Dear Friends of the McPherson Eye Research Institute,

2017 welcomed many new initiatives, including a grant program for vision research trainees, expanded vision science learning opportunities, and a visiting scholar program. We are also on the verge of announcing a first-of-its-kind Grant Summit Program, which is designed to assist our researchers in obtaining multimillion dollar federal grant support to accelerate their efforts to understand, preserve, and restore vision. The Grant Summit Program idea has drawn considerable interest, and you will be hearing more about it in future correspondence.

Year-end also provides an excellent opportunity to thank the people who contribute so much to the growth of the McPherson Eye Research Institute. This year, I’d particularly like to mention both our outgoing and incoming Associate Directors, two extraordinary scientists who have made the McPherson ERI an integral part of their research lives – and who have greatly strengthened the Institute in the process. Dr. Aki Ikeda, whose term as Associate Director culminated with his assumption of the Timothy William Trout Professorship in Eye Research, held the position since 2012. His dedication to the Institute has been unstinting, and his important work on the genetic basis of retinal aging and disease holds much promise for future therapeutics. The new Associate Director is Dr. Kevin Eliceiri, an internationally recognized investigator in medical imaging who is leading our charge to develop new ways to “see” the eye and retina. Dr. Eliceiri is a living embodiment of the scientist-as-collaborator, involved in many promising investigations both at UW-Madison and elsewhere. As Associate Director, he will assume the Walter H. Helmerich Research Chair and will take an active role in fostering our team-based research efforts.

Endowed positions such as the Timothy William Trout Professorship and the Walter H. Helmerich Research Chair are essential to our researchers. Such funding is critical in a time when research funding is more difficult to obtain than ever. We are fortunate to have nine such endowed positions, provided by the Retina Research Foundation and by Dr. Monroe and Sandra Trout. We continue to seek additional endowed positions in critical areas such as vision and engineering, and the psychology and neurology of vision, among others. On these first pages of our annual report, you’ll hear from our endowed faculty as to what these positions allow them to accomplish. I am grateful to each of these scientists for pushing the boundaries of vision research, with the goal of creating better diagnostics and therapeutics for people affected by vision loss.

Thank you for being part of our ongoing work, and for your help and inspiration.

David M. Gamm, MD, PHD
RRF Emmett A. Humble Distinguished Director
Sandra Lemke Trout Chair in Eye Research

Kevin Eliceiri, PhD
New Associate Director Kevin Eliceiri, holding the Retina Research Foundation Walter H. Helmerich Research Chair
Computational and Optical Approaches for Visualizing the Cellular Microenvironment of the Eye

“...The RRF Walter H. Helmerich Research Chair provides valuable resources in support of new research directions. This funding will advance the generation of key preliminary data for grant proposals and help initiate new collaborations in vision research and imaging of the eye. It is particularly gratifying to hold this Chair through the Retina Research Foundation, as I have admired their support for vision research in my years as a member and Leadership Committee member of the McPherson Eye Research Institute.”

Akihiro Ikeda, DVM, PhD
Past Associate Director Aki Ikeda, recipient of Timothy William Trout Professorship in Eye Research
Identification of Genetic Factors Affecting Aging of the Retina

“...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. The Timothy William Trout Professorship in Eye Research will help us dive further into these and other molecular mechanisms. For instance, we recently found that chondroitin sulfate modification of proteins is essential to maintain normal retina. Support from this professorship will allow a graduate student in my lab to focus research on identifying key proteins with chondroitin sulfate modification in the retina, which can be a therapeutic target for age-related retinal diseases.”

Cover design:
Farming Photoreceptors

ENDOWED CHAIRS AND PROFESSORSHIPS AT THE MCPHERSON EYE RESEARCH INSTITUTE
“Our overall research involves the effects of ischemia – the restriction of blood supply and resulting lack of oxygen and glucose – on the outer retina (the rods and cones). The Murfee Chair is allowing our research to expand in two important areas. It has enabled us to purchase equipment to better control the oxygen/air mixture in animal subjects (which ensures that ischemia is only produced in the experimental eye). It has also aided us in our attempts to develop a reliable model of branch retinal vein occlusion (BRVO). This will prove useful for testing new pharmaceuticals that target the retinal edema and ischemia associated with this condition.”

