MORGRIDGE
INSTITUTE FOR RESEARCH

FALL 2022

YOU make a difference

INSIDE

A SPECIAL REPORT FOR SUPPORTERS OF THE MORGRIDGE INSTITUTE FOR RESEARCH

BRAD'S UPDATE

In science, we often talk about collaborations. In this report, I want to underscore this work's importance.

Moreover, we depend on donors like you. You are a collaborator and you truly make a difference here.

I'm sure you've seen our slogan in materials and stories: "Fearless Science." That means we take risks and press against boundaries. We aim for science that we can't currently imagine.

And as an independent organization, we can move quickly and decisively, to follow interesting and important questions, wherever they may lead.

But we are also unique — we have the best of two worlds. We are deeply engaged with the University of Wisconsin-Madison, a world-class public university. That university culture helps science to flourish. Here, people build collaborations to get new ideas off the ground.

THANK YOU
for being a donor and supporter of the Morgridge Institute for Research.

These are more than just "collaborations;" they are true partnerships. We genuinely have each other's backs. And these partnerships are thriving because they are based on trust, transparency, and a shared vision.

In this report, you can read more about a promising frontier of eye disease research that leverages the imaging expertise of the Melissa Skala Lab. You can also meet our newest investigator, Daniela Drummond-Barbosa, who joined our growing metabolism community.

Last, we must celebrate a treasured partnership: The Summer Science Camp. After two years of virtual-only events, we welcomed high school students and teachers back to meet with researchers and scientists in many fields of science and medicine.

All of these collaborations, and many more, are built with your support. Your donations empower scientists, educators, and scholars to advance science and discovery.

You truly make a difference.

Thank you for helping us pursue the joy and curiosity of science. With your support, we will improve human health together.

Brad Schwartz, M.D.
Chief Executive Officer
Morgridge Institute for Research

P.S. Your voice matters. If you have any questions about the stories in this report, please don't hesitate to contact me at giving@morgridge.org

SUMMER SCIENCE CAMPS RETURN TO CAMPUS

CELEBRATING HANDS-ON SCIENCE WITH STUDENTS AND TEACHERS

After two years of virtual-only events, students and teachers from rural Wisconsin high schools returned in-person for the 16th annual Summer Science Camp.

Over the course of three camps, 67 students and 15 educators came to the UW-Madison campus to explore science firsthand. The weeklong camps covered topics ranging from stem cell differentiation to fluorescent microscopy to gene editing.

"We were anxiously awaiting the day we could welcome students back to camp in our building, and this summer did not disappoint," says Sam Mulrooney, program manager at WARF and the Discovery Connections team.

At the heart of the summer camp is the opportunity for students and teachers to build relationships with top scientists at Morgridge and UW-Madison.

Campers become immersed in topics like microscopy and biomedical imaging, stem cell science, drug discovery, and more through several presentations and hands-on experiments — often using the same tools and technologies used by the research experts.

Each camp concludes with a science showcase where the participants become the presenters. Students present a poster session and share their experiences with researchers and scientists.

The Summer Science Camp is a unique program in Wisconsin that exclusively focuses on high schools in rural and underserved communities who might not typically have access to experience advanced, cutting-edge science.

Linda Dworschack teaches middle school and high school science in the North Crawford School District, a small school located southwest of Viroqua, Wis. Dworschack has sent five students from her district annually to Madison for the last four years.

THANK YOU
Your support ensures summer camps are free to students and teachers.

"The opportunity for our students to see real science in real lab settings and to talk to researchers and grad students is pretty amazing," says Dworschack. "It helps them see that being a scientist is attainable — and that the people are real people."

The camps also help teachers and educators bring science back to their home districts.

Thanks to ongoing donor support, schools receive a supply stipend that helps teachers purchase lab materials and incorporate what they've learned at the summer camp back into their own curriculum.

"We have heard such resounding positive feedback — many include the phrase 'life-changing' when referring to our camp," Mulrooney says. "It is truly an incredible opportunity that we are proud to continue to improve and evolve year after year."

In addition to the in-person camps, more than 80 remote participants tuned in to the Summer Science Camp Online Workshop Series. The online series gives students who cannot travel to Madison the opportunity to meet with scientists and learn together over six weeks. This year's workshop covered topics such as quantum physics, materials science and engineering, biomedical imaging, and science communication.

