

The Road to Clinical Trials for Stem Cell Therapies

JOE PHILLIPS, PhD

PP. 7-9

Living With a “Watch” Dog

FREYA MOWAT, PhD

PP. 12-14



From the Director

Dear Friends of the McPherson ERI,

Most people understand that developing a treatment for any disorder—especially one that has never been tried before in humans—takes creative thought and hard work as well as time and financial support. The McPherson ERI provides an ecosystem within which our over 200 researchers, who investigate many different aspects of vision, are encouraged to bounce ideas off one another and empowered to achieve goals that advance science and medicine in profound and meaningful ways. Novel technologies and therapies often result, including gene editing techniques for inherited childhood blinding diseases and macular degeneration that are now in development.

We pursue all research projects with diligence and a sense of purpose, but for patient safety and other reasons, the work cannot be rushed. Indeed, scientists often spend much of their careers fostering ideas from conception to laboratory investigation to—with tenacity and a healthy dose of good fortune—clinical product development.

To accelerate this journey without skimping on quality and safety, the McPherson ERI supports scientists and clinician-scientists at every stage of their research endeavors. In this issue of *InSights*, you'll read about the Institute's support for graduate students and postdoctoral scientists through our Kenzi Valentyn Vision Research Awards. We also highlight larger research awards that bolster work by established faculty scientists focused on diseases like age-related macular degeneration, retinitis pigmentosa, glaucoma, and optic nerve damage. Lastly, in the article detailing Dr. Joe Phillips' work, we provide a glimpse into a major academic-industry collaborative effort designed to produce a first-of-its-kind stem cell treatment for retinal degenerative diseases.

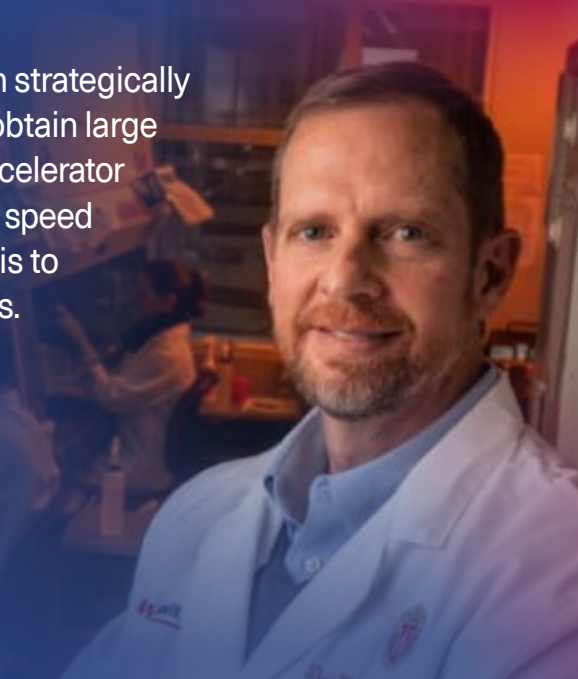
Thankfully, the resources the Institute can provide to our world-leading vision researchers allow our bite to match our bark. With the help of generous supporters, including Roger and Lynn Van Vreede (profiled below) and Sandy and the late Dr. Monroe Trout (see p.6), we are able to give our researchers a powerful leg up in their efforts to develop new therapies or assistive technologies, or to pursue studies that untangle mysteries of our visual system.

Several years ago, we started the Grant Summit Program, which strategically awards smaller funds to help researchers cross the finish line to obtain large federal grants. We are now adding another initiative—the Grant Accelerator Program—which is designed to get projects out of the gate and up to speed faster than they otherwise could. The goal of all these programs is to preserve and restore vision, which is the ultimate measure of success.

