

McPHERSON
EYE RESEARCH INSTITUTE

ANNUAL
REPORT

2020

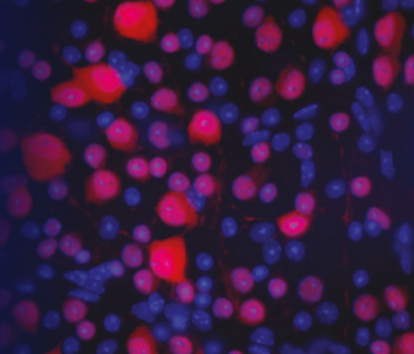
CALENDAR

2021

Special Delivery



Microscopic image of the mouse retinal ganglion cell layer after AAV2 viral vector delivery of the BCL-X gene, which produces a protein that combats ganglion cell death. Cleverly, BCL-X was engineered to glow red for ease of visualization. The nuclei of all retinal cells are shown in blue. Image courtesy of the Nickells Lab.



FROM THE DIRECTOR

We have all purchased something online or over the phone this year and then looked forward to a box arriving on our doorstep with the item we needed. Without correct delivery, however, there would be nothing to show for our efforts. Therapeutic development has a similar need for reliable delivery. Groundbreaking new treatments, including gene therapy and stem cell therapy, are in development for a wide variety of devastating diseases. But in addition to the research being done to create and refine these novel therapeutic products, McPherson ERI scientists are busy improving methods to package and place these products safely and reliably in the exact spots where they are needed in the eye.

As you might imagine with an organ so small, delicate, and complex, this is no easy task. Many areas within the eye that need treatment are in locations that are the postal equivalent of a house at the bottom of a lake or on the side of a steep mountain. In these extreme situations, the method of treatment delivery often requires as much (if not more) innovation than the treatment itself. On the next few pages, you'll learn how McPherson ERI researchers are pioneering development of the ocular packages, delivery vans, and distribution routes needed to further our work to end blindness. Some of our researchers are surgeons who are involved in advancing the tools and techniques of therapeutic delivery, while others are engineers and biologists who build viral vectors, nanocarriers, and microscaffolds that carry cellular and genetic cargo. That's what we do best—build and support the most diverse, dedicated, and talented eye research teams in the world, right here in Wisconsin.

RRF Emmett A. Humble Distinguished Director, McPherson ERI
∞ Sandra Lemke Trout Chair in Eye Research



Viral Transport

Blindness is often caused by mutations in genes, which alter proteins and disrupt healthy function. Gene augmentation therapy aims to counter these effects by introducing a healthy copy of a gene into cells before they die, which hopefully reverses the tide of the disease. But how does one go about “injecting” a healthy gene into countless microscopic retinal cells? By hijacking the most advanced gene microinjector on earth — the virus. While infamous for their disease-causing ability, **viruses can be modified so they are unable to cause disease**, yet retain their ability to deliver genetic cargo into host cells. These fit-for-purpose biological tools, known as **viral vectors**, allow scientists to insert nearly any gene, provided that it fits inside the virus (and not all do). As noted by **Dr. Curtis Brandt**, whose lab specializes in the study of viruses that affect the eye, “Nature invented gene delivery way before we took advantage of it.”

In McPherson ERI member labs, viral vectors are engineered to deliver genetic material precisely to the retinal cells that need them. As a critical first step in this process, the genes that the virus normally uses to multiply itself and to cause disease are removed. Extensive testing is then required to prove that the viral vectors have indeed turned over a new leaf and are safe for use in humans.



HOMING IN ON GLAUCOMA

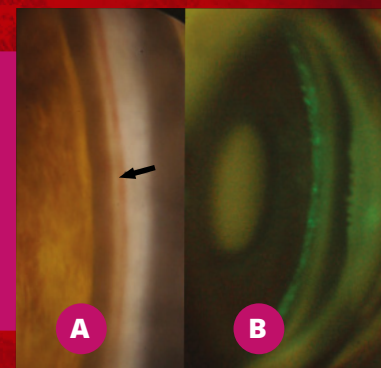
Glaucoma, the world's most common cause of irreversible vision loss and blindness, is characterized by degeneration of the optic nerve and the death of ganglion cells in the retina. While doctors can treat the high eye pressures associated with most forms of glaucoma, scientists are still searching for ways to prevent ganglion cell death and optic nerve damage that often occurs despite treatment.

UW-Madison's glaucoma group, a constellation of researchers from the Department of Ophthalmology and Visual Sciences and collaborating departments—including **Drs. Paul Kaufman, Donna Peters, Rob Nickells, Curtis Brandt, Colleen McDowell, and Gillian McLellan**—is testing various gene delivery strategies to treat glaucoma. Viral vectors play a key role in several of these approaches.

Dr. Rob Nickells' lab employs viral vectors to short-circuit the process of ganglion cell death, which is controlled by a molecular switch involving a pro-death protein called BAX and an anti-death protein called BCL-X, which serves to keep BAX in check. Using a viral vector called adeno-associated virus type 2 (AAV2), they introduce a lab-created version of BCL-X into mouse ganglion cells at the onset of glaucomatous damage. Promising early experiments have shown that ganglion cell death is indeed greatly reduced, and the Nickells Lab is now working to confirm these results and to establish the safety of their viral vector strategy in further preclinical studies.

Dr. Paul Kaufman's use of viral vector delivery is aimed at reducing pressures within the eye for those people with glaucoma who don't respond well to current treatments, or have difficulty with the high frequency and expense of their treatment regimens. To understand Dr. Kaufman's cutting-edge approach, you first need to understand how an eye is “pressurized”. Eye pressure is generated via a balance between fluid production and outflow. One of the main pathways for fluid to leave the eye is through a structure near the front of the eye called the trabecular meshwork. Dr. Kaufman's lab is pioneering ways to modulate fluid outflow using a viral vector-based gene therapy strategy that targets the trabecular meshwork and lowers outflow resistance. These viral vectors, which are injected into the front part of the eye, have shown clear potential to improve fluid outflow in preclinical tests (see Figures A, B).

Gene delivery to the trabecular meshwork after injection of a viral vector into the front of the eye. In panel A, the arrow points to the area of injection. Two years after administration of the viral vector, the trabecular meshwork continues to express the delivered gene, which shows as a thin green line in panel B. Image courtesy of Dr. Paul Kaufman.





Engineering Solutions



NANOPARTICLE PACKAGING

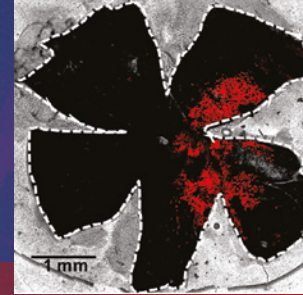
Viral vectors might be nature's gene delivery system, but they can be costly to make and are limited in what they can carry and what cells they can reach. Therefore, McPherson ERI scientists are also on the forefront of developing non-viral delivery systems that may offer superior cargo-carrying capacity, greater precision in cell targeting, broader safety profiles, and more streamlined manufacturing.

Professor Shaoqin "Sarah" Gong and her research group focus on engineering smart, non-viral nanoparticles to deliver drugs, genes, or CRISPR/Cas genome editing machinery to cells within the eye and elsewhere in the body. The uses of these "nanocarriers" are manifold—chemotherapy, gene therapy, immunotherapy, and antimicrobial therapy, among many others.

Collaborating with a group of McPherson ERI investigators that includes Drs. Pattnaik and Saha, Dr. Gong's team recently developed several patent-pending nanocarriers that can safely and efficiently deliver complex CRISPR/Cas genome editing machinery to diseased retinal cells without any apparent toxicity. Importantly, the surface of the nanocarriers can be decorated with various types of targeting molecules, thereby allowing them to "home in" on specific retinal cells in a way similar to (and perhaps better than) viral vectors.

With further development and testing, these versatile nanocarriers may enable therapies for a wide range of genetic eye diseases that currently cannot be treated with viral vectors. To achieve this goal, Professor Gong's team is broadening their collaborations with scientists and clinicians within the McPherson ERI and around the world.

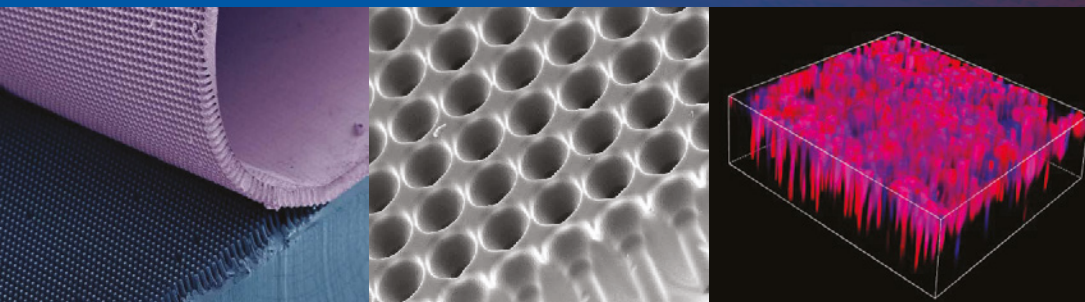
Nanocarrier delivery of CRISPR/Cas machinery results in efficient genome editing in the retinal pigment epithelium (RPE). The area in red shows RPE cells that were successfully treated in the mouse retina. Image courtesy of Dr. Pawan Shahi, Pattnaik Lab.



MICROSCAFFOLD INSERTION

Professor Zhenqiang (Jack) Ma is an exemplar of how sheer engineering know-how can advance biomedical delivery systems. Dr. Ma, the Lynn H. Matthias Professor and Vilas Distinguished Achievement Professor in the Department of Electrical and Computer Engineering, has research interests that span a wide range of engineering disciplines, including bioelectronics and biomimetics. His lab recently applied its expertise to develop biomedical devices to reconstruct the outer retina in late-stage retinitis pigmentosa (RP) and age-related macular degeneration (AMD).

Dr. Ma's lab engineered a solution to a hurdle facing Dr. David Gamm's efforts to replace photoreceptors and/or RPE cells damaged in RP and AMD, as well as many other retinal diseases and injuries. The Gamm Lab developed and patented ways to create photoreceptors and RPE from human pluripotent stem cells, but they needed a means to deliver these replacement cells deep within the retina. In collaboration with Dr. Gong, Dr. Gamm, and Dr. Joe Phillips, Dr. Ma's lab generated biodegradable microscaffolds suitable for safely transporting donor photoreceptors and RPE cells to the retina in an organized and highly controlled fashion. Various generations of these revolutionary scaffolds have been designed, built, and inserted under the retina in preclinical models that mimic damage caused by RP or AMD. Results thus far show great promise for these scaffolds to help repair the outer retina and restore vision in individuals with RP, AMD, and other degenerative disorders.



Microscopic image of a "wineglass" design photoreceptor scaffold at lower (left panel) and higher (middle panel) magnifications. The right panel shows an image of human pluripotent stem cell-derived photoreceptors (engineered to glow red) lined up neatly within the scaffold. Images courtesy of the Ma Lab (left, center) and the Gamm Lab (right).

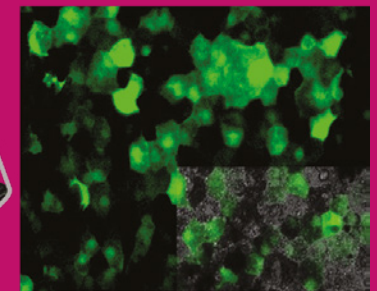
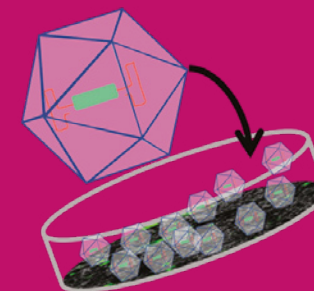


TARGETING RETINITIS PIGMENTOSA

Viral vectors also can be used to deliver therapeutic genes to the back of the eye to treat inherited retinal diseases such as retinitis pigmentosa, or RP. Dr. Bikash Pattnaik is using viral vectors in efforts to prevent blindness caused by an early onset form of RP known as Leber congenital amaurosis, or LCA. Dr. Pattnaik has a particular interest in genes that make ion channels, which are molecular gateways that control many cell functions. Mutations in some ion channel genes lead to LCA and rapid blindness in infants and young children. Dr. Pattnaik's viral vectors successfully delivered healthy copies of one type of ion channel gene to the retina of a mouse with LCA, which resulted in recovery of ion channel function and improvement in vision. Efforts are now underway to further develop this gene therapy for future clinical trials.

A large team of McPherson ERI researchers, including Drs. David Gamm, Krishanu Saha, Bikash Pattnaik, Sarah Gong, and Sushmita Roy, is employing a similar viral vector strategy to fight Best disease, one of the most common forms of inherited macular degeneration. This same group of investigators, as well as Dr. Melissa Skala at UW-Madison and Dr. Daniel Lipinski at the Medical College of Wisconsin, are using viral vectors to deliver genetic machinery capable of silencing or fixing mutant genes, not just replacing them. This latter technology, known as CRISPR/Cas genome editing, received the 2020 Nobel Prize in Chemistry and has opened the door to treating genetic disorders that gene augmentation cannot help.

