel. This PIC map demonstrates the structure of this and all other coral skeletons, which is called spherulitic—that is, a radial distribution of acicular crystals, starting from so-called centers of calcification. • IMAGE COURTESY OF PUPA GILBERT, PHD, DEPARTMENT OF PHYSICS.

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AUGUST

For various reasons, zebrafish provide a useful animal model to study visual function in the laboratory. This image is of a one day old zebrafish embryo showing expression of *foxe3* (green) and *mab21l2* (yellow) genes in the developing eye and brain. Disruption of this early activity results in abnormal development. Variants in the *FOXE3* and *MAB21L2* genes causing human ocular disease are identified and studied in Dr. Elena Semina's lab at the Medical College of Wisconsin. • IMAGE COURTESY OF ELENA SEMINA, PHD.

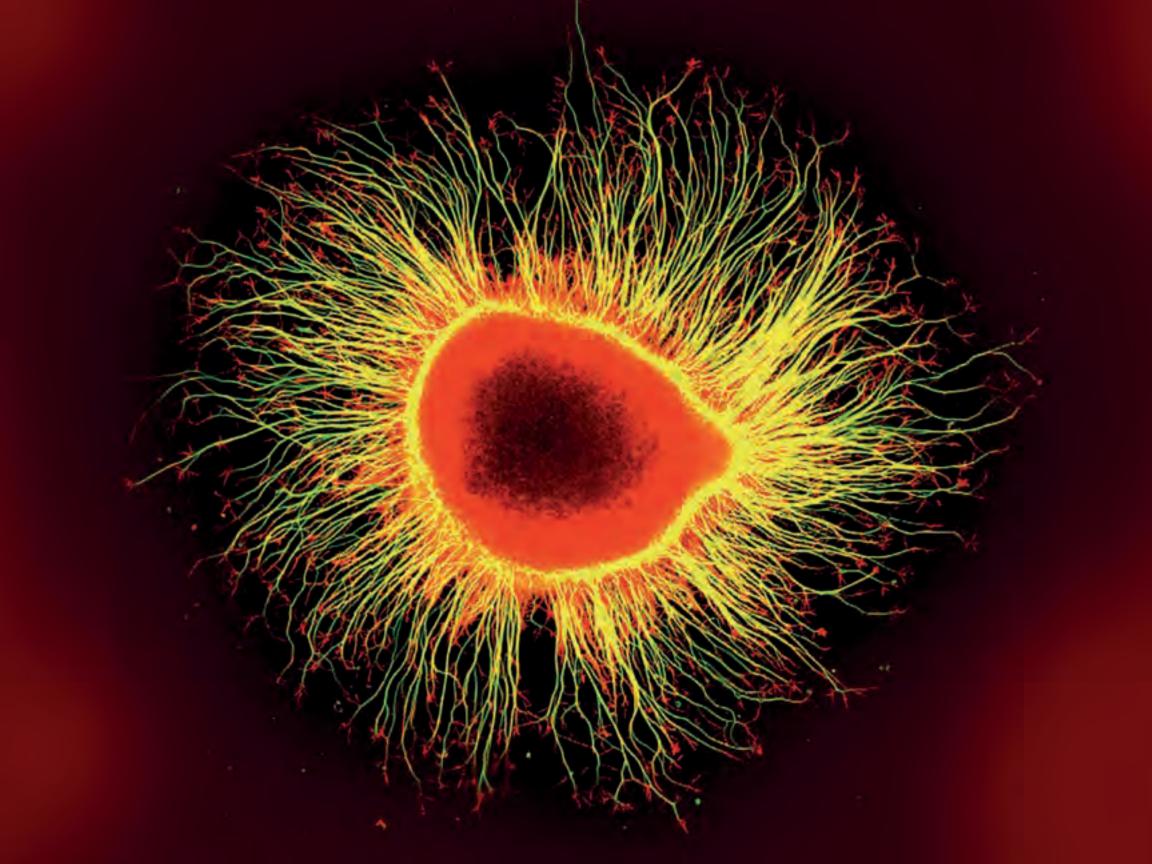
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SEPTEMBER

The eyes of a queen conch peer out nervously from an overturned shell in a seagrass meadow in the Turks and Caicos Islands. Conchs eat and recycle organic matter, an important role in seagrass habitats that are, in turn, important in stabilizing shorelines with their dense root systems. This image, taken by Assistant Professor Robert Johnson (Integrative Biology), was one of the winning images in UW-Madison's Cool Science Image contest in 2023. • IMAGE COURTESY OF ROBERT JOHNSON, PHD.

