Dear Friends,

By all accounts this has been a momentous year for the McPherson Eye Research Institute (MERI). We witnessed dramatic growth in many key areas, including facilities and resources, collaborative research initiatives, and grant opportunities. Most importantly, we continued to attract the best and brightest investigators, who work collectively to advance vision research and help those with sight-threatening diseases. This annual report highlights these recent accomplishments and provides a sense of what is yet to come.

Early in 2014, we celebrated the formal opening of our state-of-the-art research laboratories and gallery space on the 9th floor of the Wisconsin Institutes for Medical Research (WIMR II). The new and fully operational MERI labs, led by Nader Sheibani (Ophthalmology and Visual Sciences), Chris Sorenson (Pediatrics), and Jeremy Rogers (Biomedical Engineering), are expanding efforts to monitor, study, and treat eye disorders such as diabetic retinopathy, retinopathy of prematurity, and age-related macular degeneration. The Mandelbaum & Albert Family Vision Gallery, which showcases the breadth of MERI’s mission bridging the science and art of vision, has hosted two highly publicized exhibits and recently added an engaging sculpture, *Man Alone*, donated by Mildred and Marv Conney.

Critical to the McPherson ERI’s growing influence has been our ability to facilitate collaborative research initiatives and provide new scientific equipment (see highlights below). We were particularly pleased to partner with the Morgridge Institute for Research and the Department of Ophthalmology and Visual Sciences to sponsor grant competitions aimed at fast-tracking research on macular degeneration. We received numerous excellent applications and awarded three $25,000 seed grants. Opportunities like this help us fulfill MERI’s mission to promote cutting edge vision science and demonstrate how we can pool resources to maximize the impact of research dollars.

The discoveries and hard work of the now 150+ researchers who comprise the Institute continue to extend awareness of the McPherson ERI within the wider vision research community. World-renowned visiting scientists such as Dr. David Williams (University of Rochester) and Dr. Paul Sieving (Director of the National Eye Institute) were impressed by the quality and depth of vision research at UW-Madison. Both initiated further dialogue with MERI members and proposed novel collaborative projects that capitalize on the diversity and strength of our Institute.

As you peruse this calendar, I hope you enjoy reading – and seeing – how the McPherson ERI is achieving its aspiration of becoming one of the top vision research institutes in the world. Even in the face of a difficult funding climate, we continue to accelerate research efforts and pursue breakthroughs by sharing knowledge, resources, and skills. These are the hallmarks of the McPherson Eye Research Institute, and it is how the tough problems are solved.

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

McPherson ERI Director Dr. David Gamm with Dr. Alice McPherson in Lausanne, Switzerland. Dr. McPherson received the prestigious Gonin Medal in 2014, honoring her outstanding work in ophthalmology and her dedication to research advocacy and support.
MERI now provides shared access to critical new vision research equipment that will expand our members’ research capacity and help secure future grant funding. This year the Institute purchased an electroretinography (ERG) machine—a device that records the electrical properties of the retina—which is housed in the WIMR II vision core facility directed by members Aki Ikeda and Bikash Pattnaik. MERI also supported a successful bid by Gillian McLellan to obtain an optical coherence tomography (OCT) machine, which provides ultra-high resolution retinal images in living subjects.

New scientific collaborations capitalize on the ingenuity, resources and diversity of our research members. UW-Madison MERI members Jeremy Rogers and Kevin Eliceiri are collaborating with new associate MERI members Joe Carroll and Alfredo Dubra (Medical College of Wisconsin) to develop better tools to image the retina. By blending expertise in adaptive optics—a tool capable of imaging individual photoreceptors (on screen above) in patients—with expertise in computational analysis and optical scattering in tissue, the team will explore new quantitative methods to study the retina in health and disease.

As the 2014 McPherson ERI Endowed Lecturer, Dr. David Williams spoke about “Imaging Single Cells in the Living Eye.” He is a world-renowned vision scientist and engineer who developed a now-famous method to measure and correct optical defects of the eye far more accurately than previously possible. This adaptive optics development is a key technology in a camera that can take the sharpest pictures ever of the retina inside the living human eye.
GILLIAN MCELLELAN, BVMS, PHD, DACVO  
**OPHTHALMOLOGY AND VISUAL SCIENCES, SMPH SURGICAL SCIENCES, VETERINARY MEDICINE**

Loss of vision in glaucoma, a leading cause of irreversible blindness worldwide, results from damage to the optic nerve. Despite conventional treatments that lower eye pressure, inexorable vision loss continues unabated in many glaucoma patients. In her clinical work as a veterinary ophthalmologist at UW-Madison’s School of Veterinary Medicine, Dr. Gillian McLellan routinely diagnoses and treats glaucoma in dogs and cats and has identified a form of inherited glaucoma in animals.