A therapeutic gene that produces a protein (tagged with a green fluorescent marker) was delivered via a viral vector to stem cell-derived human retinal pigmented epithelium (RPE) cells created from a patient with LCA (left). The number of green cells in the microscopic image on the right reveals that nearly all of the patient's RPE cells express the new gene. Images courtesy of the Pattnaik Lab.



Optimizing Surgical Techniques

IMPLANTING PHOTORECEPTORS AND RPE CELLS

All of the wonderful new therapeutic viral vectors, nano-carriers, and microscaffolds must be safely and accurately placed where they are needed. In many cases, that requires not only skilled surgeons, but innovative ones as well.

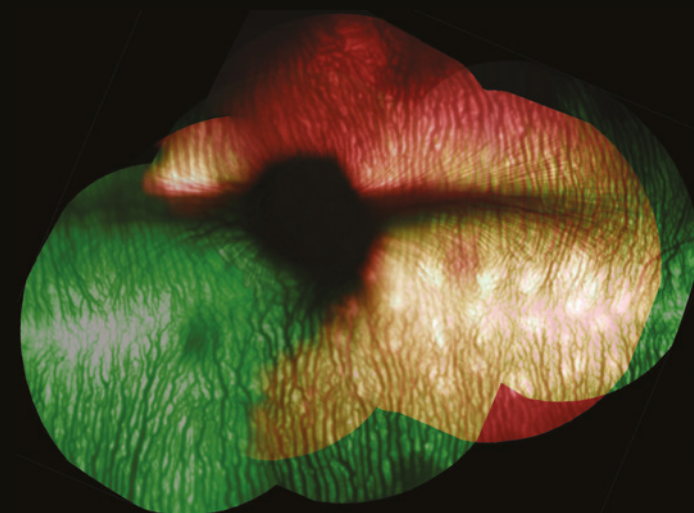
Vitreoretinal surgeon and newly named Monroe E. Trout Chair in Eye Research, **Dr. Michael Altaweel** has been working with Drs. Gamm and Phillips to optimize methods to deliver replacement photoreceptors and RPE cells (and scaffolds) beneath the retina in a safe and reliable manner that can be adopted by other surgeons. Dr. Altaweel has performed retinal surgery on children and adults with complex diseases and injuries for 20 years, and he has been an investigator for many clinical trials that have changed the standard of care for retinal disease treatment.

To proceed with clinical trials to test stem cell-based therapies for RP and AMD, it is necessary to carefully adapt surgical procedures to support the specialized handling and delivery requirements of each new therapeutic product. Dr. Altaweel is working with the McPherson ERI team to refine and test different surgical strategies, with promising results that show proper localization and widespread survival and integration of donor photoreceptors and RPE cells.

DISCOVERING BETTER ROUTES FOR DRUG DELIVERY

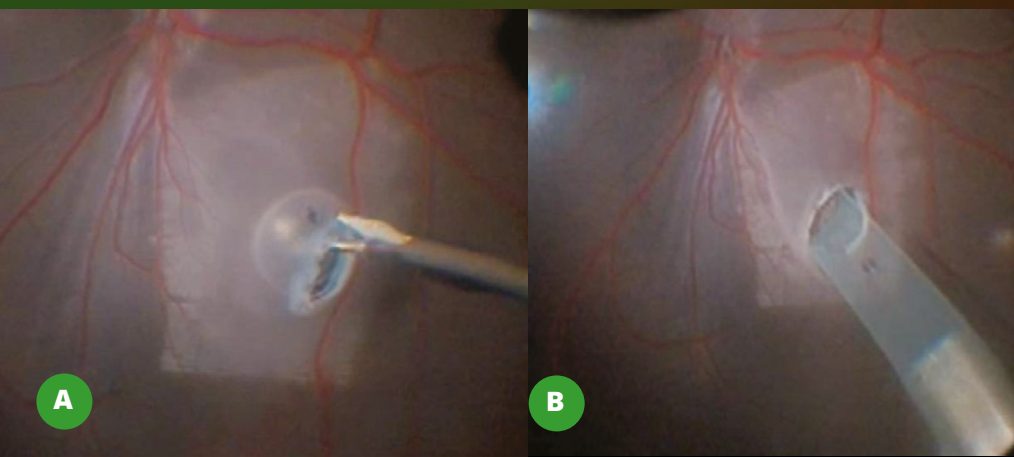
Injections remain the most effective way to deliver many types of drugs to the eye, especially those that can't penetrate the surface of the eye as drops. In collaboration with pharmaceutical companies, McPherson ERI researchers at UW-Madison are working hard to develop better means and new routes for drug delivery. Vitreoretinal surgeon and researcher **Dr. Michael Nork** and his colleagues have developed and tested many approaches to get a wide range of therapeutics to the retina, the tissue primarily affected by most untreatable blinding disorders. Recently, Dr. Nork's lab has begun testing a method to deliver drugs to the retina through the suprachoroidal space—a potential space between the sclera and the large choroidal blood vessels that supply oxygen and nutrients to the outer retina. The procedure, which involves the use of newly developed microneedles, could revolutionize retinal drug delivery.

Dr. Paul Kaufman's lab is also testing new devices and procedures to deliver novel therapeutics to treat glaucoma. Dr. Kaufman's group has had success using microcatheters threaded directly through Schlemm's canal, a drainage structure that abuts the trabecular meshwork, to inject his viral vectors exactly where they are needed to lower eye pressure.

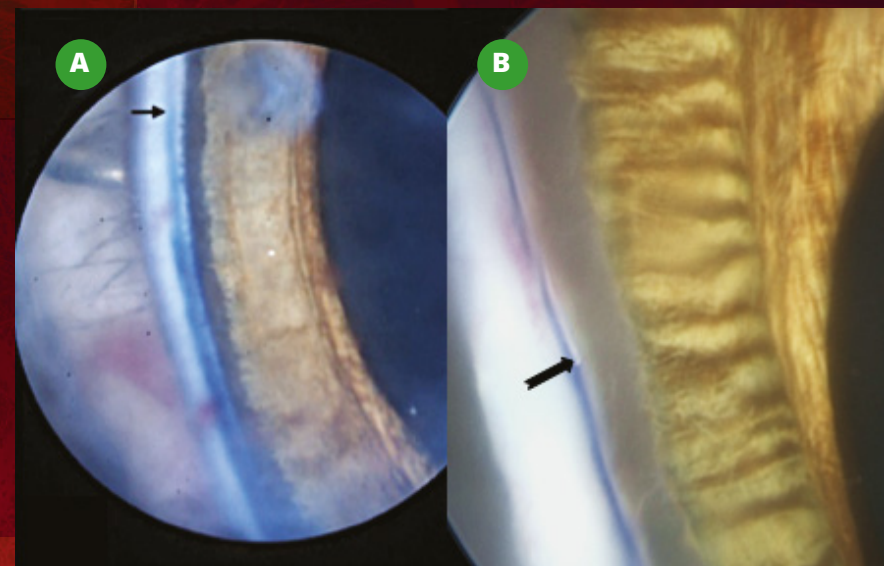


TOP: Image of a rabbit eye that has had two suprachoroidal injections. The areas at the lower left and top show the distribution of a green or red test dye after injection, respectively, with the area of overlap shown in yellow toward the right side of the image. The image demonstrates that two injections are needed to achieve good retinal coverage via the suprachoroidal route. Image courtesy of Dr. T. Michael Nork.

BOTTOM: A blue dye (arrow in panel A) confirms the accurate injection of material into Schlemm's canal, which is located next to the trabecular meshwork and is part of the fluid drainage system of the eye. The arrow in panel B shows the tip of the microcatheter used to inject material into Schlemm's canal. Images courtesy of Dr. Paul Kaufman.



LEFT: Retinal surgeon's view during a procedure to implant a photoreceptor scaffold under the retina. Panel A shows an intraocular scissor being used to create an opening in the retina. In panel B, a custom injector tip is placed into the opening and the scaffold is gently inserted under the retina with high precision. Images courtesy of Dr. Michael Altaweel and Dr. Kapil Bharti of the National Eye Institute.



FEATURED RESEARCHERS 2020

Mid-infrared image of some of the members of the Kats group, standing behind a Fourier transform infrared (FTIR) spectrometer. Image courtesy of Mikhail Kats.



MIKHAIL KATS PhD

Electrical & Computer Engineering
∞ College of Engineering

Dr. Mikhail Kats' research group engages in a broad-ranging experimental and theoretical exploration of topics across optics and photonics, from the visible to the far infrared. Kats—the Jack St. Clair Kilby Associate Professor of Electrical and Computer Engineering and an affiliate faculty member in the departments of Physics and Materials Science and Engineering—works on engineering advances that include the development of ultrathin optical components such as flat lenses, tunable optical components that protect cameras and other sensors against laser damage, and privacy coatings that can conceal information from infrared cameras. His work often involves new understanding of optical properties of emerging materials, including those with complex behaviors such as phase transitions, where a material changes to a different physical state. Kats' current projects also include hyperspectral light sensors, light sails, new measurement techniques for optical and thermal properties of materials, and, importantly, vision-enhancement technologies.

For example, Kats and colleagues recently demonstrated an optical material with a world-record degree of birefringence (a.k.a. double refraction) in the mid-infrared spectral range. His team expects that this demonstration will enable new types of polarization optics for infrared cameras, sensors, and free-space communications.

Optical coherence tomography is used to measure the macular ganglion cell-inner plexiform layer, outlined by the purple and yellow lines in this image, to determine if it is an early marker of neurodegeneration in the brain. Image courtesy of Adam Paulsen.



KAREN CRUICKSHANKS PhD

Ophthalmology & Visual Sciences, Population Health Sciences ∞ School of Medicine and Public Health

As people age, changes in vision and other senses can make everyday activities more challenging. Recently, there has been growing concern that vision changes and age-related eye diseases like cataract and macular degeneration may increase the risk for developing cognitive problems and Alzheimer's disease.

Dr. Karen Cruickshanks' research group is studying whether cognitive decline and dementia can be predicted by a person's visual health and function and by the thickness of particular layers in the retina (the macular ganglion cell layer and inner plexiform layer) as measured using optical coherence tomography (OCT). This is monitored in the Beaver Dam Offspring Study, which began in 2005 and includes thousands of adult children of participants in the long-running Beaver Dam Eye Study. Participants are examined every five years. Results have shown that even in these middle-aged people, small changes in visual contrast sensitivity and the thickness of the macular ganglion cell-inner plexiform layer were associated with cognitive decline. Currently, the study aims to determine whether these changes can be used to identify people at high risk for dementia decades before clinical symptoms such as memory loss appear. Early identification may help high-risk people get the medical care they need to improve control of blood pressure and diabetes which are critical for maintaining a healthy brain.

Image courtesy of Andrea Mason.



ANDREA MASON PhD

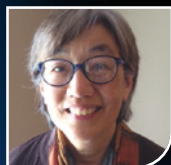
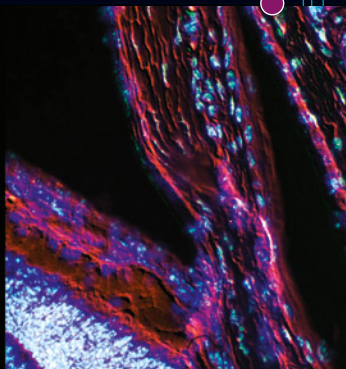
Kinesiology, Motor Behavior & Control
∞ School Of Education

Dr. Andrea Mason's main research interest involves understanding how people use visual and haptic (touch) feedback to plan and perform simple and complex movements with their hands. She has also studied how people combine the movements of the upper and lower body when grasping objects while walking. Her aim is to determine what people need to see and feel, and when that information is needed, to efficiently move and interact with objects in their environment. In Mason's Motor Behavior Laboratory, research projects have involved children and adults in order to determine how the planning and performance of these coordinated movements change across the lifespan. Mason also compares performance between natural environments, where there is an abundance of accurate sensory feedback, and virtual environments, where synthetic feedback can be crude and suffer from lag.

Mason's recent work, in collaboration with Drs. Kevin Ponto and Kristen Pickett, explores how people use visual information about objects and their surroundings to navigate their environment. For example, do features of the environment that we are walking in, such as the width of a hallway, affect the length of the steps we take, the speed at which we walk, or how long we keep both feet on the ground? These spatiotemporal measures are known to be related to fall risk in older adults. Using virtual reality technology, her group can easily manipulate these types of environmental features and test their effects on walking performance. Their results have indicated that visual features such as the width of the hallway do, in fact, lead to subtle changes in walking performance in older adults but not in young adults. In follow-up work, Mason and her collaborators are looking at the effects of performing a visual dual-task, such as reading information off a computer screen mounted to a wall, while walking in a hallway. She hopes to use findings from this work to create an objective measure of fall risk.

FEATURED RESEARCHERS 2020

Blocked iridocorneal angle in the eye of an 8-day-old PPCD1 mouse. Image courtesy of Anna Shen.



ANNA SHEN PhD

Oncology ∞ School of Medicine and Public Health

Dr. Anna Shen's research, carried out in the laboratory of Dr. Chris Bradfield, centers on a mouse model of a human corneal dystrophy, posterior polymorphous dystrophy (PPCD). PPCD is characterized by abnormal differentiation and growth of the corneal endothelium, a cell layer on the inner surface of the cornea. Although many cases are asymptomatic, some affected individuals develop corneal clouding, decreased visual acuity, and increased intraocular pressure and glaucoma, requiring treatment with medication and/or surgery. Overgrowth of abnormal corneal endothelial cells can, in some cases, lead to severe vision loss. Clinical management of this condition would be improved with better identification of the factors influencing disease progression and severity.

