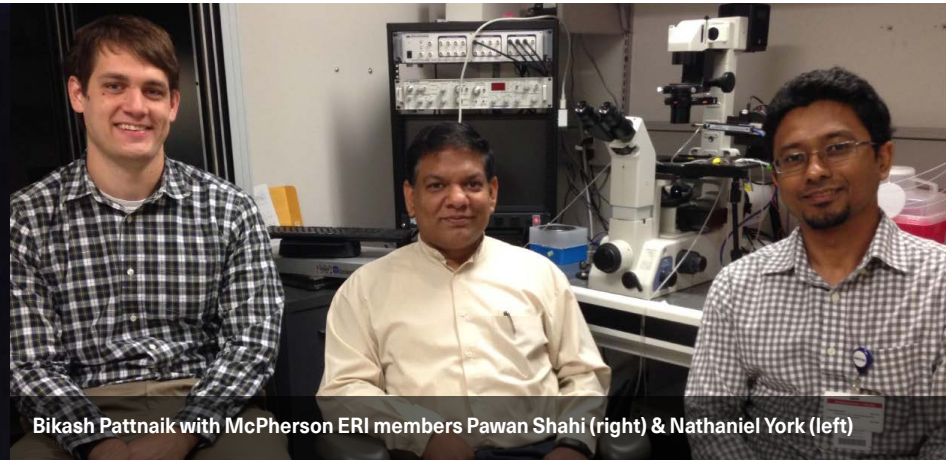


RESEARCH NEWS

## Hope for LCA Therapies

WITH BIKASH PATTNAIK, PHD, MS



Bikash Pattnaik with McPherson ERI members Pawan Shahi (right) & Nathaniel York (left)



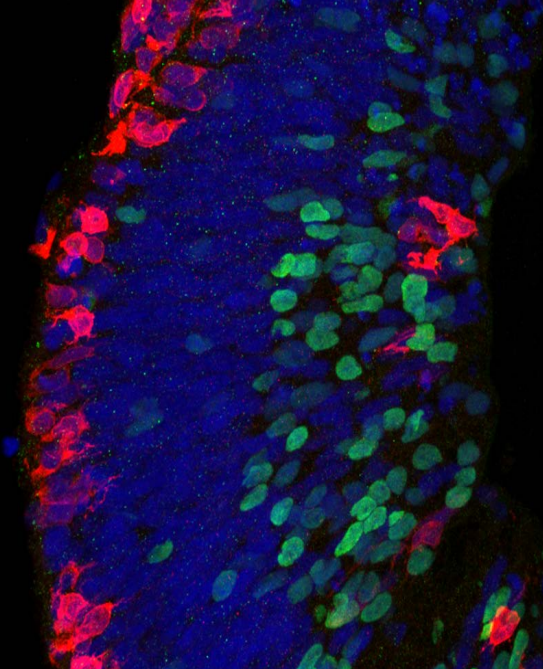
“Bench-to-bedside” is the popular term for research that begins in a lab and progresses to direct clinical applications. For Bikash Pattnaik, Assistant Professor in the Department of Pediatrics at UW-Madison, the appropriate term might be “bedside-to-bench-to-bedside.” Dr. Pattnaik’s highly promising work on Leber congenital amaurosis (LCA), a childhood blinding disease with multiple genetic causes, was boosted several years ago by a \$1 million-plus gift from the family of a young boy affected by LCA. The family, whose members have also donated genetic material for the creation of retinal stem cells, was introduced to Dr. Pattnaik’s lab by collaborators at the Casey Eye Institute in Portland, Oregon. While wishing to remain anonymous, they continue to inspire the work of his lab’s researchers (including McPherson ERI members Pawan Shahi and Nathaniel York), as well as collaborators in David Gamm’s lab. “The family’s interest and our research focus and collaborations are a natural fit, as both of us are trying to find a cure for blindness,” Pattnaik says. “I truly admire their generosity and honest desire to contribute to a cure.”

There are about 20 types of Leber congenital amaurosis – each likely resulting from different genetic mutations – and the number is growing. All types cause blindness at or soon after birth; combined, they affect approximately one child in 80,000. (The disease received widespread attention in 2008 when one variation, LCA2, was treated by gene therapy, with some success, by Dr. Jean Bennett and her collaborators at the University of Pennsylvania). Dr. Pattnaik’s initial focus was LCA16, a form of the disease first identified in 2011. His lab had long studied the molecular mechanisms of potassium channels, which conduct potassium ions and shape the activity of many cells. LCA16 is associated with a gene mutation that blocks the function of potassium channels in the retinal pigment epithelium (RPE), the pigmented layer that nourishes photoreceptor cells, resulting in blindness.

