McPherson Eye Research Institute
UNIVERSITY OF WISCONSIN–MADISON

InSights

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FALL *2022*

Saving Sight from a Distance

YAO LIU, MD

Advances in teleophthalmology allow remote patients to receive diagnoses and proper care earlier than ever before.

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An Infinite Variety of Animal Eyes

LEANDRO TEIXEIRA, DVM

Discover COPLOW, UW-Madison's internationally-known diagnostic laboratory for animal vision.

More on pp. 9

FROM THE DIRECTOR, FALL 2022

Dear Friends of the McPherson ERI,

Welcome to our Fall 2022 *InSights*, which will now come your way twice-yearly—in fall and spring—in addition to our annual calendar and year-end report. We have also expanded the page count to increase readability and keep you informed of the many advances in eye research, technology, and therapies within the Institute. For even more timely updates, you can now find the McPherson ERI on Twitter (@McPherson_ERI), as well as on Facebook (McPhersonERI) and our website (vision.wisc.edu).

When vision is impaired, the first step is diagnosing the problem, and the McPherson ERI has multiple researchers who focus on this process. In the following pages, you'll read about an important new telehealth program called "I-SITE" (Implementation for Sustained Impact in Teleophthalmology), developed by Dr. Yao Liu and her group in UW-Madison's Department of Ophthalmology and Visual Sciences. The program targets diabetic eye disease, the leading cause of blindness in American adults. Dr. Liu is currently overseeing an NIH-funded multicenter clinical trial of I-SITE, which has already shown great promise in preserving sight.

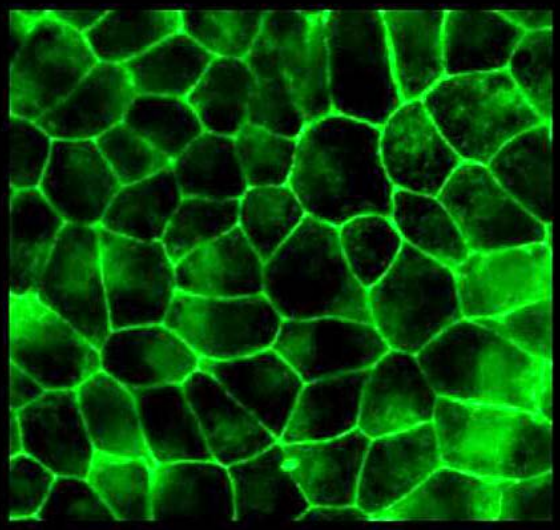
Diagnosing eye disease in animals is also critical for maintaining their health and well-being, and it also improves our understanding of human vision disorders. However, veterinary eye pathology laboratories are rare as hens' teeth. UW- Madison is fortunate to be the home of COPLOW, the Comparative Ocular Pathology Laboratory of Wisconsin—perhaps the world's foremost center for the analysis of ocular diseases in animals. Veterinarians and veterinary ophthalmologists from around the world send tissue samples to COPLOW in the hope of saving animal sight and lives and of contributing to potential future treatments. The McPherson ERI has long been inspired by COPLOW members' dedication to all creatures, and we are delighted to showcase them in this issue.

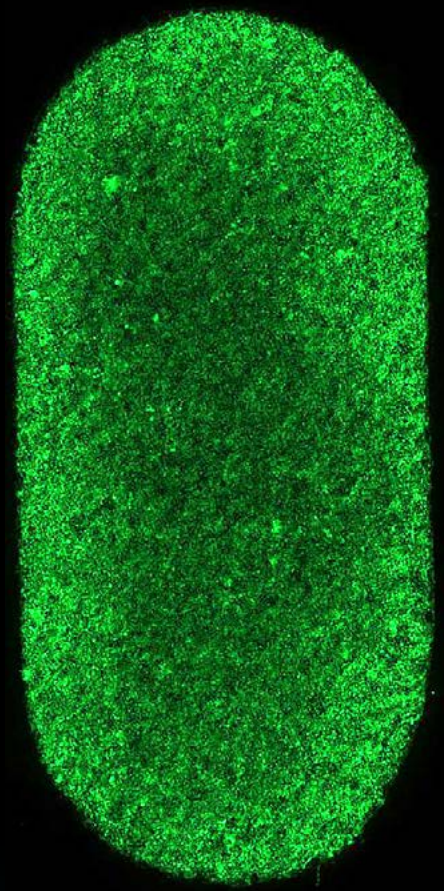
Thank you for your help and interest,

Professor, Department of Ophthalmology and Visual Sciences
RRF Emmett A. Humble Distinguished Director, McPherson ERI