My research background is in kidney development and renal cyst formation, and more specifically the role that the Bcl-2 family of proteins play in these processes. During these studies I noted that certain kidney defects which occur in the absence of these proteins also occur in the retinal vasculature. Intrigued by these observations, I wanted to study the role these proteins play in retinal vascular development. These studies will give new insight into the regulation of ocular vascular homeostasis, and how the alteration of pathways under pathological conditions drives neovascularization. This knowledge will aid in development of new therapeutics for eye diseases with a neovascular component, such as diabetic retinopathy and ‘wet’ AMD.”

“The most exciting advances in science and engineering come from the interface of cross-disciplinary research and cross pollination of ideas from one field to another. However, breaking into a new field presents challenges—from developing collaborations, to securing funding, to recruiting personnel. This professorship has made it possible to meet these challenges, enabling me to build a lab and recruit trainees so that we can bring our expertise in biophotonics to bear on the field of vision science.”

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Vision Research Trainee Grant

The McPherson Eye Research Institute’s first grant opportunity for trainees—the Vision Research Trainee Grant—was established this year to encourage the next generation of vision scientists. These grants will advance vision research in McPherson ERI member groups by funding trainee research, giving graduate students and postdoctoral researchers experience writing grant applications, and augmenting their professional development. After competitive review, two one-year grant awards of $3000 each were funded by the Institute’s annual Cycle for Sight event, which raises money to support research by McPherson ERI members.

2017 Vision Research Trainee Grant recipients:
- Wei-Hua Lee, a postdoctoral researcher in Professor Aki Ikeda’s lab in the Department of Medical Genetics, who is pursuing a project to find “The molecular mechanism regulating mitochondrial dynamics through TMEM135.”
- Hilary Miller, a graduate student in Professor Vanessa Simmering’s lab in the Department of Psychology who, in collaboration with Professor Heather Kirkorian in the Department of Human Development and Family Studies, is exploring “The role of visual attention and language in spatial cognitive development.”

TOP: Heather Kirkorian, Hilary Miller, & Vanessa Simmering
BOTTOM: Wei Lee and Aki Ikeda

Visiting Scholar Opportunity

Interaction with researchers from other institutions is an important pathway to future scientific collaborations. The Visiting Scholar Award was created to facilitate collaborations or expert training by bringing an invited guest researcher to UW-Madison for a short, active stay in order to advance research goals. Scholar visits may include lab presentations, lectures, training using specific equipment or techniques, and basic research and writing collaborations. Proposals to invite scholars are submitted by McPherson ERI-member faculty and competitively reviewed.

In the 2017 academic year, two Visiting Scholars were brought to Madison:
- Shannon Ross-Sheehy, PhD (Department of Psychology, University of Tennessee-Knoxville) was hosted by Vanessa Simmering, PhD (Department of Psychology) in December, 2016. With Dr. Ross-Sheehy, Dr. Simmering and her lab group focused on the relationships among visual attention, visual memory, and other cognitive skills bridging infancy and early childhood. Together they crafted ways to assess attention and memory that can be used in multi-level developmental design, and held a roundtable discussion on behavioral assessments of visual cognition from infancy through adulthood.
- Alex Huang, MD, PhD (Department of Ophthalmology, Doheny Eye Institute, University of California, Los Angeles) was hosted by Gillian McLellan, BVMS, PhD (Ophthalmology and Visual Sciences) in August, 2017. In lab and clinical settings, Dr. Huang worked with Dr. McLellan’s group to refine imaging techniques using aqueous angiography and outflow pathway optical coherence tomography (OCT) in various animal models of glaucoma—precursor steps that may facilitate translation of the aqueous angiography technique to human glaucoma patients. In the Department of Ophthalmology & Visual Sciences, Dr. Huang gave a seminar for the glaucoma research group as well as a Grand Rounds presentation.

