Dear Friends of the McPherson Eye Research Institute,

The McPherson ERI is proud to support one of the largest and most scientifically diverse groups of distinguished and dedicated vision-related researchers in the world. While we have an abundance of expertise, technology, and innovative ideas in each of our laboratories, we also know that true breakthroughs rarely occur in isolation. Instead, they come about through open collaboration and sharing of ideas and resources. That is why ‘team research’ is the Institute’s (and the UW-Madison’s) modus operandi.

A parallel can be drawn between the McPherson ERI’s mission and methods and those of another large and carefully crafted team—the scientists and engineers of the James Webb Space Telescope Project. The deep space images that the Webb has dazzled us with over the past year were not only the inspiration for this year’s calendar cover, but a reminder of what can be accomplished when we pool our strengths and work together. It is also worth noting that when the Webb Project began in the 1990s, the technology necessary to achieve its goals hadn’t been fully developed yet.

In the pages of this calendar, we will update you on some of the Institute’s ongoing team-based efforts to push the envelope when it comes to combating blindness. We hope to convey the very real sense that the Institute is much greater than the sum of its parts (impressive though the parts may be). Highlighted projects include those using (1) induced pluripotent stem cells to grow photoreceptors with the potential to rebuild the human retina; (2) gene editing to fix mutations that cause blindness in children; and (3) novel imaging systems to monitor the health of the living human retina in ways never before achieved.

In the end, our purpose is to preserve and restore vision by advancing science and medicine with focus, innovation, and integrity. We remain united with you in seeking an end to the most devastating diseases that impact vision.

We are also grateful for your interest in our work, and for your support of the McPherson ERI. In recent years, McPherson ERI donors have provided funds for all of the projects highlighted in this calendar—thank you!

Please have a wonderful holiday season and New Year’s, and a happy and healthy 2023.

Sincerely,
David M. Gamm, MD, PhD
Professor, Department of Ophthalmology and Visual Sciences • RRF Emmett A. Humble Distinguished Director, McPherson Eye Research Institute • Sandra Lemke Trout Chair in Eye Research

BRINGING IT ALL TOGETHER

Diseases that result in vision loss are as diverse as they are numerous. Many we know well enough to treat effectively today, but others have perpetually evaded our understanding and thus lack any meaningful therapies.

At the McPherson ERI, we have tasked ourselves with addressing the toughest remaining vision problems—the ones that don’t follow the rules as we currently know them. To be successful in this endeavor, we have to approach vision science and medicine differently, mixing and matching our varied perspectives and skills to see and fight disease in new ways. In the next few pages, we highlight inroads that McPherson ERI researchers have made in advancing knowledge and developing future treatments for some of the most prevalent and devastating causes of vision loss—age-related macular degeneration, retinitis pigmentosa, diabetic retinopathy, and glaucoma.
Age-related macular degeneration (AMD) and retinitis pigmentosa (RP)

The McPherson ERI Stem Cell Consortium: Looking toward human clinical trials

Until very recently, the idea of replacing the cells in human eyes that initiate vision—the photoreceptors—was considered science fiction. Those who have followed the McPherson ERI’s research for the past 10 years, though, know that what was once a fanciful dream is moving towards reality. In the last decade, David Gamm (Sandra Lemke Chair in Eye Research) and his lab members, along with multiple collaborating researchers at UW-Madison and around the world, have used induced pluripotent stem cells (iPSCs) to create functional human photoreceptors and other retinal cells in the lab, as well as whole retinal tissues. The McPherson ERI’s stem cell team, led by Dr. Gamm, includes biologists, statisticians, engineers, surgeons, and industry leaders.

2022 has seen strong forward movement towards transplantation of photoreceptors for retinitis pigmentosa and RPE (or RPE + photoreceptors) for age-related macular degeneration (AMD). Other inherited diseases that will benefit from these efforts include Usher syndrome, Stargardt disease, and Best vitelliform macular dystrophy, among many others. Pioneering research and patents from the McPherson ERI’s stem cell team led to the establishment of Opsis Therapeutics, a subsidiary of FujiFilm Cellular Dynamics Inc. (FCDI), in Madison, WI. In 2021, Opsis and FCDI joined forces with BlueRock Therapeutics (Boston, MA) and Bayer AG (Germany) to take their iPSC-derived photoreceptor and RPE cell technology to patients. At least two human clinical trials are planned in the coming years—the first for retinitis pigmentosa and Usher syndrome, and the second for AMD and other forms of macular disease.