"We turned a challenge of the pandemic into an opportunity," says Dan Murphy, outreach and lab manager for the Discovery Connections team which is supported in part by the Morgridge Institute. "We got feedback from the teachers and our partners that it was really great for many of them to have the flexibility of an online camp."

Gifts from donors like you ensure the summer science experiences are free for teachers and students. Thank you for bringing science, research, and education to communities across Wisconsin.

"The opportunity for our students to see real science in real lab settings and to talk to researchers and grad students is pretty amazing."

— LINDA DWORSCHACK, NORTH CRAWFORD SCHOOL DISTRICT

Danielle Desa (left), the Melita F. Grunow Postdoctoral Fellow, works with a high school student during a Summer Science Camp session analyzing microscopy images using the ImageJ software.

CHANGING LIVES

YOU MAKE A DIFFERENCE — THANK YOU!

Support from donors like you helps students and teachers from across Wisconsin. Thank you for making a difference for our camp participants.

2022 Participating Schools:

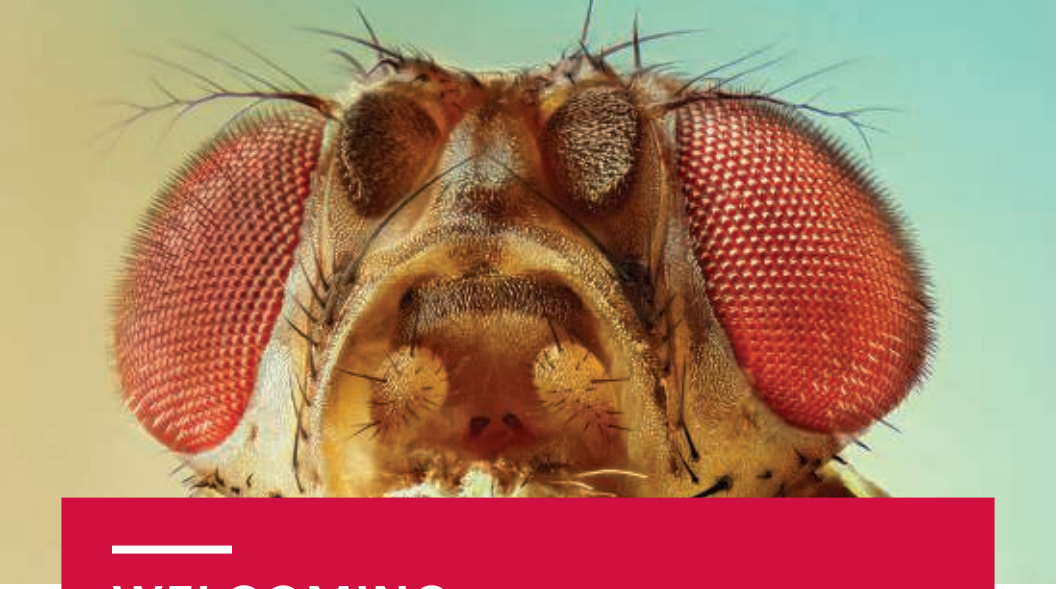
Birchwood School District
Chetek-Weyerhaeuser High School
Forward Service Corporation – Upward Bound
Independence High School
Janesville Craig High School
John Edwards High School
Kickapoo High School
Markesan High School
Mauston High School
Mayville Senior High School
McFarland High School
Mercer School District
Mineral Point High School
Necedah Area Schools
North Crawford High School
River Valley High School
Solon Springs School District
Waupaca Learning Center
Wonewoc-Center High School

Since 2007, the Summer Science Camp and the Summer Science Camp Online Workshop Series have helped over 700 high school students and 150 teachers from more than 100 state high schools. The camp has been offered free of charge thanks to the support of private donors and sponsors like you, including the Wisconsin Rural Opportunities Foundation, BioForward, the Kathy Smith Fund, the Melita Grunow Fund, and through a grant from the National Science Foundation.

CAMP HONORS ED JACKSON

The first camp session was named the "Ed Jackson Summer Science Camp" in memory of the UW-Madison emeritus professor and chair of medical physics, who was a dedicated member of the Morgridge Scientific Advisory Board and a passionate supporter of the Summer Science Camp.