The mouse model of PPCD that Dr. Shen works with carries the genetic defect seen in one form of human PPCD, and it also exhibits the pathological features of human PPCD. Shen uses this mouse model to identify the signaling pathways that lead to aberrant growth of corneal endothelial cells. In addition, the severity of corneal and retinal disease in this mouse model is dependent on the genetic background. Using genetic mapping techniques, Shen and her colleagues are engaged in an effort to identify the specific genes that influence the severity of corneal endothelial cell overgrowth and resulting glaucoma. This mouse model will also be used to test therapeutic interventions for PPCD.

Colormap data visualizations used by the Schloss Lab to study the dark-is-more bias, from a recent paper in-press at *Journal of Vision*. Images courtesy of the Visual Reasoning Lab.



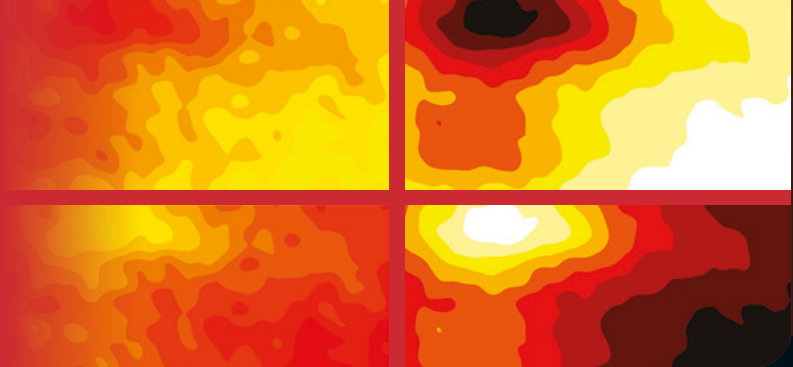
KAREN SCHLOSS PhD

Psychology ∞ College of Letters and Science, Wisconsin Institute for Discovery

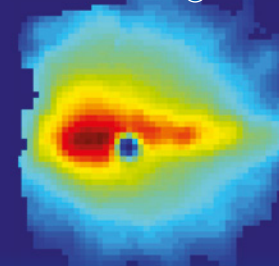
Dr. Karen Schloss is the Principal Investigator of the Schloss Visual Reasoning Lab in the Department of Psychology and Wisconsin Institute for Discovery at UW-Madison. Her lab studies how people interpret meanings from visual features like color, shape, and size during visual communication. Visual communication is fundamental to how humans share information; they communicate information about weather patterns and neural activity through colormap data visualizations, they communicate information about biological processes and mathematical properties through diagrams, and they communicate information about where to find destinations or discard different types of recyclables through signs. Observers have expectations about how visual features will map onto concepts, such as the "dark-is-more" bias to infer that darker colors map to larger quantities in colormap data visualizations. It is easier to interpret visualizations that match those expectations. Thus, the primary goal of the Visual Reasoning Lab is to understand the nature of these expectations, including how they are formed, and how they can be leveraged in visualization design to make visual communication more effective and efficient.

In a secondary line of work, Dr. Schloss's lab also aims to use information visualizations to facilitate science education in formal and informal learning environments. In the UW Virtual Brain Project, they have developed immersive virtual reality (VR) lessons that enable learners to travel through 3D diagrams of the human visual system and auditory system. Evidence suggests these VR lessons provide more enjoyable learning experiences than two-dimensional alternatives, indicating they have exciting potential to motivate interest in science in the classroom and beyond.

Dr. Karen Schloss's research is funded by a National Science Foundation CAREER award and has been supported by the McPherson ERI Grant Summit program and McPherson ERI Expanding Our Vision program. She was also recently awarded the Steven Yantis Early Career Award from the Psychonomic Society.



Cone photoreceptor distribution in the dog retina, showing the presence of a macula-like area (red) adjacent to the optic nerve (center blue spot). Image courtesy of Freya Mowat.



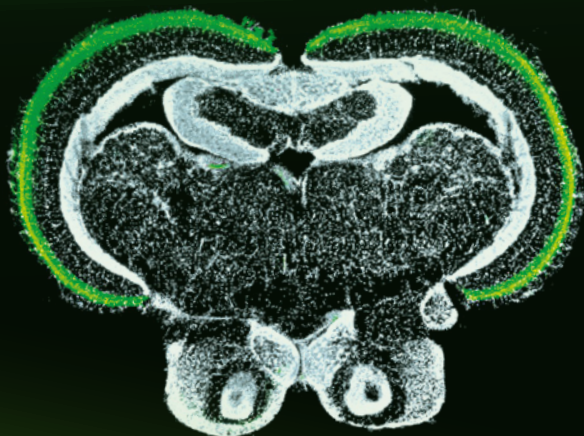
FREYA MOWAT BVSc, PhD

Surgical Sciences ∞ School of Veterinary Medicine Ophthalmology & Visual Sciences ∞ School of Medicine and Public Health

Dr. Freya Mowat's research seeks to define the metabolic pathways important in retinal aging, and to pinpoint ways to ameliorate metabolic decline in the outer retina that occurs with aging. These pathways determine how well the neurons of our retina endure the changes that come with age. They can also predispose us to loss of visual sensitivity and blinding diseases such as age-related macular degeneration (AMD), the most common cause of vision loss in persons over the age of 65 years.

A substantial part of Dr. Mowat's work involves the study of vision in companion (pet) dogs. In addition to cohabiting in their environment and sharing their lifestyles, dogs share many of the features of their human owners' retinal anatomy. Mowat focuses on the unique features of the macula of dogs—the central area of the retina that closely mirrors the macula of people and is the region most susceptible to AMD. She is particularly interested in the function of a protein called PGC1-α, which regulates the growth of mitochondria, the "energy factories" in cells. The study of the age-related vision decline of companion dogs will help us to better and more quickly understand the effect of environment and lifestyle on retinal aging and susceptibility to disease.

Green fluorescent protein labels the projections from the eye into this coronal section of zebrafish brain tissue. The projections into this part of the brain, called the optic tectum, mediate prey capture, among other visually guided behaviors. The *isl2b:GFP* transgene expression in retinal ganglion cells labels the projection green, while the brain section is counterstained white for cell nuclei. Image courtesy of the Veldman Lab.



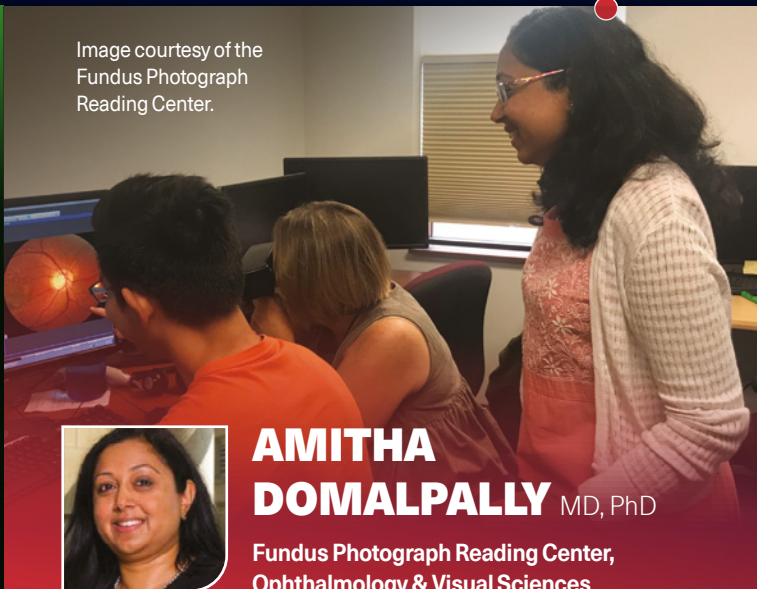
MATTHEW VELDMAN PhD

Cell Biology, Neurobiology, and Anatomy
 ∞ Medical College of Wisconsin

Optic nerve injury is thought to be the critical step in vision loss due to glaucoma and other optic neuropathies and, unfortunately, no treatments are currently available to recover lost vision in these diseases. This is also true in most animal models of glaucoma such as rats and mice. Remarkably however, zebrafish can successfully recover from optic nerve injury and completely recover lost vision. Dr. Matthew Veldman's lab at the Medical College of Wisconsin studies optic nerve injuries and the differences in response to these injuries in animals such as mice and fish, including the zebrafish.

The Veldman Lab uses molecular, genetic, and pharmacological tools to understand the ability of zebrafish to recover lost vision. Thus far, the lab group has identified multiple signaling molecules and pathways that are activated in zebrafish during optic nerve regeneration. The lab is currently testing their importance in cell survival and visual recovery. Their goal is to translate these findings in zebrafish to mammalian models of glaucoma to identify therapeutic targets for enhancing vision in patients with glaucoma or other optic neuropathies.

Image courtesy of the Fundus Photograph Reading Center.



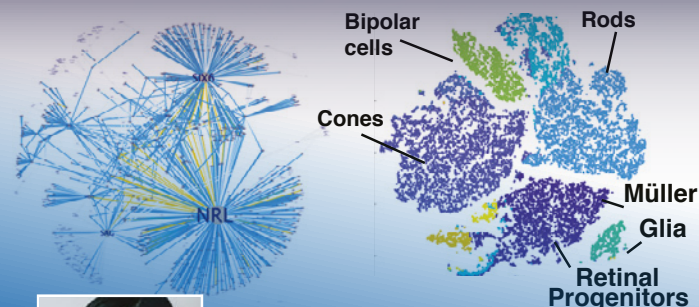
AMITHA DOMALPALLY MD, PhD

Fundus Photograph Reading Center,
 Ophthalmology & Visual Sciences
 ∞ School of Medicine and Public Health

Ophthalmology is fortunate to have cutting-edge imaging technologies available to diagnose eye diseases. UW-Madison's Fundus Photograph Reading Center (FPRC) is one of the world's leading diagnostic imaging centers for both patient diagnosis and clinical trials. Dr. Amitha Domalpally, Research Director of the FPRC, investigates clinical trial imaging endpoints for retinal diseases, with a focus on employing new imaging techniques to understand the natural history and prognostic markers of diseases such as age-related macular degeneration (AMD), diabetic retinopathy, and many others.

Dr. Domalpally's research also involves interpretation of the abundant and complex ocular imaging data that the FPRC collects. A better understanding of potential errors in imaging technologies, for instance, reduces false interpretation of data and improves patient management. Domalpally has detailed artifacts that are intrinsic to OCT angiography technology that help clinicians quickly flag unreliable images that should be discarded. She is also involved in developing diagnostic artificial intelligence (AI) algorithms for retinal diseases. In collaboration with the National Eye Institute, she has developed a deep learning algorithm that assists in detecting reticular pseudodrusen, a feature associated with AMD that is difficult to identify by a human observer. In another collaboration, her ongoing work with Dr. Kevin Eliceiri at UW-Madison has resulted in machine learning models for quantifying retinal lesions.

Left. A gene regulatory network for photoreceptors. Circles denote genes and lines denote interactions between genes. The NRL gene is shown as a major hub. **Right.** Two-dimensional plot of cells of a complex retinal cell population. Each color represents a different cell population and each dot is a single cell. Images courtesy of Sushmita Roy.



SUSHMITA ROY PhD

Biostatistics & Medical Informatics
 ∞ School of Medicine and Public Health

Changes in a cell's genetic activity are controlled by complex gene regulatory networks that connect regulatory proteins to target genes in order to control which genes are expressed at what time. In effect, these networks convert the information encoded in an organism's genome to actual responses and functions within a cell. Dr. Sushmita Roy's lab develops computational methods to understand these networks and to examine how they change across different cell types and tissues or during development and across evolution.

Together with Dr. David Gamm at the Waisman Center and Dr. Kris Saha and other collaborators at the Wisconsin Institute for Discovery, Dr. Roy's lab is developing and applying these computational methods to capture cellular responses to genetic and environmental perturbations in the retina. The group has identified various retinal populations from human stem cell-derived retinal organoids, from which Roy has inferred gene network changes that occur in response to genome-based therapies. In this way, they can optimize the safety and efficacy of burgeoning gene therapy technologies. This technique was used to assess the safety of genome editing for Best macular dystrophy in a study by a team of McPherson ERI scientists published earlier this year. Overall, the ability of Roy's lab to mine and extract hidden information from large, complex genomic datasets provides an unprecedented opportunity to understand retinal cells in their normal and abnormal states.

McPHERSON ERI/TROUT FAMILY ENDOWMENT CHAIRS

In early 2020, Monroe and Sandra Trout endowed their third vision research chair at UW-Madison, the Monroe E. Trout Chair, and increased the Timothy William Trout Endowment Fund to a Chair level. The trio of research chairs that the Trouts have endowed will lead the way to better therapies—and, we hope, a cure—for age-related macular degeneration (AMD), the leading cause of blindness in older Americans. We are grateful to the Trouts for their visionary—no other word will do!—leadership in combatting AMD.