In 2022, two different studies published by McPherson ERI stem cell team members have provided strong evidence that lab-grown photoreceptor cells have “what it takes” to function in the human eye. Early in the year, neuroscientist and David and Nancy Walsh Family Professor Raunak Sinha published a study in collaboration with the Gamm Lab showing that stem cell-derived cone photoreceptor cells can respond to light in a very similar way as those in adult non-human primates. An equally important finding came later in the year, when neuroscientist Tim Gomez’s lab reported that these same stem cell-derived cone photoreceptors have the innate ability to extend “wires”—termed axons—in order to contact other retinal cells. That study, led within the Gomez lab by Sarah Rempel in collaboration with the Gamm lab, bolsters confidence that transplanted photoreceptors can forge the links necessary to re-establish vision-generating retinal circuits in patients whose photoreceptors have been terminally damaged.

This past year, the McPherson ERI stem cell team continued to explore innovative ways to deliver photoreceptors and RPE cells to their home in the very back of the eye using the latest engineering advances. Working with Dr. Gamm, the labs of Sarah Gong (RRF Edwin and Dorothy Gamewell Professor) and Jack Ma have created a 4th generation biodegradable micro-scaffold that can safely and accurately place photoreceptors and/or RPE cells under the thin, delicate retina. The team is now testing these scaffolds in preclinical studies in collaboration with the lab of Kapil Bharti with support from the U.S. Department of Defense and the National Eye Institute. Refining the subretinal transplant procedure has also been a major Institute focus in 2022, with key improvements being made by lead retinal surgeon and stem cell team member Michael Altaweel (Monroe E. Trout Chair in Eye Research).
Childhood-onset glaucoma

Mapping the microscopic pathways of the eye’s fluid drainage system

It is possible to treat or cure a disease without understanding its origin or exact pathways, but there’s no doubt that knowledge of these can point to new and effective treatments. We know that primary congenital glaucoma (PCG), a devastating ocular disorder affecting infants, is triggered by elevated pressure within the eye which leads to painful enlargement of the globe and severe damage to tissues, including the light-processing retina. The disease is caused by a failure to correctly develop the eye’s main fluid drainage tissues—the aqueous humor outflow pathway. Only surgical treatment is currently possible and that is challenging and often fails, resulting in blindness and removal of the eye in a significant proportion of children.

The molecular causes of PCG are largely unknown, but we do know that one-quarter of cases can be attributed to mutations in four genes important for outflow pathway development. McPherson ERI researcher Stuart Tompson, PhD, was a key player in identifying two of these genes, TEK and ANGPT1. To progress further, more understanding is needed as to which exact molecular pathways are important for the formation of these crucial ocular structures. The Tompson lab is moving forward on this, utilizing state-of-the-art gene sequencing technologies to comprehensively identify all cell types and molecular pathways involved in the normal development of these tissues. Once this “atlas” is complete, it will greatly help researchers discover the elusive PCG mechanisms, enable gene-based diagnostic testing, and aid the development of more effective treatments directed at the fundamental disease biology.

Retinal organoid image courtesy of the Gamm Lab

Childhood-onset inherited retinal diseases

Bringing the power of gene editing to pediatric eye disease

The human eye—despite being one of the body’s most complex and intricate organs—is an ideal target to test treatments that use CRISPR, the Nobel Prize-winning tool that can precisely alter, or ‘edit’, DNA associated with inherited disease. The Institute has been investigating this potential through an interdisciplinary partnership involving McPherson ERI scientists at UW-Madison, the Morgridge Institute for Research (MIR), and the Wisconsin Institute for Discovery (WID). Our team, led by Kris Saha, is organized around a variety of cutting-edge techniques that enhance the safety, reproducibility, and efficacy of gene editing aimed at curing inherited forms of childhood blindness.

