

# MCPHERSON EYE RESEARCH INSTITUTE

## 2013 ANNUAL REPORT

## 2014 CALENDAR







## Mandelbaum & Albert Family Vision Gallery

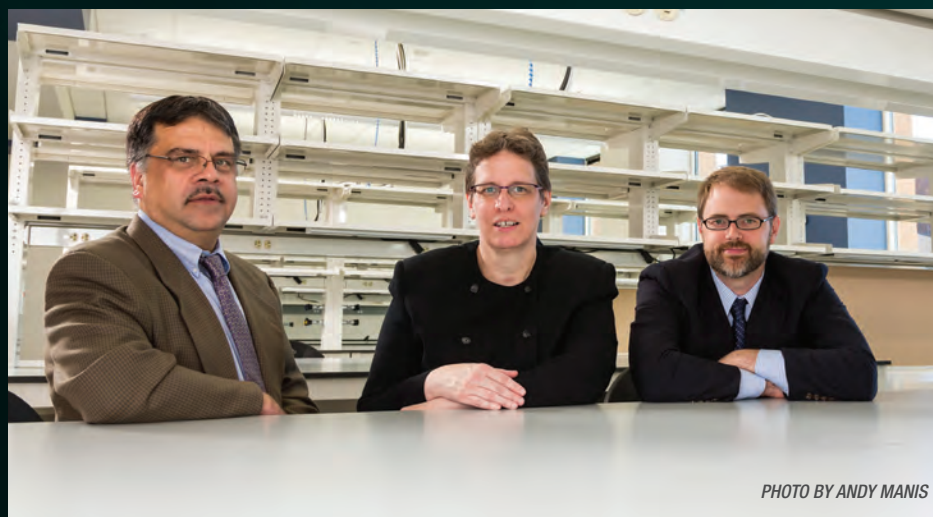


PHOTO BY ANDY MANIS

**TOP LEFT:** Dr. Jean Bennett, honored as the inaugural McPherson ERI Endowed Lecturer, with Dr. David Gamm. **TOP RIGHT:** Dr. Alice McPherson, MERI namesake and inspiration, with Founding Director Dr. Daniel Albert. **CENTER LEFT:** Vision Gallery sign for WIMR II. **BOTTOM:** WIMR II investigators (from left) Nader Sheibani, Christine Sorenson, and Jeremy Rogers.

# Dear Friends,

2013 has been a year of exciting growth for the McPherson Eye Research Institute, culminating this December with our occupancy of new laboratory and office space on the top floor of Tower II of the Wisconsin Institutes for Medical Research (WIMR II). We have talked about and anticipated this move for several years, and couldn't be more excited about it. It has been made possible through support from both donors and the many people who worked on the design, planning, and construction of some of the most advanced lab space in the world. We're very grateful to everyone for making this a reality.

Our lab space in WIMR II will be occupied by three outstanding McPherson ERI (MERI) researchers. Nader Sheibani, in the Department of Ophthalmology & Visual Sciences, studies abnormal blood vessel growth in the eye with the goal of developing treatments for age-related macular degeneration and other retinal illnesses. Christine Sorenson, in the Department of Pediatrics, investigates normal and pathogenic retinal vessel remodeling. Jeremy Rogers, in the Department of Biomedical Engineering, devises new optical instrumentation with a goal of advancing imaging methods for vision research. We are confident that this cluster of research perspectives will spark collaborative interactions among MERI members across the spectrum of vision science.

WIMR II will also be home to the Mandelbaum & Albert Family Vision Gallery, an art display space created with the help of MERI members and associates in the visual arts. The gallery is named for the families of David and Nathan Mandelbaum – longtime supporters of the Eye Research Institute – and our Founding Director Dr. Daniel Albert.

Growth continued this past year in the number of endowed chairs held within the McPherson ERI. In January, we were delighted to establish the Sandra Lemke Trout Chair in Eye Research as the result of a generous gift from Monroe and Sandra Trout; Sandra Trout is a UW-Journalism alumna. We are also thankful for the ongoing generosity of Dr. Alice McPherson and the Retina Research Foundation, who fully endowed the Daniel M. Albert Chair – capping the support of many donors who have helped develop this Chair over the past four years.

Our outreach and education efforts experienced considerable expansion this past year as well. One highlight among many was the inaugural McPherson ERI Endowed Lecture, given by Dr. Jean Bennett (University of Pennsylvania), a pioneer in gene therapy research for retinal diseases. Dr. Bennett epitomizes the type of researcher that fills the ranks of the McPherson ERI – dedicated, collaborative, and utterly focused on understanding key issues in vision research and the needs of the visually impaired.

We hope that you'll spend a few minutes with this report to learn more about some of these researchers, and to enjoy the remarkable images generated from their work. Their research holds the promise of improving many lives, and I'm honored to know and serve them.

