McPherson Eye Research Institute
UNIVERSITY OF WISCONSIN–MADISON

InSights

Published each semester

SUMMER *2019*

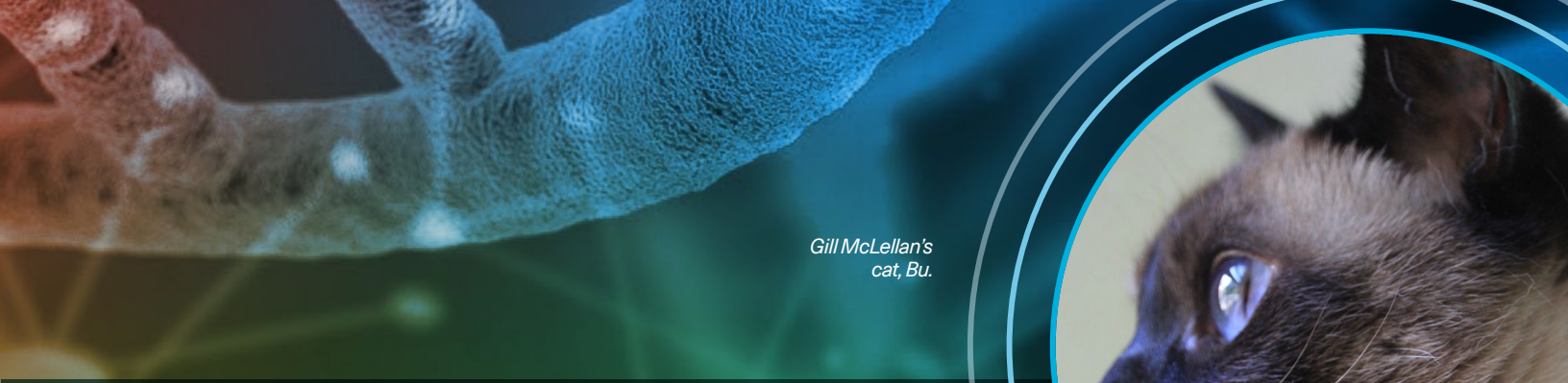
Understanding Glaucoma Across Species

WITH GILLIAN MCLELLAN, BVMS, PHD, DECVO, DACVO

Glaucoma affects more than 3 million people in the U.S. alone, and is also a devastating disease in companion animals. According to Dr. Gillian McLellan, "It is a complicated disease to study and to treat. The pathway to disease involves many factors, including differences in underlying genetics and individual lifestyle contributions that affect vision loss." Applying the principles of "One Health," she studies diseases in veterinary patients, which share our environment and are often long-lived, but have high rates of naturally occurring genetic disease such as glaucoma due to many years of selective breeding. Dr. McLellan's laboratory aims to discover new treatments for vision loss due to optic nerve and retina damage in glaucoma, in both humans and animals.

In the course of her clinical work as a veterinary ophthalmologist, Dr. McLellan has treated glaucoma in many types of animals. She discovered a family of Siamese cats with congenital glaucoma and, working with a team of national and international collaborators, showed that glaucoma in these cats was caused by a mutation in the gene ***LTBP2***. Mutations in this gene are associated with glaucoma in children and adult humans, as well as in cats.

Glaucoma in dogs can have a particularly sudden onset, and is a painful and devastating disease that most closely resembles acute angle closure glaucoma in humans. The disease is highly prevalent in certain breeds of dog, including Basset Hounds and Siberian Huskies. Over the past few years, it appears to be getting more severe and affecting increasingly younger animals of these breeds. The McLellan lab is working in collaboration with colleagues in the Comparative Orthopedics Research Laboratory of the School of Veterinary Medicine, and with the support of



Gill McLellan's cat, Bu.

Understanding Glaucoma
Across Species

the American Kennel Club, to unravel the genetic basis of glaucoma in the Siberian Husky. The goal is to identify the gene defect (or defects) responsible, which in turn will reduce incidence of the disease in dogs by selective breeding. Furthermore, it will provide important insight into underlying mechanisms for glaucoma development and ultimately inform better treatment strategies for people as well as animals.