With the initial gift from the family affected by LCA16 – and more recently, with a four-year, \$1.5 million grant from the National Eye Institute’s Audacious Goals Initiative – Dr. Pattnaik has been able to work on a number of therapeutic approaches. One promising route begins with RPE cells derived from induced pluripotent stem cells (iPSC-RPEs), and uses the remarkable new CRISPR technique of gene editing to create models of different LCA16 mutations in a dish. The pathophysiology of these different mutations can then be studied at the level of the gene (Pattnaik’s lab has focused on the mutated *KCNJ13* gene as a possible cause of LCA16.) With CRISPR, there is then potential to correct the section of the mutated gene if a causal connection is identified. The lab is also investigating viral vectors which could ultimately deliver a corrected *KCNJ13* gene into RPE stem cells, theorizing that this could resolve the potassium channel defect and treat the disease.

Another promising approach taken by the Pattnaik lab is to test therapeutic “read-through” drugs. These specific small molecules (like antibiotics) are able to overcome the potassium channel defect due to the *KCNJ13* gene mutation and result in a natural protein product without any other adverse reactions. Several of these drugs are being used to treat muscular dystrophy & cystic fibrosis. A potassium channel defect, as in this study, provides a measure for the ion-channel functional cure in LCA.

The through-line in Dr. Pattnaik’s research is the patient. “In this unique collaboration we have been able to decode the disease cause through the generous donation – both in biological material and gift support – from the affected family,” he says. “We’re now preparing ourselves to take the results to the bedside.” It’s an approach that Dr. Pattnaik hopes will bear fruit in the form of vision-saving therapies that will help this family, and thousands of others.



*FROM THE DIRECTOR:*

## Dear Friends of the McPherson Eye Research Institute,

At the McPherson ERI, we prize opportunities to interact with the people we strive to help through the research and influence of our more than 180 members. Thus, it gives us great pleasure to highlight community partners like the “Blind Take Off” Cycle for Sight team. Just as these extraordinary individuals work together to inspire and support us, we work in synergistic research teams to address the most challenging diseases, like retinitis pigmentosa, that continue to rob our family, friends, and neighbors of their eyesight.

As just one example, a McPherson ERI research team recently received a nearly \$1 million Foundation Fighting Blindness Gund-Harrington grant (only one awarded worldwide) to support production of bioengineered scaffolds, or “support structures” to deliver photoreceptors to the subretinal space in patients with retinitis pigmentosa and other retinal degenerative diseases that cause death of photoreceptors. Work done over the past few years in my own lab has advanced methods to produce photoreceptors from adult human induced pluripotent stem cells, which have the potential to be used as spare parts to restore vision in some patients. However, to realize that potential, it was clear that we needed additional expertise in how best to package and deliver these stem cell-derived photoreceptors and then to evaluate their impact on vision. Therefore, we reached out to multiple expert McPherson ERI scientists to tackle these issues as rigorously and expeditiously as possible. Dr. Joe Phillips and other researchers in my lab continue to improve photoreceptor production, while Zhenqiang “Jack” Ma (Electrical Engineering) and Shaoqin “Sarah” Gong (Biomedical Engineering) are developing the actual micro-patterned scaffolds that will contain the photoreceptor replacement cells. In addition, Drs. Paul Kaufman, Mike Nork, and James Ver Hoeve (Ophthalmology and Visual Sciences) are authorities in retinal surgery and analysis who will help take this collaborative effort to the clinical trial stage.

This project is only one of many that McPherson ERI members explore daily. The pioneering work of Dr. Bikash Pattnaik (Pediatrics), profiled on the cover, is a sterling example of research with landmark potential, and we will update you on others in future communications. In the meantime, please know how grateful my McPherson ERI colleagues and I are for your interest in, and support of, our collective goal to understand, protect, and restore sight — our most precious sense.

**David M. Gamm, MD, PhD**

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





Jim Tormey (center left), Gary Doering (center front), and Gerard Xavier (right front) at Cycle for Sight

## TEAM PROFILE

# Blind Take Off: Riders for Vision

In this year's Cycle for Sight indoor fundraising ride, the Blind Take Off team showed once again that the blind can do more than take off – they can soar! Blind Take Off consists of Jim Tormey, Gary Doering, and Gerard Xavier, three men with retinitis pigmentosa – a degenerative eye disease which affects photoreceptor cells in the retina, causing vision to deteriorate from the periphery inward and progressively leading to blindness. Riding for the third consecutive year, the team was active in helping to promote Cycle for Sight, underlining the need for ongoing vision research by recounting their own experiences.

The teammates met at the RP support group at the Wisconsin Council of the Blind and Visually Impaired in Madison. Jim and Gerard were diagnosed with RP in their teens. "It was very hard to take then," Jim says. "Being a kid, hearing that...it kind of puts you in a bubble." Jim got through, and continues to get through, because of his family's support and his love of hunting and fishing – ice fishing in particular. In an interview that he and his teammates did for WKOW TV before the ride, Jim emphasized that "You can live and survive...you gotta keep your head up. It [the research] gives me hope for the future, and I hope other people see this, young and old." Gerard, who works as a counselor at Madison College and whose vision began to deteriorate when he was 11 years old, agrees. "I think that within the next couple of years there'll be that option...where I'll be able to go through some kind of procedure that will increase the amount of vision I have."