Thank you for your help and interest,



Professor, Department of Ophthalmology and Visual Sciences
RRF Emmett A. Humble Distinguished Director
McPherson ERI Sandra Lemke Trout Chair in Eye Research





Lynn and Roger
Van Vreede

Supporting MERI's Greatest Needs

Roger and Lynn Van Vreede have been married for 35 years and have also counted 35 years of supporting charitable causes together. Their interests align well—both are lovers of the arts, and passionate gardeners and environmentalists. (As Lynn says: “When we were kids, we’d take our shoes and socks off and run in the water.... we want to make sure that future generations can do that.”) For the past five years, vision research has topped their list of interests, leading to their recent pledge of \$1 million to endow the Van Vreede McPherson ERI Greatest Needs Fund.

Their interest starts close to home. Roger’s mother Lorraine, who passed away in 2023 at the age of 100, had age-related macular degeneration; as does Lynn’s father, Allen, now 87. For Lorraine Van Vreede, AMD was frustrating but not incapacitating, as she retained some vision. For Lynn’s father, AMD has been worse. “I started taking him to the Wisconsin Council of the Blind and Visually Impaired after my mother died,” Lynn says, “and the devastating effects of the disease became apparent. My dad can’t really do much at all, but he’s handled it with grace.”

Lynn herself has suffered from various eye issues over the years, a topic which came up socially with their friends Monroe and Sandy Trout. The Trouts quickly introduced them to the McPherson ERI, and the Van Vreedes were just as quickly fascinated by the range of research taking place at the Institute.

“The connections throughout the world were impressive. It’s not just one lab working on one issue; the number of individual studies going on is surprising,” notes Lynn. “You’re studying diseases from many different angles.” They began supporting the Institute soon after and joined the McPherson ERI Advisory Board in 2017.

Although intimately familiar with age-related macular degeneration, the Van Vreedes decided not to focus their Institute support on only one area. Both are highly aware that an organization’s needs can change each year (Roger, whose father started Van Vreede’s appliance stores in the Fox River Valley in the 1950s, grew up watching the ever-changing needs of a retail business). They began by sponsoring successful annual matches for the Institute’s year-end giving and are fervent believers that match offers create excitement and increase support. More recently, their support switched to underwriting major research grants for AMD and retinitis pigmentosa.

In planning a large-scale gift, the Van Vreedes became interested in the idea of a Greatest Needs fund—an endowment that would be flexible enough to respond to the McPherson ERI’s research needs each year. The Shapiro Foundation’s match offer sealed the one-million-dollar amount: “That was how we came up with that big of a number,” says Roger. “The more we band together, the more synergy is created and the better the outcome,” Lynn adds.

Their hope is for transformative change. “I know it may take some time before the average person can get a transplant or other treatment that will help their sight,” says Roger. “But it’s moving along faster than I thought it would. And we want to help solve these problems.”



The Herman and Gwen Shapiro Foundation

Herman “Murph” Shapiro, MD ‘32, and Gwen Shapiro, BS in Nursing (’53)—a longtime faculty member of the University of Wisconsin School of Medicine and Public Health (SMPH) and head nurse at UW Hospital and Clinics, respectively—had a strong desire for their legacy to shape educational experiences for future generations of physicians and nurses. Established in 1995, the Herman and Gwen Shapiro Foundation memorializes the couple, who worked hard, loved life and followed their hearts about ways they could assist others well beyond their lifetime, notes David Walsh, JD, chair of the foundation’s board of directors. “They wanted to improve the human condition—the words from the Wisconsin Idea—and that’s why they were involved in academic medicine,” says Walsh, whose parents were friends with the couple.

Walsh and the Shapiro Foundation Board approved the \$1 million match to the McPherson ERI because, according to Walsh, the Shapiro Foundation “has continued to identify and support unique and exciting new initiatives in medicine and nursing.” He notes that, “the McPherson Eye Research Institute is home to many innovative initiatives, and the Shapiro Foundation is glad to support MERI and the tremendous generosity of Roger and Lynn Van Vreede with this matching grant.”