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





## MCPHERSON EYE RESEARCH INSTITUTE ADVISORY BOARD 2012-2013

**DANIEL M. ALBERT, MD, MS**  
*Founding Director, McPherson ERI*

**ROSE BARROILHET**  
*Chair, McPherson ERI Advisory Board*

**DARRELL BEHNKE, JD**

**OSCAR C. BOLDT**

**PATRICIA BOLDT**

**DERILYN CATTELINO**

**ERIK CHRISTIANSON**

**KENNETH FRAZIER**

**BRUCE E. HARVILLE**

**EMMETT A. HUMBLE**

**ALICE R. MCPHERSON, MD**

**SHARON MADNEK**

**ALAN R. MORSE, JD, PHD**

**NELL R. RAY**

**HARRY ROTH, MD**

**DAVID G. WALSH, JD**

**MARILYN VANDERHOOF YOUNG**

## MCPHERSON EYE RESEARCH INSTITUTE LEADERSHIP COMMITTEE 2012-2013

**NANSI JO COLLEY, PHD**  
*School of Medicine and Public Health*

**RICHARD R. DUBIELZIG, DVM**  
*School of Veterinary Medicine*

**KEVIN W. ELICEIRI, MS**  
*Graduate School*

**DAVID M. GAMM, MD, PHD**  
*School of Medicine and Public Health*

**AKIHIRO IKEDA, DVM, PHD**  
*School of Medicine and Public Health*

**HONGRUI JIANG, PHD**  
*College of Engineering*

**ANDREA H. MASON, PHD**  
*School of Education*

**MARGARET J. MCFALL-NGAI, PHD**  
*School of Medicine and Public Health*

**SHIELA I. REAVES, MA**  
*College of Agricultural and Life Sciences*

**VANESSA R. SIMMERING, PHD**  
*College of Letters and Science*

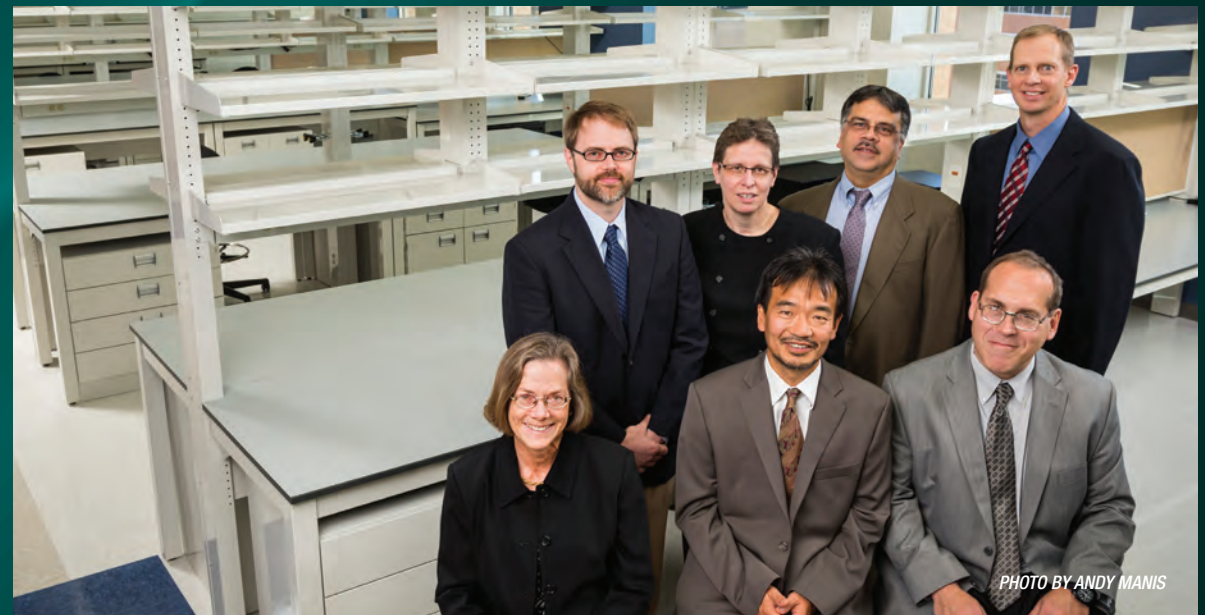


PHOTO BY ANDY MANIS

**TOP:** Advisory Board members including (L to R) Erik Christianson, Nell Ray, Darrell Behnke, Rose Barroilhet (Chair), Kenneth Frazier, and David Walsh tour the almost finished WIMR II laboratory space, led by Mark Wells, Assistant Dean for Facilities at the School of Medicine & Public Health (at right). **BOTTOM:** Lab occupants in the McPherson ERI's new space, along with McPherson ERI staff. **Back row L to R:** Jeremy Rogers, Christine Sorenson, Nader Sheibani, David Gamm; **front row L to R:** Gail Stirr, Akihiro Ikeda, Michael Chaim.