Kris Saha started exploring the idea of CRISPR-based therapies many years ago. Saha, the RRF Kathryn & Latimer Murfee Chair, is a biomedical engineer at the WID and a member of the NIH’s Somatic Cell Genome Editing Consortium who has pioneered gene editing technologies. He was joined by David Gamm (Sandra Lemke Trout Chair in Eye Research), Bikash Pattnaik (RRF M.D. Matthews Research Professor), Sushmita Roy (WID), and MIR biomedical engineer Melissa Skala (RRF Daniel M. Albert Chair). Drs. Gamm and Pattnaik bring expertise in stem cells and retinal function assessment to the gene editing team. Dr. Roy is an expert in bioinformatics and computational analysis, and Dr. Skala develops non-invasive imaging methods to assess gene editing outcomes.

This NIH-supported project, now in its fourth year, uses human stem cell-derived retinal organoids created in the Gamm Lab to replicate the cellular dysfunctions of inherited pediatric eye diseases in a dish. There are many genetic conditions that cause childhood blindness, so creating organoids from patients allows the team to test gene editing strategies in the lab safely and efficiently.

The Skala Lab contributed a key technique to the project called autofluorescence lifetime imaging, which can track the natural fluorescence produced during photoreceptor activity. This experimental approach, spearheaded by Skala lab assistant scientist Kayvan Samimi, was capable of detecting subtle biochemical changes within organoid photoreceptors. Using this technique, the team can now determine whether CRISPR-mediated gene editing is hitting its intended disease target in the human genome.

Adapted from an article by Brian Mattmiller, Morgridge Institute
Clinical trial description adapted from an article by Joslin Diabetes, www.joslin.org, 5/18/21.
Shawn Green’s research focuses on developing and evaluating behavioral training methods to enhance human vision. Behavioral training of this type can help in overcoming all kinds of vision-related obstacles. Among other things, the Green lab works to understand an obstacle known as “the curse of specificity.”

If you have an individual repeatedly practice a given visual task (for example, to indicate whether a line is oriented clockwise or counterclockwise from vertical), they will improve at the task. However, the benefits of that practice rarely transfer to new tasks—such as, for instance, asking the individual to indicate whether a line is oriented clockwise or counterclockwise from horizontal, after training on the vertical task. This presents a significant problem if the goal is to use behavioral training to improve vision in the real world. It does an individual no good if they’ve improved their ability to detect visual cues via a computer training exercise if they can’t then use that training in real life to, for example, detect a deer on the side of the road.

The Green lab uses a host of different approaches to attack this problem, including deploying various highly visually demanding commercial video games (“action video games”) as training platforms. They have shown that dedicated training on such games improves everything from very basic visual skills to much higher cognitive abilities, such as memory and attention. Dr. Green’s hope is that by better understanding which components of commercial video games allow them to produce such benefits, his lab can improve vision training outcomes for those with various low-vision conditions.
Roomasa Channa, MD

Roomasa Channa is a clinician-scientist whose research focuses on diabetes-related retinal diseases, the leading cause of vision loss among working-age adults. Artificial intelligence (AI)-based tools and techniques figure heavily in her work.

One key area of her research is the use of point-of-care artificial intelligence (AI) techniques to decrease disparities in access to disease screening and follow-up eye exams. We know that point-of-care screening can significantly improve the number of people who get diagnosed in a timely fashion. A recent study from Dr. Channa and her collaborators showed that implementation of AI-based detection of diabetic retinopathy improved compliance with screening exams from 46% to over 90%. The study used retinal cameras located at primary care sites that were connected to an AI software platform that provided immediate (within 1-2 minutes) identification of diabetic eye disease. The next steps will focus on improving the cost-effectiveness of AI screening as well as decreasing disparities in eye care access.

It is also possible to identify novel causes of vision loss in diabetes by leveraging various technological advances. Evaluation of diabetes-related eye diseases has historically been based on manual grading of fundus photos. In the past decade, there have been advances in retinal imaging, improved AI image analysis techniques, and improved handling of big data, which allow us to study diseases in much more detail than was previously possible. Dr. Channa’s team is studying how to incorporate data from optical coherence tomography (OCT) images to evaluate retinal damage from diabetes. They are also using AI techniques to extract subtle disease features, called “endophenotypes,” from retinal images. These features, invisible to the naked eye, can be correlated with genetic data to identify novel disease mechanisms that can point the way to more effective treatments.