Dr. Monroe E. Trout

1931-2024

Monroe Trout, a true friend of the McPherson ERI, passed away on March 4th after a short illness. Dr. Trout connected with the Institute following an event held at the Trout Museum in Appleton in 2012 and was an outstanding supporter and advisor in the years since. His ongoing struggle with macular degeneration gave him insight into the patient's experience, and his extensive background in medicine, the pharmaceutical industry, law, and business left him well-equipped to advise the Institute in its growth. Alongside his wife, Sandy, Dr. Trout endowed the Trout Director's Fund to broadly advance sight-saving science, four Chairs to support world-renowned vision researchers, and, most recently, the Trout AMD Project to specifically advance therapies for macular degeneration. Certainly, the Trout family's legacy to vision research will live and grow in the Institute forever.

Beyond his support for eye research, we will miss Monroe Trout's good humor and penchant for envisioning impactful projects and his over-arching concern for the well-being of others. He told his extraordinary life story in his autobiography, *Winter Galley*, and captured many of his experiences and passions in his paintings. Monroe lit up whenever he spoke about his family, and his and Sandy's love of children found an outlet in their sponsorship of the PBS Kids Channel at PBS Wisconsin, which was established in honor of their late son Timothy. The Trouts have also supported veterans, numerous schools and universities, the arts, and their Appleton church, among other philanthropic ventures. Dr. Trout led a life of true meaning, and we will hold his memory in our hearts.

A portrait of Dr. Joe Phillips, a middle-aged man with grey hair, a beard, and glasses, wearing a dark button-down shirt. He is smiling slightly and looking towards the camera. The background is a soft-focus outdoor scene with green trees and a warm, orange-toned light source, possibly the sun, creating a lens flare effect.

The Road to Clinical Trials for Stem Cell Therapies

Dr. Joe Phillips is a scientist whose research focuses on the development of induced pluripotent stem cell (iPSC)-based therapeutics for the treatment of blinding disorders of the retina. Dr. Phillips has been working towards this goal since 2010, when he moved from Texas to Wisconsin to leverage and combine his knowledge of animal models testing and background in retinal therapeutics with Dr. David Gamm's pioneering development of iPSC-derived retinal organoid technology.

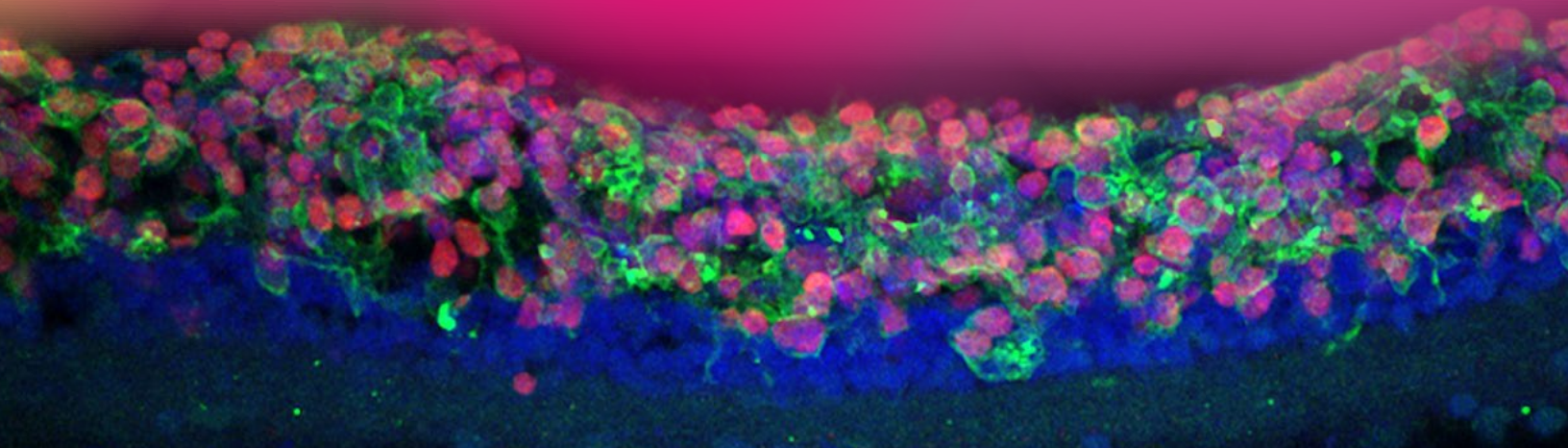
Their developmental work on iPSC-derived retinal cell therapeutics led to a partnership with Fujifilm Cellular Dynamics Inc. and the formation of Opsi Therapeutics in 2016, a company focused on bringing this therapy to the clinic.