# 2013 MEMBERSHIP MCPHERSON EYE RESEARCH INSTITUTE

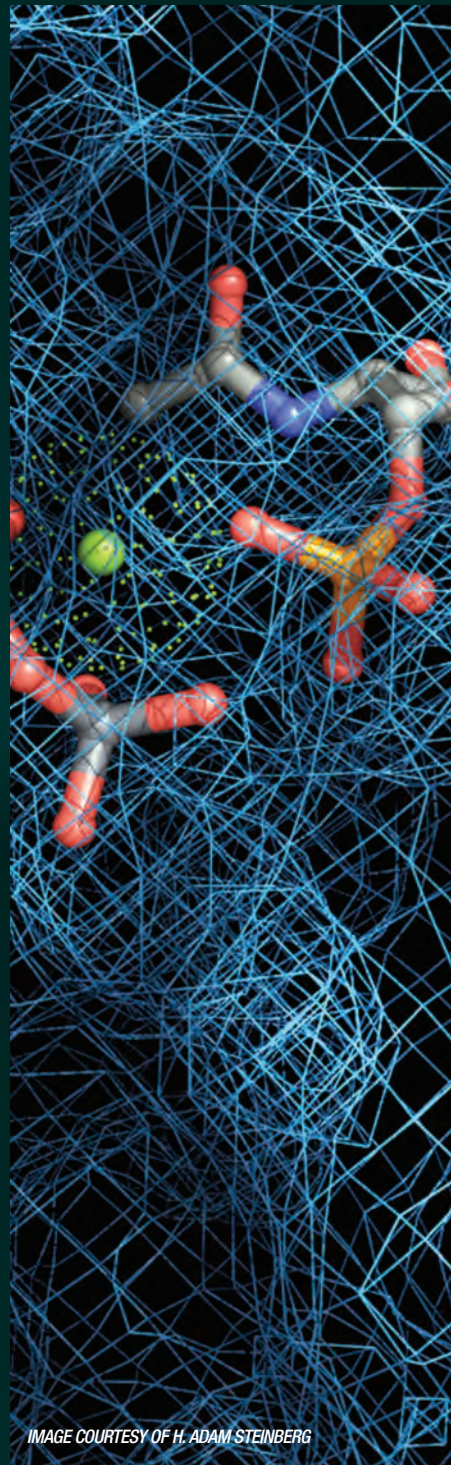


IMAGE COURTESY OF H. ADAM STEINBERG

**DANIEL M. ALBERT, MD, MS**  
Ophthalmology and Visual Sciences

**AIMEE ARNOLDUSSEN, PHD**  
Center for Clinical Knowledge Management  
UW Hospitals & Clinics

**AMIR H. ASSADI, PHD**  
Mathematics

**AMIR AZARI, MD**  
Ophthalmology and Visual Sciences

**NEAL P. BARNEY, MD**  
Ophthalmology and Visual Sciences

**MICHELE A. BASSO, PHD**  
Psychiatry & Biobehavioral Science  
University of California, Los Angeles

**BILLIE BECKWITH-COHEN, DVM, MBA**  
Pathobiological Sciences, Veterinary Medicine

**ELLISON BENTLEY, DVM**  
Surgical Sciences, Veterinary Medicine

**JAMES P. BLANCHARD, PHD**  
Engineering Physics

**BARBARA A. BLODI, MD**  
Ophthalmology and Visual Sciences

**M. DERIC BOWNDS, PHD**  
Zoology; Cell & Molecular Biology (Emeritus)

**CHRISTOPHER A. BRADFIELD, PHD**  
Oncology

**CURTIS R. BRANDT, PHD**  
Ophthalmology and Visual Sciences

**JILL H. CASID, PHD**  
Art History

**PAUL J. CAMPAGNOLA, PHD**  
Biomedical Engineering

**SURESH R. CHANDRA, MD**  
Ophthalmology and Visual Sciences

**MOO K. CHUNG, PHD**  
Biostatistics & Medical Informatics

**NANSI J. COLLEY, PHD**  
Ophthalmology and Visual Sciences

**ELLEN B. COOK, PHD**  
Ophthalmology and Visual Sciences

**YURI DANILOV, PHD**  
Biomedical Engineering

**RONALD P. DANIS, MD**  
Ophthalmology and Visual Sciences

**C. THOMAS DOW, MD**  
Ophthalmologist, Eau Claire, WI

**DORIS DUBIELZIG**  
Certified Mentor, Science Teachers

**RICHARD R. DUBIELZIG, DVM**  
Pathobiological Sciences, Veterinary Medicine

**FELICIA DUKE, DVM**  
Laboratory for Animal Medicine  
University of Michigan, Ann Arbor, MI

**IAN D. DUNCAN, BVMS, PHD, FRSE**  
Medical Sciences, Veterinary Medicine

**CHARLES R. DYER, PHD**  
Computer Sciences

**JANIS T. EELLS, PHD**  
Biomedical Sciences  
University of Wisconsin-Milwaukee

**KEVIN W. ELICEIRI, MS**  
Laboratory for Optical & Computational Instrumentation

**NICOLA J. FERRIER, PHD**  
Mathematics & Computer Science Division  
Argonne National Lab, Argonne, IL

**CATHERINE TADDY FICK**  
DVM Candidate, Veterinary Medicine

**MARSHALL FLAX, MS, CLVT, COMS**  
Vision Rehabilitation Services  
Wisconsin Council of the Blind & Visually Impaired

**DAVID M. GAMM, MD, PHD**  
Ophthalmology and Visual Sciences

**ALIREZA GHAFFARIEH, MD**  
Ophthalmology and Visual Sciences

**MICHAEL L. GLEICHER, PHD**  
Computer Sciences

**TIMOTHY M. GOMEZ, PHD**  
Neuroscience

**JUSTIN GOTTLIEB, MD**  
Ophthalmology and Visual Sciences

**C. SHAWN GREEN, PHD**  
Psychology

**ANNE E. GRIEP, PHD**  
Cell and Regenerative Biology

**YEVGENYA GRINBLAT, PHD**  
Zoology and Neuroscience

**LIAN-WANG GUO, PHD**  
Surgery

**ZAFUR GUREL, PHD**  
Ophthalmology and Visual Sciences

**REBECCA PERKINS HARRINGTON, MS**  
Industrial Engineering – Human Factors  
PhD Candidate

**CAROL J. HIRSCHMUGL, PHD**  
Physics  
University of Wisconsin-Milwaukee

**XIN HUANG, PHD**  
Neuroscience

**YIJUN HUANG, PHD**  
Ophthalmology and Visual Sciences

**LARRY D. HUBBARD, MAT**  
Ophthalmology and Visual Sciences (Emeritus)

**AKIHIRO IKEDA, DVM, PHD**  
Medical Genetics

**SAKAE IKEDA, DVM**  
Medical Genetics

**MICHAEL S. IP, MD**  
Ophthalmology and Visual Sciences

**NASIM JAMALI**  
Ophthalmology and Visual Sciences  
PhD Candidate

**HONGRUI JIANG, PHD**  
Electrical and Computer Engineering

**RONALD E. KALIL, PHD**  
Ophthalmology and Visual Sciences

**MOZHGAN REZAEI KANAVI, MD**  
Ophthalmology and Visual Sciences

**PAUL L. KAUFMAN, MD**  
Ophthalmology and Visual Sciences

**THERESA M. KELLEY, PHD**  
English

**ADAM L. KERN, PHD**  
East Asian Languages and Literature

**HEATHER L. KIRKORIAN, PHD**  
Human Development and Family Studies

**BARBARA E. K. KLEIN, MD, MPH**  
Ophthalmology and Visual Sciences

**RONALD KLEIN, MD, MPH**  
Ophthalmology and Visual Sciences

**APARNA LAKKARAJU, PHD**  
Ophthalmology and Visual Sciences

**VIVIAN LEE, MD**  
Ophthalmology  
University of Pennsylvania, Philadelphia, PA

**LEONARD A. LEVIN, MD, PHD**  
Ophthalmology and Visual Sciences

**SARA J. LILIENSIEK, PHD**  
ibidi, LLC  
Verona WI



# 2013 MEMBERSHIP MCPHERSON EYE RESEARCH INSTITUTE

**THOMAS R. MACKIE, PHD**  
Medical Devices, Morgridge Institute for Research  
Medical Physics

**JULIE A. MARES, PHD**  
Ophthalmology and Visual Sciences

**ANDREA H. MASON, PHD**  
Kinesiology

**MARGARET J. MCFALL-NGAI, PHD**  
Medical Microbiology and Immunology

**GILLIAN J. MCLELLAN, PHD,  
DECVO, DACVO**  
Ophthalmology and Visual Sciences  
Surgical Sciences, Veterinary Medicine