Elena Semina, PhD

Elena Semina’s research program studies genetic causes of human pediatric eye conditions, with an emphasis on prenatal disorders that disrupt eye development. Dr. Semina’s lab uses cutting edge DNA testing to analyze samples from individuals with a broad range of eye problems. They then study newly discovered gene mutations in zebrafish, a commonly-used animal model for such studies, to better understand what went wrong. The Semina lab has uncovered multiple new genes involved in eye disorders, including those that result in small eyes (microphthalmia) or malformed eyes (coloboma, aniridia, and Peters anomaly). Since many of the genes involved in forming the eye also play a role in the development of other parts of the body, affected children may have additional non-ocular health concerns that need to be addressed.

The ability to anticipate symptoms before they start (based on the genetic diagnosis) allows for timely interventions that can lessen the severity of disease and improve quality of life. Through participation in their studies, genetic testing is provided to eligible families free of charge, many of whom would not otherwise have received a diagnosis. In many cases, the genetic results provide a clinical diagnosis to finally explain health issues experienced by the affected individual. In addition to these benefits, identification of new genes and mutations that cause human eye disorders can ultimately lead to better clinical management and perhaps even future treatment options.
**MACULAR DEGENERATION: LEADING THE FIGHT**

**MONROE & SANDRA TROUT 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.

**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 enabled my lab to advance efforts to produce and test a next-generation micro-scaffold for the dual delivery of retinal pigmented epithelial (RPE) cells and photoreceptors as a potential treatment for advanced age-related macular degeneration (AMD) and other macular disorders. AMD results in the loss of both of these critical cell types, and thus it is of paramount importance to devise new ways to replace them. This work also involves close collaborations with fellow McPherson ERI labs headed by Drs. Sarah Gong and Jack Ma as well as the lab of Dr. Kapil Bhartli at the National Eye Institute.”

**Michael Altaweel** MD  
Ophthalmology and Visual Sciences > Monroe E. Trout Chair in Vision Research

“One of the great benefits of the Monroe E. Trout Chair in Vision Research is the team-based approach this supports, fostering collaboration in the effort to bring stem cell therapy to clinical trials. Our team has been dedicated to the surgical delivery of stem cell-derived photoreceptors to the sub-retinal space. This has progressed in concert with refinement of the process to produce these retinal organoids, led by Dr. David Gamm. The studies that are required prior to human clinical trials are planned for this winter.”

**Akihiro Ikeda** DVM, PhD  
Medical Genetics > Timothy William Trout Chair in Eye Research

“Support from the Timothy William Trout Chair in Eye Research has allowed my lab to identify that TMEM135, a protein involved in retinal aging, is a regulator of docosahexaenoic acid (DHA), which is an important fatty acid for retinal health. We were also able to discover that over-expression of the Tmem135 gene results in the abnormal appearance and degeneration of retinal pigment epithelium (RPE) cells, the severity of which is determined by genetic makeup. And, importantly, we have found the genetic location of the modifiers that determine the severity of these RPE abnormalities, which should lead to the development of new therapeutic targets for RPE atrophy in human AMD patients.”

**YOU CAN SUPPORT AMD RESEARCH**

by giving to the McPherson ERI’s Macular Degeneration Fund, **Fund #132580419**. This endowed fund was established by the Trouts and Dr. Alice McPherson in February 2022 to support AMD research until a cure is found.

**PAT AND JAY SMITH: FILLING THE GAPS**

Jay Smith, Chairman of Teel Plastics, has been an insightful and valuable member of the McPherson ERI’s Advisory Board since 2017. By the time Pat Smith developed age-related macular degeneration, Jay had already heard much about potential therapies in development at UW-Madison. With characteristic energy, the Smiths decided to help move AMD research forward at a quicker pace. With a gift of $1 million early in 2022, they established the Pat and Jay Smith Macular Degeneration Treatment Innovation Program.