THANK YOU to the Jackson Family for honoring Ed's life and legacy with a gift to help students and teachers.



WELCOMING DANIELA DRUMMOND-BARBOSA

NEW MORGRIDGE INVESTIGATOR EXPLORES ROLE OF DIET AND METABOLISM IN STEM CELL FUNCTION

Daniela Drummond-Barbosa has been fascinated by genetics her entire life, but her biggest turning point in science came courtesy of the humble fruit fly, Drosophila melanogaster.

Drummond-Barbosa joined the Morgridge Institute and the Department of Genetics at UW-Madison on July 1, 2022. She came to Wisconsin from Johns Hopkins University, where she was a professor of biochemistry and molecular biology since 2009.

Drummond-Barbosa is an acknowledged leader in her field working to understand the metabolic and physiological factors that link the behavior of stem cell lineages to diet, stress, and other systemic inputs. The work has major implications for understanding the genetic drivers of stem cell disorders, obesity, infertility and a variety of diseases related to metabolism.

The backbone of Drummond-Barbosa's research is the model organism Drosophila, but that wasn't the case early in her academic career. She earned her PhD at Yale University in 1995 under the mentorship of renowned genetics professor Daniel Dimaio, but she couldn't help but be captivated by her fellow graduate students using the flies.

"I was watching the graduate students working on Drosophila who could make a mutation in a single gene, and suddenly something would change completely about the fly. So there was no question that what they were studying was important," she says.

Her interest was cemented when taking the course "Cells in Development," where she learned about the Nobel Prize-winning work of scientists who used Drosophila and the power of genetics to figure out how an embryo develops — basically following the hierarchy of genes that determine the entire segmentation pattern, including where and how the head, thorax and abdomen will develop.

Her lab is interested in fundamental questions about how tissues develop from stem cells, how fertility is controlled, and how the physiology of an organism connects to the reproduction. The team also looks at how the external environment, physiology and reproduction are connected. In particular, they are studying the strong correlation between diets, obesity and infertility.

THANK YOU
Donor support makes it possible to recruit world-class scientists.

Drummond-Barbosa also has a strong commitment to training the next generation of scientists from all backgrounds, including women and groups historically excluded from science. She says her status as a Latina woman in science might help her seem more approachable to a diverse range of students.

Drummond-Barbosa was born in Los Angeles and grew up in Belo Horizonte, Brazil. After getting her PhD, she did her postdoctoral training at the Carnegie Institution for Science, and in 2002 became an assistant professor of cell and developmental biology at the Vanderbilt University Medical Center.

"Daniela's research connects stem cell biology and metabolism and is therefore a superb fit for the Morgridge Institute," says Morgridge CEO Brad Schwartz. "Even before arriving here, Daniela has sparked many conversations with her Morgridge colleagues on possible research collaborations, which is exactly the type of scientist we strive for. We are delighted to have her on our team."

RESEARCH PARTNERSHIP BRINGS GENE EDITING PROMISE TO EYE DISEASE

SKALA LAB CONTRIBUTES IMAGING EXPERTISE

In order to tap the tremendous potential of CRISPR gene editing technology for reversing human disease, Wisconsin scientists are working with a star pupil.

The human eye — though one of the body's most complex and intricate structures — happens to be an ideal early candidate for treatments that incorporate CRISPR, the Nobel Prize-winning tool that may help precisely target and alter sequences of DNA associated with disease.

David Gamm, director of UW-Madison's McPherson Eye Research Institute (McPherson ERI) and professor of ophthalmology and visual sciences, describes a number of important attributes. Eyes are a self-contained, compact system. They are readily accessible to treatments, unlike the brain or other organs. They are somewhat immune privileged, making them less prone to tissue rejection. We have two of them — in case something goes wrong.

And there's major clinical momentum, Gamm says. A gene therapy called Luxturna — used to treat a rare inherited form of vision loss — recently became the first gene therapy approved in the U.S. that targets a disease caused by mutations in a specific gene.

That interest has coalesced at UW-Madison through an interdisciplinary partnership involving scientists at the McPherson ERI, the Morgridge Institute and the Wisconsin Institute for Discovery (WID). The team is organized around a variety of techniques to identify the safety, reproducibility and efficacy of gene editing targets in the eye.

