

Adaptations of Animal Vision

Nature, after millions of years of evolution, provides a plethora of intriguing visual systems with superb optical designs. These natural eyes have always fascinated Dr. Hongrui Jiang, a leader in micro-scale optical imaging whose work has been guided by these bio-inspired approaches. His lab works to selectively incorporate the useful elements of nature's visual systems into integrated, intelligent micro-optical imaging systems.

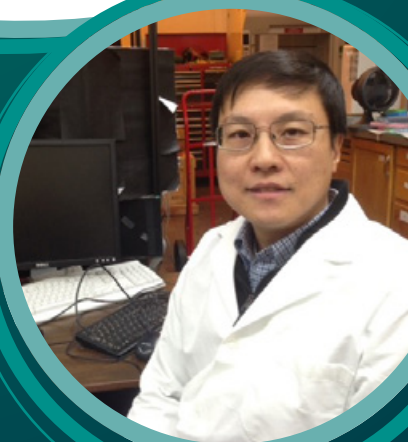
There is a distinct difference between inspiration and simple mimicking. Natural ocular adaptations are often exquisitely matched to specific visual demands of an ecological niche, and are in many cases limited by structural, morphological and physiologic constraints. The resulting visual solutions furnished through evolution are usually "good enough" rather than superior. Keeping this issue in mind, Jiang is always aware that his research should not aim to simply replicate the natural eyes, but to adapt key features for new and targeted uses. This puts his research in stark contrast with other works that seek to mimic specific biological eye constructions.

In 2006, Dr. Jiang's group published a landmark paper on smart liquid microlenses that could sense aspects of their surroundings (such as temperature and pH) and self-adaptively vary their focal length. This smartness was achieved by incorporating stimuli-responsive hydrogels mimicking ciliary muscles in human eyes. Jiang followed this trailblazing work by developing so-called "super artificial eyes," microlens arrays on spherical surfaces with each lens individually tunable in focal length. These "super artificial eyes" merged the best features of the two most prevalent types of natural eyes, compound eyes and mammal eyes. Fusing hydrogels as actuators with flexible electronics, this work solved a long-time engineering dilemma by enabling both a large field of view and high spatial resolution.

In another work, Jiang developed artificial reflecting superposition compound eyes, inspired by the eyes of some decapods including lobsters, shrimps and crayfish. This extraordinary work allows for extremely acute motion detection and high sensitivity of light and low chromatic aberration (due to superposition and reflection-based imaging, rather than refraction). Recently, Jiang's group unveiled a strategy reliant entirely on optics to significantly enhance the photosensitivity of any imaging system, independent of the electronic imagers used. The design was inspired by intriguing features in the retina of elephant-nose fish, which possess funnel-shaped nanostructures for the concentration of light. This work opens up a new direction in the development of low-light imaging systems such as cameras.

Dr. Jiang's technology has already led to impressive biomedical applications. He pioneered flexible endoscopes that implement tunable liquid lenses at the distal ends for endoscopic surgeries, solving the persistent problems of current endoscopes (which use fixed lenses). This allowed for the first scanning of the colon with minimal physical movement, a potentially revolutionary tool for colonoscopies and other endoscopic surgeries. Dr. Jiang also developed a prototype multiple-micro-camera laparoscopic imaging tool that provides a large field and depth of view, which is a much needed breakthrough in laparoscopic imaging (a technique that had been based on a single fixed camera for fifty years, causing multiple issues for surgeons). Dr. Jiang and his surgical collaborators currently have NIH funding to refine this technology.