The new program is addressing critical gaps in our understanding of AMD, and applying that knowledge to create more effective therapies. Three initial projects are underway: (1) AMD drug development in Nader Sheibani’s lab, (2) stem cell-based AMD model systems and cell-based AMD therapeutics in David Gamm’s lab, and (3) advanced imaging of the human retina in health and disease by Jeremy Rogers’ lab. All have great potential for successful near-term advances in AMD treatment, and we are grateful for the Smiths’ support and focus on high-priority needs.
**Melissa Skala PhD**
Biomedical Engineering and Morgridge Institute for Research * RRFDaniel M. Albert Chair

“Improved methods for retinal imaging could provide early markers of disease to enable treatment before vision loss, and allow better tracking of treatment response to optimize therapies for each patient. We have used the Albert chair to develop methods to image molecules in the retina related to disease onset (such as melanin and retinoids), and to image individual cells in patients through adaptive optics. Ongoing work will translate these methods into human eye imaging, and streamline instrumentation so these technologies can be used across numerous medical centers.”

**David Gamm MD, PhD**
Ophthalmology and Visual Sciences * RRFEmmett A. Humble Distinguished Directorship

“Support from the RRF Emmett A. Humble Distinguished Directorship was utilized in 2022 to further my lab’s efforts to refine methods to generate human red and green cone photoreceptors for use in cell therapies aimed at individuals with late-stage inherited retinal degenerations (such as retinitis pigmentosa, Stargardt disease, and Best disease) as well as AMD. In all of these conditions, it is the cone photoreceptors that are most important as they convey high resolution and color/daytime vision. By focusing on production of these two types of cones, we seek to make future generations of photoreceptor therapies more effective.”

**Bikash Pattnaik PhD**
Pediatrics * RRFM. D. Matthews Research Professor

“Our lab has found that ion channel defects cause rare pediatric blindness due to defective ion channel genes, which affect photoreceptor (PR) and RPE cell function. We have generated induced pluripotent stem cell (iPSC) RPE and PR harboring molecular defects to serve as suitable models for further research. We have also used our disease models to demonstrate the effectiveness of genome editing as a possible therapy, and to note its current limitations, which will need further research.”

**Mrinalini Hoon PhD**
Ophthalmology and Visual Sciences * RRF Rebecca Meyer Brown Professor

“Retinal neurons communicate and transfer visual information at specialized junctions called ‘synapses’. Our recent research has revealed that early visual cues are instrumental in establishing the correct synaptic junctions between inner retinal neurons. The support of the RRF Rebecca Meyer Brown Professorship has enabled us to make progress on this exciting study which shows that a mammalian retina that develops without early visual signals forms erroneous connections leading to an impairment in the visual information that is processed by the retina. We are currently investigating the reversibility of these alterations.”

**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.”

**Kevin Eliceiri PhD**
Associate Director * McPherson Eye Research Institute > Director/LOCI * Morgridge Institute for Research * RRF Walter H. Helmerich Research Chair

“My research interests are in the areas of developing optical and computational approaches to non-invasively study dynamic cellular processes like those in the eye. The RRF Walter H. Helmerich Research Chair supports the development of novel optical imaging methods and instrumentation for investigating the cellular microenvironment, and the development of open-source software for multi-dimensional imaging informatics.”

**Sarah Gong PhD**
Ophthalmology and Visual Sciences and Wisconsin Institute for Discovery * RRFE Edwin & Dorothy Gamewell Professor

“The RRF Edwin and Dorothy Gamewell Professorship will help my laboratory to develop innovative non-viral nanocarriers for safe and efficacious gene therapy and genome editing therapy.”
RAUNAK SINHA, PhD, Neuroscience

“The David and Nancy Walsh family professorship has enabled us to figure out more details about how the cone photoreceptors, which mediate daylight vision, vary in their functional properties across the visual field. In particular, we were able to determine that cones in the central part of the primate retina, the fovea, adapt to changing light levels quite differently than cones present in the peripheral part of the primate retina. The Walsh professorship has also allowed us to further understand how cone photoreceptors in the human stem cell-derived retina mature with time which provides interesting insights into human retinal development.”

In 2021, the Walsh family began a new fundraiser for vision research—spearheaded by then eight-year-old Audrey Olsen, David and Nancy Walsh’s granddaughter. Audrey was determined to do something to support her uncles, John and Michael Walsh, both of whom have Usher Syndrome Type 2C, a condition that leads to loss of vision and hearing. Audrey looped in her brother Charlie, her parents, Molly Walsh and Jeff Olsen, and her grandparents, and the result was their first annual Walk for Sight, which raised $22,000 for research at the McPherson ERI.