As a clinician-scientist, Dr. McLellan is committed to improving animal and human health through research. Working with collaborators in Iowa, she has identified the gene mutation responsible for this form of inherited glaucoma in cats. In children, mutations in this same gene cause severe glaucoma, as well as lens abnormalities. Mounting evidence points to an important role for chemicals known as growth factors, including Transforming Growth Factor Beta (TGF-ß), in processes leading to blindness in glaucoma. The McLellan lab, in the Department of Ophthalmology and Visual Sciences within the School of Medicine and Public Health, has measured high levels of TGF-ß in the front of the eye in affected animals.

In ongoing research, Dr. McLellan is examining how TGF-ß might influence development and progression of damage to the optic nerve. A recent Grant-in-Aid from Fight for Sight has funded her study examining patterns of gene expression in the optic nerve as glaucoma progresses. Study results will aid in confirmation and discovery of genes and pathways that contribute to optic nerve damage in glaucoma—knowledge that will help to establish new treatment strategies to preserve sight in human as well as veterinary glaucoma patients.

MARSHALL FLAX, MS, CLVT, COMS  
**DIRECTOR, VISION REHABILITATION SERVICES**  
**WISCONSIN COUNCIL OF THE BLIND & VISUALLY IMPAIRED**

The ability to travel independently is basic to being human—but how do you get around if you can’t see? When fully sighted people think of suddenly having no vision, their first concern is, “I can’t move. It’s not safe.” And the idea of crossing streets without vision is often terrifying. Yet people who are blind or have vision impairments travel independently on a daily basis.

Learning how to travel with limited or no useful vision requires adaptive skills and techniques. Orientation and mobility (O&M) is the discipline that teaches people with vision impairments how to travel safely and efficiently. A certified orientation and mobility specialist (COMS) with the Wisconsin Council of the Blind and Visually Impaired, Marshall Flax works with people across the life span and in a variety of settings to provide one-on-one O&M instruction in the “real world” (as opposed to a clinical setting). This forces the student to address the endless variations that can occur on a routine trip: construction or maintenance blocking the sidewalk, weather, crowds, and traffic.

With recent developments in artificial vision (such as the Argus II retinal implant) and with stem cell and gene therapies, researchers are moving a group of people with little or no useful vision into the world of low vision. Even when post-treatment changes may be impossible to measure objectively on a visual acuity chart, subjects may report improved functional vision. Assessment of orientation and mobility can provide insight into these gains. Marshall has been involved in O&M assessment of subjects in clinical trials with the Argus II (Second Sight Medical Products) and in gene therapy trials with people with Leber Congenital Amaurosis (CCMT Phase 3 Protocol for LCA2: Evaluating Functional Mobility & Activity of Daily Living Performance in Patients with Gene Therapy).

HEATHER L. KIRKORIAN, PHD  
**HUMAN DEVELOPMENT AND FAMILY STUDIES**  
**SCHOOL OF HUMAN ECOLOGY**

Heather Kirkorian, assistant professor in the Human Development and Family Studies Department of the School of Human Ecology, seeks to better understand how viewers of different ages (infants, children, and adults) watch and learn from screen media. With specialized, non-invasive cameras that record exactly where a person is looking—for example, recording moment-to-moment changes in visual attention while young children watch television and play video games—she and her research group can observe human visual attention in a natural setting.

Dr. Kirkorian’s research has demonstrated that older viewers (especially adults) look at video in a systematic way. For example, adult TV-viewers tend to look at the same things at the same time as one another, to process information more quickly, and to “look ahead” in order to anticipate what will happen next. All of these factors likely make it easier for adults to understand and learn from video. Infants, on the other hand, are less systematic. They process visual information more slowly and are less prone to look at the same things as other infants. Instead of anticipating what is going to happen next, infants respond to things that have already happened—likely making it harder for infants to comprehend and learn from video.