**DANA K. MERRIMAN, PHD**  
Biology and Microbiology  
University of Wisconsin-Oshkosh

**OLACHI MEZU-NDUBUISI, OD, MD**  
Pediatrics

**PAUL E. MILLER, DVM**  
Surgical Sciences, Veterinary Medicine

**LEIGH ANN MROTEK, PHD**  
Kinesiology  
University of Wisconsin-Oshkosh

**CHRISTOPHER J. MURPHY, DVM, PHD**  
Surgical and Radiological Sciences  
University of California, Davis, CA

**BILGE MUTLU, PHD**  
Computer Sciences

**PAUL F. NEALEY, PHD**  
Institute for Molecular Engineering  
University of Chicago, Chicago IL

**ROBERT W. NICKELLS, PHD**  
Ophthalmology and Visual Sciences

**T. MICHAEL NORK, MD**  
Ophthalmology and Visual Sciences

**CAMERON F. PARSA, MD**  
Ophthalmology and Visual Sciences

**BIKASH R. PATNAIK, PHD**  
Pediatrics

**TRACY PERKINS, MPH**  
The Emmes Corporation

**DONNA M. PETERS, PHD**  
Pathology and Laboratory Medicine

**SUZANNE M. PEYER, PHD**  
Medical Microbiology and Immunology

**M. JOSEPH PHILLIPS, PHD**  
Waisman Center

**DE-ANN PILLERS, MD, PHD**  
Pediatrics

**ARTHUR S. POLANS, PHD**  
Ophthalmology and Visual Sciences

**LUIS C. POPULIN, PHD**  
Neuroscience

**BRADLEY R. POSTLE, PHD**  
Psychology; Psychiatry

**GORDANA RACA, MD, PHD, FACMG**  
Pathology and Laboratory Medicine  
University of Chicago Medical Center, Chicago IL

**MATTHEW F. RAREY**  
Art History, PhD Candidate

**SHIELA I. REAVES, MA**  
Life Sciences Communication

**JEREMY D. ROGERS, PHD**  
Biomedical Engineering

**BAS ROKERS, PHD**  
Psychology

**ERICA E. ROSENBAUM, PHD**  
Ophthalmology and Visual Sciences

**ARNOLD E. RUOHO, PHD**  
Neuroscience

**ERIN M. SCHAMBURECK**  
Design Studies, MFA Candidate

**DIETRAM A. SCHEUFELE, PHD**  
Life Sciences Communication

**CHARLES S. SCHOBERT, PHD**  
Pathobiological Sciences, Veterinary Medicine

**RODNEY SCHREINER, PHD**  
Chemistry

**ERIN SCOTT, VMD**  
Comparative Ophthalmology, Veterinary Medicine

**DOLORES J. SEVERTSON, RN, PHD**  
School of Nursing

**BASSAM Z. SHAKHASHIRI, PHD**  
Chemistry

**NADER SHEIBANI, PHD**  
Ophthalmology and Visual Sciences

**ANNA L. SHEN, PHD**  
Oncology

**JANE Y. SHEPARD, MA**  
Academic Affairs, SMPH

**DUSKA J. SIDJANIN, PHD**  
Cell Biology, Neurobiology and Anatomy  
Medical College of Wisconsin, Milwaukee WI

**VANESSA R. SIMMERING, PHD**  
Psychology

**RUCHIRA SINGH, PHD**  
Waisman Center

**VIKAS SINGH, PHD**  
Biostatistics & Medical Informatics  
Computer Sciences

**AHNA R. SKOP, PHD**  
Genetics

**CHRISTINE M. SORENSON, PHD**  
Pediatrics

**LINDSEY SPENCER, MS**  
Wicab, Inc.  
Middleton WI

**JAMES L. STAHL, PHD**  
Ophthalmology and Visual Sciences

**H. ADAM STEINBERG, DBA**  
artforscience

**LEANDRO B. C. TEIXEIRA, DVM, MS**  
Pathobiological Sciences, Veterinary Medicine

**BAOHE TIAN, MD**  
Ophthalmology and Visual Sciences

**KIMBERLY A. TOOPS, PHD**  
Ophthalmology and Visual Sciences

**DANIEL J. UHLRICH, PHD**  
Neuroscience

**JAMES N. VER HOEVE, PHD**  
Ophthalmology and Visual Sciences

**DONNA L. WEIHOFEN, RD, MS**  
WISC-TV Channel3000.com

**TOM C. T. YIN, PHD**  
Neuroscience

**CHUNMING ZHANG, PHD**  
Statistics

**LI ZHANG, PHD**  
Computer Sciences

**XIAOJIN (JERRY) ZHU, PHD**  
Computer Sciences

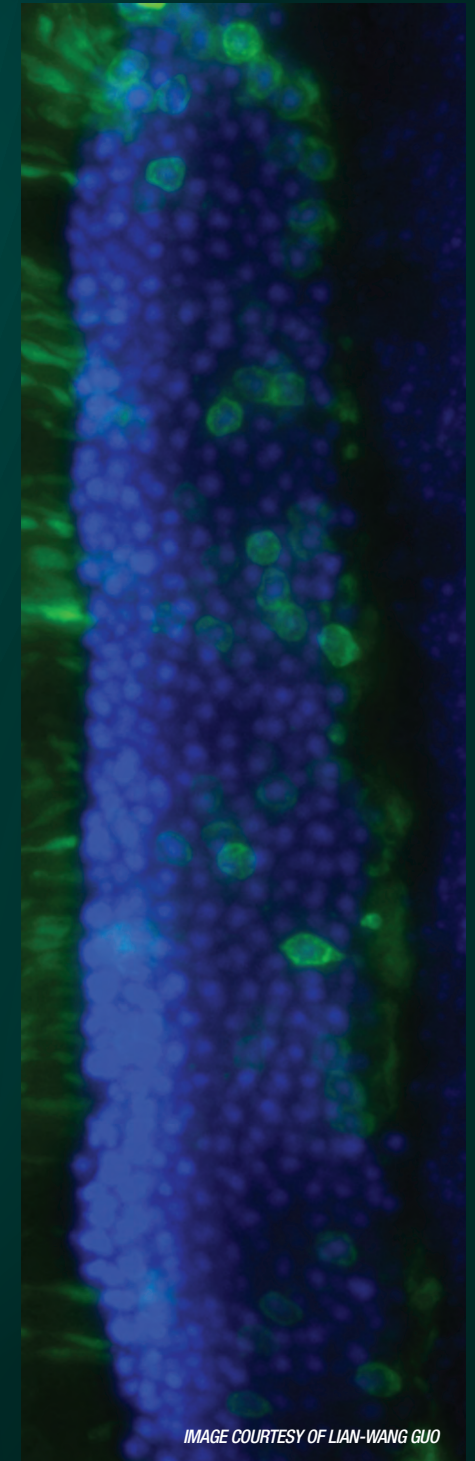


IMAGE COURTESY OF LIAN-WANG GUO



## FEATURED FACULTY AND SCIENTISTS AT MCPHERSON EYE RESEARCH INSTITUTE



### AKIHIRO IKEDA, DVM, PHD

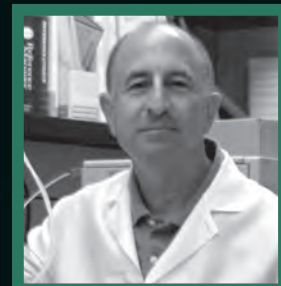
RRF WALTER H. HELMERICH CHAIR, ASSOCIATE DIRECTOR

Dr. Akihiro Ikeda, associate professor in Medical Genetics, and his lab are focused on understanding the genetic and molecular mechanisms that cause age-dependent retinal abnormalities and their association with retinal diseases. For age-dependent diseases to manifest themselves across a lifespan of development, there must be tight association between the disease-causing mechanisms and cellular changes that occur with normal aging. The retina, due to its well-organized layered structure, offers an excellent model to monitor such age-dependent changes in the neuronal tissue.

Recent studies in mice and humans have shown that the normal aging retina goes through pathological changes, including the formation of abnormal photoreceptor synapses and gradual photoreceptor cell degeneration. Similar retinal abnormalities are observed in a number of

age-dependent retinal degenerative diseases. Using mouse genetics as a tool, the Ikeda lab determined the progression of age-dependent retinal changes — noting differences in the severity of these changes between two strains of mice, and concluding that genetic factors indeed do affect age-dependent retinal abnormalities. By taking full advantage of mouse genetics resources, the lab intends to efficiently map and identify these gene mutations leading to early onset of aging phenotypes in the mouse retina, even when multiple factors are involved.

The identification of specific modifier genes affecting the severity of age-dependent synaptic abnormality in the mouse retina will provide entry points into the molecular mechanisms regulating the aging process. These modifier genes may be involved in the retinal regulation of oxidative stress, which is considered a major contributor to the aging process in general. Ultimately, Dr. Ikeda hopes to prove the feasibility of this genetic approach, which can potentially be applied to a larger study to identify genes regulating other aspects of retinal aging. Elucidating the molecular mechanisms causing common age-dependent retinal abnormalities will enhance our understanding of age-dependent retinal diseases.