Sandra Lemke Trout Chair in Eye Research

Above shows a close-up of a patch of RPE cells at higher magnification. Right image shows the full-RPE-patch (2 x 4 mm). Each dot is an RPE cell with the borders stained green. Each patch contains approximately 75,000 RPE cells. (Image courtesy of Kapil Bharti, PhD, NEI)





FIRST U.S. PATIENT RECEIVES AUTOLOGOUS STEM CELL PATCH FOR DRY AMD

In early September, the National Institutes of Health (NIH) announced that the first patient has been treated in its phase 1/2a clinical trial (NCT04339764) of an autologous induced pluripotent stem (iPS) cell therapy for the treatment of dry age-related macular degeneration (AMD). The patient received the therapy in a clinical trial overseen by Kapil Bharti, PhD, a senior investigator at the National Eye Institute. The trial is the first in the United States to use replacement tissues from patient-derived iPS cells.

The technology used in the trial was developed in collaboration with FUJIFILM Cellular Dynamics Inc. and Opsis Therapeutics, two Madison-based iPS cell companies established by McPherson ERI members Jamie Thomson and David Gamm, respectively. The process converts a person's own white blood cells to iPS cells, which are subsequently coerced to become retinal pigment epithelial (RPE) cells, the primary cell type that degenerates in AMD. The RPE cells are then surgically implanted as a patch under the patient's central retina, also known as the macula. According to Dr. Bharti, "the protocol, which prevented blindness in animal models, is the first clinical trial in the United States to use replacement tissues from patient-derived iPS cells." Patients will be followed for 5 years after surgery to monitor changes in visual acuity and the occurrence of adverse events.

Adapted from an article by David Hutton, Ophthalmology Times, 9/2/22

MOVING FORWARD ON MACULAR DEGENERATION

Two New Donor-Established Funds Aim to Develop New Therapies

The McPherson ERI is thrilled to announce two new donor-established funds that will boost research for age-related macular degeneration, one of the most prevalent and rapidly growing health problems in the U.S. and western world. The Pat and Jay Smith Macular Degeneration Treatment Innovation Program will provide immediate funding for projects with the greatest potential to lead to AMD treatments, serving as a "rapid response" fund. The McPherson ERI Macular Degeneration Fund is an endowment that will grow funding for AMD until a cure is found, and welcomes support from additional donors.

The statistics on age-related macular degeneration are staggering. Currently, 15 million people in the U.S. have the disease, and 1.7 million Americans have it in advanced form. 2% of all individuals 50-59 have AMD, rising to nearly 30% in individuals over the age of 75. With increasing life expectancies, by 2050 the number of people affected by AMD in the U.S. is expected to double.

The need for rapid progress on new therapies and a cure couldn't be more pressing, and UW-Madison and the McPherson ERI have expertise and technology to bring to bear to develop and advance treatments for AMD. Fortunately, the Institute also has generous and forward-thinking donors to support that expertise.

PAT AND JAY SMITH: BRIDGING 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, they established the Pat and Jay Smith Macular Degeneration Treatment Innovation Program. Use of the funds is targeted toward addressing critical gaps in our understanding of AMD and applying that knowledge to create more effective therapies. Three initial projects have been identified: (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.

BUILDING AN AMD FUND

Even as we work toward near-term advances in AMD research and treatment, we know that the fight against AMD will require research for years to come. The McPherson ERI Macular Degeneration Fund provides an endowment for the length of that battle. Started in December 2021 with gifts of $100,000 each from the Trout Family Endowment and from Dr. Alice McPherson, the fund will invest, as it grows, in a variety of near- and long-term AMD research opportunities at UW-Madison. The McPherson ERI AMD Fund will be a great source of support for Institute scientists who focus on the disease, including the three current holders of Trout-endowed Chairs. We're thankful to the fund's founding donors, as well as to all who give support in the future.