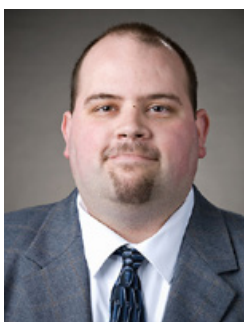
The Jiang lab's advances have multiple uses for adaptive technologies for vision. In 2011 Dr. Jiang was given an NIH New Innovator Award to support integration of his tunable liquid lenses into contact lenses. The resulting "accommodative contact lenses" have the potential to correct presbyopia on a large scale for millions of elderly patients with deteriorating vision. Recently, Jiang received the prestigious Stein Innovation Award from Research to Prevent Blindness, rarely given to engineers, for his cutting-edge work enabling optical imaging technology to study the pathophysiology of glaucoma. He currently collaborates with Paul Kaufman, Mary Ann Croft and Michael Nork (all in the Department of Ophthalmology and Visual Sciences at UW-Madison) to develop implantable nanophotonic sensors to monitor choroidal tension and intraocular pressures. Jiang hopes to use this technology to advance understanding of the underlying mechanism of glaucoma and its potential correlation with presbyopia, which ultimately could lead to new therapies.



FROM THE DIRECTOR:

Dear Friends of the McPherson Eye Research Institute,

Recently, the Institute underwent a transition in the Associate Director position, which offers an opportunity to highlight two of McPherson ERI's extraordinary scientists and leaders. The Associate Director serves as an important link to McPherson ERI members and plays a key role in encouraging vision research collaborations. For the past five years, Dr. Aki Ikeda has held this position in addition to his long-standing role on our Leadership Committee. As an exemplar of McPherson ERI research, Dr. Ikeda is unparalleled. His work on the genetic causes of retinal aging and disease shows great promise and ultimately led to his appointment as the first McPherson ERI Timothy William Trout Professor in Eye Research. He has played a key role in strengthening the Institute, and I am personally grateful to him for his wise advice.



McPherson ERI's new Associate Director, Dr. Kevin Eliceiri, is well-equipped to pick up the baton. Dr. Eliceiri directs the UW Laboratory for Optical and Computational Instrumentation (LOCI) and is an investigator in Medical Engineering at the Morgridge Institute for Research. He is an outstanding scientist and imaging specialist with boundless energy and intellectual curiosity, and is particularly sought after as a collaborator by investigators across UW and the nation. Dr. Eliceiri's research is situated at the frontiers of medical imaging – one of the most promising areas of vision research in the Institute. In the coming years he will take a lead in helping the McPherson ERI open new pathways for discovery, innovation, and treatment.

These two outstanding researchers are prime examples of the breadth and depth of the over 190 members of the McPherson ERI. **I am fortunate to share a common Institute with all of them.**

A handwritten signature in blue ink that reads "David M. Gamm".

David M. Gamm, MD, PhD

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



In the Sheibani and Sorenson Vision Laboratories, Discovery Advances on Multiple Fronts