Strong collaborative relationships with other investigators underpin the McLellan Lab's efforts to answer other challenging questions, including: where does pathological change begin in glaucoma? When do secondary responses kick in that might offer additional targets for treatment, and are these responses protective or harmful? Her lab's wide-ranging collaborations include:

- **Developing better optical imaging tools** to screen for differences in the sclera (white) of the eye, possibly predictive of susceptibility to vision loss in glaucoma (a collaboration with Dr. Jeremy Rogers' lab);
- **Postdoc Kara Vogel's work** (in collaboration with Dr. Colleen McDowell's lab) to refine methods to culture different cell types from the eye relevant to glaucoma, which can then then be studied "in a dish";
- **Work on imaging the fluid outflow pathways** in living eyes done by trainee veterinary ophthalmologists Kevin Snyder and Becky Telle, and recent DVM graduate Jake Nilles;
- **Innovative microscopy studies** (involving collaborators in UW's Morgridge Institute) to view these same pathways in mouse eyes that have been rendered completely transparent, done by lab members Kore Chan and Kazuya Oikawa.

All of these studies provide routes to earlier diagnosis and better treatment for veterinary – and ultimately human – glaucoma patients. "Through these collaborations with other talented researchers, including many fellow McPherson ERI members, our lab is often at the forefront in the development and application of cutting edge technologies," notes McLellan. "We never lose sight of our overarching goal: to improve quality of life for those people and animals who suffer from this debilitating disease."

From the Director

Summer 2019

The McPherson ERI draws its members from a broad spectrum of vision researchers across UW-Madison's extensive campus, as well as other Wisconsin institutions. While unique in our backgrounds and abilities, we share a passion for understanding, preserving, and restoring the magnificent but fragile visual system. Achieving these goals requires expertise from many disciplines, as reflected by this year's new members (below). In 2018-19, we added world-class researchers from several specialties, including cell biology, genetics, cognitive psychology and perception, epidemiology, and engineering, among others. As these new members build collaborations, the potential for advancements in vision science and therapeutics increases.

There is also a range of longitudinal experience among our membership. Some have worked in vision science and medicine their entire careers, while others, including some who we welcomed this year, are new either to the University or vision research in general. The McPherson ERI's focus on team building and knowledge sharing has helped persuade many supremely talented researchers to work on eye and vision problems. And when dedicated, gifted people come together, good things happen.

In addition to fostering collaborations that tackle tough issues in vision research, the Institute sponsors gatherings that shed light on these activities so that other members can see synergistic opportunities. These events include our annual MERI-at-a-Glance presentation, which features updates from a cross-section of McPherson ERI researchers (November 22nd this year), and our fall scientific poster session, which will be held on October 24th. Neurobiologist Margaret Livingstone will deliver a keynote lecture immediately following the poster session (see the announcement on the back page), and you are invited to join us at her talk. I hope to see you there, and as always, thank you for your interest and support.

David M. Gamm, MD, PhD

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

New McPherson ERI Members

Amitha Domalpally, MD, PhD

Research Director • *Fundus Photograph Reading Center* • UW-Madison

Dr. Amitha Domalpally is the Research Director at the UW-Madison Fundus Photograph Reading Center in the Department of Ophthalmology and Visual Sciences, and is actively involved in clinical trial imaging research with a focus on retinal diseases. Her research interest involves novel outcome measures and imaging techniques designed to better understand the natural course and prognostic markers for complex retinal diseases such as macular degeneration and diabetic retinopathy. A second area of interest is in imaging artifacts and ways to interpret quantitative data. She is also involved in developing diagnostic artificial intelligence algorithms for retinal diseases.