Vision Science Instructional Lectures

One of the goals of the McPherson ERI is to encourage researchers in widely varying fields to begin research in vision science. McPherson ERI Vision Science Instructional Lectures are intended to fill training gaps for those entering a new research domain and to provide background knowledge to support development of new collaborations. They offer foundational instruction in the fundamentals of vision for graduate students, postdocs, research scientists, faculty and staff in any department. In an introductory series of lectures offered this academic year, Dr. Christopher Murphy gave an overview of the architecture and function of the eye in three lectures on the “Functional Morphology of the Vertebrate Eye.” Dr. Murphy, a Board Certified Veterinary Ophthalmologist and Professor of Comparative Ophthalmology in the Schools of Veterinary Medicine & Medicine at the University of California-Davis, grounded his lectures in the morphology of both human and animal eyes. A longstanding member of the McPherson Eye Research Institute and Professor Emeritus at the School of Veterinary Medicine at UW-Madison, Dr. Murphy was welcomed back to campus for these informative and engaging 90-minute talks, held in February, May, and August 2017.
Gerard Xavier has been a counselor for 25 years, including his current job at Madison Area Technical College. There’s an upside to counseling students as a blind man. Some students tell him that they don’t feel judged, as he may not notice an attribute that they’ve felt judged on previously. “Counseling is one of those fields where you can do so much without vision,” he says. It took time, though, for Gerard to become optimistic. When he first started losing his sight, as a preteen in Kuala Lumpur, Malaysia, his doctor downplayed his condition. Only after moving to London for school and consulting the distinguished ophthalmologist Barrie Jay was he diagnosed with retinitis pigmentosa – and Jay’s assessment was bleak. Gerard was told not to hope for cures “because we’re so far away from that.” He moved to the States, hoping that research and treatment would be more advanced, and went to the University of Illinois at Chicago for treatment (getting his bachelor’s and graduate degrees at UW-Whitewater and UW-Madison). But hope was elusive, and for the better part of a decade he didn’t even bother going to an ophthalmologist.

In the early 2000s, Gerard became hopeful about potential technological adaptations, but nothing panned out at that time. A few years later he met a neighbor, Dr. David Gamm, who updated him on the promise of stem cell therapies. “He was very cautious,” Gerard recalls, “but psychologically it was a turning point in terms of optimism. The idea that there may be something that happens in my lifetime was incredibly encouraging and uplifting.” Since 2014, Gerard has ridden in Cycle for Sight on the Blind Take Off team, and has helped raise thousands of dollars for vision research. “It’s a great way to give back and really appreciate what Dave and all of you do,” he says, and notes how “every breakthrough that happens in stem cell research related to blindness…also has large-scale implications across the board. Every dollar that goes into research has a universal impact.”

It’s hard to imagine how Gerard even finds time to ride, given his full time job, his part-time real estate business, and his family time. He and his wife, LeAnn, and their two sons (Eashan, 20, and Krishan, 16) travel frequently – throughout Asia, as well as to Europe, various stateside destinations, and Canada – and their house remains a neighborhood gathering place. He has no useful vision left, occasionally a bit of light perception, but remains upbeat. “I really hold optimism that there will be a commercially viable, medically plausible solution to getting rid of blindness,” he says. “And if a solution could be arrived at that could stop or arrest RP – I think about young kids who get diagnosed with this – not to have blindness as an outcome would be so incredible.”

Dr. Kimberly E. Stepien is a medical retina specialist and serves as the director of the adult Inherited Retinal Degeneration Clinic at UW Health Ophthalmology, which was established in order to offer expanded services such as specialized examinations and testing, physician consultation, genetic counseling, imaging, lab work and information about ongoing clinical trials and current research about inherited eye diseases. She has a particular interest in inherited retinal disease, exploring how changes in our genetic makeup can result in degeneration of the retina, the nerve tissue we see with, and vision loss.