In blinding diseases like retinitis pigmentosa (RP) and age-related macular degeneration (AMD), specific retinal cells required for vision are progressively and irrevocably lost. The retinal cell types affected in these patients include the light-sensitive photoreceptors and/or supportive retinal pigment epithelium (RPE) cells, which are required for photoreceptor survival. In Dr. David Gamm's laboratory, Dr. Phillips leads a team of researchers that evaluates the safety and efficacy of iPSC-derived photoreceptors and RPE in animal models of retinal disease.

Animal models of human disease are essential for the evaluation of new therapeutics, prior to proceeding to human clinical trials. As there are many animal models that have the same disease etiology as diseases found in humans, performing testing in these models provides critical insight into how the therapeutic will perform in human patients. The studies performed by Dr. Phillips's team involve transplanting iPSC-derived photoreceptors and RPE into animal models of RP and AMD and evaluating the engraftment, differentiation, and integration of these cells, as well as testing retinal function following transplantation. These studies have guided the development and optimization of these therapeutics.

Translating laboratory research to the clinic is an enormous undertaking. Towards this end, Dr. Phillips and Dr. David Gamm collaborate closely with industry leaders in cell-based therapies, and in 2021 formed a strategic research alliance between their laboratory, Opsis Therapeutics, Fujifilm Cellular Dynamics Inc., BlueRock Therapeutics, and Bayer to bring these therapies to patients. The first of these therapies is an iPSC-derived photoreceptor cell product designed to treat patients with RP and other retinal diseases leading to primary photoreceptor loss.

Over the past 2 years, Dr. Phillips has overseen multiple large-scale, multi-million-dollar, Investigational New Drug (IND) enabling studies that are required by the Food and Drug Administration (FDA) to initiate clinical trials for this novel iPSC-derived photoreceptor replacement therapy. In the lab, this included a large-scale efficacy study that systematically evaluated iPSC-derived photoreceptor transplantation in an RP animal model. In these studies, Dr. Phillips' team demonstrated that transplanted human iPSC-derived photoreceptors will become fully mature rod and cone photoreceptors in vivo, survive long term, and integrate into a retina of an animal model affected by a severe form of RP.



Transplanted human iPSC-derived photoreceptors survive long-term in a rat model of retinitis pigmentosa, replacing photoreceptors that are otherwise missing in this model. Over time, rod and cone photoreceptors mature and integrate within the host rat retina. In this image, transplanted human cells (red cells) express a marker for photoreceptors (green cells) and have reformed a new photoreceptor layer. Image courtesy of the Gamm Lab.

Dr. Phillips also oversaw independent safety studies performed at Labcorp. In these studies, multiple safety parameters were evaluated, including toxicology, tumorigenicity, and biodistribution. Additional studies were performed to develop, optimize, and evaluate the safety of the surgical procedure that will be performed in humans. Currently, these animal studies, along with additional extensive product safety and characterization studies, are being compiled into a comprehensive IND package for submission to the FDA for approval to initiate clinical trials.