Ross Collery, PhD

Assistant Professor • *Ophthalmology & Visual Sciences* • Medical College of Wisconsin

Ross Collery's research centers on the study of retinoids (vitamin A analogs) and other signaling pathways that participate in eye growth, health, and control of refractive state. He uses zebrafish and stem cell-derived retinal pigment epithelial cells to study how retinoids support the visual cycle and affect gene expression. His research investigates biological and perceptual variables that contribute to emmetropia – "ideal vision" – and retinal health. To that end, he uses CRISPR/Cas9 gene editing techniques to delete or mutate genes associated with human diseases affecting refractive state or leading to retinal degeneration.

Ronald Gangnon, PhD

Professor • *Biostatics and Medical Informatics* • UW-Madison

Ronald Gangnon has served as senior biostatistician for the Beaver Dam Eye Study and the Wisconsin Epidemiologic Study of Diabetic Retinopathy, and collaborated with Dr. Matthew Davis on the development of severity scales for age-related macular degeneration and for diabetic macular edema. In a recent series of papers, he and his colleagues advocated for the use of multistate models for incidence, progression and regression of age-related macular degeneration (AMD). Using these models, they have greatly enhanced our understanding of multiple aspects of the epidemiology and progression of AMD.

New McPherson ERI Members

Colleen McDowell, PhD

Associate Professor • *Ophthalmology and Visual Sciences* • UW-Madison

Colleen McDowell's laboratory focuses on the molecular pathways associated with the development and progression of glaucoma. More specifically, she studies the development and regulation of elevated intraocular pressure (IOP), as well as the effect of elevated IOP on retina ganglion cell (RGC) survival and optic nerve head (ONH) damage. For example, using various techniques her lab discovered that mutation in TLR4 (toll-like receptor 4) rescues ocular hypertension in a mouse model of glaucoma. These and other data are invaluable because they provide model systems to study glaucoma damage and to test novel therapeutics.

Beth Meyerand, PhD

Vilas Distinguished Achievement Professor • *Medical Physics* • UW-Madison

Beth Meyerand develops new methods to create maps of human brain connections in different patient groups using Magnetic Resonance Imaging (MRI) data and ways to visualize diffusion and activation in the human brain. As part of this effort, she conducts research with patients who have had tumors and lesions in the visual cortex. She also studies changes within the visual cortex in patients who have had a stroke or traumatic brain injury. Her goal is to develop new MRI methods to visualize the structure and function of the brain and to translate these methods to the hospital for clinical diagnosis.

Emily Ward, PhD

Assistant Professor • *Psychology* • UW-Madison

Emily Ward directs the Visual Cognition Lab in the Department of Psychology. Her lab explores the nature of visual awareness, with an emphasis on the ways in which visual perception interacts with and constrains other processes in the mind. Some current questions her lab is exploring are: What determines whether we become aware of something? How does the format of information in the brain correspond to what we see? Do artificial visual systems suffer from the same failures of awareness that people do? To address these topics, her lab uses a combination of behavioral and functional neuroimaging methods, creates novel visual tasks, and employs state-of-the-art machine learning to explore both human and artificial visual systems.

New McPherson ERI Members

Donna Neumann, PhD

Associate Professor • *Ophthalmology and Visual Sciences* • UW-Madison

HSV-1 is a common infection associated with cold sores and ocular infections that can result in blindness. **Donna Neumann's** laboratory focuses on understanding how HSV-1 infections lead to corneal scarring and blindness in some individuals but not others. Her laboratory uses a global approach to answer this question, starting at the neuron level so as to define the mechanisms through which HSV-1 causes ocular pathogenesis.

Jacob Notbohm, PhD

Assistant Professor • *Engineering Physics* • UW-Madison

Jacob Notbohm's research interests are in cell mechanics, mechanotransduction (the conversion of mechanical stimuli to biochemical signals in cells), cell migration, and quantitative image analysis with applications in human health and disease. Numerous conditions of the eye are related to mechanics and cell response – two examples are changes in intraocular pressure and transport across the retinal pigment epithelium (RPE).