In her lab research, Dr. Stepien focuses on better understanding of retinal disease, including inherited retinal degenerations, through the use of ocular imaging and genetic testing. She has worked with a novel imaging technique called Adaptive Optics to image retinal disease on a cellular level, and is currently exploring vascular anomalies in inherited retinal degenerations using ocular coherence tomography angiography (OCTA). Her clinical work keeps her in close touch with potential therapeutic treatments for inherited retinal degenerations; she is now principal investigator on three clinical trials for choroideremia and X-linked retinitis pigmentosa. Recently relocated to UW-Madison, Dr. Stepien is a sterling example of the clinician-researcher whose multidisciplinary approach to understanding and treating eye disease is helping patients today.
Temporal dynamics of motion-based image segmentation. In this image, a river runs on the surface of a planet and bifurcates into two rivers as they flow to their distant destinations, mimicking the experimental findings of neural activity. Artistic design and rendering by Xiaofeng Zhu.

Temporal dynamics of motion-based image segmentation. In this image, a river runs on the surface of a planet and bifurcates into two rivers as they flow to their distant destinations, mimicking the experimental findings of neural activity. Artistic design and rendering by Xiaofeng Zhu.

Dr. Vikas Singh’s research deals with the design of algorithms for image analysis – the mining of useful information from images. One area of his work is motivated by applications in machine vision, so that images and video can be interpreted and meaningful information derived with little to no human intervention. Such algorithms will enable his lab to make sense of large amounts of image data on various photo sharing and media platforms, as well as the automated analysis of video data from both online platforms and handheld devices.

A significant portion of Singh’s methodological work in image analysis is driven by important scientific applications in neuroscience and neuroimaging. In these contexts the algorithms do not merely seek to mimic human perception, but instead are able to identify statistical patterns in the images not easily perceivable by human vision. For example, an ongoing NIH-funded collaboration with Sterling Johnson’s group in the Wisconsin Alzheimer’s Disease Research Center is exploring ways of statistically modeling how brains change (or age) over time, and how mathematical representations of changes in brain structure— together with various genetic factors—may identify individuals at increased risk for Alzheimer’s disease. In this project, Dr. Singh’s goal is to use the Artificial Intelligence methods his group is developing to better utilize MRI and other types of brain images when designing clinical trials for Alzheimer’s disease drugs and therapies.

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A turning point for Kelsey came when her mother taped a TV feature about runner Marla Runyan, the first legally blind athlete to compete in the Olympics. Runyan, who also has Stargardt disease, was shown teaching deaf and blind children, and Kelsey – a runner herself – had her “aha” moment. “How awesome would it be that I could fully relate to those students who have a visual impairment just like me?” Kelsey thought. (Years later, she talked with Runyan on the phone, and watched her compete in the Olympic trials).

Kelsey Tiradani

Stargardt disease, like many degenerative blinding diseases, progresses at different rates for different people. Kelsey Tiradani’s vision deteriorated “pretty quickly” after she was diagnosed at 13 – “especially in high school.” Twenty years later, she still recalls how difficult it was. Stargardt damages the macula of the retina, severely affecting central vision. Although Kelsey’s rate of loss has slowed in recent years, her central vision is limited, making everyday tasks extremely difficult.

“Sometimes I don’t recognize my own husband in a store,” she notes with a laugh. A turning point for Kelsey came when her mother taped a TV feature about runner Marla Runyan, the first legally blind athlete to compete in the Olympics. Runyan, who also has Stargardt disease, was shown teaching deaf and blind children, and Kelsey – a runner herself – had her “aha” moment. “How awesome would it be that I could fully relate to those students who have a visual impairment just like me?” Kelsey thought. (Years later, she talked with Runyan on the phone, and watched her compete in the Olympic trials).

Kelsey received her undergraduate degree from Wisconsin Lutheran College and was trained in the field of Visual Impairments at Northern Illinois University. Now a Teacher of the Blind and Visually Impaired in the Madison Metropolitan School District, Kelsey instructs students of varying visual impairments, ages, and abilities. They work on developing skills in the areas of assistive technology, braille, and advocacy to increase their level of independence. “I see so much resilience in my students,” she says. “I really struggled when I was first diagnosed, and I see my students having positive personalities, positive outlooks, positive dispositions. They really are an inspiration to me.”