The Walsh family’s 2022 Walk for Sight was equally successful, despite a brief rain squall. Neither rain nor snow dampens the energy of this family! We’re very grateful for the time and initiative put in by Audrey and her entire family, and we highly recommend this type of event for anyone wishing to lead a vision fundraiser in their neighborhood.
This year’s annual David G. Walsh Graduate Student Support Initiative award was given to two McPherson ERI members, C. Shawn Green, PhD, and Emily Ward, PhD—both in the Department of Psychology—to support the work of PhD candidate Mohan Ji. Mohan’s thesis focuses on understanding the visual cues that we use to determine animacy (the state of being alive) and intentionality, which is critically important for evolutionary fitness. The $12,000 GSSI grant is financed by the David G. Walsh Research Fellowship Endowment.

Kenzi Valentyn Vision Research Awards are named in honor of Kenzi’s courage and positive attitude throughout her long battle with Kearns–Sayre syndrome. As always, the McPherson ERI is grateful for the Valentyn family’s dedication to vision research and outstanding participation in Cycle for Sight.

Fall/Winter 2021-22 award recipients:

Jennifer Heyward, DVM, a graduate student in Comparative Biomedical Services, Veterinary Medicine, mentored by Freya Mowat.

Jenna Nagy, a graduate student in Cellular & Molecular Pathology, Neuroscience, mentored by Raunak Sinha.

Ziyun Ye, a graduate student in Ophthalmology & Visual Sciences, mentored by Donna Neumann.

Clementine Zimnicki, a graduate student in Psychology, mentored by Karen Schloss.

Walsh Research Travel Awards restarted in Fall 2022, after a hiatus during COVID. These awards, generously supported by the David G. Walsh Research Fellowship Endowment, allow trainee researchers to present their findings and connect with other researchers at conferences. Fall 2022 Walsh Research Travel Award recipients are Jacob Khoussine (Ophthalmology and Visual Sciences), mentored by Mrinalini Hoon, who presented his work on night blindness at Neuroscience 2022 in November; and Ziyun Ye (Ophthalmology and Visual Sciences), mentored by Donna Neumann, who will present her work on ocular HSV-1 infections at ARVO in April, 2023.

Yin Li, PhD, (Biostatistics and Medical Informatics) was awarded the 2022 Expanding Our Vision Award ($10,000), for research in visual communication, cognition, perception, computer science, data visualization, or imaging advances. Dr. Li’s project will develop and evaluate video-based, automated surgical skill assessment tools for cataract surgery using computer vision and machine learning.

The McPherson ERI distributed a variety of student and trainee awards in 2022, including:

The Dan & Ellie Albert Student Vision Research Award, supporting a summer vision research project for an SMPH student through the Shapiro Summer Internship Program, to Tammy Zhong, working with Yao Liu, MD, to advance teleophthalmology.

Lillian Li and her advisor, Ari Rosenberg, PhD (Neuroscience), were awarded a Hilldale Undergraduate Award for work which aims to elucidate the neuronal mechanisms that transform 2D retinal images into accurate and precise 3D representations.

Once again, six McPherson ERI trainees received StoryForm Science Course Awards, underwriting their participation in the StoryForm Science workshop developed by Holly Kerby and Adam Steinberg.

The McPherson ERI will add further research awards in the coming year, including a Distinguished Paper Award for McPherson ERI trainee members; a resumption of our Visiting Scholar Awards, on hiatus since 2020 due to COVID; and, excitingly, multiple $50,000 pilot grants for research on age-related macular degeneration and retinitis pigmentosa, thanks to the generosity of Roger and Lynn Van Vreede and the Robert A. Brandt Macular Degeneration Fund. Stay tuned for more information!
During the summer of 2022 in the Vision Gallery, the *Art from Science* exhibit featured artworks created in response to science images from McPherson ERI member research. Artists were offered a collection of over 60 images from which to select one on which to base an artwork. Madison artist Lauren Harlowe’s striking contribution, an oil painting entitled *Sight Lines* (above), is based on an image of the eye of a zebrafish embryo (right) from the lab of Yevgenya Grinblat, PhD.  • IMAGES COURTESY OF LAUREN HARLOWE AND YEVGENYA GRINBLAT.
The image above shows a 3D reconstruction of a primate retinal neuron (dark green) receiving input from several photoreceptor terminals (light green). This is the first stage of information transfer in the retina between the dim-light photoreceptor and the downstream retinal neuron, and enables the retina to convey dim-light visual signals. The pictured reconstruction was generated from a serial electron microscopy image stack.