Recently, Dr. Kirkorian has used eye-tracking technology to understand how toddlers learn from interactive media, discerning that they learn more when they interact with a touchscreen tablet than when they passively view a video, but only when the application—unlike many on the market—helps children pay attention to the right information at the right time. Interactive media may improve learning by young children when it actively guides visual attention. This line of research may eventually help media creators to develop content that is educationally valuable, and may help parents to select beneficial content if they choose to let their toddlers use screen media.
The formation of new blood vessels (angiogenesis) occurs under both normal and pathological conditions. Professor Nader Sheibani and his lab are working to learn how angiogenesis is regulated in the eye, focusing specifically on the role of two proteins that our body makes normally in order to keep this process in check—thrombospondin-1 (TSP1) and pigment epithelium-derived factor (PEDF)—proteins that naturally inhibit angiogenesis. The Sheibani group has shown that the levels of these proteins change under various pathological conditions including diabetic retinopathy, age-related macular degeneration (AMD), and ocular tumor formation. Most interestingly, they have used animal models to demonstrate that transgenic expression of these proteins has significant protective effects in these eye diseases, with the potential to stop new blood vessel growth.

An area of current investigation in the Sheibani lab is the development of novel mimetic peptides from these protein molecules for treatment of exudative (wet) AMD. This is a multidisciplinary endeavor among three universities including UW-Madison, Northwestern University, and the University of Nebraska—each of which is providing unique expertise to accomplish the objectives of this translational project. Dr. Sheibani’s goal is to have multiple candidates from these molecules identified and tested in preclinical models of wet AMD, for subsequent initiation of human clinical trials.

Dr. Sheibani is hopeful that these new compounds will have significant advantages over current treatments. As a class of drugs that mimic the body’s natural defenses, these therapeutic candidates will potentially be more effective, with fewer side effects. Along with novel methods of delivery, they may lead to better and safer treatment of wet AMD.

Research in the Rokers Vision Laboratory, under the direction of assistant professor Bas Rokers in the Department of Psychology, focuses on the neural mechanisms underlying visual perception. One of their goals is to understand the consequences of amblyopia (“lazy eye”) on the human visual system in an effort to improve clinical treatment.

Amblyopia, a developmental disorder caused by poorly coordinated binocular input, occurs in approximately 5% of the normal population. Individuals with amblyopia are subject to reduced visual acuity and impairments in binocular depth perception. It has been well established that these visual deficits are neuronal in nature—visual input leads to normal responses in the eye, but subsequent neural activity in the visual cortex is reduced. Accordingly, amblyopia is of interest not only as a clinical disorder, but also as a human model of the interplay between sensory input and neural development.

In a recent study, Dr. Rokers and his group used diffusion-weighted magnetic resonance imaging (DWI) to identify the pathways that relay visual input from the eyes to specific visual brain areas (shown in image). When investigating these pathways, they found that connections between the thalamus and the visual cortex were abnormal in amblyopes, suggesting that reduced activity in the visual cortex is directly associated with structural changes in these visual pathways.

They are currently exploring whether these structural abnormalities can be reduced with behavioral treatment using video games. Study results could lead to new clinical interventions that eliminate the visual deficits associated with amblyopia.

In the SCORE2 trial, all patients undergo monthly imaging with optical coherence tomography (OCT) scans. Each scan is analyzed for the thickness and anatomic features of the retina. In addition, new OCT software is used that allows for evaluation of the individual layers of the retina. The photoreceptor layer is of particular interest, since there is evidence to suggest that changes in photoreceptor layer thickness in eyes with CRVO may be a surrogate marker for visual function.

Another novel component of the SCORE2 trial is the ultra-wide-field angiography images that provide a panoramic (200°) view of the retina. FPRC research staff evaluate these wide angle angiograms in order to identify retinal leakage and retinal ischemia throughout the retina (see figure). This allows Dr. Blodi to correlate the anatomic features of retinal imaging with the visual acuity and long-term prognosis of patients with central retinal vein occlusion.
Small organelles called mitochondria play a key role in cellular energy metabolism and intracellular signaling processes; they are involved in many complex signaling cascades regulating both cell survival and cell death. Importantly, mitochondrial dysfunction and the resulting oxidative stress are central in the pathogenesis of retinal aging and retinal degenerative disease. In Professor Janis Eells’ laboratory, research is directed at understanding the mitochondrial signaling pathways that regulate the processes of cellular aging and degeneration in the retina, with the long-term goal of learning how to protect the retina against these degenerative processes.

The Eells’ laboratory has pioneered investigations into the mechanism of action and therapeutic efficacy of photobiomodulation in retinal injury and disease. Evidence is growing that exposure of cells to low-energy photon irradiation in the near-infrared (NIR) range of the spectrum, collectively termed photobiomodulation (PBM), can restore the function of damaged mitochondria, upregulate the production of cytoprotective factors, and prevent cell death. Photobiomodulation studies by Dr. Eells and her colleagues have documented retinoprotection in animal models of retinal injury, diabetic retinopathy, and retinal degeneration. They have shown that NIR photons are absorbed by the mitochondrial photoacceptor molecule, cytochrome c oxidase—triggering intracellular signaling pathways that culminate in improved mitochondrial energy metabolism, increased cytoprotective factor production, and cell survival.

