ANNUAL REPORT 2023

Stem Cell & Regenerative Medicine Center
UNIVERSITY OF WISCONSIN–MADISON

Our Mission

The UW–Madison Stem Cell and Regenerative Medicine Center (SCRMC) operates under the School of Medicine and Public Health (SMPH) and the Office of the Vice Chancellor for Research and Graduate Education. The center provides a central point of contact, information, and facilitation for campus stem cell researchers.

SCRMC faculty members collaborate across multiple UW–Madison schools, colleges, and centers, including SMPH, UW Health, College of Engineering, Wisconsin Institute for Discovery, Morgridge Institute for Research, Waisman Center, Wisconsin National Primate Research Center, School of Veterinary Medicine, and many others.

The center's mission is to advance the science of stem cell biology and foster breakthroughs in regenerative medicine through faculty interactions, research support, and education.

Our Goals:

- Maintain UW–Madison as a leader in stem cell and regenerative medicine research and application.
- Foster increased stem cell and regenerative medicine communication within campus and beyond its borders.
- Support stem cell and regenerative medicine research: basic, translational, clinical, bioethics, and public policy.
- Develop educational, training, and outreach programs.
- Enhance philanthropic support.

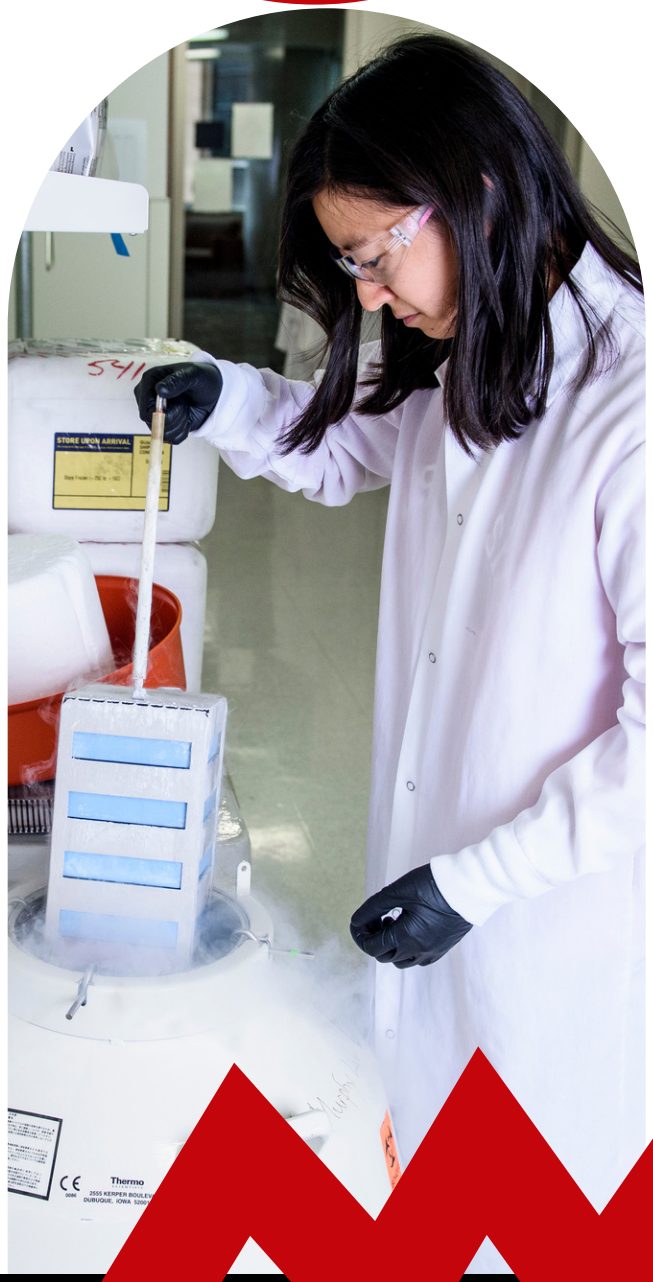

Photo Credit: University of Wisconsin-Madison

SNAPSHOT

118

Members from across campus

50

Departments represented

DIRECTORS' STATEMENT

Dear Colleagues and Friends,

Thanks to your support, 2023 has been a year of innovation. Whether it was confirming that lab-grown retinal cells have the capacity to replace diseased cells (pg. 3) or using new nanocapsules to deliver therapy brain-wide (pg. 5), SCRMC members have been making huge strides. But to get these discoveries and others to the public, interactions and collaborations with industry are essential. For that reason, this year the SCRMC is initiating the Industry Partnership Program.