Clinical trials are organized into different phases. This work will support an upcoming Phase 1/2 clinical trial for the treatment of RP and other photoreceptor-based diseases. Phase 1 clinical trials are designed to test the safety of new therapies in a small number of patients. If safety is demonstrated in Phase 1, Phase 2 is initiated and both safety and efficacy parameters are evaluated. Phase 3 involves a larger number of patients and is designed to gather safety and efficacy data and compare those findings to any current standard treatment. Increasing numbers of patients are evaluated in each phase, and the optimal dose of the drug is determined. Following Phase 3, the performance of the drug (which in this case is human iPSC-derived photoreceptors) is evaluated by the FDA for potential approval and release of the new drug on the open market.

Dr. Phillips and his team are also currently performing studies to develop and test new AMD therapeutics, which involves the replacement of both photoreceptors and RPE. This combined cell therapy product for the treatment of AMD will follow the same approval path with the FDA, and IND-enabling studies are planned to begin in the near future.

L-R, Suzanne Litscher BS, Ashley Willes BS, Tyra Moyer BS, Joe Phillips PhD, Lindsey Jager PhD, Mari Feudner BS, Lydia Bowar BS



Targeting AMD, RP, and Glaucoma

The McPherson ERI exists to support promising research avenues identified by our scientists. With the support of a range of generous donors, including Roger and Lynn Van Vreede and the Robert A. Brandt Macular Degeneration Fund as well as an anonymous donor, MERI was able to fund these projects with \$50,000 grants in Fall 2023.

Nader Sheibani, PhD



Professor, Ophthalmology and Visual Sciences
☛ *Caffeine and Mitigation of Angioinflammatory and Fibrotic Processes in Exudative AMD*

“Age-related macular degeneration (AMD) is mediated by local chronic inflammation. Our recent studies show an important role for caffeine in mitigating ocular inflammatory processes in pre-clinical models of AMD. The studies proposed here begin to expand on these initial findings in order to identify the molecular mechanisms involved at the cellular levels. This knowledge will allow us to discern points of intervention to halt development and progression of AMD.”

Kim Stepien, MD



Professor, Ophthalmology and Visual Sciences
☛ *Comparison of Clarus and Optos Ultrawide Field Imaging for Retinitis Pigmentosa (COCO – RP)*

“Retinitis Pigmentosa (RP) is a group of rare inherited retinal disorders that are characterized by early onset loss of night vision, peripheral vision, and, in end stage disease, loss of central vision. Ocular imaging plays a crucial role in the diagnosis and management of RP, as well as monitoring potential therapeutic responses in emerging clinical trials for RP. Our study works to systematically compare standardized images taken on several different types of ocular imaging cameras to ensure that these diverse imaging tools yield equivalent results for standardized measurements in RP clinical trials.”

Ismail Zaitoun, PhD

Assistant Professor, Ophthalmology and Visual Sciences • *Undesirable Outcomes of Wound Healing in Exudative AMD*

“Macular scar formation is an unfavorable outcome of the abnormal growth of new blood vessels in the wet form (neovascular form) of age-related macular degeneration. Unfortunately, there are limited therapy options available to prevent scar formation, and many patients with wet AMD do not respond to the current therapy. Our studies established that blood vessel cells contribute to choroidal neovascularization (CNV) development and its associated scarring in mice and humans. This new funding will allow us to advance our understanding of the underlying cellular and molecular mechanisms responsible for CNV and scar formation in these patients, potentially leading to novel options to treat patients with wet AMD.”