### ARTHUR S. POLANS, PHD

RRF KATHRYN AND LATIMER MURFEE CHAIR

Unwanted blood vessels are a component of many different human diseases; the formation of these new blood vessels from existing ones is a process referred to as angiogenesis. Considerable research is devoted towards understanding the molecular mechanisms regulating angiogenesis as well as the discovery and development of new drugs to treat these often leaky, new blood vessels. Diabetic retinopathy, exudative or “wet” age-related macular degeneration (AMD), and retinopathy of prematurity are just a few of the diseases of the eye with blood vessels that contribute to visual impairment or

blindness. Ocular tumors as well as other types of solid cancers also require new blood vessels to grow and to disseminate to other regions of the body. Eye tumors not only impair vision, but their metastases can be fatal.

To inhibit the growth of undesirable blood vessels that characterize disease states, Professor Arthur Polans (Ophthalmology and Visual Sciences) and his lab are focusing research on a subset of natural, non-toxic plant



### DAVID M. GAMM, MD, PHD

RRF EMMETT A. HUMBLE DISTINGUISHED DIRECTOR  
SANDRA LEMKE TROUT CHAIR IN EYE RESEARCH

Retinal diseases that cause degeneration of photoreceptors and retinal pigment epithelium (RPE) are a significant cause of visual loss. The ability to produce stem cells from adult human tissue (which are termed “induced pluripotent stem cells,” or iPSCs) provides an essential source of biological material for studying retinal disease and developing cell-based treatments for blinding disorders. Dr. David Gamm (Ophthalmology and Visual Sciences) and his lab group focus on investigating events that occur within stem cells as they decide to become retinal cell types (e.g., photoreceptors), and using these retinal cells for rescue or replacement therapies for retinal degenerative diseases. To meet these goals, the lab has developed methods to direct induced pluripotent stem cells to become retina. This in turn allowed them to create cell-based

laboratory models of human retinal degenerative diseases and begin transplantation experiments.

By understanding the behavior of these cell types, they hope to optimize strategies to delay or reverse the effects of inherited and acquired eye diseases such as retinitis pigmentosa and macular degeneration.

In 2013 the Gamm lab published an article describing the first iPSC “disease-in-a-dish” model of a human macular degenerative disease (Best disease). Using this novel system, lab researchers gained important insights into the disease, which they are now using to develop pharmacological treatment strategies. Lab research also extended into the realm of stem cell transplantation. His lab remains actively involved in the pursuit of hiPSC-based therapies for retinal degenerative diseases, and recently published a study that addressed issues related to the clinical production of RPE cells from iPSCs.

Funding was awarded this year from the Foundation Fighting Blindness to produce bilayered (RPE + photoreceptors) outer retinal constructs from immune-matched “super donor” hiPSC lines for future use in cell-based therapies for retinal degenerative diseases. It is Dr. Gamm’s hope that these and other efforts that now engage his lab will prove beneficial to patients with outer retinal degenerations in the foreseeable future.

products. They have determined that these natural products instigate specific calcium signals in activated endothelial cells which comprise new blood vessels; these calcium signals then inhibit endothelial cell division and migration and their ability to form vessels. Further, the Polans lab has shown that the delivery of low levels of these plant products inhibits the development of new vessels in a rodent model of choroidal neovascularization which resembles the wet form of AMD.

By understanding the mechanism of action of these natural products, the lab is now able to design new drugs for the treatment of wet AMD, with improved properties that will allow their delivery by intravenous injection or through consumption. This compares favorably with current treatments using other agents which require injections into the eye. Based on their initial findings, the Polans group is also modifying their synthesized agents to be more resistant to metabolic processes that otherwise would limit their bioavailability in humans.

By enhancing bioavailability, they are making the drugs more effective.



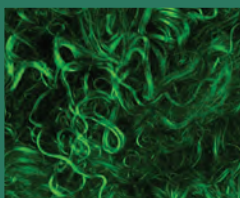
## FEATURED FACULTY AND SCIENTISTS AT MCPHERSON EYE RESEARCH INSTITUTE



### KEVIN W. ELICEIRI

DIRECTOR, LOCI

In his many interactions with various departments and institutes at UW-Madison, Kevin Eliceiri epitomizes the collaborative nature of the McPherson ERI. As director of the Laboratory for Optical and Computational Instrumentation (LOCI) – a federally funded biophotonics laboratory with the mission of developing new optical and computational instrumentation for live cell imaging – he is at the forefront of cutting-edge work in medical imaging techniques. As an investigator in the Graduate School's Laboratory of Molecular Biology and in the Morgridge Institute for Research and Wisconsin Institute for Discovery, he collaborates with top researchers in many areas.



3D stack of collagen in sclera of human eye (SHG image)

Currently, Eliceiri is focusing on the development of novel optical imaging methods and instrumentation for investigating cell signaling and cancer progression, and the development of software for multidimensional image informatics. Vision is a driving theme in his research. He has long been interested in how to capture and visualize multidimensional-based phenomena, and in designing tools that best allow for human interpretation of 3D biological events.

Much of this work is based on his interest in the role of the collagen-rich extracellular matrix (ECM) in normal and abnormal disease function, including

the part it plays in breast cancer and cardiac disease. Through MERI member collaborations, he has become very interested in discerning how collagen composition might be involved in the pathology of the eye. With members Richard Dubielzig and Leandro Teixeira of the Comparative Ocular Pathology Laboratory, he has been investigating the differences and similarities in corneal anatomy between terrestrial and aquatic animals. Eliceiri also works with MERI members David Gamm and Jeremy Rogers, examining the role of collagen makeup in macular degeneration. Early work using advanced techniques such as second harmonic generation (SHG) to image the sclera of the human eye has been successful; they are now focused on imaging the Bruch's membrane and other membranes of the eye for collagen composition changes.



### MARGARET J. MCFALL-NGAI, PHD

MEDICAL MICROBIOLOGY AND IMMUNOLOGY

The McFall-Ngai laboratory has two major focuses: 1) the influence of beneficial bacteria on health and 2) the 'design' of tissues that interact with light. These seemingly disparate areas of research come together with the symbiotic association between the Hawaiian bobtail squid and its luminous bacterial partner, *Vibrio fischeri*. The animal is a night-active predator, using the light produced of their bacterial partner in its camouflage. Specifically, the squid, which hangs in the water column while hunting, emits ventral luminescence to match down-welling moonlight and starlight so that predators on the sea floor cannot look upward and see its silhouette.



The symbiotic organ, or light organ, is remarkably convergent with the eye. Instead of receiving light, it emits light; but it modulates the light with cornea, lens, tapetum, and choroid analogues. In studies of the light organ tissues that modify light, Dr. McFall-Ngai and her lab have found that these elements, to function, use the same biochemistry as the eye. For example, the 'lens' of the light organ, although muscle derived, shares the same protein, an aldehyde dehydrogenase, as a crystallin; in both eye and light organ, the lens produces crystallin proteins at high concentrations to refract light. The animal controls the amount of light emitted.