This SCRMC Industry Partnership Program will help advance stem cell and regenerative medicine research while supporting the biotechnology ecosystem throughout Wisconsin and beyond. By supporting the Center through this new partnership model, industry will interact with campus experts and gain insight on cutting-edge research advances while also having the opportunity to connect with SCRMC-trained job applicants through the Center's Job Board, the Job Fair, the Fall Conference, and more. Likewise, the SCRMC will benefit by connecting with companies who can provide important insights, networking opportunities for students, and the critical connections needed to move discoveries forward.

We hope you will join us in 2024 as we further our mission to increase stem cell and regenerative medicine innovation on campus and beyond its borders. We are grateful for your support, both in-kind and financially, as every donation aids our efforts to positively transform the future of human health via stem cell and medical breakthroughs.

Sincerely,

Timothy Kamp, MD, PHD

Director, Professor of Medicine and Cell and Regenerative Biology, School of Medicine and Public Health

Randolph Ashton, PhD

Associate Director, Associate Professor of Biomedical Engineering, College of Engineering

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Design by Bekah McBride

Cover photo credit: Ana Caroline Gandara, image of drosophila melanogaster testis filled with individualizing GFP-labeled sperm.

Page 3 circle photo credit: UW–Madison image courtesy of Gamm Laboratory
Page 5 circle photo credit: UW–Madison
Page 11 photo credits: Hollie Thompson

INDUSTRY PARTNERSHIP PROGRAM

Please visit **stemcells.wisc.edu** and click on the **Industry Partnership** tab in the main menu to learn more about the Industry Partnership Program, the job fair, or the job board.

We also invite you to contact Bekah McBride at **bmcbride@medicine.wisc.edu** with any questions.

Thank you for your continued support of the SCRMC!

Lab-grown retinal eye cells make successful connections, open door for clinical trials to treat blindness

By Chris Barncard

Retinal cells grown from stem cells can reach out and connect with neighbors, according to a new study, completing a "handshake" that may show the cells are ready for trials in humans with degenerative eye disorders.

Over a decade ago, researchers from the University of Wisconsin–Madison developed a way to grow organized clusters of cells, called organoids, that resemble the retina, the light-sensitive tissue at the back of the eye. They coaxed human skin cells reprogrammed to act as stem cells to develop into layers of several types of retinal cells that sense light and ultimately transmit what we see to the brain.

David Gamm is the RRF Emmett A. Humble Distinguished Director, McPherson Eye Research Institute and a Professor of Ophthalmology & Visual Sciences at the Waisman Center Stem Cell Research Program.
Photo credit: UW-Madison

"We wanted to use the cells from those organoids as replacement parts for the same types of cells that have been lost in the course of retinal diseases," says David Gamm, the UW–Madison ophthalmology professor and director of the McPherson Eye Research Institute whose lab developed the organoids. "But after being grown in a laboratory dish for months as compact clusters, the question remained — will the cells behave appropriately after we tease them apart? Because that is key to introducing them into a patient's eye."

During 2022, Gamm and UW–Madison collaborators published studies showing that dish-grown retinal cells called photoreceptors respond like those in a healthy retina to different wavelengths and intensities of light, and that once they are separated from adjacent cells in their organoid, they can reach out toward new neighbors with characteristic biological cords called axons.

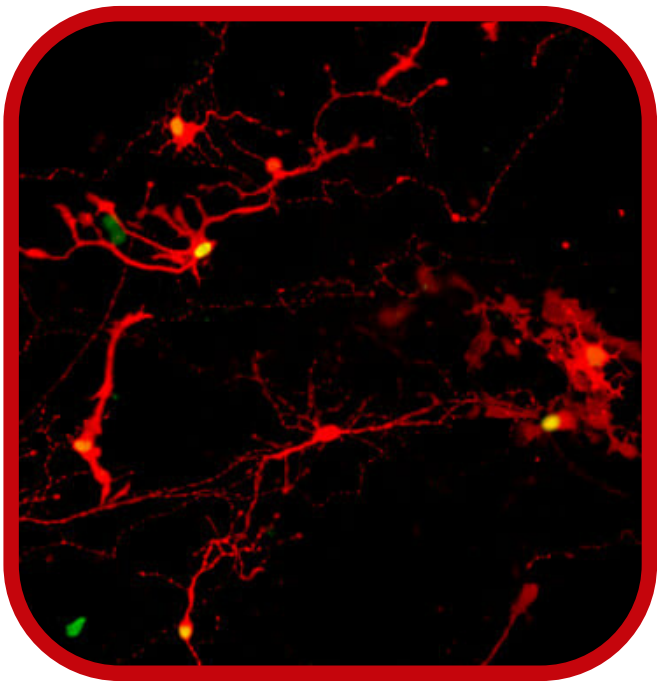
"The last piece of the puzzle was to see if these cords had the ability to plug into, or shake hands with, other retinal cell types in order to communicate," says Gamm, whose new results on successful connections between the cells was published today in the Proceedings of the National Academy of Sciences.