Saving Sight from a Distance

Even prior to COVID-19, regular eye checkups were difficult for Larry, a retired truck driver with diabetes living in rural Mauston. Fortunately, Larry had access to remote care through the University of Wisconsin Teleophthalmology Program.

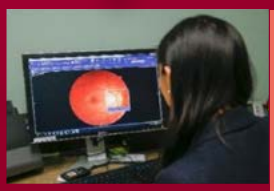
Founded in 2015 by Dr. Yao Liu, an ophthalmologist and assistant professor at UW-Madison, the program has become a nationally known model for telemedicine and the basis for an exciting National Eye Institute-funded multicenter clinical trial. For Larry, its impact was more immediate. Without the program, said Larry, "I probably would have went blind in my right eye. [I] wouldn't have been able to see anything." Larry's primary care provider was able to use a special camera to photograph the back of his eye at Mile Bluff Medical Center in Mauston. The photos were quickly reviewed by UW Health eye doctors in Madison, who identified diabetic eye disease in Larry's right eye. A quick referral to a retina specialist saved Larry's vision while the disease was in its early stages.

OVERVIEW OF TELEOPATHALMOLOGY FOR DIABETIC EYE SCREENING IN PRIMARY CARE

Eye photos are taken at primary care clinic

Photos are sent to an Eye Specialist

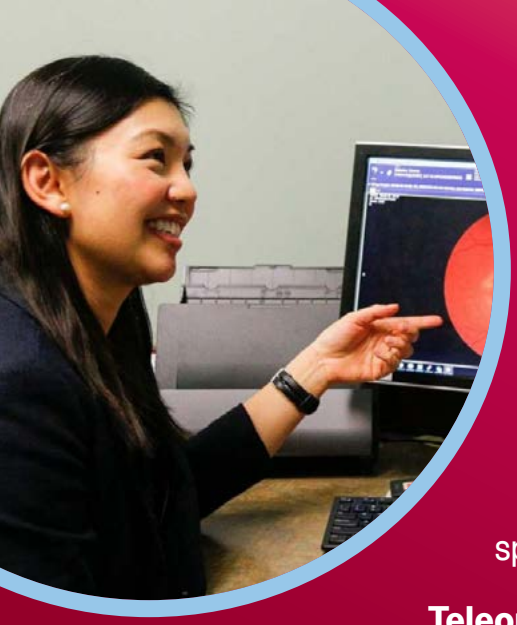
Eye Specialist reviews the photo



Diabetic Retinopathy Report

Primary Care Provider identifies eligible patients

Patients identified for further clinical evaluation and treatment



37.3 million Americans have diabetes, and diabetic eye disease is the leading cause of blindness in American adults. Blindness from diabetes is preventable with early screening and timely treatment, but half of Americans with diabetes do not obtain regular eye screening for a variety of reasons. Traditional screening requires patients to schedule a dilated eye exam with an eye doctor, which can be uncomfortable, time-consuming, and costly if insurance coverage is limited. In rural communities, the barriers of distance and access to specialists are even greater.

Teleophthalmology provides a clinically-proven, low-cost alternative to screening that can be done conveniently at a primary care clinic without dilating eye drops. But providing cameras is only the first step; too often, those cameras just end up gathering dust in a closet. Dr. Liu began the UW Teleophthalmology program to increase the use of this vision-saving technology. "The goal of our research is to make eye care more accessible, particularly for people in rural communities who have to travel longer distances to get eye specialty care," she notes.

In partnership with Mile Bluff Medical Center, Dr. Liu's research team interviewed patients, doctors, and medical staff to understand major barriers to teleophthalmology use. The team then used industrial systems engineering principles to develop a structured process called I-SITE (Implementation for Sustained Impact in Teleophthalmology). With I-SITE, a coach works with the primary care clinic to tailor a site-specific design for the teleophthalmology program. After I-SITE implementation, teleophthalmology use at Mile Bluff increased dramatically and diabetic eye screening rates at Mile Bluff increased from 47% to 64%—from below the national average to the top 25th percentile.

Based on her initial success, Dr. Liu's team was awarded over $4 million in 2021 from the National Eye Institute to test I-SITE in a multicenter clinical trial. The I-TRUST (Implementation of Teleophthalmology in Rural Health Systems) Study will include eight rural health systems in six states and expand the reach of the UW Teleophthalmology program, which currently serves eleven primary care clinics across four Wisconsin health systems, with more to come (see sidebar).