DAVID M. GAMM MD, PHD

Director, McPherson Eye Research Institute
∞ Sandra Lemke Trout Chair in Eye Research

“The Sandra Lemke Trout Chair in Eye Research provides critical funds to advance our pioneering retinal stem cell technology toward the clinic to treat patients with devastating degenerative diseases of the retina such as age-related macular degeneration (AMD). Over the years, support from this chair has facilitated studies that have improved our ability to generate photoreceptors (rods and cones) and retinal pigment epithelium (RPE) in the lab, and to test their capacity to replace these same cell types in diseased or damaged retinas. As a result, we are now in a public-private partnership to generate the cells on an industrial scale, which is needed to begin clinical trials for both AMD and retinitis pigmentosa (RP) in the foreseeable future. To specifically treat AMD, we have worked with McPherson ERI researchers Shaoqin Gong and Zhenqiang Ma to create next-generation biodegradable scaffolds that can replace both RPE and photoreceptors. These scaffolds are now being tested in preclinical studies by colleagues at the National Eye Institute and here at UW by McPherson ERI researcher and retina surgeon Dr. Michael Altaweel.”



MICHAEL M. ALTAWHEEL MD

Monroe E. Trout Chair in Vision Research

“The Monroe E. Trout Chair will allow me to develop and optimize surgical techniques to deliver stem cell-derived photoreceptors and RPE cells to the retina in a safe, effective, and reproducible manner. This will be accomplished through collaborations with a team of McPherson ERI colleagues, including Dr. Gamm (who grows the stem cell-derived retinal cells in his lab) and Drs. Gong and Ma (whose labs have developed biodegradable scaffolds to house the photoreceptors). As a vitreoretinal surgeon at UW-Madison with 20 years of experience, I have participated in many clinical trials to advance therapeutics for AMD, retinal vascular disorders, inflammatory eye disorders, and other indications. For example, I was the lead UW investigator for a series of clinical trials that led to the FDA approval of the first commercially available anti-VEGF drug that was shown to block abnormal vascular growth in the eye and improve vision in AMD. My surgical and research career at UW has led me to this new opportunity to restore sight with stem cell therapies developed entirely here at UW, and I’m enormously excited to be part of this effort.”

Further information on Dr. Altaweel's work can be found in the Delivery feature, above.



AKIHIRO IKEDA DVM, PhD

Timothy William Trout Chair in Eye Research

“Our overall research goal is to identify mechanisms underlying aging and age-related diseases in the retina. Using mouse models, we have successfully discovered several key molecules associated with aging of the retina. One such mouse model showed similar symptoms as those observed in patients with age-related macular degeneration (AMD). We identified a mutation in a mitochondrial gene called Tmem135 that is responsible for accelerated aging and AMD-like phenotypes in the mouse retina. Most recently, we discovered that over-expression of Tmem135 results in abnormal morphology and degeneration of retinal pigment epithelium (RPE) cells, suggesting that the proper level of this gene is essential for the health of RPE cells. Interestingly, we found that other genes also contribute to the health of the RPE in these mice. This finding allows us to search for “modifier genes” that interact with Tmem135 to determine how they affect the severity of the RPE abnormalities. Ongoing studies of Tmem135 will lead to a better understanding of how RPE cells are maintained in their normal state and how they become diseased. It will also help us understand why some people are affected by eye diseases like AMD while others are protected. Support from the Timothy William Trout Chair in Eye Research is vitally important for us to move our research effort towards this goal.”

McPHERSON ERI/RETINA RESEARCH FOUNDATION CHAIRS AND PROFESSORSHIPS

DAVID M. GAMIM ∞ Retina Research Foundation
Emmett A. Humble Distinguished Directorship

"The RRF Emmett A. Humble Distinguished Directorship supports my lab's efforts to generate human "disease-in-a-dish" models of inherited retinal disease (for example, retinitis pigmentosa) using induced pluripotent stem cell (iPSC) technology that my laboratory patented at UW-Madison. These models are created from blood samples donated by individuals with blinding disorders, which we employ as platforms to understand what causes the diseases and how best to treat them (using drug or gene therapies) in order to preserve or restore vision. Recently, in collaboration with McPherson ERI researchers Bikash Pattnaik, Krishanu Saha, and Sushmita Roy, we published a study that used retinal pigment epithelial (RPE) cells generated from patient-derived iPSCs to build a lab-based model of an inherited macular blinding disorder called Best disease. We then used these cells to show how two different types of gene therapies (gene augmentation and CRISPR/Cas genome editing) could potentially be used to treat all forms of this disease. We are now using the same approach using iPSCs from patients with retinitis pigmentosa and Usher syndrome."



BIKASH PATTNAIK PhD

Retina Research Foundation M. D. Matthews
Professorship

"Our lab research focus is on inherited and acquired pediatric blindness. We have made some important discoveries regarding the functioning of ion channels—proteins that facilitate cellular communication. When the ion channels are non-functional, they give rise to specific vision problems in children. We have used patient-derived induced pluripotent stem cells as disease-in-a-dish models to develop a gene therapy treatment for retinal diseases arising from both potassium and chloride channel mutations. Currently, a gene therapy for one type of Leber congenital amaurosis (LCA16) is headed toward clinical trials through our close partnership with Hubble Therapeutics. In separate studies, we are also investigating new therapeutic strategies that may be able to correct a broad class of mutations known as "nonsense mutations". These mutations, which make up about 15% of all genetic defects, result in the production of incomplete and nonfunctional proteins. We are using several approaches, such as small molecules or engineered tRNA, to overcome the effects of nonsense mutations. We then employ biochemical tests and advanced electrophysiological techniques that directly measure recovery of ion channel function in order to optimize therapeutic dosage and efficacy."



BARBARA A. BLODI MD

Retina Research Foundation Daniel M.
Albert Chair

"The focus of my vision research as the Daniel M. Albert Chair has been to help create the Wisconsin Advanced Imaging of the Visual System (WAIVS) program that has begun building and augmenting Adaptive Optics (AO) retinal imaging systems at UW. AO technology will allow us to visualize the structure and function of photoreceptors and other retinal cell types in animals and humans in greater detail than has ever been possible. This year, in order to use our AO systems in clinical research, our AO team has designed and written a clinical trial protocol that will compare AO images and data from 12 human participants across four AO laboratories in the Midwest. This trial is being done in order to standardize AO image capture techniques and the formal assessment of AO images. In addition, this comparative trial will use the UW Fundus Photograph Reading Center to grade the AO images in a masked fashion."



JEREMY ROGERS PhD

Retina Research Foundation Edwin and
Dorothy Gamewell Professorship

"The RRF Edwin and Dorothy Gamewell Professorship enables my lab to pursue the development of new methods to image retinal cells in patients. We are investigating how light is scattered and reflected by the retina and using this information in computational models as we optimize and advance cutting-edge imaging capabilities, including Adaptive Optics instrumentation and Optical Coherence Tomography. Our long-term goal is to develop functional cellular imaging to aid diagnosis, optimize therapies, and improve our understanding of the visual system."

McPHERSON ERI/RETINA RESEARCH FOUNDATION CHAIRS AND PROFESSORSHIPS



KEVIN ELICEIRI PhD

Associate Director, McPherson Eye Research
Institute ∞ Retina Research Foundation Walter
H. Helmerich Research Chair

"The support of the Retina Research Foundation Walter H. Helmerich Research Chair has allowed me to advance my current research on computational optics and to develop new imaging and computational approaches for characterizing changes in the cellular microenvironment. Some highlights of this work include the following:

- With McPherson ERI members Dr. Amitha Domalpally and Dr. Barb Blodi, we have enjoyed a successful collaboration on automated image analysis at the UW Fundus Photograph Reading Center (FPRC). The Center is using this program for several segmentation tasks in eye images. Recently, we finished implementing a new platform on machine learning for automated analysis of their data.
- With McPherson ERI members Dr. Paul Campagnola and Dr. Jeremy Rogers, we have commissioned a novel multimodal imaging instrument that combines four tissue-imaging methods ranging from nanometers to millimeters in spatial sensitivity. This is being explored for multiscale image analysis of sclera organization.
- My lab continues to develop the open-source image analysis software package ImageJ. We recently received an NIH grant to develop and expand this tool. The grant includes the addition of new capabilities to our open-source platform, including improved approaches for automated analysis and pattern recognition."

David and Nancy
Walsh and family
with Dr. Alice
McPherson



MRINALINI HOON PhD

Retina Research Foundation Rebecca Meyer
Brown Professorship

"Our recent research has uncovered a novel role for a cell adhesion protein called LRRTM4 in the mammalian retina. Using mouse models that lack LRRTM4, we discovered that LRRTM4 is necessary for correctly wiring the night-vision (dim-light) circuit of the retina. The retinal neurons that form this circuit communicate at specialized junctions called synapses. Without LRRTM4, the formation and function of several types of synapses—'ribbon' synapses and inhibitory GABAergic synapses surrounding the ribbon synapses—are severely perturbed. Importantly, these alterations are specific for synapses only along the night vision pathway. The support of the RRF Rebecca Meyer Brown Professorship was crucial in enabling us to complete this study by combining approaches such as 3D electron microscopy, high-resolution confocal microscopy, and single-cell electrophysiology. As a follow up to these exciting findings, we are currently investigating the mechanistic basis of LRRTM4 function in the retina and extending our findings in mouse retina to primate retina, as mutations in LRRTM4 have been linked to hereditary macular degeneration and macular dystrophy."

THE DAVID AND NANCY WALSH FAMILY PROFESSORSHIP IN VISION RESEARCH



RAUNAK SINHA PhD

"Research in our lab is focused on understanding how visual signals are converted in the photoreceptors and how they are subsequently processed by the downstream neural circuitry in the vertebrate retina. The David and Nancy Walsh Family Professorship supports our lab's efforts to understand the functional properties of photoreceptors in the fovea—a specialized retinal area unique to diurnal primates that mediates our high-definition central vision. Even though the



KRISHANU SAHA PhD

Retina Research Foundation Kathryn and
Latimer Murfee Chair

"Support from the Retina Research Foundation Kathryn and Latimer Murfee Chair has enabled me to build further momentum for our genome-editing projects in the eye. With the Chair support, we are developing new methods to understand the safety and efficacy of various genome-editing approaches in close collaboration with McPherson ERI members David Gamm, Bikash Pattnaik, Sarah Gong, Melissa Skala, and others. My lab has now designed additional viruses and nanoparticles that can be injected into the eye through intravitreal or subretinal injection in order to edit the genome of cells within the retina directly.

We have also started to better understand two critical concerns with genome-editing strategies in the field: genomic specificity and potential off-target adverse effects. We are now identifying gene regulatory network changes following the administration of a viral genome editor. This work involves machine learning and bioinformatics, and this pandemic year has been an excellent time to "double-down" on efforts like these, which can be done outside the lab. We are also now able to detect off-target modifications to the genome at a higher resolution within retinal pigment epithelial cells and photoreceptors. This work is helping us to understand, and ultimately avoid, adverse events in patients who are treated with genome-editing therapeutics."

perceptual and anatomical specializations of central vision and foveal cone photoreceptors have been known for almost a century, our understanding of cone function in the fovea remains elementary. Using single-cell electrophysiology in primate cone photoreceptors, our lab is exploring how cone function in the fovea may be distinct from the rest of the primate retina. Our goal is to use this information about cone physiology as a baseline for testing cone photoreceptor function in human stem cell-derived 3D retinal organoids. This will help establish a functional assay to probe abnormalities in cone photoreceptor function in retinal organoids derived from human patients with disease mutations, and allow for testing novel pharmaceuticals."



Kenzi Valentyn Vision Research Awards

Kenzi Valentyn Vision Research Awards, the McPherson Eye Research Institute's research grant opportunity for trainees, were established in 2017. They are named after Kenzi Valentyn, in honor of her courage and positive attitude throughout her long battle with Kearns-Sayre syndrome, a degenerative disease with symptoms including vision loss. Kenzi's many friends and family members, including her parents Nancy and Tim, brothers Brett and Connor, and sister-in-law Mackenzie, have ridden in Cycle for Sight as "Kenzi's Team" since 2014. Each award recipient receives a grant of \$4,000 to support their vision research project.

In 2020, three Kenzi Valentyn Vision Research Award recipients were chosen:

Anjani Chakrala, a graduate student in Neuroscience mentored by Xin Huang. **Project title:** *Neural Representation of Overlapping Motion Surfaces Located at Different Depths in Visual Area MT: Effects of Selective Attention on this Representation.*

Ralph W. Nelson, a graduate student in Kinesiology – Motor Control & Behavior, mentored by Andrea Mason. **Project title:** *The Assessment of Dual-Task Interference Using Walking and Carrying Tasks in Children With and Without Autism Spectrum.*

Abhilash Sawant, a graduate student in Neuroscience, mentored by Raunak Sinha. **Project title:** *Understanding the Mechanism and Function of Postsynaptic Inhibition in the Mouse ON-Alpha Retinal Ganglion Cell.*

We are grateful to the Valentyn family for continued support for these awards, which go to the next generation of young vision researchers!

RESEARCH AWARDS & GRANTS

Expanding Our Vision Research Grants

NEW IN 2020!