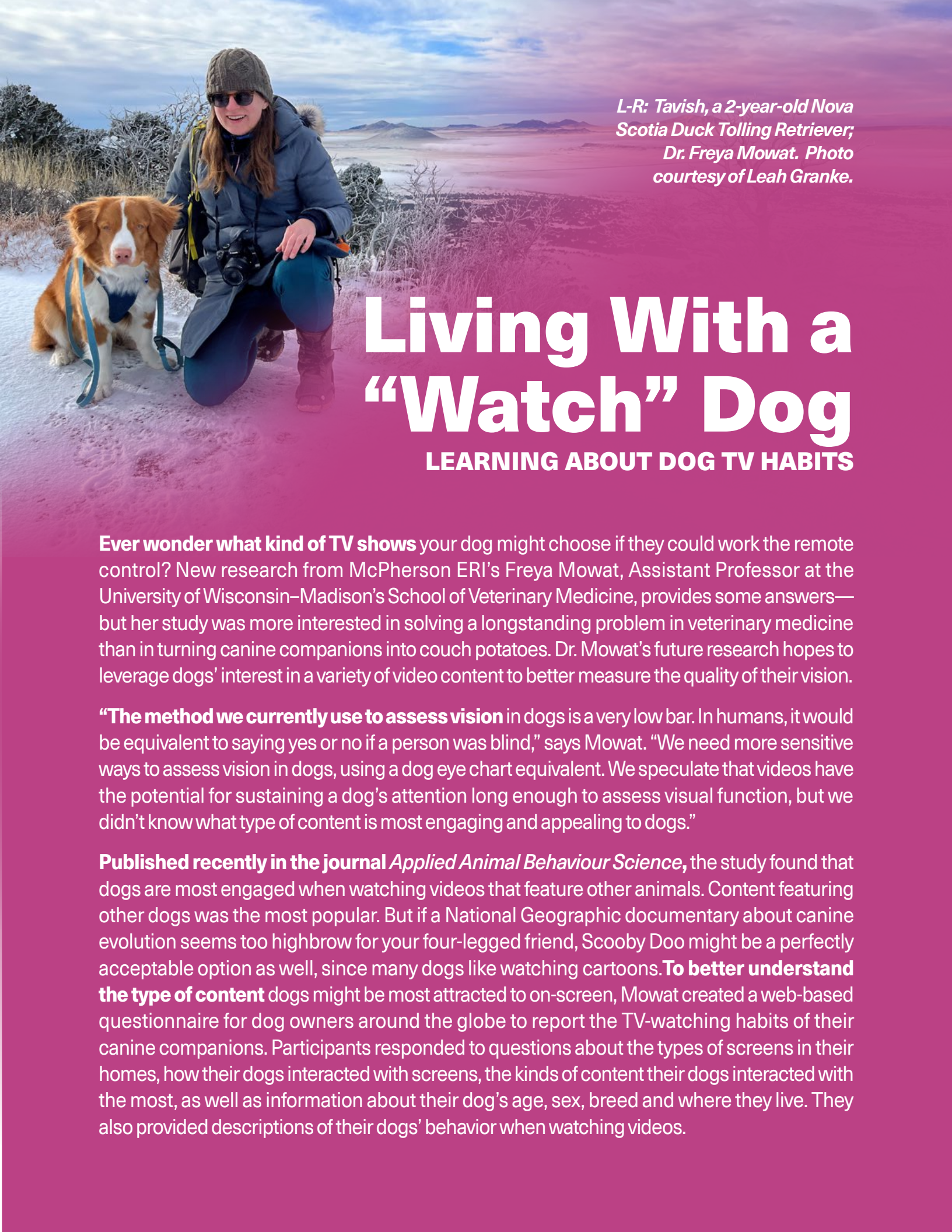


Robert Nickells, PhD

Professor, Ophthalmology and Visual Sciences • *Measuring and mapping mitochondria in retinal ganglion cells*

“Retinal ganglion cells (RGCs) are neurons that transmit visual information from the retina to the brain via the optic nerve. In glaucoma, or after traumatic injuries that affect the optic nerve, RGCs die. Studies indicate that the resilience of RGCs is dramatically impacted by the health of organelles called mitochondria, which provide all cells with high energy substrates needed for normal function. While we know mitochondria are important to RGCs we know very little about how they function, where they are, or how they are affected in damaged RGCs. This work aims to provide some answers to these questions including developing new tools that will allow us to study them in greater detail in models of glaucoma and acute optic nerve injury. Understanding more about the mitochondria in RGCs will hopefully reveal ways to boost their function and in turn strengthen the RGCs to prevent their loss in blinding diseases.”