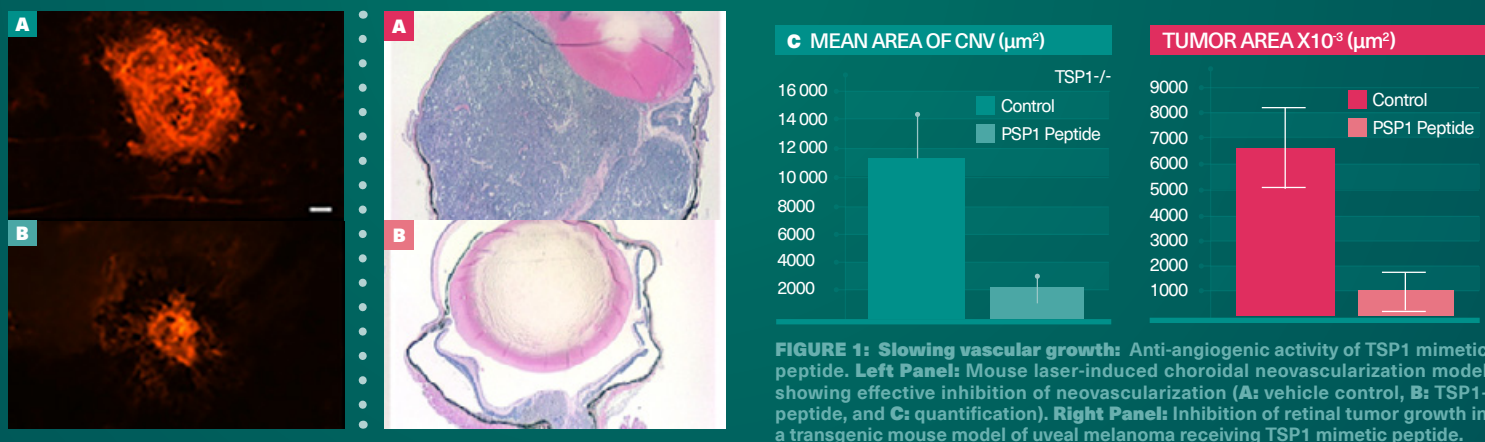
The maintenance of vascular homeostasis – stability within the blood vessels of the eye – is vital to ocular health. This homeostasis is maintained through a tightly regulated balanced production of positive and negative factors. Compromises in this balance lead to abnormal vascular function and growth of new and dysfunctional blood vessels, and if left untreated lead to retina traction and detachment and loss of vision. Some of the major vision-threatening eye diseases are tied to growth of abnormal new blood vessels, including age-related macular degeneration, diabetic retinopathy, and retinopathy of prematurity. A major focus of the Sheibani and Sorenson Vision Laboratories' research is to delineate the molecular mechanisms that are responsible for dysregulation of ocular vascular homeostasis. Once these mechanisms are identified the lab focuses on inhibiting angiogenesis and restoring normal homeostasis. These efforts are highly collaborative and take advantage of expertise from colleagues in imaging, drug development and testing, and pathological evaluations. On these pages are a sampling of four current research projects in the laboratories.

INHIBITING BLOOD VESSEL GROWTH IN AMD

Work from the Sheibani and Sorenson labs has established that thrombospondin-1 (TSP1) and pigment epithelium derived factor (PEDF) are key regulators of ocular vascular homeostasis -- and that their alteration contributes to ocular diseases with a neovascular component (including exudative or wet AMD, diabetic retinopathy, and the growth of ocular tumors such as uveal melanoma). An increase in TSP1 (through a TSP1 mimetic peptide or unabridged TSP1 expression) has been shown to significantly inhibit ocular neovascularization and tumor growth (Figure 1). Dr. Daniel Albert as well as collaborators at Northwestern University (Drs. Jack Henkin, Olga Volpert, and Hao Zhang) are currently working to develop such mimetic peptides from TSP1 and PEDF for treatment of exudative AMD.

EARLY INTERVENTION IN DIABETIC RETINOPATHY

Diabetic retinopathy is a complication of diabetes and a major cause of vision loss in middle age. Unfortunately, there are no treatments available to protect the eye from retinal vascular changes during diabetes or to stop progression to the proliferative stage, when active neovascularization is a major threat to vision. The Sheibani and Sorenson labs have been interested in determining the steps by which diabetes leads to retinal vascular dysfunction. They have shown that in diabetes, an overall decreased ocular level of TSP1 is a major contributing factor to retinal vascular dysfunction and non-proliferative changes such as loss of vascular cells.