Cells in the retina and brain communicate across synapses, tiny gaps at the tips of their cords.

To confirm that their lab-grown retinal cells have the capacity to replace diseased cells and carry sensory information like healthy ones, the researchers needed to show that they could make synapses.

Xinyu Zhao, UW–Madison professor of neuroscience and co-author of the new study, worked with the Gamm lab's cells to help study their ability to form synaptic connections. They did this using a modified rabies virus to identify pairs of cells that could form the means to communicate with one another.

The research team, including graduate students and co-first-authors Allison Ludwig and Steven Mayerl, broke apart the retinal organoids into individual cells, gave them a week to extend their axons and make new connections, exposed them to the virus, and then took a peek. What they saw were many retinal cells marked by a fluorescent color indicating a rabies infection had infected one across a synapse successfully formed between neighbors.



Proof of synapses connecting pairs of retinal cells derived from human pluripotent stem cells comes from the red coloring of infection by a modified rabies virus passed from one cell with a yellow nucleus across the synapse to a cell that glows only red. UW–Madison image courtesy of Gamm Laboratory.

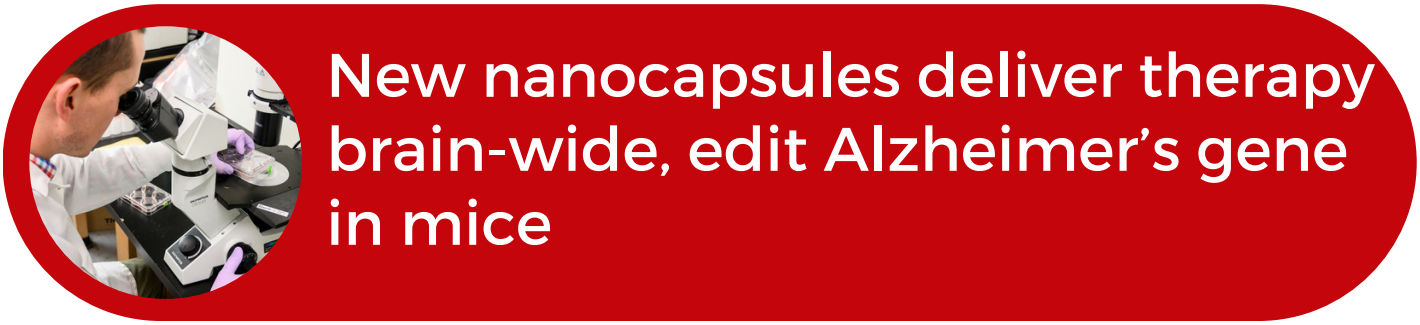
"We've been quilting this story together in the lab, one piece at a time, to build confidence that we're headed in the right direction," says Gamm, who patented the organoids and co-founded Madison-based Opsis Therapeutics, which is adapting the technology to treat human eye disorders based on the UW–Madison discoveries.

> "It's all leading, ultimately, to human clinical trials, which are the clear next step."

After they confirmed the presence of synaptic connections, the researchers analyzed the cells involved and found that the most common retinal cell types forming synapses were photoreceptors – rods and cones – which are lost in diseases like retinitis pigmentosa and age-related macular degeneration, as well as in certain eye injuries. The next most common cell type, retinal ganglion cells, are degenerate in optic nerve disorders like glaucoma.

"That was an important revelation for us," says Gamm. "It really shows the potentially broad impact these retinal organoids could have."

This research was supported by federal grants from the National Institutes of Health (U01EY027266, U24EY029890, MH116582, U54HD090256, P50HD105353 and F30EY031230), the Department of Defense (W81XWH-20-1-0655), the Sandra Lemke Trout Chair in Eye Research, and the RRF Emmett A. Humble Distinguished Directorship of the McPherson ERI.