A woman wearing a grey knit beanie, sunglasses, and a dark blue winter jacket is kneeling in a snowy, open landscape. She is holding a camera. To her left, a brown and white dog is sitting. The background shows a vast, flat, snow-covered field under a cloudy sky.

L-R: Tavish, a 2-year-old Nova Scotia Duck Tolling Retriever; Dr. Freya Mowat. Photo courtesy of Leah Granke.

Living With a “Watch” Dog

LEARNING ABOUT DOG TV HABITS

Ever wonder what kind of TV shows your dog might choose if they could work the remote control? New research from McPherson ERI’s Freya Mowat, Assistant Professor at the University of Wisconsin–Madison’s School of Veterinary Medicine, provides some answers—but her study was more interested in solving a longstanding problem in veterinary medicine than in turning canine companions into couch potatoes. Dr. Mowat’s future research hopes to leverage dogs’ interest in a variety of video content to better measure the quality of their vision.

“The method we currently use to assess vision in dogs is a very low bar. In humans, it would be equivalent to saying yes or no if a person was blind,” says Mowat. “We need more sensitive ways to assess vision in dogs, using a dog eye chart equivalent. We speculate that videos have the potential for sustaining a dog’s attention long enough to assess visual function, but we didn’t know what type of content is most engaging and appealing to dogs.”

Published recently in the journal *Applied Animal Behaviour Science*, the study found that dogs are most engaged when watching videos that feature other animals. Content featuring other dogs was the most popular. But if a National Geographic documentary about canine evolution seems too highbrow for your four-legged friend, Scooby Doo might be a perfectly acceptable option as well, since many dogs like watching cartoons. **To better understand the type of content** dogs might be most attracted to on-screen, Mowat created a web-based questionnaire for dog owners around the globe to report the TV-watching habits of their canine companions. Participants responded to questions about the types of screens in their homes, how their dogs interacted with screens, the kinds of content their dogs interacted with the most, as well as information about their dog’s age, sex, breed and where they live. They also provided descriptions of their dogs’ behavior when watching videos.

Most commonly, dog owners described their pets' behavior as active—including running, jumping, tracking action on screen and vocalizing—compared with passive behaviors like lying down or sitting. Dog owners also had the option to show their dog(s) four short videos featuring subjects of possible interest, including a panther, a dog, a bird, and traffic moving along a road. They were then asked to rate their dog's interest in each video and how closely the dog tracked the moving objects on the screen.

Dr. Mowat received 1,600 responses from dog owners across the world, including from the United States, Canada, the United Kingdom, the European Union, and Australasia. Of those respondents, 1,246 ultimately completed the study.

Some of the most interesting results included:

- Age and vision were related to how much a dog interacted with a screen.
- Sporting and herding purebred dog breeds appear to watch more than other purebred breeds.
- Video content featuring animals was the most popular, with other dogs being by far the most engaging subjects to watch.
- Humans do not appear to be very appealing for dogs to watch, ranking ninth out of 17 predetermined animal categories.
- Cartoons were engaging for more than 10% of dogs.
- Movement on screens was a strong motivator for screen attention.



Below, one of Dr. Mowat's study subjects, watching the moving dog in the larger image. Image courtesy of the Mowat lab.



Dr. Mowat plans to build on the results of this study. Future research will focus on the development and optimization of video-based methods that can assess changes in visual attention as dogs age as well as answer questions that could help our four-legged friends age as gracefully as possible.

“We know that poor vision negatively impacts quality of life in older people, but the effect of aging and vision changes in dogs is largely unknown because we can’t accurately assess it,” she says. “Like people, dogs are living longer, and we want to make sure we support a healthier life for them as well.”

Another of Dr. Mowat’s goals is to compare how a dog’s vision ages compared with the human or humans they share a home with. “Dogs have a much shorter lifespan than their owner, of course, and if there are emerging environmental or lifestyle factors that influence visual aging, it might well show up in our dogs decades before it shows up in us,” she explains. “Our dogs could be our sentinels—the canine in the proverbial coal mine.”