Matthew Veldman, PhD

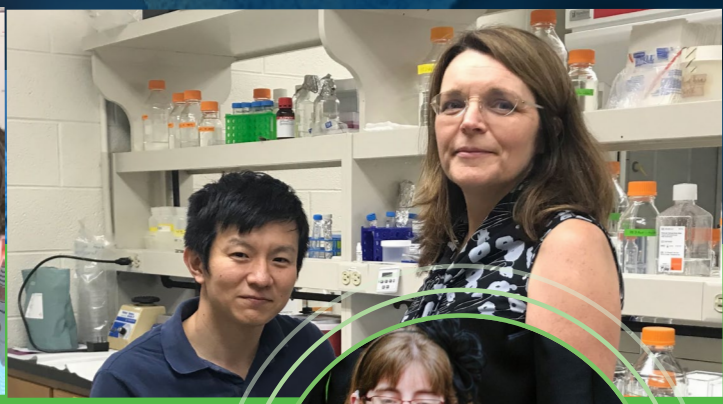
Assistant Professor • *Cell Biology, Neurobiology and Anatomy* • Medical College of Wisconsin

Matthew Veldman's research is focused on optic nerve and retinal degenerative disease and injury models and on methods to stimulate regeneration within the visual system following these pathological events. Specifically, he is studying the molecular mechanisms of successful optic nerve regeneration in the zebrafish model, with the hopes of translating these findings into new therapies for patients with conditions such as glaucoma.

Sushmita Roy, PhD

Associate Professor • *Biostatistics and Medical Informatics* • UW-Madison

Dr. Sushmita Roy collaborates with several McPherson ERI investigators on projects focused on gene expression and repair. She is currently working with David Gamm to study the transcriptional programs of retinal development, as well as regulatory networks that might be involved in cell fate decisions in different photoreceptor cells. She is also a co-investigator on a major grant led by Kris Saha, the goal of which is to monitor therapies designed to correct gene defects in retinal cells to assure they do not introduce new genetic mutations.



Kenzi Valentyn Vision Research Trainee Grants Commemorate a Brave Spirit

The McPherson Eye Research Institute's annual Cycle for Sight fundraiser has, beginning in 2017, funded four Vision Research Trainee Grants (two annually). This year and in future years these grants have been renamed the **Kenzi Valentyn Vision Research Trainee Grants** – in honor of Kenzi's courage and positive attitude throughout her long battle with Kearns-Sayre syndrome, a degenerative disease with symptoms including vision loss, which ended with her passing at age 30 in March 2017. Her many friends and family members, including her parents Nancy and Tim, brothers Brett and Connor, and sister-in-law Mackenzie, have ridden in Cycle for Sight as "Kenzi's Team" since 2014. The Valentyn family's dedication to vision research once again enables the award of two one-year grants of $4000 each to trainees selected by Research and Leadership Committee members in the 2019 competition.

Michael Landowski, PhD, a postdoctoral researcher working with Professor Aki Ikeda's lab group in the Department of Medical Genetics, will pursue a project exploring a protein that may be important in maintaining mitochondrial dynamics, **"A role of TMEM135 in retinal glucose and lipid metabolism."** His work will also explore age-dependent retinal pathology development in a mouse model.

Kazuya Oikawa, BVSc, a graduate student in the Comparative Biomedical Science Program in the School of Veterinary Medicine who is mentored by Dr. Gillian McLellan (Department of Ophthalmology and Visual Sciences; Department of Surgical Sciences), will be advancing understanding of "Optic nerve head neuroinflammation in a spontaneous large animal model of glaucoma," correlating inflammation with disease severity over different stages of feline glaucoma.

We are grateful to the Valentyn family and to all Cycle for Sight supporters for making this award program possible.

SAVE THE DATE!

11th Annual **Vision Science Poster Session**

Thursday, October 24, 2019

3:00pm – 5:30pm Poster Session
Atrium, Health Sciences Learning Center (HSLC)
750 Highland Ave, UW-Madison
Registration opens late August

5:45pm Distinguished Guest Lecture
HSLC Room 1335
What Art Can Tell Us About the Brain

Margaret S. Livingstone, PhD
Department of Neurobiology
Harvard Medical School