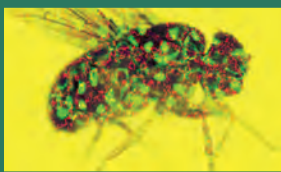
The lab has asked: 'How do they see this light, when the light organ is distant from the eye?' Their research showed that the light organ has all the components of the visual transduction cascade, including rhodopsin, rhodopsin kinase, and arrestin, and the tissues were physiologically capable of responding to a light stimulus in a similar manner to that of the eye. Thus, the light organ 'sees' the light that it makes. Recently published results show that, during development, the light organ expresses the proteins that are conserved and essential for the development of eyes in animals. Using the 'experiments' that nature has done through evolutionary selection, the McFall-Ngai lab seeks to shed light on shared properties in the form and function of tissues that interact with light.



### NANSI J. COLLEY, PHD

RRF M. D. MATTHEWS RESEARCH PROFESSOR

The long-term objective of Professor Nansi Colley's lab, in the department of Ophthalmology and Visual Sciences, is to understand the molecular genetics of hereditary human retinal diseases, such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD). Human RP and AMD are highly complex diseases with multiple subtypes, each with a distinct genetic and biochemical basis. This complexity, along with the limited availability of suitable tissues from RP and AMD patients and the wealth of *Drosophila* genome knowledge, makes use of the fruit fly a powerful animal model for studying inherited retinal degeneration disorders.



Unraveling the basic mechanisms of protein biosynthesis, transport, and assembly required for vision is a process demanding detailed tracking of cellular activities. Protein assembly and transport are error-prone processes.

In a normal sequence, the cell must ensure that a variety of steps occur correctly: protein translocation, glycosylation, folding, assembly, quality control, transport and targeting. A malfunction in any of these steps can lead to disease-producing pathology in tissues and cell death. The Colley lab focuses on two particular aspects of protein processing and transport: the first is the role of a group of proteins termed SNARE proteins in transport of rhodopsin; the second is the family of enzymes called mannosidases and their key roles in trimming carbohydrates during rhodopsin biosynthesis. (The protein rhodopsin is paramount because, in the retina, it is responsible for capturing light for vision).

Dr. Colley's lab has discovered important links between errors in these processing and transport steps and retinal degeneration. Their discoveries in *Drosophila* are used to screen a highly defined set of human AMD and RP pedigrees for similar defects. Dr. Colley anticipates that this work will greatly impact our understanding of the fundamental mechanisms of protein processing and will also provide important insights into retinal diseases such as RP and AMD.



## FEATURED FACULTY AND SCIENTISTS AT MCPHERSON EYE RESEARCH INSTITUTE



### BILGE MUTLU, PHD

DIRECTOR, HUMAN-COMPUTER INTERACTION LABORATORY

A key research objective at the Human-Computer Interaction Laboratory is the development of virtual and robotic agents that afford natural, intuitive, and effective interactions with people. To achieve this goal, assistant professor Bilge Mutlu (Computer Sciences) and his lab build computational models of human behavior from observations of human interactions, enabling them to simulate humanlike behaviors in these agents. Achieving humanlike gaze behavior has been a particular focus of this research, as gaze plays a key role in human interactions. To date, in collaboration with MERI member Michael Gleicher (Computer Sciences), the Mutlu lab has built a number of models for controlling the eyes, the head, and body orientation of artificial agents from observations of human data or findings from human and primate neurophysiology.



The lab's most recent work seeks to model the role that gaze plays in instructional scenarios. To build such a model, they developed a task in which an instructor teaches a student how to make a sandwich, and then created a dual mobile eye-tracking setup that captures the gaze targets of both teacher and student. This task and equipment setup has uniquely enabled the Mutlu lab to model the interplay between the gaze behaviors of the two parties engaged in the interaction.

For instance, they found two key uses of gaze in instruction: (1) the instructors supplemented their teaching with gaze cues directed toward objects of interest to clarify what objects they were referring to; and, (2) following an instruction, the instructors monitored the students' gaze behavior in order to assess their understanding of the teaching, which would be indicated by whether or not they gazed toward the objects to which the instructor referred. The lab is currently building an instructional virtual agent that will similarly use its gaze to convey information, as well as to follow the gaze of its user – assessing the user's understanding of the information. Dr. Mutlu expects agents and robots that use his lab's gaze model will serve as more effective instructors.



### JEREMY D. ROGERS, PHD

RRF EDWIN AND DOROTHY GAMEWELL PROFESSOR

Spectral scattering, although long-studied as a scientific phenomenon, has only recently shown promise as a method for studying the eye. Jeremy Rogers, assistant professor in Biomedical Engineering, sees tremendous potential in the development of spectral scattering techniques and tools for non-invasive study and screening of eye diseases, including age-related macular degeneration.

To understand spectral scattering, consider the question: Why is the sky blue? Used for centuries by countless children to puzzle parents, this question had no rigorous answer until Lord Rayleigh refined his theory of scattering in the late 1800's. His work showed that light scattered from very small particles, like nitrogen and oxygen molecules in the atmosphere,

depends strongly on the wavelength. Shorter blue wavelengths scatter much more strongly than longer red wavelengths. Blue light is thus scattered by the atmosphere while red light travels through it. The result is that the daytime sky appears blue, while a sunset appears red (when the sun is low in the sky, sunlight travels through enough atmosphere that most of the blue light is scattered, with only the un-scattered red light reaching the eye).

Cells and tissues that make up our bodies also scatter light; but in the body, scattering is caused not by particles, but by continuous variations in the way light refracts from water, lipids, proteins, and other molecules that make up cells, organelles, and extracellular matrix (ECM). By precisely measuring this scattering within tissues, subtle changes in tissue nano-architecture can be quantified – changes with great potential for disease diagnostics.

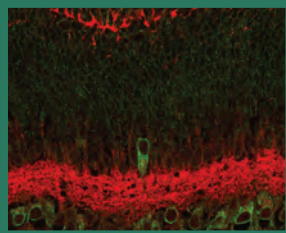
Spectral scattering techniques are remarkably sensitive to changes in tissue that cannot even be resolved with microscopy. The technology is currently being developed for cancer screening, for instance, where changes in nuclear size, chromatin texture, and alterations of the ECM are associated with risk of many types of cancer. The Rogers lab, in collaboration with other McPherson ERI investigators, aims to apply these methods in the study of retinal disease.



### ARNOLD E. RUOHO, PHD

RRF EDWIN AND DOROTHY GAMEWELL PROFESSOR (ENDED JUNE 2013)

Many McPherson ERI researchers investigate aspects of genetics, cell, or molecular biology that have broad implications not only for vision, but for multiple areas of pathology. Neuroscience Professor Arnold Ruoho, who studies cellular stress, is a case in point.



Some diseases that occur in the eye (glaucoma) and in spinal nerves that control muscles (Lou Gehrig's Disease or ALS) are due in part to cell death resulting from increased levels of oxidative stress. Using a mouse model, the Ruoho lab and its collaborators have discovered a naturally occurring compound, derived from the essential amino acid tryptophan, which increases the activity of a special protein called the Sigma-1 receptor.