The Expanding Our Vision (EOV) grant program was started this year to provide awards of up to \$10,000 to researchers performing vision-related research in visual communication, visual cognition, visual perception/performance, data visualization, development of novel imaging techniques for the visual system, computer sciences, and/or bioinformatics. Research in these areas is essential for understanding the intricacies of human vision and for enhancing our ability to visualize cells and processes in the eye, and to analyze large and complex datasets.

Five projects were awarded EOV Research Grants in this initial year:

Andrea Mason (Kinesiology) and **Leigh Ann Mrotek & Robert Scheidt** (Biomedical Engineering, Marquette University), *Impact of visual cue saliency during bimanual visually guided reach-to-grasp*

Ari Rosenberg (Neuroscience), *Hierarchical cortical processing of three-dimensional visual motion*

Sushmita Roy (Biostatistics & Medical Informatics), *Computational approaches for characterizing cell type dynamics in human retinal tissue*

Karen Schloss (Psychology), *Understanding dimensional structure underlying color-concept associations to advance visual communication*

Andreas Velten (Biostatistics & Medical Informatics), *Measuring ocular retroreflectance for remote ocular diagnostics*

Student Awards

The McPherson ERI sponsors two student awards, which were given this year to students who were able to perform their research remotely (as mandated during the COVID-19 pandemic). The undergraduate **Hilldale Award** (\$4,000) was given to **PJ Derr**, a neurobiology and psychology double major in **Raunak Sinha's** lab. The **Dan and Ellie Albert Student Vision Research Award** (\$2000), matched through the Shapiro Summer Internship Program and funded by Dr. Daniel and Eleanor Albert, supports a summer vision research project for an SMPH student. **Claire Vanden Heuvel**, in **Dr. Julie Mares' lab**, was the recipient for Summer 2020.

Grant Summit Program (GSP), 2019-2020 Awards

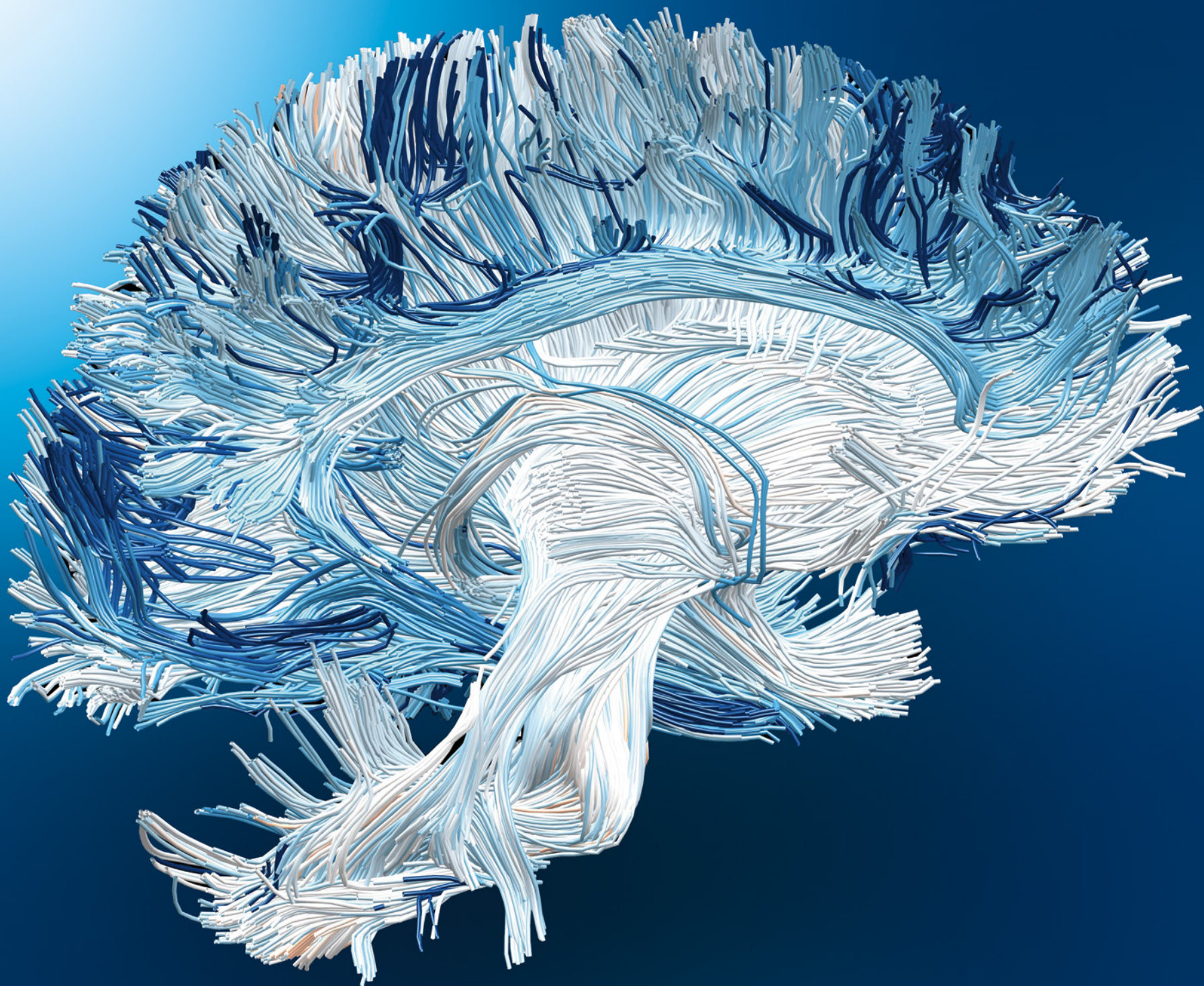
The McPherson ERI initiated the Grant Summit Program (GSP) in 2018 to provide critical and timely support to bolster projects that are under consideration for federal awards but require additional experiments. Since the program's inception, multiple grants have been resubmitted and successfully received funding that far exceeded the GSP contribution (typically a greater than 20-fold return on investment). Thus, the GSP is a very cost-effective way to support vision research within the Institute.

In 2019 and 2020, GSP awards were given to three McPherson ERI researchers:

Colleen McDowell, Ophthalmology and Visual Sciences, received \$10,000 for her grant resubmission, titled *Toll-like receptor 4 signaling in the glaucomatous optic nerve head.*

Ismail Zaitoun, Ophthalmology and Visual Sciences, received \$10,000 for his grant resubmission, titled *Gender impact and retinal damage in hypoxic-ischemic encephalopathy.*

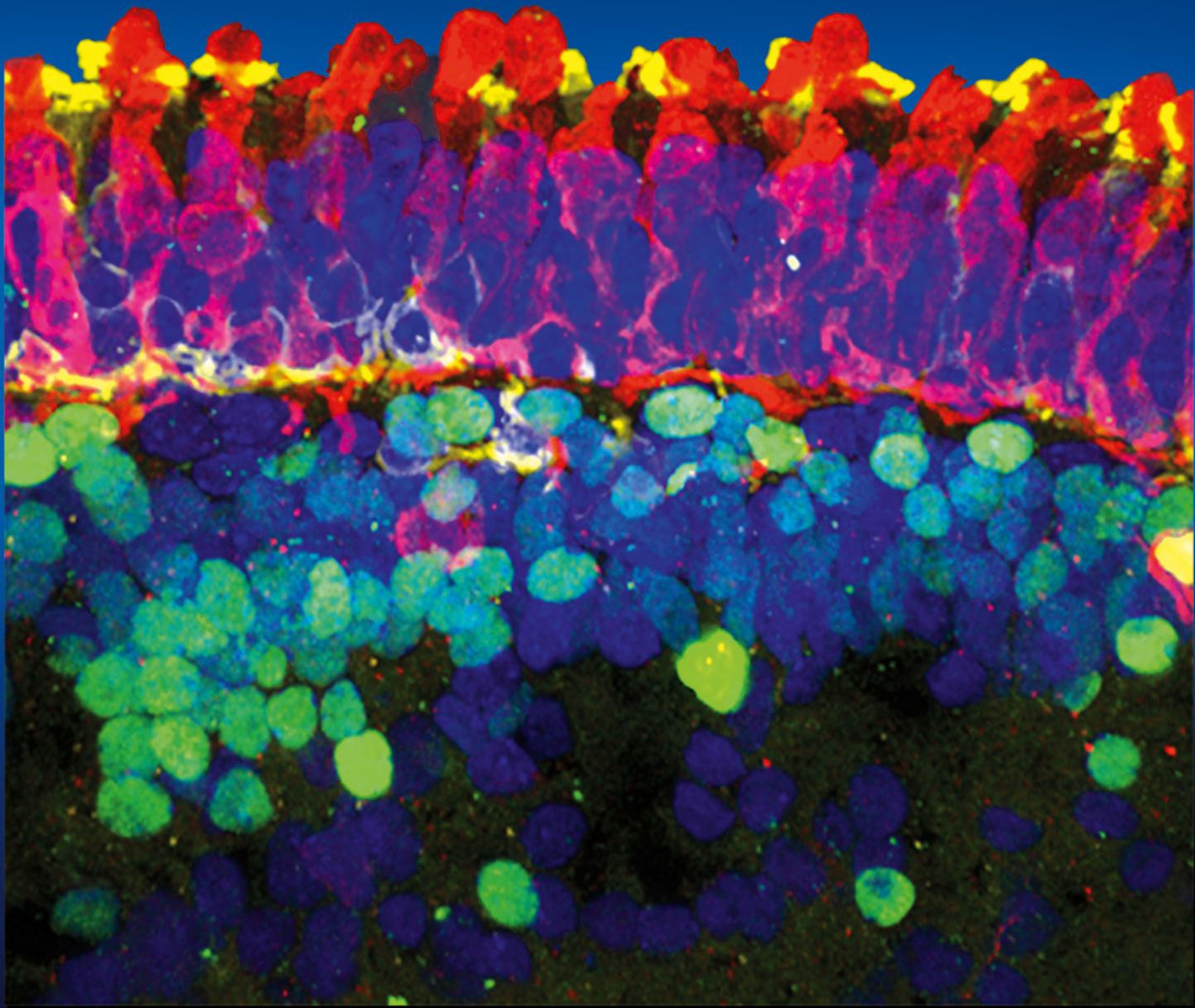
Karen Schloss, Psychology, received \$9,686 to facilitate resubmission of an NSF CAREER award proposal, titled *Understanding visual reasoning for scientific communication.* Dr. Schloss's proposal was recently approved for \$558,702.



JANUARY

Image Credit: Visualization by Tananun Songdechakraiwut, Moo K. Chung; Processing by Zhan Luo, Ian C. Carroll; Acquisition by Andrew L. Alexander, H. Hill Goldsmith. | In the above image, the reconstructed white matter fibers of the human brain from diffusion tensor imaging (DTI) reveal the structural connectivity between brain regions. The fibers are colored based on the strength of functional connectivity obtained from resting-state functional magnetic resonance imaging (rsfMRI).

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FEBRUARY

Image courtesy of Elizabeth Capowski, PhD | This is a confocal microscope image of the inner and outer nuclear layers of a self-organizing, human stem cell-derived retinal organoid. Cones (in red) form a single line at the top of the outer nuclear layer while rods (blue nuclei and yellow outer segments) form 4-6 layers under the cones, as seen in human retinas. The green nuclei in the inner layer are bipolar cells which form the second link in the neuronal chain that detects light and projects the signal to the visual cortex. Retinal organoids such as these, grown in the laboratory of Dr. David Gamm, are used to model human retinal development and to test novel therapeutics for blinding disorders.

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Image courtesy of Briana Ebbinghaus, Hoon Lab | Dr. Mrinalini Hoon's lab studies the development of connectivity in the neural retina and how this connectivity is affected in disease states. Shown here is a retinal ganglion cell, the type of output neuron for this circuit. This is a maximum intensity projection of a 3D image taken with a confocal microscope. Ganglion cells transmit visual information to the brain, so a problem with this cell type will have a noticeable effect on vision. Glaucoma and diabetic retinopathy are two of the known diseases which involve changes in the retinal ganglion cells.