Adapted from a UW News article by Gian Galassi.

This study was supported in part by an NIH career development grant to Mowat (K08EY028628), a Companion Animal Fund Grant from the UW–Madison School of Veterinary Medicine, a grant from Research to Prevent Blindness, Inc. to the UW–Madison Department of Ophthalmology and Visual Sciences and a core grant for Vision Research from the NIH to UW–Madison (P30 EY016665).

Kenzi Valentyn Vision Research Awards

2023

Kenzi Valentyn Vision Research Awards support work by outstanding young vision scientists at the grad student or postdoc level. These awards kickstart promising research projects that likely would otherwise go unfunded. Kenzi Valentyn Awards are funded by Cycle for Sight and named in honor of a brave young woman with vision loss who passed away in 2017; her family continues to cycle each year as Kenzi's Team in her honor. In late 2023, five Kenzi Valentyn Awards were given to the researchers on this page.

Bikalpa Ghimire, Graduate Student

Department of Neuroscience, SMPH

 **Mentor:** Xin Huang

 *Neural processes of motion integration and segmentation in the primary visual cortex (V1)*



Jake Khoussine, PhD/MD Student

Department of Ophthalmology and Visual Sciences, SMPH

 **Mentors:** Mrinalini Hoon and Jeremy Rogers

 *Combining adaptive optics, electrophysiology and serial electron microscopy to investigate photoreceptor integrity in retinitis pigmentosa*



Michele M. Salzman, Graduate Student

Department of Surgical Sciences, SVM

 **Mentor:** Freya Mowat

 *In utero cadmium exposure: effects on murine retinal development and postnatal function – a pilot study*



Tania Sharmin, Graduate Student

Department of Ophthalmology and Visual Sciences, SMPH

 **Mentor:** Colleen M. McDowell

 *Role of Integrin $\alpha 4$ and $\alpha 9$ in the development of elevated IOP and trabecular meshwork damage*



Theodore Bucci, Graduate Student

Department of Neuroscience, SMPH

 **Mentor:** Raunak Sinha

 *Effects of Rhodopsin Phosphorylation Perturbation on Sensitivity and Timing of the Retinal Output*





Sight Beyond Limits

Works by Wisconsin Artists with Vision Loss

Among the 100,000+ Wisconsinites with severe vision loss are a notable number of fine artists. The McPherson ERI's **Mandelbaum & Albert Family Vision Gallery** has displayed the work of eight of these artists in our Spring 2024 exhibit, *Sight Beyond Limits*. Please join us for a closing reception on the last day, May 31st, from 4:30-6:00 PM.

- 1 WARMTH (DESERT AT NIGHT)**
Duncan Hamilton - Crayon, pastel
- 2 PARTIAL ACUITY**
Duncan Hamilton - Crayon, pastel
- 3 SECOND CHANCES**
Lynn Olson - Oil and cold wax on canvas
- 4 PLANET SQUASH**
Rose Fortney - Digital photo on metal
- 5 GLOBAL WARMING**
Albert Schmiede - Oil on canvas



Cycle for Sight 2024

Thank you for making Cycle for Sight 2024 so successful!

With your help, Cycle for Sight again hit an all-time high, raising more than \$70,000 for vision research grants. Our Princeton Club kickoff hosted more than 100 riders and walkers, with team events continuing outdoors in late March and April. We're grateful for your support.



Birds' Eye Views

This summer's exhibit in the Mandelbaum & Albert Family Vision Gallery will explore bird vision through photos by four wildlife photographers: Arlene Koziol, Paul Ludden, Rob Streiffer, and Tom Yin.

🏠 9th floor of WIMR II, 1111 Highland Ave

Birds' Eye Views
opens on Thursday,
June 20th.

Please join us from **4:30-6:30 PM**,
for the gallery opening and ICE
CREAM reception, featuring
a selection of Babcock
Dairy ice creams.

Please follow the McPherson ERI on

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