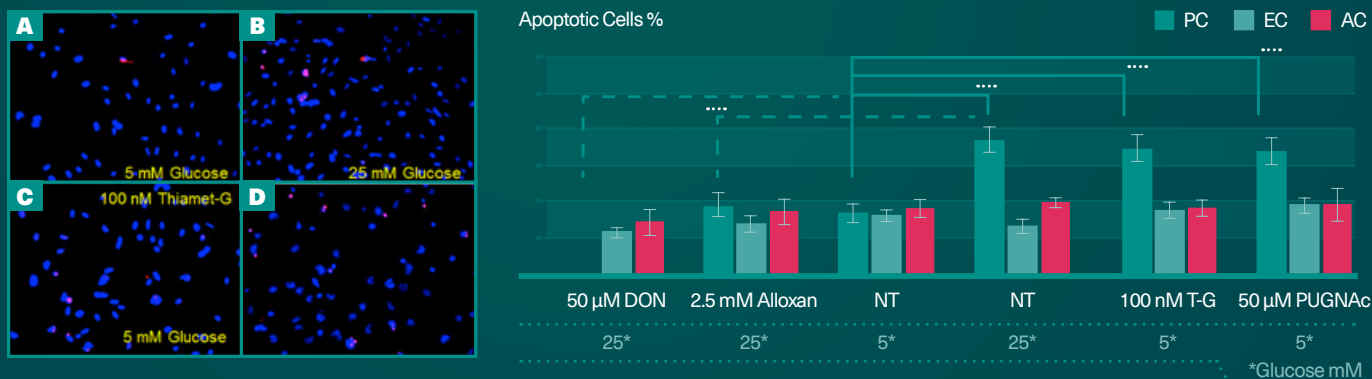
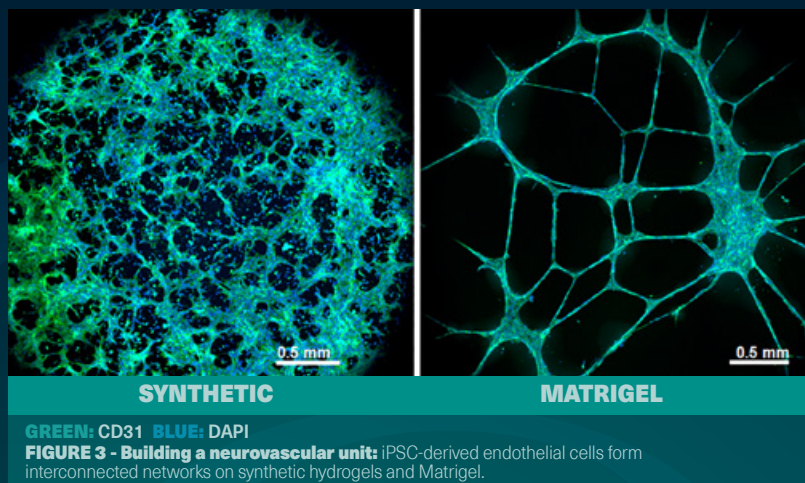


FIGURE 2: Sensitivity of retinal pericytes to high glucose or increased O-GlcNAc modification in normal glucose. (A): represents retinal PC grown in 5 mM (normal) glucose medium, (B): in 25 mM (high) glucose medium, (C): treatment with 100 nM Thiamet-G (increase O-GlcNAc pharmacologically) for 1 day in 5 mM glucose medium, (D): positive control, cells treated with 1 μ M staurosporine (STP) for 6 h. These images are representative of images evaluated at least 1000 cells for each condition with 3 replicates (original magnification x200). (E): Bar graphs quantify apoptosis (programmed cell death), which is expressed as a percentage of apoptotic cells for each.

Understanding the contribution of cell death to vascular failure in early-stage diabetic retinopathy is key to reducing this dysfunction and preventing later vascular proliferation. Using a culture of various retinal vascular cells, the Sheibani and Sorenson labs have found that one type of vascular cell, perivascular supporting cells (pericytes), is sensitive to changes in glucose levels and undergoes cell death (Figure 2), while other types of vascular cells do not exhibit this response. The labs' current studies focus on determining why pericytes respond so differently to high glucose conditions by investigating the metabolic activity of these cells – especially the modification of intracellular proteins by glucose. The ultimate goal is to intercede with the process of cell death at an early stage, halting or delaying further vascular degeneration.