*IMAGE COURTESY OF AINDRILA SAHA, JUAN ZUNIGA AND KAINAT MIAN, SINHA LAB.*
A single amino acid change in a potassium channel (shown above) that is present in the retinal pigment epithelium causes a form of childhood blindness. Bikash Pattnaik’s lab found that this mutation affects the structure of the protein in the inner surface of the cells that constricts the opening without affecting any other aspects of the protein structure. The narrowing of the space does not let potassium go through, but other small-sized ions can pass through without any hindrance. • IMAGE COURTESY OF KATIE BEVERLY & BIKAH PATNIAK, PATNIAK LAB, AND H. ADAM STEINBERG OF ARTFORSCIENCE.COM.
Every cell in a developing eye of a young zebrafish embryo can be seen using a specialized stain. Here, in an image from Yevgenya Grinblat’s lab, cell outlines are stained in yellow and the cell nuclei are in cyan. Ease of imaging makes zebrafish an ideal model for studying the formation of eyes during embryogenesis. Because this process is largely the same in all vertebrate embryos, including humans, we can use zebrafish to understand congenital eye disorders and to find potential treatments.

* IMAGE COURTESY OF THE GRINBLAT LAB.
The protein composition and structure of the sclera (the tough outer coat of the eye) plays an important role in determining how the eye responds to internal pressure in glaucoma. In this side-by-side comparison, we can see that the collagen fibers in the sclera of a cat with inherited glaucoma (right) are organized very differently than those of a normal cat (left). Collagen fibers that go in the same direction are depicted here in the same color. • Image courtesy of Odalys Torné in the McLellan Lab.
These stylistically different takes on chest X-rays were created by Dalton Griner and Xin Tie using generative adversarial networks, computing networks designed to “learn” like the human brain learns. While these particular works of art are more beautiful than useful in radiology, GANs are used in medical imaging to enhance, classify and reconstruct information and understand the differences between X-rays of a COVID case (top row), pneumonia (bottom row) and healthy lungs (center row). The image received a Cool Science Image Award for 2022 and hung in the McPherson ERI’s Mandelbaum & Albert Family Vision Gallery. • IMAGE COURTESY OF DALTON GRINER AND XIN TIE.
Scallops are bivalve mollusks that lack a brain—but they have many dozens of eyes. The image above shows two scallop eyes prepared for microscopic viewing and stained with hematoxylin and eosin. The small eyes are at the end of small tentacles. Light reflects on the curved back of the eye like a reflecting telescope. • IMAGE COURTESY OF COPLOW.
Shown above is a mouse retina, with different cell and protein types indicated in different colored stains. For instance, microglia, immune cells which are thought to play important roles in the inflammatory response of glaucoma and optic nerve damage, are in green. mRNA for Sigma type 1 receptors are in red. It has been suggested that targeting these receptors along with other receptors could increase neuron survival and function in neurodegenerative disease. *IMAGE COURTESY OF TIMUR MAVLYUTOV, MCDOWELL LAB.*
Glial cells serve as support cells for neurons. Above is a 3D reconstruction of a glial process (orange) wrapping around a retinal photoreceptor (grey) with specialized 'ribbon' contact zones (magenta). In a healthy retina, glial processes do not contact photoreceptors; however, the pictured image is from a retina where photoreceptor activity has been suppressed. Several hundred consecutive electron microscopic images were used to reconstruct the cells and connections in this image.