FEB

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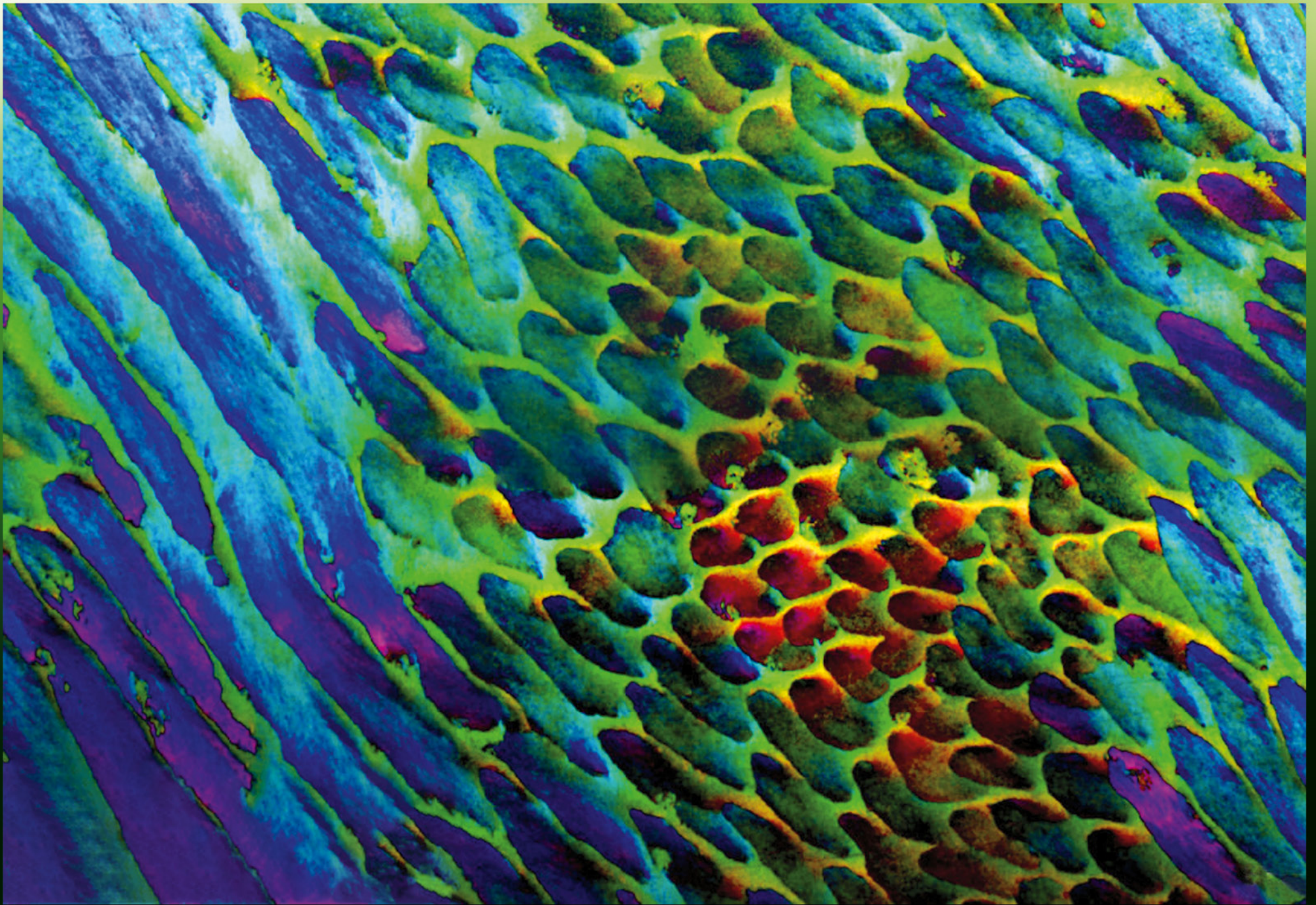
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APRIL

Image courtesy of Michael Taylor, PhD | This image, generated by laser confocal microscopy, displays the blood vessels in the brain of a zebrafish larva. The color is false color—the color spectrum represents depth in the image, with red/yellow being nearest the surface, green intermediate, and blue/violet the deepest. Dr. Michael Taylor is an Assistant Professor in the School of Pharmacy, Pharmaceutical Sciences Division.

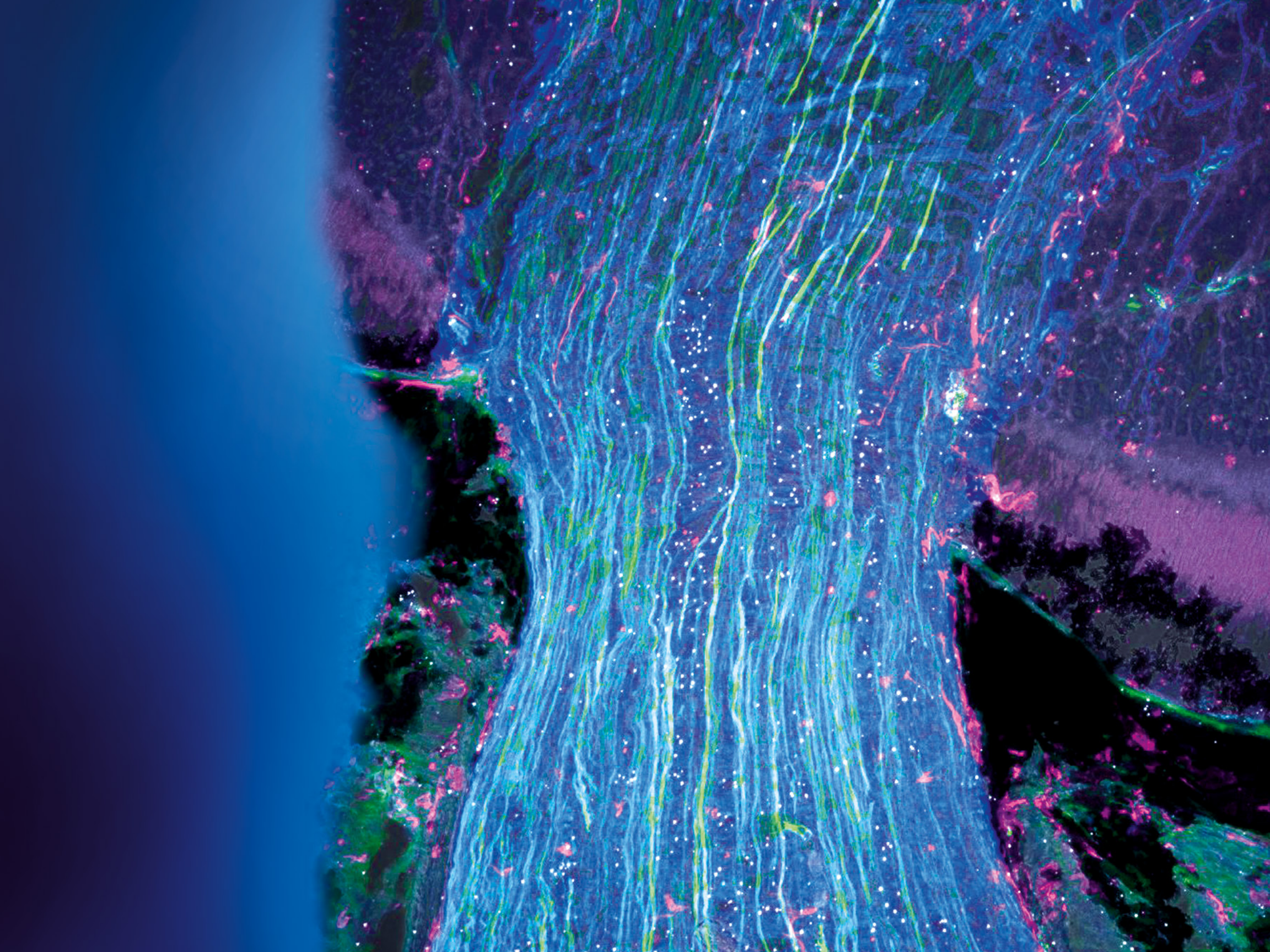
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MAY

Image courtesy of Pupa Gilbert, PhD | Dr. Pupa Gilbert's image of human tooth enamel, displayed in the Mandelbaum & Albert Family Vision Gallery show *Demystify: Seeing the Unseeable*, was generated by Polarization-dependent Imaging Contrast (PIC) mapping. The technique uses polarized X-rays to detect the orientation of individual crystals in a microcrystalline material such as tooth enamel. Variations in orientation are displayed as variations in color and intensity. Dr. Gilbert is a Professor in the Department of Physics at UW-Madison.

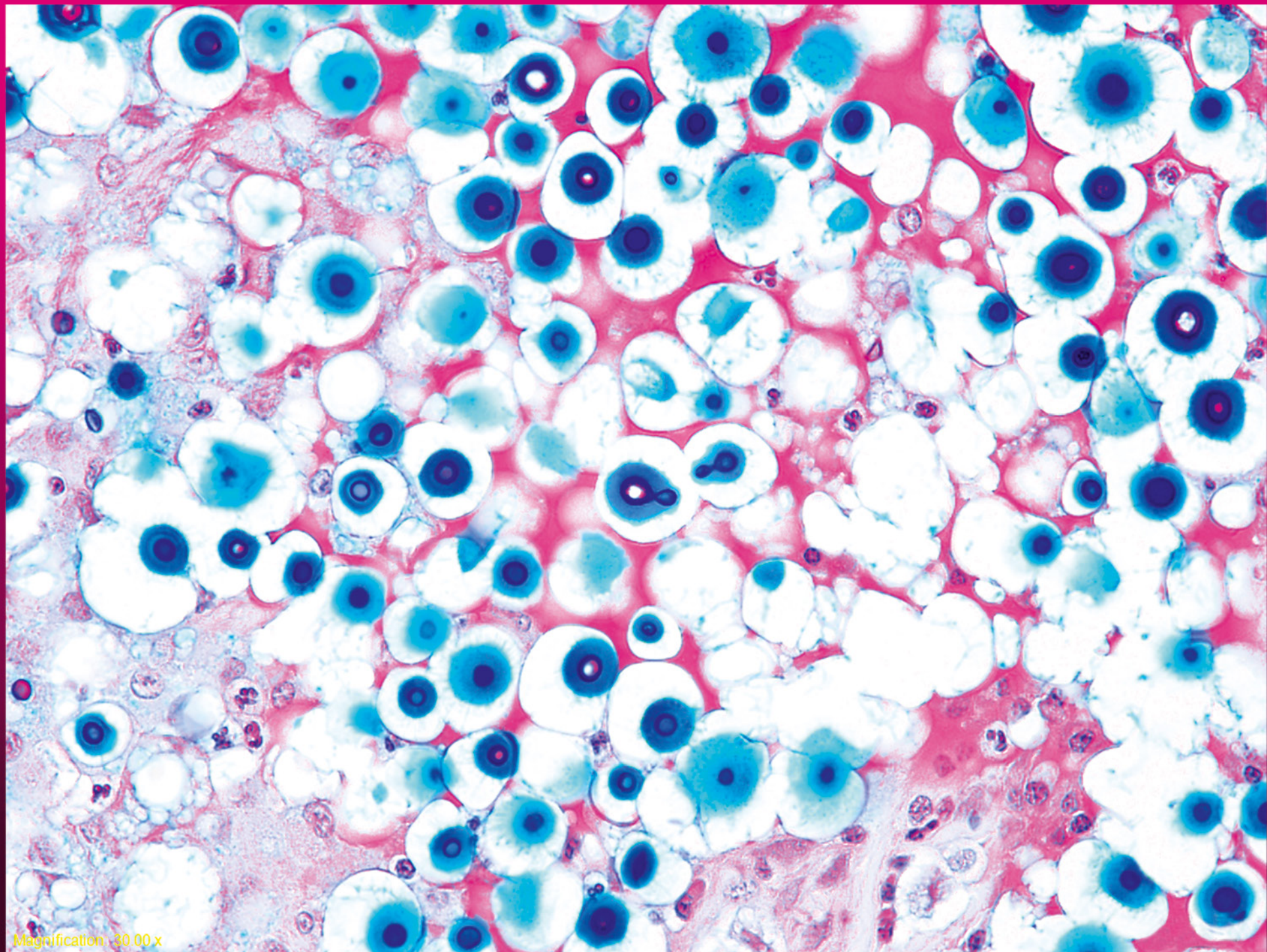
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JUNE

Image courtesy of Dr. Timur Mavlyutov, Senior Research Specialist in Dr. Colleen McDowell's laboratory | The image above is an immunohistochemical analysis of the mouse optic nerve head. The optic nerve head is where the axons of retinal ganglion cells (RGCs) converge. This region is particularly vulnerable in glaucoma. The green streaks are the axons of the retinal ganglion cells; the blue cells are astrocytes, which are specialized glial cells; the pink cells are microglial cells; and the white dots are mRNA of Toll-like receptor 4 (TLR4), a potentially important gene in regulating glaucomatous damage.