New nanocapsules deliver therapy brain-wide, edit Alzheimer's gene in mice

By Laura Red Eagle

Gene therapies have the potential to treat neurological disorders like Alzheimer's and Parkinson's diseases, but they face a common barrier — the blood-brain barrier. Now, researchers at the University of Wisconsin–Madison have developed a way to move therapies across the brain's protective membrane to deliver brain-wide therapy with a range of biological medications and treatments.

"There is no cure yet for many devastating brain disorders," says Shaoqin "Sarah" Gong, UW–Madison professor of ophthalmology and visual sciences and biomedical engineering and researcher at the Wisconsin Institute for Discovery.

Shaoqin "Sarah" Gong
Photo Credit: UW-Madison

"Innovative brain-targeted delivery strategies may change that by enabling noninvasive, safe and efficient delivery of CRISPR genome editors that could, in turn, lead to genome-editing therapies for these diseases."

CRISPR is a molecular toolkit for editing genes (for example, to correct mutations that may cause disease), but the toolkit is only useful if it can get through security to the job site. The blood-brain barrier is a membrane that selectively controls access to the brain, screening out toxins and pathogens that may be present in the bloodstream. Unfortunately, the barrier bars some beneficial treatments, like certain vaccines and gene therapy packages, from reaching their targets because in lumps them in with hostile invaders.

Injecting treatments directly into the brain is one way to get around the blood-brain barrier, but it's an invasive procedure that provides access only to nearby brain tissue.

> "The promise of brain gene therapy and genome-editing therapy relies on the safe and efficient delivery of nucleic acids and genome editors to the whole brain," Gong says.

In a study recently published in the journal Advanced Materials, Gong and her lab members, including postdoctoral researcher and first author of the study Yuyuan Wang, describe a new family of nano-scale capsules made of silica that can carry genome-editing tools into many organs around the body and then harmlessly dissolve.

By modifying the surfaces of the silica nanocapsules with glucose and an amino acid fragment derived from the rabies virus, the researchers found the nanocapsules could efficiently pass through the blood-brain barrier to achieve brain-wide gene editing in mice.

In their study, the researchers demonstrated the capability of the silica nanocapsule's CRISPR cargo to successfully edit genes in the brains of mice, such as one related to Alzheimer's disease called amyloid precursor protein gene.

Because the nanocapsules can be administered repeatedly and intravenously, they can achieve higher therapeutic efficacy without risking more localized and invasive methods.

The researchers plan to further optimize the silica nanocapsules' brain-targeting capabilities and evaluate their usefulness for the treatment of various brain disorders. This unique technology is also being investigated for the delivery of biologics to the eyes, liver and lungs, which can lead to new gene therapies for other types of disorders.

CELEBRATING THE 25TH ANNIVERSARY OF A STEM CELL SCIENCE MILESTONE

In November 1998 , the world learned of the first successful isolation of human embryonic stem cells (ESCs) accomplished by the team led by Dr. Jamie Thomson. ESCs are master stem cells that can be grown in the laboratory indefinitely and under appropriate conditions form any cell type present in the human body. This discovery launched a whole new era of stem cell research and empowered the promise of regenerative medicine.

To celebrate this milestone, SCRMC member and Steenbock Professor in Neural and Behavioral Sciences, Su-Chun Zhang, MD, PhD, gave a presentation, "Human Stem Cells 25 Years Later, Where are We?" for the November 8, 2023 edition of Wednesday Nite @ the Lab.

Jamie Thomson, who isolated five stem cell lines from surplus in vitro fertilization human embryos for the first time in 1998. Photo Credit: Morgridge Institute for Research

CASEY OSTHEIMER KNOWS HOW TO NURTURE

By Jordana Lenon

Recent University of Wisconsin–Madison College of Agricultural and Life Sciences (CALS) graduate Casey Ostheimer knows how to nurture herself and others. She managed classes in genetics, neuroscience, and kinesiology. She earned a double major in neurobiology and genetics, along with a certificate in Global Health. She even held a few part-time jobs, which included working in a stem cell lab, taking care of patients, and engaging in outreach to middle and high school students.

Ostheimer was an undergraduate research assistant in Stem Cell and Regenerative Medicine Center (SCRMC) and School of Medicine and Public Health faculty member Owen Tamplin's Cell and Regenerative Biology lab. She was involved in projects related to hematopoietic stem cell development in mice and zebrafish, and live imaging of hematopoietic stem cells. Ostheimer, who was on the CALS Dean's List, also received a Genetics and Genomics Distinguished Research Fellowship in 2021 for her lab work, which involved inserting a single nucleotide mutation into both leukemia and human embryonic kidney cells.