Gamm, whose expertise is in cell-based therapies to fight diseases of the retina, started exploring the idea of CRISPR-based therapies about a decade ago with Kris Saha, a biomedical engineer at WID and member of the NIH's Somatic Cell Genome Editing Consortium. Saha has pioneered new gene editing technologies.

They were joined by Morgridge biomedical imaging investigator Melissa Skala, who provides non-invasive ways to measure off-target effects of gene editing. The team also includes Sushmita Roy at WID, who is an expert in computational methods for genome network analysis.

Their NIH-supported project, now in its fourth year, uses stem cell-derived retinal organoids (or tiny 3-D retinal tissue cultures) created in the Gamm Lab to replicate the cellular makeup of eye diseases in a dish.

Gamm notes there are more than 250 different genetic diseases that cause human blindness, so creating organoids en masse allows the team to test literally thousands of gene editing combinations to identify beneficial effects and unforeseen safety issues.

"The vast majority of human eye diseases do not have animal models," Gamm says. "In the case of gene editing, you need to work within the human genome to know if your therapy will be safe and on-target."

The Skala Lab contributed a technique called autofluorescence lifetime imaging — which can track the natural fluorescence produced during cellular activity. The technology is highly sensitive to retinoids, which are pigments in the eye that change their conformation during visual cycles.

The experimental approach designed by Skala Lab assistant scientist Kayvan Samimi proved to be effective for tracking the dynamics of cellular changes across these organoids. Importantly, it provides a way to confirm whether changes are occurring as a direct result of the gene editing. Right now, getting that validating proof is one of the major challenges of CRISPR technology.

"It came out of left field," Skala says. "We all knew that retinoids were in the eye and that they fluoresce, but we thought they weren't useful to identify function. Kayvan discovered how he could image different conformations of retinoids that were meaningful in

determining the function of the cell. So, that was a really fun journey."

The next step in the journey, Saha says, is to build on the current work to actually develop an investigational new drug based on gene editing of the retina within a patient, rather than treating cells outside the body and returning them. It would represent a monumental step forward, not only in preventing eye diseases but providing gene-editing proof of concept for other diseases.

"This is a great example of team science and working across colleges and disciplines," Saha says. "I could tell that we were pushing the boundaries when we first sketched out the project. We were constantly asking: 'What did you mean by that? What is that term?' We had to be very specific with our language, we had to slow down. That's a signal that we're really bringing together people that normally don't talk to one another."

Gamm says the project reflects how the McPherson Eye Research Institute approaches basic research. It draws on talented scientists from across the university — many of who have not worked within the eye before — out of the recognition that one field of research won't have all the answers.

"We're tapping into what's already the greatest resource that the UW-Madison has, which is that all of its talented people actually like to work with one another," Gamm says. "Researchers here are excited to get outside of their own swim lane, and working together is like having a noodle to hang onto as you venture into the deep end."

THANK YOU

You've made a difference for scientists, educators, researchers, and students.

Your donations provide critical resources that help scientists working on cutting-edge research and support educators who bring science to communities around Wisconsin.

CELEBRATING AWARDS AND HONORS

Morgridge alum awarded for "FANTM" limb virtual technology

Finn Kuusisto, an alumnus of the Morgridge Postdoctoral Fellowship Program, was honored for his work developing information technology to improve virtual reality applications that could one day be applied to biomedical devices.

Eliceiri named Open Hardware Trailblazer Fellow

Morgridge Investigator **Kevin Eliceiri** was recently named an Open Hardware Trailblazer Fellow by the Open Source Hardware Association (OSHWA) for his work in imaging innovation. Eliceiri is a pioneer in open source hardware and software design that allows for richer data collection and supports innovative research on campus and around the world.

Cantor wins research award to study aggressive blood cancer

Morgridge Investigator **Jason Cantor** received a 2021 Hartwell Individual Biomedical Research Award to help identify new therapeutic targets for T-cell acute lymphoblastic leukemia (T-ALL). The aggressive blood cancer accounts for 15 percent of all newly diagnosed ALL cases in the United States each year.

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— LINDA DWORSCHACK, NORTH CRAWFORD SCHOOL DISTRICT

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