Larry is among the program's biggest supporters.

"Tell everybody: Make sure you get your eyes checked if you want to enjoy the world and enjoy seeing it better!"

To learn more about the UW Teleophthalmology program and hear Larry's story in a 7-minute video, go to:

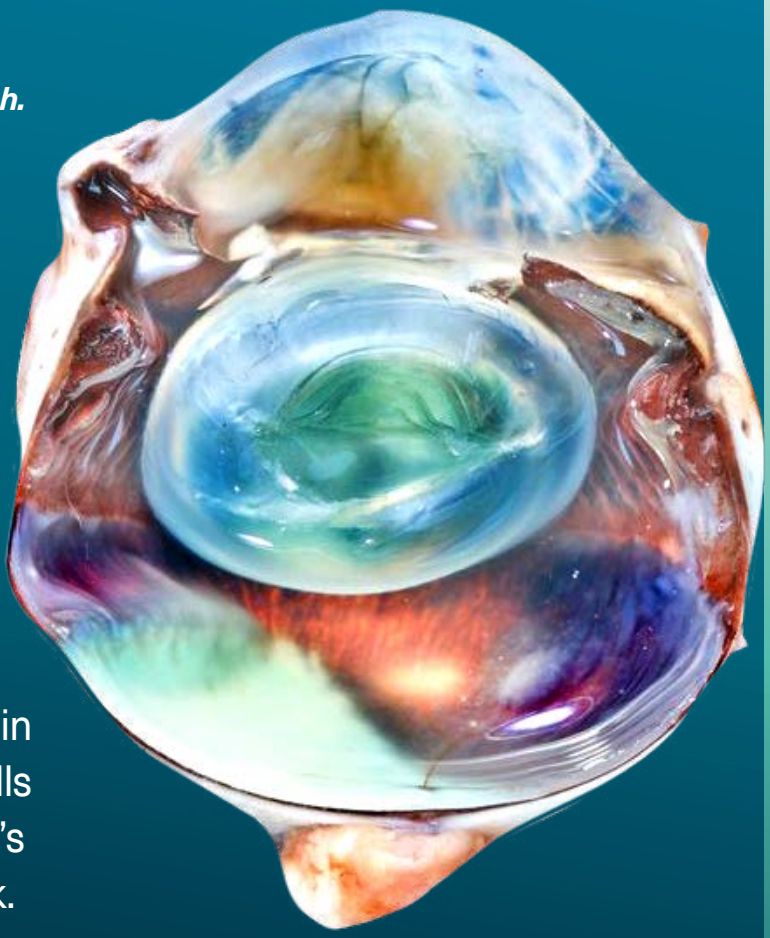
uwmadison.app.box.com/s/48jc27uhq8z4qivmzq0hw6pakhiygltr

or visit **eyephoto.wisc.edu**

Dr. Liu's research team is adapting the I-SITE program for underserved, urban communities of color to address racial and ethnic disparities in vision loss from diabetes.

Black Americans are three times more likely to develop vision-threatening diabetic eye disease than non-Hispanic whites. People of Latinx background have the highest rates of visual impairment and blindness of any ethnic group in the country. UW researchers are interviewing Black and Latinx patients with diabetes to identify their unique barriers to eye screening and boost teleophthalmology use. Working with community partners, they aim to design strategies to bridge gaps in eye screening and improve access to effective treatment. As part of this initiative, three additional clinics at two federally qualified health centers serving low-income patients in Milwaukee and Madison are expected to launch teleophthalmology programs later this year.

Right, feline corneal defect caused by a cat scratch. All images in this article are courtesy of COPLOW.



An Infinite Variety...

Imagine being the person who opens each day's mail at the Comparative Ocular Pathology Laboratory of Wisconsin (COPLOW) at UW-Madison. Okapi eyeballs from the Bronx Zoo? Check. A blue whale's eyeball, 4 inches in diameter? Also check.

At its inception in 1983, as part of the newly founded School of Veterinary Medicine, COPLOW was envisioned primarily as a diagnostic laboratory that would support veterinary ophthalmologists with specialized eye pathology services.