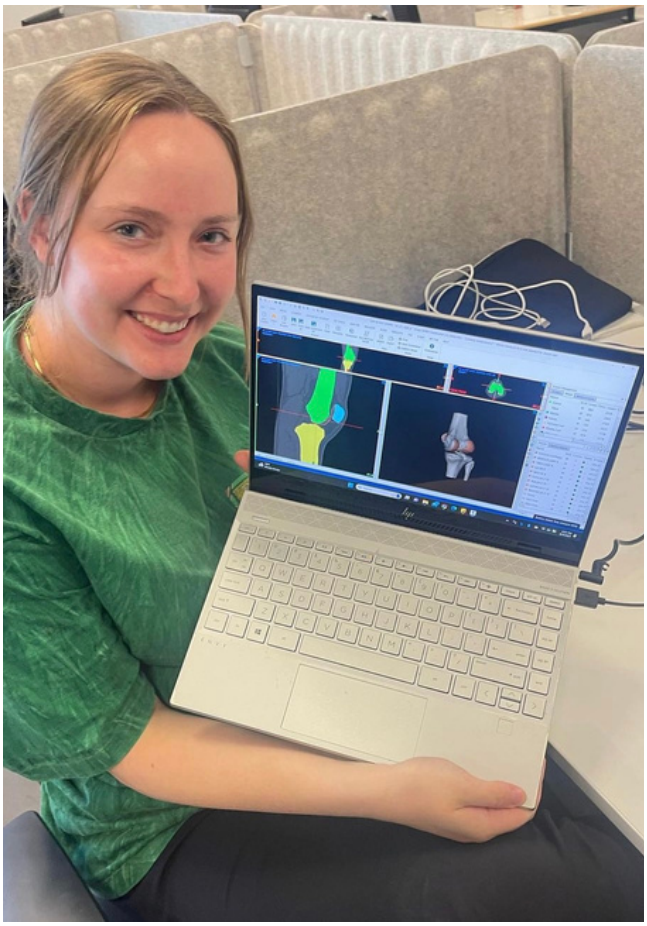
She also assisted Damola Elujoba-Bridenstine, PhD, during her graduate work by analyzing the effects of gene knockouts in mice on immune and hematopoietic stem cells and later worked independently on the project.

Ostheimer helped manage the lab's mouse colony and performed general lab maintenance. She also continued her work

Ostheimer in Iceland where she held a summer research position at Reykjavik University. Photo courtesy of Casey Ostheimer.

as a patient safety attendant at SSM-Health during this time.

Additionally, Ostheimer spent a few hours each week as the student lab assistant for the Stem Cell Learning Lab at the Biotechnology Center, a partnership with the SCRMC, Biotechnology Center, and Wisconsin National Primate Research Center launched through a grant from the Baldwin Wisconsin Idea Endowment in 2008. In that role Ostheimer set up the lab and spoke with middle school and high school students about her stem cell research.



Ostheimer evaluates a knee joint scan at the Institute of Biomedical and Neural Engineering. Photo courtesy of Casey Ostheimer.

If all that's not enough, Ostheimer was also the Primate Center's outreach and editorial intern and president of the Student Society for Stem Cell Research on campus. She was also a member of the national pre-health honor society Alpha Epsilon Delta (AED), participating in AED volunteer, professional, and advocacy events. She is now applying to medical schools and wants to specialize in trauma care and orthopedics.

While Ostheimer is deeply involved with academic organizations, she also believes in spending time on activities outside of academics and the lab. After playing on her high school volleyball team, she continued with club volleyball at UW–Madison. She thinks it's important to set realistic goals and take care of oneself. Ostheimer knows how to nurture herself – and others: she grew up breeding and showing Holland Lop rabbits with her parents in Boscobel, WI, as well as raising chickens and propagating greenhouse plants. She also nurtured the campus community by volunteering with Slow Food for its Family Dinner Night.

From serving on the volleyball court to serving sustainable comfort food, Ostheimer looks forward to medical school and serving patients. In the meantime, she just wrapped up a summer research position at Reykjavik University, where she worked in its Institute of Biomedical and Neural Engineering.

Surfing the waves of research

By Bekah McBride

The Stem Cell and Regenerative Medicine Center labs welcomed a wave of new members this summer, as five talented undergraduate students participated in the Summer Undergraduate Research Fellowship (SURF) program. This unique experience pairs mentors with motivated University of Wisconsin–Madison undergraduate students as they pursue 10-weeks of collaborative research in stem cells and regenerative medicine.