Recent studies in a rodent model of retinitis pigmentosa have demonstrated that photobiomodulation improves retinal mitochondrial function and protects against photoreceptor cell loss. Dr. Eells anticipates that this research will provide important insights into the role of mitochondrial dysfunction in the pathogenesis of retinal degenerative disease and will also demonstrate the potential of photobiomodulation for retinal disease treatment.

The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) and the Beaver Dam Eye Study (BDES). Professors Barbara and Ronald Klein have devoted their careers to decreasing blindness and impaired vision due to diabetic retinopathy, age-related macular degeneration (AMD), and cataract. They are principal investigators of two landmark population-based epidemiological cohort studies, the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) and the Beaver Dam Eye Study (BDES).

The WESDR, begun in 1980, was the earliest population-based study of diabetic retinopathy, a common and potentially devastating complication of diabetes. At that time, the importance of optimal control of blood sugar levels in reducing the incidence of diabetic retinopathy had not yet been established, and there were no uniform guidelines for ophthalmic care for persons with diabetes. The study cohort of 2,370 persons was examined 7 times over a period of 33 years—yielding unparalleled information on the long-term complications of both type 1 and type 2 diabetes.

The Beaver Dam Eye Study was launched in 1987. At that time, little was known about the prevalence, incidence, and risk factors for AMD and cataract and their effects on quality of life. A cohort of 4,926 persons 43-86 years of age was identified by a private census and examined 5 times over a 20-year period (a sixth examination is currently underway). The BDES revealed the importance of smoking as a major risk factor for AMD and cataract. It also found and described the differences in risk factors among the three most common forms of age-related cataract.

Insights from both the WESDR and the BDES have been incorporated into preventive guidelines for diabetic retinopathy, cataract, and AMD patients around the world. The methodology, protocols, and grading approaches developed for these studies by the Drs. Klein have been highly influential and have been adapted for many other epidemiologic studies and clinical trials worldwide.
In the department of Electrical and Computer Engineering lab of Professor Hongrui Jiang, research interests include micro/nano sensors and actuators, microfluidics, lab on chips, smart materials, and nanoscale surface engineering, among others. Dr. Jiang’s notable work on biological and optical applications of microelectromechanical systems (MEMS) draws expertise from surgery, ophthalmology, veterinary medicine, materials science, computer science, and chemical engineering. Jiang and his research group have developed a self-focusing, accommodative contact lens to correct vision in aging adults. They have also pioneered a liquid microlens termed “smart” due to its ability to vary focus in response to stimuli such as temperature, pH, or light—useful in instruments for laparoscopic surgery or endoscopy.

Biomimetics and bioinspiration, emulating nature’s best biological ideas to address human problems, have been key in these designs. Recently, the Jiang lab developed a new artificial compound eye mimicking the structure of a lobster eye at a life-size scale. While most compound eyes occurring in nature rely on multiple lenses, the lobster eye comprises a spherical array of very small reflecting chambers that focus the available light into a single image with a 180-degree field. Because it’s based on reflection, this design offers an advantage over conventional imaging, in which a lens uses refraction that can create color distortions and reduce light intensity.

Dr. Jiang’s small artificial compound eye—which captures light via 168,100 reflecting chambers arrayed in a perfectly hemispherical pattern—offers high acuity motion detection and detailed imaging in dark environments. Potential application areas range from medicine to astronomy to the military.

Professor Shiela Reaves, department of Life Sciences Communication, is interested in the multidisciplinary crossroads of neuroscience and visual communication, in particular the responses of the brain’s visual system across media and the visual arts.

Her research is an extension of her 8-year career in photojournalism, which was a hunt for the answer to “What makes a good picture?” Reaves explores the many facets of how digital media has challenged news editors to maintain the highest ethical standards in photojournalism. Whereas artists have great freedom to digitally manipulate and create new imagery, digital photojournalism is still accountable to notions of visual truth. News editors and photographers must attempt to preserve public trust despite computers and movable pixels, as the evolved human brain still tends to believe what it sees. This issue of visual trust has ramifications for those who might accept as real what often is unreal—such as the digitally enhanced, ultra-thin models in fashion media. Western media practices can create a ripe soil for little girls to diet, contributing to eating disorders.