It has since evolved into the world's premier comparative ocular pathology laboratory, internationally recognized for its contributions to fundamental discoveries in both animal and human ocular diseases. Along the way, it has compiled one of the world's largest collections of vertebrate and invertebrate eyes.

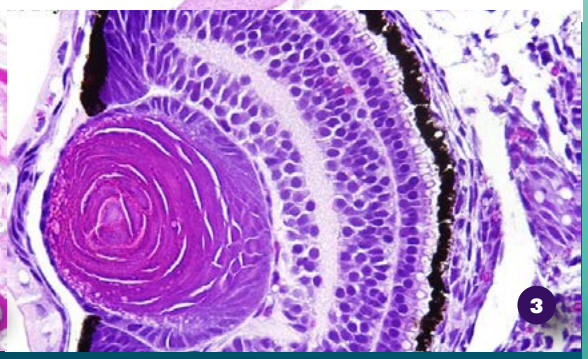
Animal eyes are startling in their variety, but common threads connect many animal species with humans. Dogs, cats, mice, and chickens can all get glaucoma. Fish, snakes, and frogs can all develop cataracts. The concept of a laboratory that focused on animal ocular diseases with the intent to better understand similar conditions in humans was wildly ahead of its time when COPLOW was founded. Visionary COPLOW founder Professor Richard Dubielzig, also an early McPherson ERI member, set the course for the lab's main translational research interests: naturally occurring ocular diseases in animals, animal models of ocular disease, and the comparative biology of glaucoma.

Glaucoma was a natural focus for COPLOW, as it is the leading cause of permanent vision loss in humans and domestic animals alike. Increased intraocular pressure, a major risk factor for glaucoma, results from dysfunction of the eye's drainage system, causing progressive optic nerve damage and blindness. COPLOW's basic science research focuses on abnormalities in the extracellular matrices

Congo River Fish

Komodo Dragon

Mouse



1 COPLOW members. Top, L-R, Heidi Clark; Richard Dubielzig, founding Director; Leandro Teixeira, COPLOW Director; and Megan Climans. Bottom, L-R, Liam Olds; Gillian Shaw; Kelsey Brakel. 2 In this lens rupture in a penguin, lens epithelial cells are proliferating and making new basement membranes. 3 Tadpole eye at 2.8 days.

(ECM), the "glue-like substances" of the eye which cause this dysfunction. Work in this area includes cats and rodents who have glaucoma at birth and dogs and cats who develop glaucoma later in life. These animals are identified through the COPLOW diagnostic service, whose research directly impacts the health and care of animal patients while also providing insights into human glaucoma. COPLOW partners with many McPherson ERI researchers on glaucoma and other eye diseases, including Dr. Gillian McLellan, who studies cats with congenital glaucoma, and Dr. Nader Sheibani, who tracks the impact of genetic abnormalities in mice who develop glaucoma.

COPLOW's unique expertise also spurs collaborations with researchers from a variety of institutions world-wide. Many of these efforts begin when an institution uses COPLOW's world-renowned diagnostic services, and proceed from there. Recent collaborations have included the development of a new intraocular hydrogel-sustained drug delivery system to treat and prevent human retinal diseases and vision loss with Dr. Jennifer Kang-Mieler from the Stevens Institute of Technology; a multidisciplinary project studying ocular abnormalities associated with Zika virus infection; and a project with Professor of Neurology Ian Duncan's lab using a dog model of multiple sclerosis (MS) to assess the usefulness of OCT scans (a form of retinal imaging) to monitor myelin loss and disease progression in MS patients.

And then there is that incredible collection of animal eyes, and the accompanying archived pathology samples and database, which serve as key tools in providing cutting-edge training in comparative ophthalmology and vision science to undergraduate, postdoctoral, and medical students. As the accompanying illustrations suggest, the quest to understand nature's variety is never-ending—but UW-Madison and COPLOW have accepted the challenge.