Kelsey and her husband, Matthew – yes, they met on a blind date – formed Team Tiradani several years ago to ride in Cycle for Sight and raise funds for vision research. “I feel so fortunate that this research is going on right where I live, and it’s been an awesome experience meeting and collaborating with people in the vision field. It’s exciting!” (As is new parenthood; their son, Conner, is four months old.) “I’ve been diagnosed for 20 years – other people have been diagnosed for much longer – I know a cure is not going to happen within the next six months or one year but I’m hopeful, and it’s surreal to think that with all this research, it’s closer now than I ever thought.”
We are in the midst of a gene editing revolution. In the past few years, bioengineering advances like CRISPR-Cas9—which enables segments of a gene's DNA to be edited out and corrected replacement segments to be inserted—have now made precision gene editing directly within patient tissues feasible, with the goal not only of treatment, but of cures. Assistant Professor Krishanu Saha is working on genetic disorders that affect the eye, specifically in the retinal pigment epithelium (RPE), the layer that underlies and serves photoreceptor cells.

One of the limitations in gene therapy has been the safety issues inherent in viral delivery of genetic materials. Dr. Saha's approach sidesteps these limitations by using advances in biomaterials to generate non-viral, synthetic nanocarriers of gene editing machinery. These non-viral tools have been used in his lab to precisely correct pathogenic mutations within cultured cells. His lab has tethered donor DNA templates (red in the illustration above) to Cas9 proteins (green) to create an all-in-one gene editing tool at the nanoscale. This and other new tools should enable new types of genetic "surgery" in the eye with unprecedented precision.

Researcher

Krishanu Saha, PhD

Biomedical Engineering | College of Engineering
Wisconsin Institute for Discovery

Dr. Krishanu Saha has a passionate research interest in retinopathy of prematurity (ROP), a potentially blinding eye disease of abnormal vascular development in premature infants. In Dr. Mezu-Ndubuisi's neonatology practice, she sees the untoward effects of exposure of fragile developing organs to a cellular process called oxidative stress, and their resulting impact on neurodevelopmental outcomes in premature infants. Her research is directed toward characterizing ROP beyond abnormal vascular development, using novel in vivo retinal imaging techniques in live oxygen-induced retinopathy (OIR) mice. This model allows Dr. Mezu-Ndubuisi to more closely study retinal vasculature, structure and function. Her innovative work led to the use of in-vivo phosphorescence lifetime imaging to measure retinal vascular oxygen tension, as well as the use of fluorescein angiography—a medical imaging technique to quantitatively depict the unique phenotypical characteristics of retinal arteries, veins and capillaries during developmental maturity. Dr. Mezu-Ndubuisi's laboratory is currently investigating novel therapies for ROP and the underlying molecular and signaling mechanisms mediating their effects.

Researcher

Olachi Mezu-Ndubuisi, MD, OD

Neonatology & Newborn Nursery, Pediatrics | School of Medicine and Public Health

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Researcher

Dana K. Merriman, PhD

AcTech International Professor of Biology | University of Wisconsin-Oshkosh
Adjunct Research Professor of Ophthalmology & Visual Sciences | Medical College of Wisconsin

Ground squirrels are diurnal, vision-dependent rodents with a retina dominated by cones (85%), the photoreceptor cells responsible for color vision. Over the years they have been used to tease out different aspects of cone function and circuitry. The ground squirrel’s status as a wild animal complicates its use in biomedical research, so in 2003 Dr. Merriman set about learning how to breed the native Wisconsin species—the 13-lined ground squirrel (13-LGS)—in captivity. She has been successful in this endeavor, providing 13-LGS and their ocular tissues to the National Eye Institute since 2007, as well as to laboratories around the world. Because the 13-LGS is an obligate hibernator, Dr. Merriman has partnered with diverse laboratories that examine the means by which squirrel tissues tolerate the strenuous hypometabolic and hypoperfusing conditions that are imposed by deep torpor. Her 13-LGS have contributed important findings in lung, liver, blood, skeletal muscle, heart, kidney, and brain. Other collaborations have yielded novel aspects of viral gene incorporation and transposable element defense.