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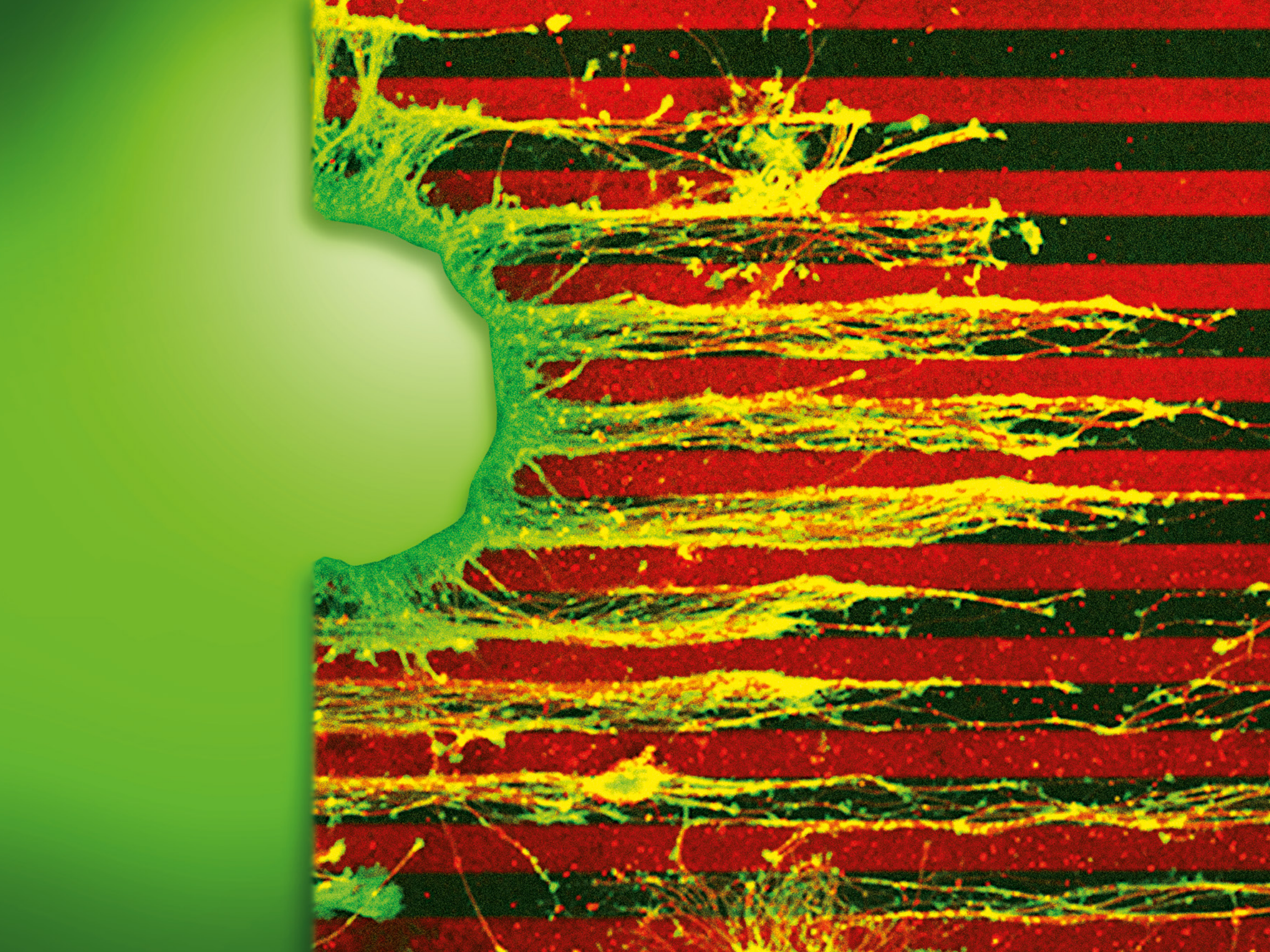


Magnification: 30.00 x

JULY

Image courtesy of Richard Dubielzig, DVM | *Cryptococcus neoformans* is a yeast form of pathogenic fungus capable of infecting the eye, particularly in cats. This photomicrograph image shows an almost pure population of yeast organisms from an infected cat's eye. The organism is made up of a central round cell body seen in dark purple surrounded by a blue polysaccharide capsule which shrinks in the space occupied by the yeast. Dr. Richard Dubielzig founded the Comparative Ocular Pathology Laboratory of Wisconsin (COPLOW) in 1983 in order to better understand the pathogenesis and prognosis of ocular diseases.

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AUGUST

Image courtesy of Timothy Catlett, PhD, of the Gomez Lab | In the image above, corrected (control) human forebrain neuron axons (yellow) are guided by patterned stripes of the inhibitory axon guidance cue EphrinA1 (red stripes). Similar assays are being used to test whether induced pluripotent stem cell-derived neurons carrying autism-related mutations are properly guided. The Gomez Lab is working to understand and guide the growth and development of neural circuits in many areas, including photoreceptor axon development.

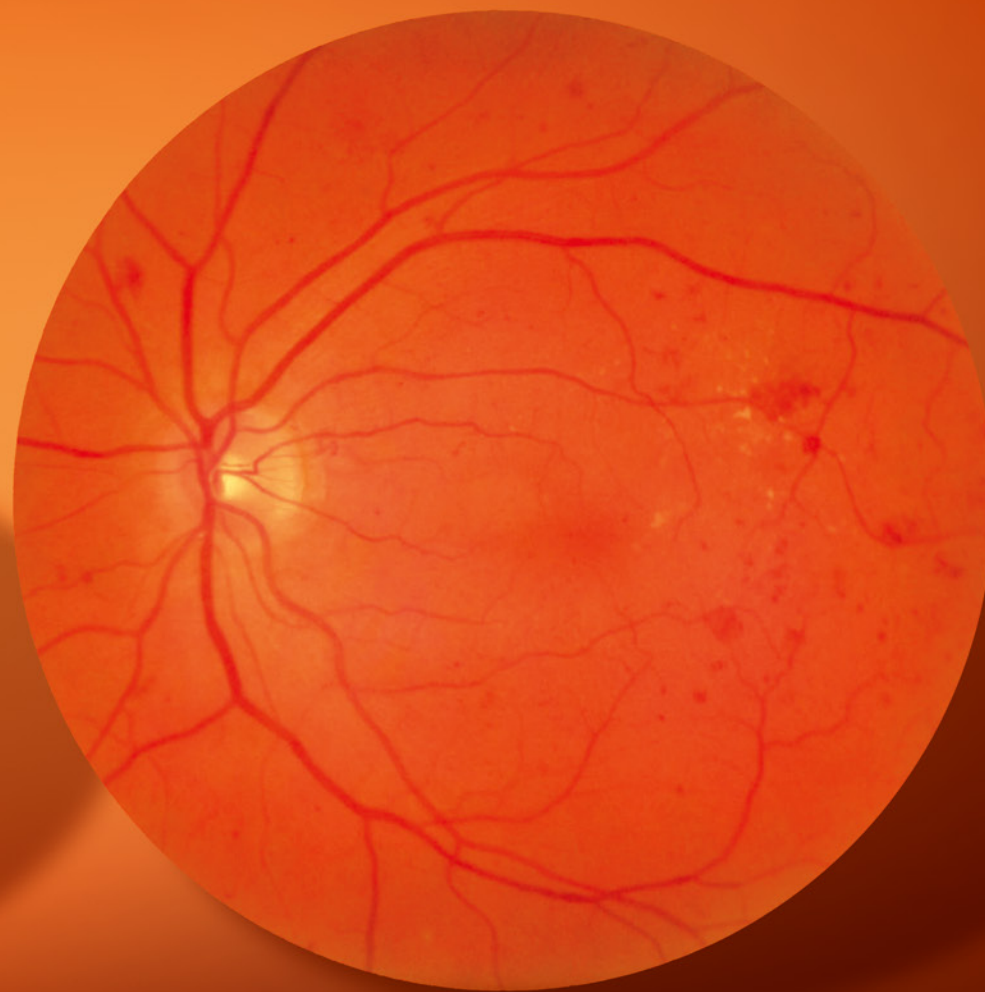
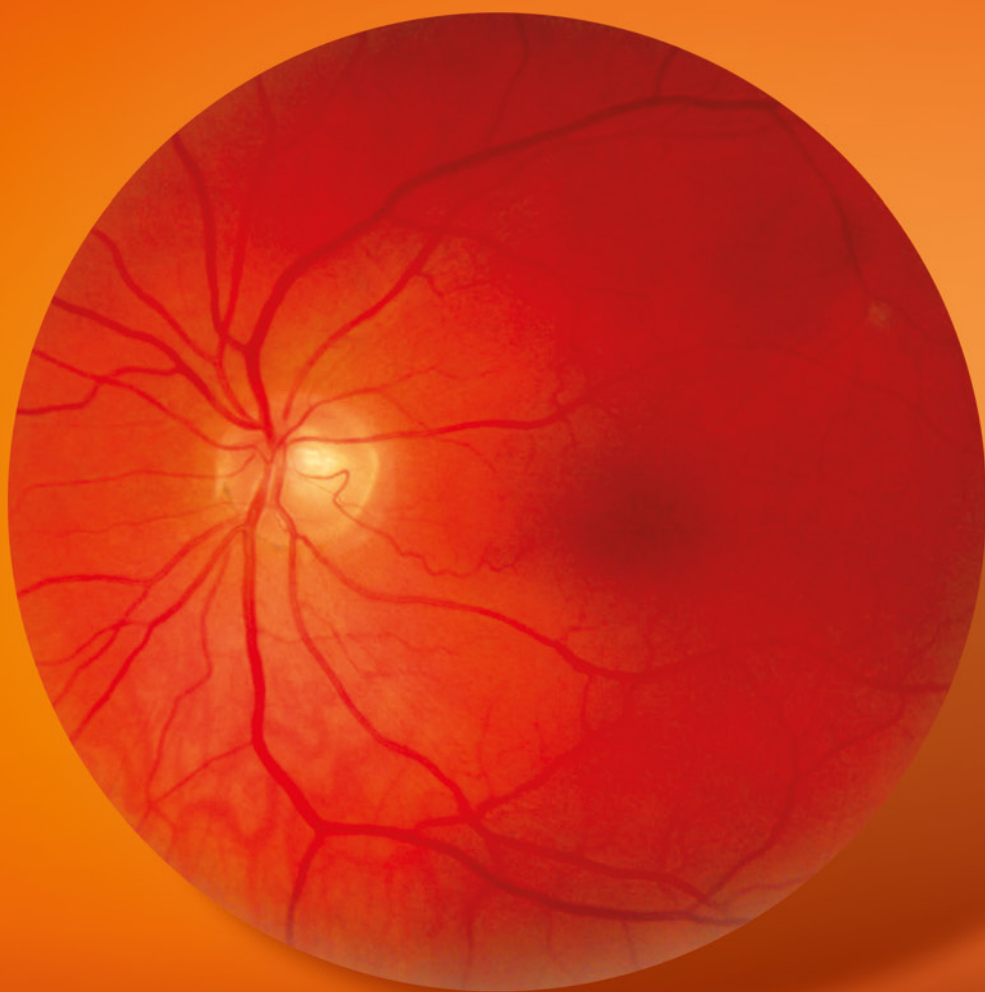
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SEPTEMBER

Image courtesy of the artist, Rick Ross | **“Color Theory,” oil and cold wax on panel** | Rick Ross is inspired by history, age, and patina as he takes nature as his subject matter, whether literally interpreted through landscapes and still life or abstractly represented by the textures and depth of oil and cold wax medium. This artwork was part of the show *Your Brain on Abstract Art*, which was presented in the Mandelbaum & Albert Family Vision Gallery of the McPherson Eye Research Institute.

AUG	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	MON	TUE
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OCTOBER

Image courtesy of the UW Teleophthalmology Program | The UW Teleophthalmology Program aims to prevent blindness through advancing innovative telemedicine technologies, including using retinal photos for diabetic eye screening. Pictured on the left is a photo of a healthy retina; on the right, we see a retina with diabetic retinopathy showing scattered retinal hemorrhages (red blotches and dots) and exudates (small yellow dots). Both images were taken with an easy-to-use touchscreen retinal camera conveniently located in primary care clinics.

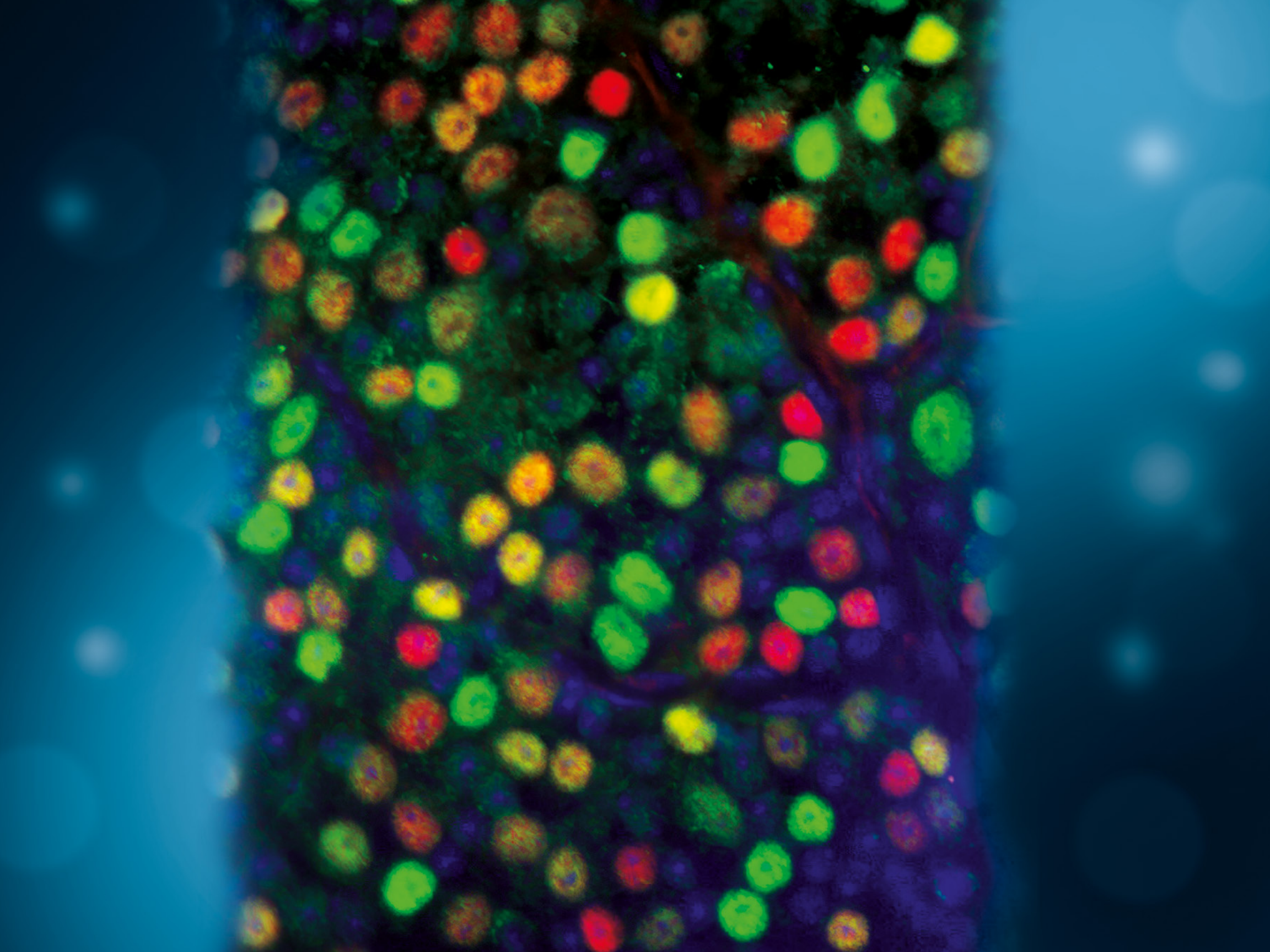
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NOVEMBER

Image courtesy of **Andreas Velten, PhD** | Dr. Velten's image was taken by a camera without a direct line of sight to the scene (shown in the background). The camera illuminates relay surfaces near the scene and captures light that travels from there to the scene and back to a relay surface. The image is computed from this data. Using this method, this camera may be able to see around corners and behind objects. Changes can also be made to the perspective and lighting of a scene in post-processing. Dr. Andreas Velten is an Assistant Professor in the Department of Biostatistics and Medical Informatics and the Department of Electrical and Computer Engineering.