This natural compound, DMT (N, N-Dimethyltryptamine) – together with the Sigma-1 receptor – may enhance cell survival under various neurodegenerative conditions. With MERI member Lian-Wang Guo, assistant professor of Surgery, Ruoho confirmed that the Sigma-1 receptor stabilizes proteins and reduces formation of destructive forms of oxygen and nitrogen within mouse retinal ganglion cells and mouse spinal cord motor neurons.

The Ruoho lab has found the enzyme that makes the compound DMT to be co-localized with the Sigma-1 receptor in the ganglion cells of the retina, as well as in the motor neurons of the spinal cord. These observations may facilitate the discovery of new drugs that increase the activity of this enzyme, and/or the activity of the Sigma-1 receptor – an essential step in advancing the treatment of human neurodegenerative diseases.



## FEATURED FACULTY AND SCIENTISTS AT MCPHERSON EYE RESEARCH INSTITUTE



### CHRISTINE M. SORENSON, PHD

RRF DANIEL M. ALBERT CHAIR

Christine Sorenson (Pediatrics) and her lab conduct work in both retina and kidney, organs in which the modulation of apoptosis (naturally occurring programmed cell death) is a critical process during development and pathogenesis of various disease states. With specific focus on two proteins – Bcl-2, which prevents cell death, and Bim, which facilitates it – the Sorenson lab seeks to understand the roles played by each. In the retina, these proteins affect cell death during retinal blood vessel growth in newborns, as occurs in retinopathy of prematurity (ROP). They are also involved in the abnormal blood vessel growth that characterizes age-related

macular degeneration (AMD). Both ROP and AMD are major causes of blindness in the United States, and the underlying mechanisms remain poorly understood. Sorenson works in close collaboration with MERI member Nader Sheibani to study how vascular development and function affect these diseases.

In the kidney, Dr. Sorenson has discovered that perhaps as a result of abnormal blood vessel growth, mice deficient in Bcl-2 develop renal hypoplasia/cystic dysplasia; the human parallel of this disorder is the second leading cause of kidney transplantation in children. Research in the Sorenson laboratory exploits their unique ability to study both retinal and kidney developmental changes and to isolate blood vessel cells from transgenic mice to study these organs in tandem. Sorenson's novel research has demonstrated that the presence of Bcl-2 and Bim proteins not only impact cell death, but also many other cell-specific functions. Alterations in these cellular functions may lead to abnormal retinal and kidney development and various disease states.

The knowledge gained from these studies will allow a better understanding of the regulatory mechanisms in these organs; understanding their alteration with various pathologies will aid the design of treatment modalities to intervene at earlier stages of these diseases, preventing their development and progression.



### VANESSA R. SIMMERING, PHD

DEPARTMENT OF PSYCHOLOGY

From the moment of birth, humans use vision to learn. Newborn infants prefer to look at faces, and visual recognition of people they see frequently emerges within days after birth. Visual memory during infancy predicts general intelligence as much as a decade later, suggesting it provides an important foundation for more general cognitive skills. Limitations in visual memory occur in a variety of atypical populations, including children diagnosed with ADHD and children born preterm. For these reasons,

assistant professor Vanessa Simmering (Psychology) focuses her research on how visual memory functions and develops over the lifespan.

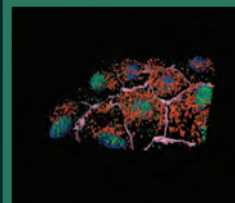
Simmering seeks to understand how children and adults use visual memory for different purposes, and how they learn to adapt to their memory limitations. For example, visual short-term memory has a severely limited capacity: adults can remember only about four simple objects for a few seconds. In children, this capacity is



### APARNA LAKKARAJU, PHD

RRF REBECCA MEYER BROWN PROFESSOR

Research in the Lakkaraju laboratory is focused on understanding the cellular basis of age-related macular degeneration (AMD), the leading cause of irreversible blindness in the aging population. Several genetic and environmental factors have been associated with AMD, but there is as yet limited insight into the exact sequence of events that eventually lead to vision loss. Aparna Lakkaraju, assistant professor in Ophthalmology and Visual Sciences, studies the retinal pigment epithelium (RPE), which sits beneath the light-sensing cells of the eye called the photoreceptors. The RPE is the initial site of damage in AMD.



The RPE performs numerous functions that are indispensable for the health of the retina, including the daily digestion of routinely shed photoreceptor tips (cellular debris), which is essential for photoreceptor renewal and healthy vision. Over a lifetime, the clearance mechanisms responsible for digesting these shed tips become less efficient and toxic aggregates accumulate both within and

beneath the RPE. Although decreased efficiency of these clearance mechanisms is a general consequence of aging in cells like the RPE and neurons, and does not fully explain susceptibility to AMD, it is an avenue worth investigation. The Lakkaraju lab is using state-of-the-art high-speed live imaging to explore lysosome (waste disposal) function in RPE.

Professor Lakkaraju was recently awarded a grant from the American Federation for Aging Research to study how complex genetic and environmental factors regulate these clearance mechanisms and how this contributes to the cellular pathology of AMD. Her lab's research is yielding valuable information about early changes in the RPE's ability to clear unwanted debris induced by genetic and cellular stressors implicated in AMD pathogenesis. This information will help identify novel therapeutic targets for the most common form of AMD, called dry AMD or geographic atrophy, which causes a slow decline in vision and currently has no approved treatments.

limited to only one or two objects. Through comparisons of different laboratory tasks, however, Simmering has shown that children can remember more objects in supportive contexts, as with shorter memory delays or viewing objects repeatedly. Moreover, she has demonstrated that children's information-seeking behavior in one task (looking back and forth to find which of two displays contains a changing color) predicts how many objects they can remember in a single-display task.

The Simmering group uses dynamic neural field models to account for how changes in neural connectivity could underlie memory improvements over development. She has shown that strengthening excitatory and inhibitory connections between cortical layers leads to faster memory formation and more stable maintenance. Future studies will address whether specific experiences could accelerate the neural changes that support memory development, with an eye toward designing interventions for populations with limited visual memory abilities.





# CYCLE FOR SIGHT

Our annual indoor cycling fundraiser took place in March 2013 and was a great success. Dedicated McPherson ERI supporters had an exhilarating workout at several athletic facilities on the UW-Madison campus, riding for an hour in support of vision research.