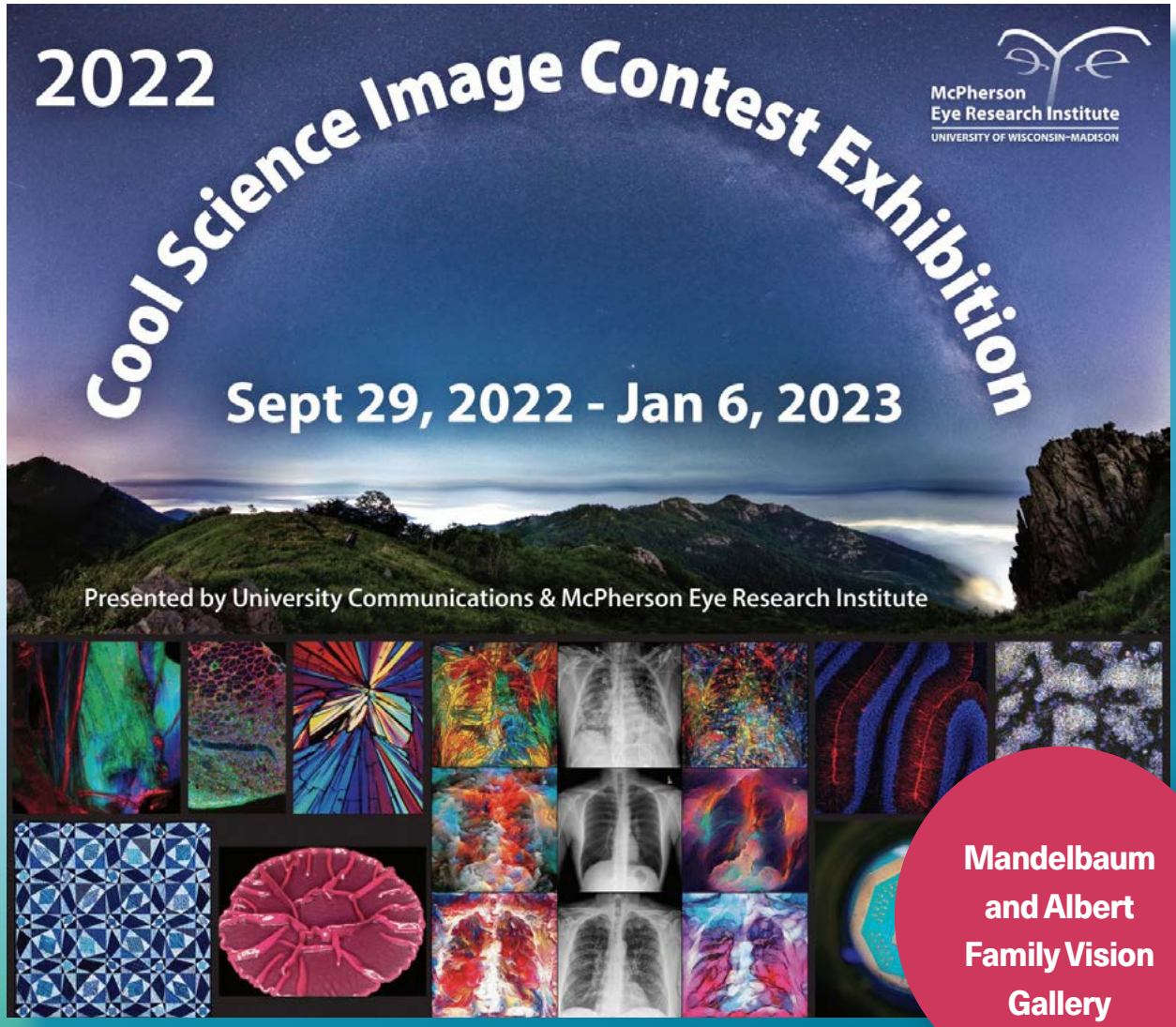
MCPHERSON ERI NOTES

ELICEIRI RECEIVES PRESTIGIOUS OPEN HARDWARE TRAILBLAZER FELLOWSHIP

Kevin Eliceiri, PhD, professor of medical physics and biomedical engineering and associate director of the McPherson ERI, was recently named an Open Hardware Trailblazer Fellow by the Open Source Hardware Association (OSHWA). The one-year fellowship provides funds to create a library of resources for others to utilize.

NATIONAL EYE INSTITUTE DIRECTOR MICHAEL CHIANG, MD, VISITS THE MCPHERSON ERI

The McPherson ERI hosted Michael Chiang, MD, for the 10th Annual McPherson Endowed Lecture on September 12th. Dr. Chiang gave a well-attended talk 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. More in our year-end report!



Mandelbaum and Albert Family Vision Gallery

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