DEVELOPMENT OF A NEUROVASCULAR UNIT

The central nervous system neurovascular unit, consisting of neurons, glial cells and vascular cells, plays a crucial role in maintaining neurological and vascular functions of tissue. Disruption of this neurovascular unit contributes to a variety of neurological pathologies, and – in the case of retina – to vision diseases such as diabetic retinopathy. The Sorenson and Sheibani labs are collaborating with Dr. William Murphy (Biomedical Engineering) and other members of the Human Models for Analysis of Pathways (HMAPS) Center (Drs. David Beebe, James Thomson, Sushmita Roy, and Krishanu Saha) on an exciting new project. Using induced pluripotent stem cell (iPSC)-derived cellular components, they will assemble a neurovascular unit using a synthetic biomaterial (Figure 3). This unit, which is amenable to high throughput screening



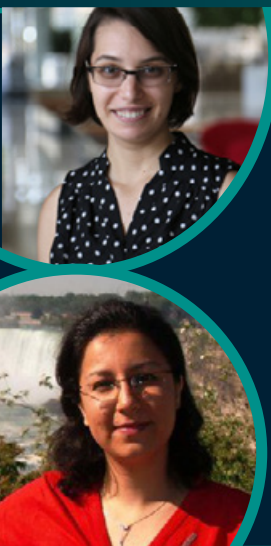
studies, will be utilized for rapid screening of many chemicals that may adversely affect the development and function of the central nervous system or create neurological disorders. The system, funded by the Environmental Protection Agency, would also allow for more dynamic study of the specific impact of high glucose on the neurovascular unit, and for better identification of cellular targets. This knowledge will aid in early detection and effective targeting of appropriate cells for preventative and therapeutic interventions.

UNDERSTANDING A LACK OF RESPONSE TO ANTI-VEGF THERAPY IN EXUDATIVE AMD

Anti-VEGF therapy is commonly used for treatment of exudative (wet) AMD. However, approximately 30% of individuals fail to respond to this treatment. A new endeavor underway in the Sheibani and Sorenson labs holds promise for this cohort of patients. In collaboration with Dr. Barbara Blodi, the lab will examine patient response and attempt to delineate the reason for this lack of effectiveness. An initial focus will be on altered expression and/or activity of one of the key proteins responsible for the activity of anti-VEGF. The goal is to gain more knowledge of who will respond to anti-VEGF treatment, and to determine whether anti-VEGF is a good option for all patients with exudative AMD.

Sheibani and Sorenson lab members, L-R TOP: Shoujian Wang, Zafer Gurel, Yong-Seok Song, M. Ali Saghir, Debra Fisk, Eric Nguyen **BOTTOM:** Soesiawati Darjatmoko, Nasim Jamali, Christine Sorenson, Nader Sheibani, Ismail Zaitoun, and Juliana Falero-Perez.





Fall 2017 Walsh Research Travel Award Recipients

McPherson ERI/David G. Walsh Research Travel Awards provide funds for MERI-affiliated graduate students and postdocs to attend conferences to present vision-related work and advance their educational and professional development. We are pleased to announce two fall 2017 award recipients! **Maryse Lapierre-Landry**, a graduate student (Morgridge Institute for Research; Biomedical Engineering; Melissa Skala, mentor), will attend the 2018 SPIE Photonics West conference. She will present her work on photothermal optical coherence tomography, which uses a contrast agent that augments eye tissue visibility for diagnosis and surgical uses. **Nasim Jamali**, a postdoctoral researcher (Ophthalmology and Visual Sciences; Nader Sheibani, mentor), will attend the 2018 Association for Research in Vision and Ophthalmology (ARVO) annual meeting and present her work on vitamin D3 and regulation of vasculature function. **Congratulations** to both award recipients, who will be invited to speak in the McPherson ERI seminar series during the 2018-19 academic year.

MARCH 10, 2018

Save the Date for Cycle for Sight 2018!

SAVE THE DATE

10TH

MAR 2018

THREE VENUES:

- **Princeton Club West**, 8080 Watts Rd
- **Capital Fitness**, 15 N. Butler
- **UW Natatorium**, 2000 Observatory Dr

Register online starting in late
December, vision.wisc.edu/cycle

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appreciate your help in advancing
vision research!