The effortlessly charismatic Gary Doering, who chairs the Wisconsin Council's retinitis pigmentosa support group, is the only one of the three riders who was diagnosed with RP as an adult. He has a long-term perspective on the research now underway. "Before 10 or 12 years ago, there was basically no hope; the research was very limited, there weren't even any funds for research. But just in the last 10 to 12 years, the door is wide open for anything and everything. It's very promising." Doering, who lives in Baraboo and has worked for years at Badger Paperboard, is also optimistic about what the next few years may bring. "They're doing research for retinitis pigmentosa that's never been done before...it's all happening right here in Madison."

Cycle for Sight was held this year on March 12th at the Princeton Club and several campus locations in Madison. The event raised more than \$34,000 for vision research at the Institute, and brought together a cross-section of McPherson ERI researchers, supporters, and friends and family members. Kenzi's Team, the extraordinary team captained by Nancy Valentyn, was once again the top fundraising team, with more than \$6,300 raised. Twenty other teams participated in the ride, including multiple teams with blind or vision impaired riders. Out of Sight, the sightpaths, the McBurney McBikers, Team Tiradani – all included riders with retinitis pigmentosa or other conditions, most riding for the second or third year in a row. And Blind Take Off? They raised almost \$5,400 for vision research this year...and will be back next year.



Gary Doering (left) and Jim Tormey (right)

## RESEARCH AND MEMBER NOTES:

### **Dan & Ellie Albert Student Vision Research Award Enables Medical Student Summer Research**

With matching funds provided by the Dan and Ellie Albert Student Vision Research Fund, two medical students and their mentors recently received Shapiro Summer Research Awards from the UW-Madison School of Medicine & Public Health. Under mentor **Yao Liu, MD** (Ophthalmology & Visual Sciences), Minbo Bai is focusing on “Macular Pigment as a Glaucoma Risk Factor in the Carotenoids in Age Related Eye Disease Study 2 (CAREDS2).” Under mentor **Bikash Pattnaik, PhD, MS** (Pediatrics), Samuel Bauer is working on the “Kir7.1 Novel LCA16 Mutation and Its Pathophysiology.” Both of these first-year medical students will participate in 10-week summer research projects.

### **Hilldale Undergraduate/Faculty Research Fellow to Focus on Cellular Vision Science**

Undergraduate student Katherine Schleck was awarded the 2016-2017 McPherson ERI-sponsored Hilldale Undergraduate/Faculty Research Fellowship for the project, “Bim Expression Affects Retinal Astrocytes Adhesion and Migration through Altered Production of ECM Proteins.” Her vision-related research will be mentored by **Christine Sorenson, PhD** (Pediatrics). This is the 3rd year that the McPherson ERI has funded a Hilldale fellowship, from which students receive \$3,000 and faculty mentors receive a stipend to sponsor a research project that will be presented at the annual UW-Madison Undergraduate Symposium.

### **Pawan Sinha, 4<sup>th</sup> Annual McPherson Endowed Lecturer, Draws Capacity Crowd**

Pawan Sinha, PhD, Professor of Vision and Computational Neuroscience at MIT's Department of Brain and Cognitive Sciences, inspiringly paired scientific and humanitarian significance in speaking about “Learning to See Late in Childhood.” His lecture focused on Project Prakash—an initiative restoring sight to blind children—and on his associated research, tracking visual learning and brain plasticity through a combination of behavioral and brain imaging studies. View his April 2016 lecture at: [www.vision.wisc.edu](http://www.vision.wisc.edu)

### **Remarkable Parallels in Eye Evolution**

Published this June in the journal *Integrative and Comparative Biology* with the title “Photoreception in Phytoplankton” is a study of photosensory pigments and light-detecting systems in a wide variety of microscopic, single-celled organisms known as phytoplankton. **Dr. Nansi Colley** (Ophthalmology and Visual Sciences) together with Dr. Dan-Eric Nilsson (University of Lund, Sweden) showed that the evolution from simple photoreception to vision seems to have independently followed identical paths and principles in phytoplankton and animals, strengthening understanding of the biological process by which eyes evolve.

# 8<sup>th</sup> Annual Vision Science Poster Session & Lecture

TUESDAY, OCTOBER 4, 2016 3:00PM – 5:30PM

Atrium, Health Sciences  
Learning Center (HSLC)  
750 Highland Ave, UW-Madison

Registration opens late August

**DISTINGUISHED GUEST LECTURE**  
**AT 5:45PM, HSLC ROOM 1335**

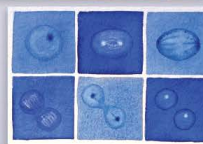
**Professor JoAnn Kuchera-Morin**  
University of California, Santa Barbara  
Departments of Media Arts & Technology and Music



## CATCHING THE EYE

of McPherson Eye Research Institute Members

An exhibition exploring how vision research  
and the artistic eye align in artworks  
created or collected by members of the McPherson ERI.



**MANDELBAUM & ALBERT FAMILY VISION GALLERY**  
**JUNE 20–AUGUST 31, 2016**

9th floor, Wisconsin Institutes for Medical Research