*IMAGE COURTESY OF SERENA WISNER, HOON LAB.*
The interphotoreceptor matrix (IPM) is a gel-like sticky substance that protects and gives structural support to the photoreceptor outer segments (POS) in the retina. This image shows the cross-section of a human pluripotent stem cell-derived retinal organoid displaying elongated POS in red, surrounded by IPM in green and cell nuclei in blue. These retinal organoids serve as powerful tools to model retinal diseases that affect the IPM.

*Image courtesy of Steven Mayerl, GAMM Lab.*
The optic nerves of a mouse are shown above, originating from the eye (to the left) and extending toward the brain (right). Each optic nerve has been labeled using a virus that fills the retinal ganglion cells with a red fluorescent protein. One of the optic nerves has been labeled chemically with a green dye, making that nerve appear yellow in this overlapping image. Optic nerves carry fibers called axons from each eye. Notice that nearly all the fibers originating from one eye project to the other side of the brain in a mouse, crossing from one side to the other at the optic chiasm. • IMAGE COURTESY OF ROB NICKELLS.
An optical coherence tomography (OCT) line scan through the fovea of a patient with non-exudative AMD is shown above. The foveal pit is at the center of the image, and multiple large drusen—the mountain-shaped projections—are seen adjacent to the fovea, resulting in alterations in the appearance of the overlying photoreceptor layers. • IMAGE COURTESY OF JOSEPH CARROLL.
IN MEMORIAM

Carl Gulbrandsen, PhD, JD

After McPherson ERI Advisory Board member Carl Gulbrandsen passed away in October, 2022, Madison.com accurately described him as "a giant in Wisconsin research". As McPherson ERI Associate Director Kevin Eliceiri notes, "Carl was a tireless and passionate champion of innovation and idea discovery at the University of Wisconsin and beyond. He had major impact across campus and the state of Wisconsin on basic research, translational and commercialization activities."

Over Carl’s 16 years as Managing Director of the Wisconsin Alumni Research Foundation (WARF), WARF was able to double its investment portfolio to $2.6 billion, and more than triple its annual research support to UW-Madison. The McPherson ERI was one of many research entities on the UW campus that benefited from his drive, foresight, skill, and dedication to service. Among other accomplishments, Carl was instrumental in the creation of the Morgridge Institute for Research and the Wisconsin Institute for Discovery. Carl, a Viroqua native, received both his Ph.D in physiology and his JD from UW-Madison. We were very pleased that his interests extended to vision research, and that he was an involved and thoughtful McPherson ERI Advisory Board member since 2018.
Cycle for Sight Plus 2022

Cycle for Sight Plus 2022, held in late April, kept the “choose your own event” format, with teams cycling, walking, or running on their own. Once again, teams participated across the state and around the country, raising $56,300—slightly more than in 2021.

We're grateful for all of our teams, and to our terrific major sponsors, Opsis Therapeutics and the Chippewa Valley Eye Clinic. As you can see elsewhere, Cycle for Sight allows us to keep adding research grants and awards, and to increase funding for already-established awards, such as the Kenzi Valentyn Vision Research Awards. Thank you to all who participated and donated, and stay tuned for information on Cycle for Sight 2023!

Visiting Lecturers, 2022

The McPherson ERI was fortunate to host two highly distinguished visiting lecturers in 2022, and it is an understatement to say that researchers enjoyed the return to in-person lectures and conversations!

In September, National Eye Institute Director Michael Chiang, MD, visited UW-Madison and gave the 10th Annual McPherson Endowed Lecture, speaking on Artificial Intelligence and Data Science for Health Care: Perspectives from the National Eye Institute. He was able to connect with a wide range of McPherson ERI scientists during his visit.

In October, noted zoologist Dan-Erik Nilsson spoke on The Evolution of Eyes and Vision for the 14th Annual Vision Science Lecture, which followed the McPherson ERI’s annual Poster Session—back for the first time since 2019.

The Mandelbaum & Albert Family Vision Gallery

Our art gallery on the 9th floor of WIMR II was back to a full schedule of new shows in 2022, kicking off the new year with The Eye as Image, featuring works in which the image of the eye played a prominent role. Summer 2022 brought Art from Science, with artwork created in response to science images from McPherson ERI member research. And Cool Science Images 2022 filled up our gallery space in the fall, featuring the winners of UW-Madison's annual contest for the year's best science-related images.
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