Exploring the emerging field known as neuro-aesthetics, Professor Reaves is asking, “What attracts the visual brain?” Answers vary depending on cultural diversity, individual experience, and personal motivation. But by combining principles from perceptual psychology, evolutionary biology, and functional brain anatomy, neuro-aesthetics augments understanding of human visual response. Reaves finds that something marvelous happens when she calls attention to the brain’s processing centers of motion, color, form, and pattern, and the pre-attentive search for faces: the relatively conservative biology of the visual system becomes accessible in new ways. She notes that as visual behavior deepens, non-neuroscientists and non-photographers can apply vision science to enrich their lives and powers of observation – almost as easily as visual artists and photographers who spend their entire lives steeped in visibility.

Professor Brian Link and his lab utilize zebrafish as a model to study eye development and disease. Their main focus is to understand the interactions and signals between cells that regulate critical steps during retinal development. Utilizing genetic and cell biological tools, including mutational analysis and in vivo live cell imaging, they are learning about the mechanisms, cellular behaviors, and underlying genes that influence retinal layer formation.

Another focal point of Dr. Link’s research involves modeling disease processes of the eye including photoreceptor degenerations and glaucoma. Most recently, he initiated a collaboration with Dr. Terri Young’s group at UW-Madison to study the genetic interactions and mechanisms underlying myopia. For disease modeling, both mutational analyses and targeted gene manipulations are being conducted to shed light on the mechanisms of pathogenic phenotypes.

Finally, the Link lab is part of a multidisciplinary team, led by Dr. Howard Jacob, that is studying the significance of genetic variants identified through whole genome sequencing of young patients from Children’s Research Hospital / Medical College of Wisconsin in Milwaukee. Patients can show a spectrum of anomalies, including neurological and ophthalmological disorders, but are bound by the fact that the causes are undiagnosed. This work has impact for defining methodology for the practice of personalized medicine.
ENDOWED PROFESSORSHIPS AND CHAIRS AT THE MCPHERSON EYE RESEARCH INSTITUTE

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Retina Research Foundation Emmett A. Humble Distinguished Directorship
Modeling and Treating Retinal Disease with Human Induced Pluripotent Stem Cells (hiPSCs)
Sandra Lemke Trout Chair in Eye Research
Applications of stem cell technology to the study and treatment of age-related macular degeneration

Jeremy Rogers, PhD
Retina Research Foundation Edwin and Dorothy Gamewell Professor
Optical Instrumentation and Technology Platforms for the Study and Screening of Retinal Disease

Nansi J. Colley, PhD
Retina Research Foundation M. D. Matthews Research Professor
Molecular Genetic Studies of Retinal Degeneration in Drosophila

Akihiro Ikeda, DVM, PhD
Associate Director, McPherson Eye Research Institute
Retina Research Foundation Walter H. Helmerich Research Chair
Identification of Genetic Factors Affecting Aging of the Retina

Aparna Lakkaraju, PhD
Retina Research Foundation Rebecca Meyer Brown Professor
Insight into the Cellular Basis of Retinal Degenerative Diseases

Arthur S. Polans, PhD
Retina Research Foundation Kathryn and Latimer Murfee Chair
New Agents for the Treatment of Ocular Tumors and Neovascular Diseases of the Eye

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Retina Research Foundation

Dr. Monroe Trout and Sandra Trout

WITH GRATITUDE TO . . .

Alice R. McPherson, MD
Founder, President, and Scientific Director
Retina Research Foundation
The Mandelbaum & Albert Family Vision Gallery, adjacent to the McPherson ERI’s new laboratory space on the 9th floor of the Wisconsin Institutes for Medical Research, was dedicated on May 8th, 2014. Named for the related families of Dr. Daniel Albert, the McPherson ERI’s Founding Director, and David & Nathan Mandelbaum, key supporters of the institute since its inception, the gallery brings an exciting new exhibit space to the medical campus.

Two exhibits were featured in 2014: The Delighted Eye, a show of exceptional artwork from UW-Madison’s Tandem Press, and Cool Science Images 2014, featuring winners of the annual campus-wide science images contest sponsored by the online UW magazine The Why Files. Exhibits in this McPherson ERI gallery, which is open to the public during building hours, will rotate 2-3 times per year. We encourage you to visit!
CYCLE FOR SIGHT

Our March 2014 indoor cycling fundraiser expanded this year, taking place at two UW campus locations and at the Princeton Club in Madison. More than 150 riders participated in raising funds for vision research—and had a great workout near the end of a long Madison winter.

Cycle for Sight 2015 will be held on campus as well as at the Princeton Club on Madison's west side.

SIGN UP NOW FOR CYCLE FOR SIGHT 2015
SATURDAY MARCH 14TH, 2015!

Visit Cycleforsight.wisc.edu or contact Michael Chaim (chaim@wisc.edu)
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