## SIGN UP FOR THIS YEAR'S CYCLE FOR SIGHT — MARCH 8TH, 2014!

Cycle for Sight will return on Saturday, March 8th, 2014 with new support from the Shopko Foundation and the Princeton Club, among others. Please sign up to ride, as an individual or on a 4-person team! For more information:

**VISIT [CYCLEFORSIGHT.WISC.EDU](http://CYCLEFORSIGHT.WISC.EDU) OR CONTACT MICHAEL CHAIM ([CHAIM@WISC.EDU](mailto:CHAIM@WISC.EDU))**





# WITH THANKS AND APPRECIATION

to the Following Contributors to the McPherson Eye Research Institute:

**FROM JULY 1, 2012 — JUNE 30, 2013**

- Dan A. Ainsworth
- Daniel M. & Eleanor Albert
- Kathryn A. Allen
- Robert G. Allen
- Alliant Energy Foundation
- Caroline Anderson
- Roxanne & Brad Anderson
- Leigh & Neeraj Arora
- Sarah L. Atzen
- Jason Austin
- Jessica & Greg Barrett
- Rose Barroilhet
- Billie Beckwith-Cohen
- Janice M. Beers
- Lisa Beers
- Pearl Beers
- Darrell & Michelle Behnke
- Melissa J. Behr
- Cindy Bell
- Ellison Bentley
- Ronald Berg & Karen Leonard-Berg
- Saswati Bhattacharya
- Nathan Blankenheim
- Oscar C. & Patricia Boldt
- The Boldt Company
- Jo Ann K. Bradley
- Jill Bradshaw & Curtis Slover
- Simran Brar
- Steven C. Briggs
- Paul J. Bryar
- Budget Bicycle Center
- Craig Butler
- Lynn A. Caravello
- Jason Roy Carr
- Michael F. Chaim
- Erik & Rachel Christianson
- Robert & Nancy Chritton
- Marsha Cohen
- Chandra Darjatmoko
- Laura S. Darjatmoko
- Soesiawati Darjatmoko
- Matthew & Nancy Davis
- R. Christian & Kathy Davis
- Delta Gamma Sorority
- Lori A. Devine
- Ronald J. Diamond
- Direct Fitness Solutions
- C. Thomas Dow
- Jennifer M. Dreyfus
- Richard & Doris Dubielzig
- Felicia Duke
- Kathryn Duke
- Mary Anne Duke
- Richard A. Duke
- Christine Echtner
- Darlene Edge
- Janis T. Eells
- Daniel Eimer
- Erik's Bike Shop
- Stephane Esnault
- Marilyn Essex & Michael Skindrud
- Ingrid E. Feder
- Finance & Investments Society, UW-Madison
- Marshall E. Flax
- Neil & Peggy Ford
- Susan G. Frackman
- Kenneth Frazier
- Kristen R. Friedrichs
- B'Ann T. Gabelt
- David J. Gagnon
- David & Marilyn Gamm
- Jeffrey A. Georgson
- Nicole Belle Gile
- Kate S. Gladding
- Janine Glaeser
- Nancy Godfrey
- Jackie Gong
- Wright Goodwin
- Niki A. Graham
- Steve & Judith Grahovak
- Michael & Lori Granberg
- Sally Grantee
- Kathryn Graves
- Andrew J. Haertel
- Patrick Halbach
- John Hancock Financial Services
- Christopher Harrison
- Bruce E. Harville
- Jesse Heiden
- John & Judy Heim
- Michele J. Heim
- Steven & Joyce Henning
- Robert R. M. Holloway
- Virginia J. Holoubek
- Ann & Terry Holterman
- Nancy J. Homburg
- Andrea L. Hotchkiss
- Elizabeth Pace Hughes
- Emmett A. Humble
- Denise Imai
- Phil Ingwell
- John H. Jenson
- Vicki Johnson
- Tonia Jorgenson
- Sherry F. Kaiman
- Steven & Faith Kamps
- Paul & Anne Karch
- Kyungmann Kim & Youngsook Lee
- Mike Knowlton
- Julia Lam
- Ronald & Jean Lewis
- Liberty Tax Service
- Kathleen S. Lieber
- Linda Linssen
- Lions Club of Lancaster
- Steven Lipton
- Kathryn Mace
- Madison Central Lions Club
- Madison Evening Lions Club
- Madison Monona Lioness Club
- Sharon Madnek
- David Maggs & Lynelle Johnson
- Ronald R. Magness
- Deborah J. Mahaffey
- Earl & Carmen Marley
- Charles D. McCanna
- Alice McPherson, MD
- Tod & Marcia Melotte
- Jenna Mertz
- Judy A. Middendorf
- Sigurd H. Midelfort
- Jennifer H. Mitchell
- Monticello Lioness Club
- Monticello Lions Club
- Jonathon & Amy Morgan
- Alan R. Morse
- Anantharaman Muthuswamy
- Barbara & Stephen Napier
- Ashley Nault
- Melissa J. Nelson
- Jeff E. Niesen
- Nikon Instruments
- T. Michael Nork
- Melissa Novinski
- Kevin J. O'Connor
- Samuel A. Packer
- Panera Bread
- Bikash Pattnaik
- Helda Perez
- Todd & Tracy Perkins
- Douglas & Michelle Peters
- Marie & Mark Pinkerton
- Arthur Polans & Myra Schultz
- Judy & John Post
- Walter & Karen Pridham
- Beth & Greg Puleo
- Patricia Rasmussen
- Paul J. Rathouz
- Nell & Harmon Ray
- Shiela Reaves
- Division of Recreational Sports, UW-Madison
- Christopher M. Reilly
- Retina Research Foundation
- Antoinette R. Richards
- Rachelle J. Richardson
- Harry & Karen Roth
- Bryan K. Rutledge
- Saris Cycling Group
- Jessica L. Schlumpf
- Wanda Schmitt
- Michael Schroeder
- Erin M. Scott
- Jane & Bill Shepard
- Milton B. Shields
- Joseph & Jeanne Silverberg
- Harry & Bonnie Spiegelberg
- Dale & Betty St. John
- Christy J. Stadig
- James L. Stahl
- Howard Steinberg & Barbara Andrews
- Gail & Richard Stirr
- Daniel Stoudt
- Leandro B. Teixeira
- Kristin & Viren Thakkar
- Michelle Tollakson
- TOSA Foundation
- Trek Stores of Madison
- Sandra & Monroe Trout
- Charlotte A. Tusler
- University Bookstore, HSLC
- US Bancorp
- Paul & Elise Van Ginkel
- Eva Vasiljevic
- Michelle R. Vetterkind
- Edward & Janice Vidruk
- Jena Rae Voss
- Walgreen's
- David & Nancy Walsh
- Jay Wayne & Noelle C. LaCroix
- The Laurence & Frances Weinstein Foundation
- Guilford Mitchell Wiley Jr.
- Wisconsin Distributors
- Wright Vision Care LLC
- Frederick & Mary Ann Yahr
- James F. Yahr
- Aleksandr Yelenskiy
- David York & Linda Bergren-York
- Helen Yu
- David & Karen Zimmerman
- Rolland & Janet Zimmerman





Mission Statement:

The McPherson Eye Research Institute is a multidisciplinary community of scholars working to gain critical knowledge about the science and art of vision and apply it to the prevention of blindness.

For more information on how to partner with the McPherson Eye Research Institute in support of research, education and treatment advances in the visual sciences, please contact us at

**T** (608) 265-4023

**E** [info@vision.wisc.edu](mailto:info@vision.wisc.edu)

**W** [www.vision.wisc.edu](http://www.vision.wisc.edu)

**A** McPherson Eye Research Institute  
9431 WIMR  
1111 Highland Avenue  
Madison WI 53705

© 2013-2014 The Board of Regents of the University of Wisconsin System  
MERI logo design by H. Adam Steinberg