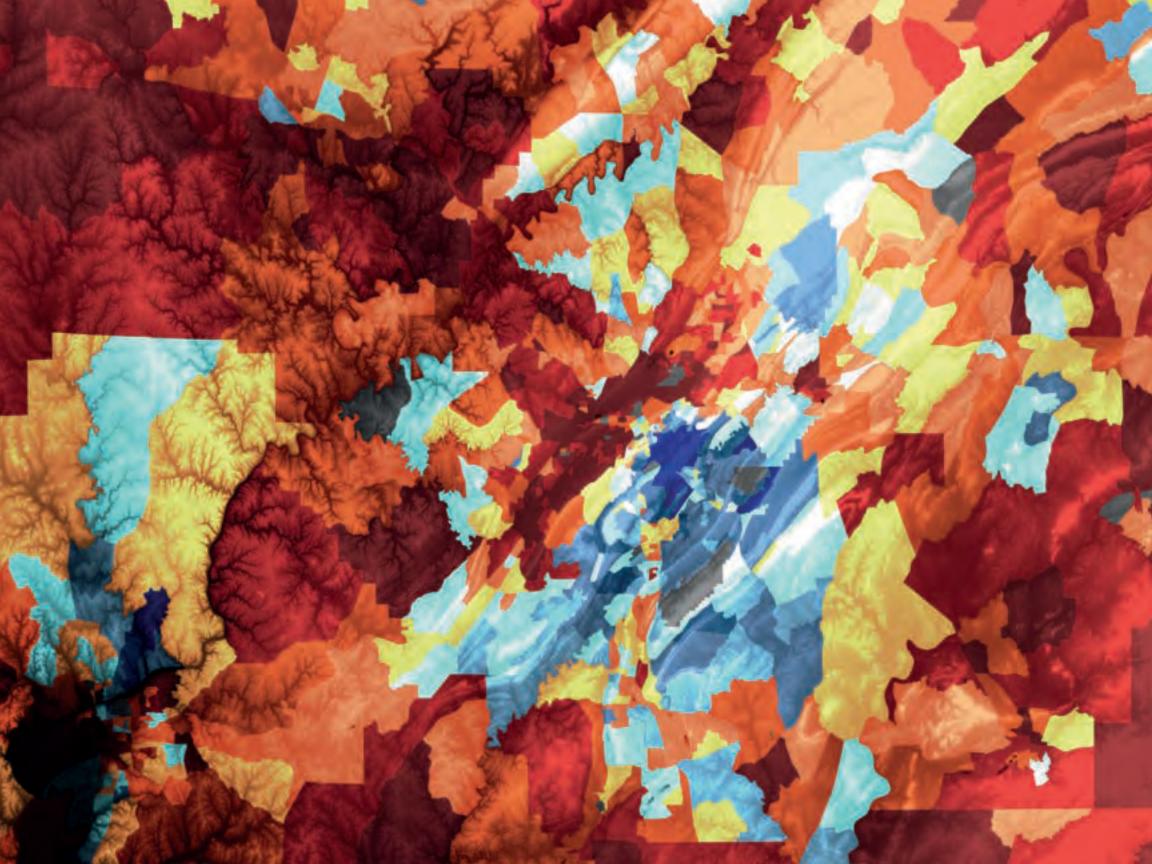
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OCTOBER

Low-magnification confocal microscope image of a human motor neuron (MN) neurosphere derived from induced pluripotent stem cells (iPSCs), with hundreds of extending MN axons. Microtubules (yellow) make up the core of developing axons; and filamentous actin (red) concentrates within the tips, called growth cones, that are capable of movement and extension. The Gomez lab uses stemcell derived MNs and other classes of neurons that differentiate from stem cells to understand mechanisms of axon growth and guidance. • IMAGE COURTESY OF TIM GOMEZ, PHD, DEPARTMENT OF NEUROSCIENCE.

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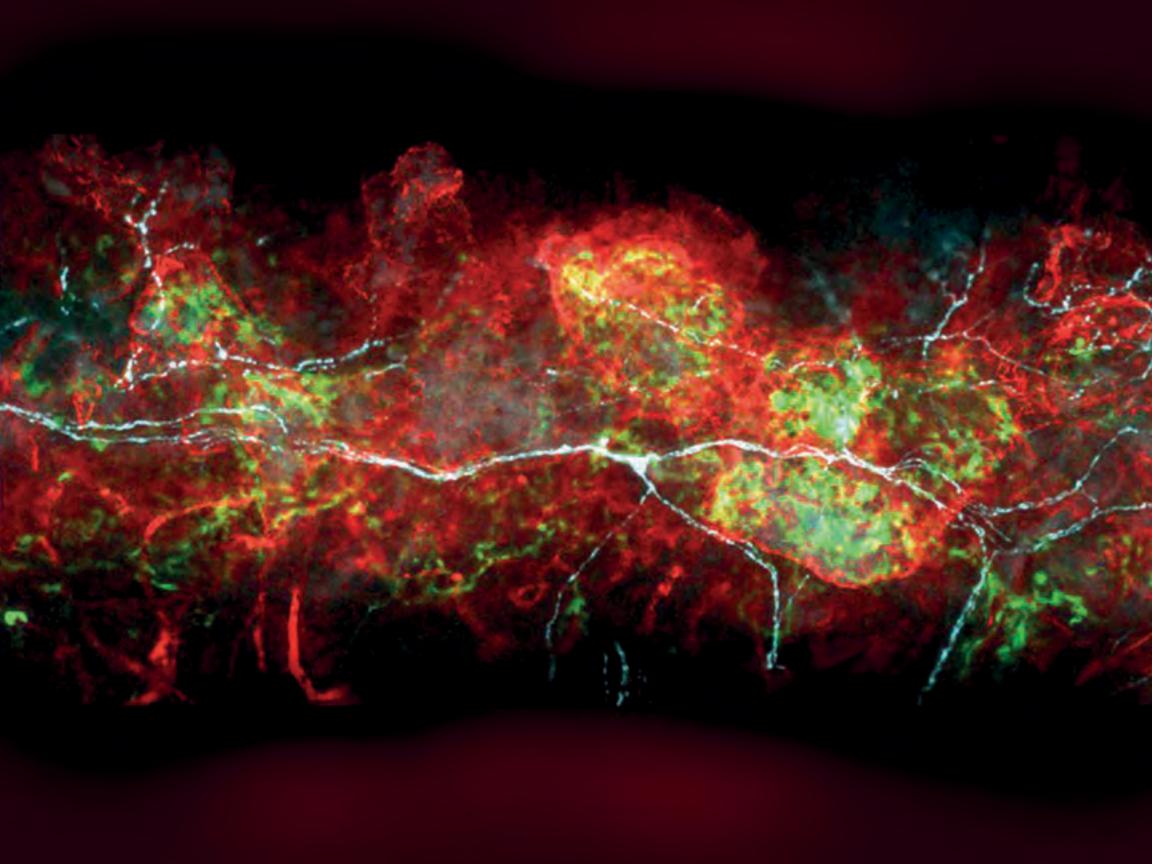