OCT	FRI 1	SAT 2	SUN 3	MON 4	TUE 5	WED 6	THU 7	FRI 8	SAT 9	SUN 10	MON 11	TUE 12	WED 13	THU 14	FRI 15	SAT 16	SUN 17	MON 18	TUE 19	WED 20	THU 21	FRI 22	SAT 23	SUN 24	MON 25	TUE 26	WED 27	THU 28	FRI 29	SAT 30	SUN 31
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DECEMBER

Image courtesy of Robert Nickells, PhD | This image shows different types of retinal ganglion cells (RGCs) in the mouse retina stained for two different RGC-specific proteins (red and green). Some RGCs express just the green protein (called BRN3B), some just the red protein (BRN3A), and some cells express both, making them appear yellow or orange depending on the respective amounts of each. These proteins play an important role in determining RGC identity and, therefore, function in the retinas of all animals.

NOV	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		
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KWANZAA BEGINS																NEW YEAR'S EVE				NEW YEAR'S DAY												
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2019 2020

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IN MEMORIAM

➤ **Oscar C. Boldt** ➤

The McPherson ERI deeply regrets the passing of Oscar C. Boldt, known as O.C., an extraordinary individual who was a founding McPherson ERI Advisory Board member and friend to the Institute for many years. O.C., who passed away on June 9th, 2020, was Chairman of The Boldt Company, one of the nation's largest and most highly respected construction firms. Following his service as a navigator on a 15th Air Force B24 bomber in Italy during World War II, O.C. completed his Civil Engineering education at UW-Madison, then guided Boldt Construction for 70 years, crafting many familiar and beautiful Wisconsin buildings. Included among those is the Wisconsin Institutes for Medical Research (WIMR) towers on UW-Madison's medical campus—a state-of-the-art research complex that holds the McPherson ERI's home offices and labs. O.C. and his wife Pat helped guide and support the McPherson ERI in its early years, and they continued in recent years to stay involved with the Institute's progress. Together, they had a second career as benefactors of countless organizations in Appleton and other communities. We will miss O.C.'s great personal warmth, intelligence, and common sense.



Mandelbaum & Albert Family Vision Gallery

The Mandelbaum & Albert Family Vision Gallery, on the 9th floor of WIMR II, displays vision-related artworks in rotating exhibits. In 2020, one exhibit remained in place for the entire calendar year, due to the Covid-19 pandemic. *DeMystify: Seeing the Unseeable* was a fascinating exhibit that showcased the results of various imaging techniques used to reveal what is otherwise unseeable. In the exhibit, UW-Madison scientists shared the information contained in these images and explained how they are produced.

DEMYSTIFY
seeing the unseeable

McPherson Eye Research Institute
TROUT FAMILY ENDOWMENT

MANDELBAUM & ALBERT FAMILY VISION GALLERY

JANUARY 29 - MAY 29, 2020

OPENING RECEPTION:
JANUARY 30TH, 4:30-6:30PM

We humans are visual beings. Through sight we develop our knowledge of the world—and when we understand something we say, “I see.”

We create visible images to represent and enhance our understanding. It’s what artists do when making drawings and paintings. No wonder, then, that scientists, too, create images to represent that which cannot be seen directly.

Images in this exhibition reveal what is otherwise unseeable. Using a variety of techniques to produce visible images of things invisible to our eyes, scientists share the information these images contain and explain how they are produced.

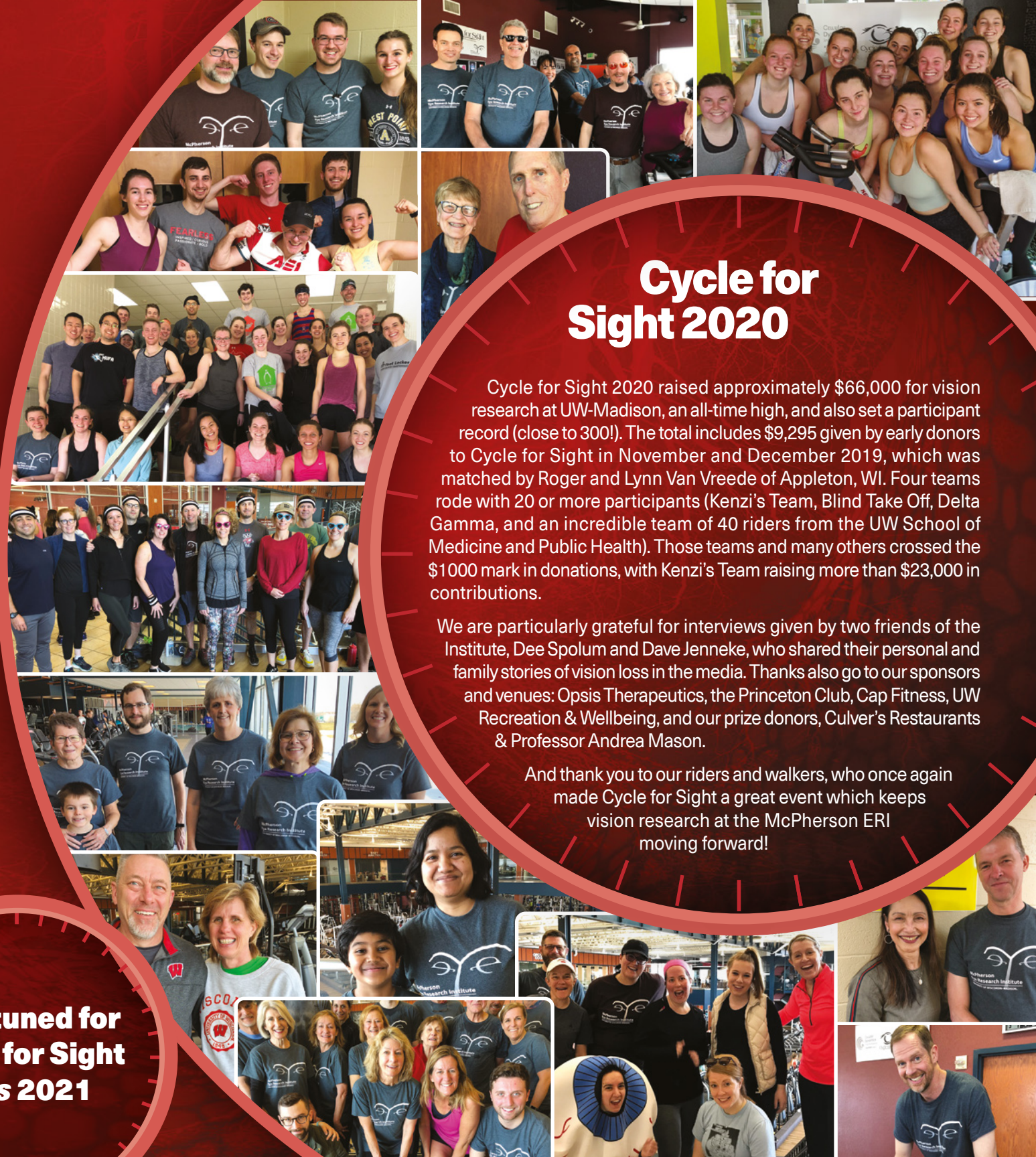
**Stay tuned for
Cycle for Sight
Plus 2021**

Cycle for Sight 2020

Cycle for Sight 2020 raised approximately \$66,000 for vision research at UW-Madison, an all-time high, and also set a participant record (close to 300!). The total includes \$9,295 given by early donors to Cycle for Sight in November and December 2019, which was matched by Roger and Lynn Van Vreede of Appleton, WI. Four teams rode with 20 or more participants (Kenzi's Team, Blind Take Off, Delta Gamma, and an incredible team of 40 riders from the UW School of Medicine and Public Health). Those teams and many others crossed the \$1000 mark in donations, with Kenzi's Team raising more than \$23,000 in contributions.

We are particularly grateful for interviews given by two friends of the Institute, Dee Spolum and Dave Jenneke, who shared their personal and family stories of vision loss in the media. Thanks also go to our sponsors and venues: Opsis Therapeutics, the Princeton Club, Cap Fitness, UW Recreation & Wellbeing, and our prize donors, Culver's Restaurants & Professor Andrea Mason.

And thank you to our riders and walkers, who once again made Cycle for Sight a great event which keeps vision research at the McPherson ERI moving forward!



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Roger and Lynn Van Vreede Match

In Fall 2019, Roger and Lynn Van Vreede initiated a match for all year-end donor giving up to \$100,000. Their generosity inspired more than \$120,000 in contributions in November and December 2019 from many of our donors. We're grateful to all of you, and to the Van Vreedes—**who are repeating their match offer from October through December 2020!**

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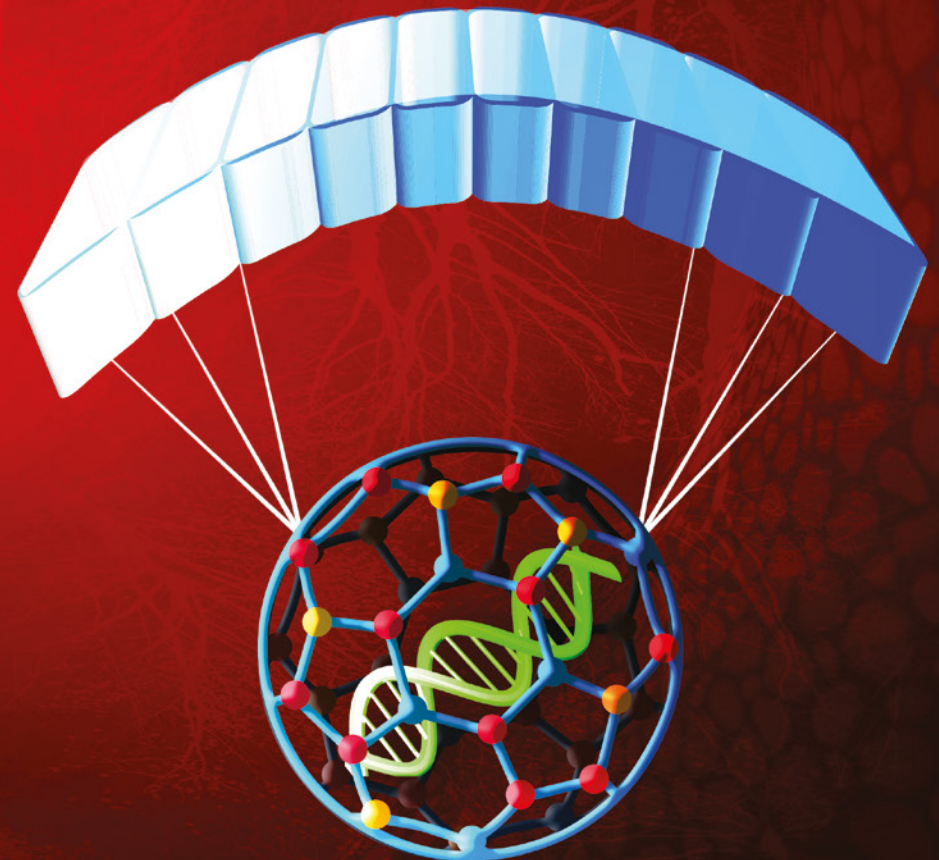
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The cover image depicts healthy genes being strategically delivered to the retina by “smart” nanocages after injection into the human eye.

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