Despite this breadth of inquiry, Dr. Merriman remains at heart a vision researcher. She and her Master's student are working to describe pre- and post-natal retinal development in the 13-lined ground squirrel. She is also part of a multi-center effort, funded by the Foundation Fighting Blindness and headed by Drs. Carroll and Besharse of the Medical College of Wisconsin, to create a 13-LGS model of Usher Syndrome—a hereditary disorder that causes visual and auditory loss.

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Philanthropists

Ken Frazier
"I was inspired to join and remain on the board by its leadership (specifically, Doctors Dan Albert and David Gamm) and by its mission: "...to prevent and cure blindness," which is ambitious to say the least. I never dreamed that the McPherson ERI would come so far in such a brief amount of time – and during these years I have learned a great deal about why the Institute has been successful. The McPherson ERI's collaborative approach to research is a perfect fit for the Wisconsin Idea. It includes interdisciplinary scientists, engineers, and scholars from the UW community, Wisconsin, and worldwide. The partners have proven to be eager to engage in fruitful cooperation for such a noble purpose. "I can’t wait to see what happens next!"

David Walsh
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Rose Barrilhlet
Advisory Board Chair
MANDELBAUM & ALBERT FAMILY VISION GALLERY

BRIGHT SIGHTS – Six Ways of Seeing
January – May 2017
Showcasing works by six Wisconsin artists whose visual impairments inspire and enrich their art: Angelynn Brown, Alison Fortney, Ron Wendt, Rosemarie Fortney, Albert Schmiege, and Dan Sullivan. Presented in partnership with the Wisconsin Council of the Blind & Visually Impaired.

Do You See What See?
June – September 2017
Displaying drawings by children, youth, and adults – each created in response to questions asking how we “see” or visualize things in our heads.

2017 Cool Science Image Contest Winners
September – December 2017
Featuring winning images from UW-Madison scientists and students competing in UW Communications’ sixth annual Cool Science Image Contest.

5th Annual McPherson ERI Endowed Lecture
Shooting in the Dark: Maintaining cone function in retinal degenerations
held April 27, 2017
José-Alain Sahel, MD, PhD
Professor and Chairman of the Department of Ophthalmology
University of Pittsburgh Medical Center
Director of Institut de la Vision
Université Pierre et Marie Curie-Sorbonne Universités, Paris

9th Annual Vision Science Lecture
Virtual Reality Video
held October 12, 2017
Steven Seitz, PhD
Computer Science and Engineering
University of Washington
Team Director, Google Seattle
Cycle for Sight 2017 took place on Saturday, March 11th and once again was a great success, raising $53,000 for vision research at the McPherson ERI. More than 250 riders participated this year. Kenzi’s Team was the top fundraising team, with the Blind Take Off and Out of Sight teams in second and third place. Members from each of these teams helped publicize the event, and TV news stories featured Chip & Christy Kaufman and Annika Konrad from the Out of Sight team. Other teams that did very well included the Retinal Research Riders, Team Tiradani, and some teams new to Cycle for Sight – Isthmus Eye Care/Eye Ballurz, the Mad Rollin’ Dolls, and the Wisconsin Council of the Blind & Visually Impaired team. We’re grateful to all of our participants and volunteers, and hope to see everyone back in 2018!

Kenzi Valentyn, Tim and Nancy Valentyn’s daughter and the inspiration for Kenzi’s Team, passed away at 30 years of age on Monday, March 6th, 2017—five days before Cycle for Sight. Her courageous battle against a harsh degenerative disease, which included vision loss, had brought together and motivated her family and friends through years of Cycle for Sight rides. In Kenzi’s honor, her extraordinary extended family—including her parents and her brothers Brett and Connor—rode in Cycle for Sight on March 11th. A celebration of Kenzi’s life, attended by hundreds of family members and friends, was held at Monona Terrace the following Saturday. Kenzi was remembered by many for her strength, honesty, fearlessness, and sense of humor. Kenzi’s Team raised a remarkable $24,605 for vision research this year, and plans to ride again in 2018. We salute and thank them for their dedication to restoring sight to all.

For more information, or to register or donate to Cycle for Sight, visit vision.wisc.edu/cycle

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