NOVEMBER

Layering measurements of socioeconomic disadvantage—a scale called the Area Deprivation Index (ADI) created by the Center for Health Disparities Research—at a neighborhood scale over a digital elevation model (DEM) allows researchers to consider how geography may affect health outcomes. In this image of Birmingham, AL, we can see the topography beneath. Rivers, valleys, and hills are visually reminiscent of the shapes of our bodies and the connections in our brains. This was a winning image in the UW's 2023 Cool Science Image contest. • IMAGE COURTESY OF NYLA THURSDAY AND LUKE CHAMBERLAIN, GIS SPECIALISTS, CENTER FOR HEALTH DISPARITIES RESEARCH.

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DECEMBER

Shown in this image is a composite confocal image of mouse trabecular meshwork—the important "drainage system" for the eye's aqueous humor. Dysfunction in this system can lead to the development of glaucoma. The colors represent the protein PECAM1 (red) and fluorescent latex beads trapped in the highflow areas of the trabecular meshwork (green), among other things. The function of sensory neurons (bright cyan) in the trabecular meshwork has yet to be elucidated. • THIS IMAGE WAS ACQUIRED AND FURTHER PROCESSED BY TIMUR MAYLYUTOV, PHD, AND SAMER BILAL, IN THE LABORATORY OF COLLEEN MCDOWELL, PHD.

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**** PAUL M. DELUCA JR ****

McPherson ERI mourns the loss of Dr. DeLuca in October 2023. Paul was a great friend to MERI and a distinguished scientist and former provost of UW-Madison; he will be missed.

MCPHERSON EYE RESEARCH INSTITUTE 2022-2023

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Cycle for Sight 2023

Hits a New High Mark with a Hybrid Event

Cycle for Sight went hybrid in 2023! We were back at the Princeton Club West for the kickoff event on March 25th with intrepid riders participating in the middle of a late winter snowstorm. Then, over the following month, other teams and individuals walked or rode in community events around Wisconsin and as far away as Cannon Beach, Oregon. Cycle for Sight raised a record \$64,102 in 2023!

We're grateful for all of our teams, and to our terrific long-term sponsors, Opsis Therapeutics, the Chippewa Valley Eye Clinic, and the Princeton Club.

And we certainly want to note the outstanding contribution of Kenzi's Team, which this year raised over half of the contribution total for the event. Their dedication, and that of all our participants, supports the Kenzi Valentyn Vision Research Awards to fund pilot projects from outstanding young vision researchers (among many other awards).





The Mandelbaum & Albert Family Vision Gallery

- Envisioning the Environment: Scenes from Plein Air Artists, in Spring 2023, featured outdoor works from a dozen Wisconsin artists, capturing the state in all its seasons.
- The Soul in Things, which ran through the summer of 2023, displayed UW-Madison Biochemistry Professor Alan Attie's outstanding portrait photographs of a range of acquaintances, including many affiliated with the McPherson ERI. The sitters were photographed with objects of their choice and of great meaning in their lives; their personal statements are viewable in full on Professor Attie's website, www.alanattiephotography.com.
- Cool Science Images 2023 is showing in the gallery in Fall 2023 (through January 10th, 2024), and features the winners of UW-Madison's annual contest for the year's best science-related images.











WITH THANKS AND APPRECIATION

TO THE FOLLOWING DONORS TO THE MCPHERSON EYE RESEARCH INSTITUTE, July 2022 - October 2023:

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Age-related macular degeneration causes the central retina, known as the macula, to deteriorate. Scientists at the McPherson ERI are striving to treat this condition on many levels, including replacing this missing "piece" of the retina with stem cell technology.

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