The program, which is sponsored by WiCell, the Stem Cell and Regenerative Medicine Center (SCRMC), and the National Science Foundation Engineering Research Center for Cell Manufacturing Technologies (CMaT) awards up to five undergraduate students a $6,000 stipend and the opportunity to collaborate on a research project while being mentored by a graduate student or postdoctoral fellow. The program is administered by the SCRMC Graduate Student Association (GSA), an organization of UW–Madison graduate student and postdoctoral researchers that aims to foster interaction, collaboration, dialogue, and support among campus stem cell and regenerative medicine researchers. Members of the GSA help to select the SURF applicants, assign them mentors, and support the participants throughout the program.

“Helping to organize the SURF program this spring and summer has been a great learning experience to understand all of the work and people necessary to coordinate a successful Research Experiences for Undergraduate (REU) program,” says Austin Feeney, a GSA officer and a MD-PhD student in the Palecek Lab. “It was my first year serving on the SURF Board this year, and it has been an extremely rewarding experience.”

Feeney shared that he is particularly proud to support undergraduate research as his own undergraduate experience is what inspired him to pursue his current academic goals.

“I became involved with SURF after becoming a board member with the SCRMC GSA because I saw the unique opportunity to help undergraduates learn more about the strong stem cell and regenerative medicine research community on campus,” Feeney said.

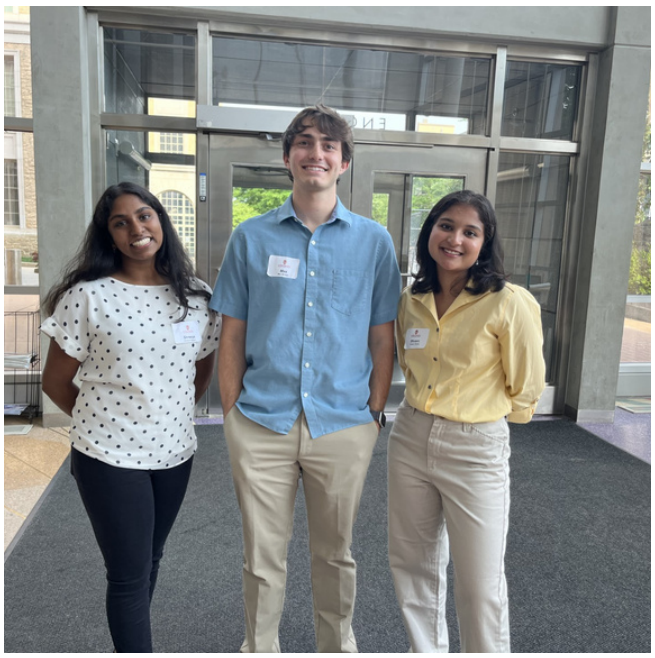
“As an undergraduate at UW–Madison myself from 2014-2018, early research experiences allowed me to discover my passion for stem cell and regenerative medicine research, leading me to pursue graduate studies.”

> “The SURF program is designed to provide an opportunity for early undergraduates to explore stem cell and regenerative medicine research. From the SURF program, many students are able to find a supportive research environment where they can continue to do research throughout their undergraduate career.”

In fact, statistics show that over 80 percent of SURF participants continue to work with their assigned lab beyond the 10-week program.

“The SURF program has given me the opportunity to not only learn new skills and protocols, but also grow as a scientist and think like a researcher,” says SURF participant and Neurobiology student Shreeya Rajesh.

“Working day after day in a such an energetic and rigorous research environment alongside my mentor has allowed me to understand and appreciate how enlightening and fast paced the research field is with new discoveries.”



A few of the SURF mentees gather including (left to right) Shreeya Rajesh, Max Herman, and Dhvani Trivedi. Photo courtesy of SURF.

Likewise, Max Herman, a SURF participant and undergraduate Biochemistry and Biology student says that the program helped him to confirm his area of interest while allowing him to gain valuable research experience.

“I’d say the most valuable thing I got from this program is an idea of what I may do post-undergrad,” says Herman.

“Having not a lot of rigorous experience in research or medicine, I came into the summer not knowing which route I wanted to pursue. Working 40 hours a week in a lab tells you pretty quickly if research is right for you or not, and I found myself greatly enjoying my time in the lab! I can definitely see myself pursuing research in the future.”

In addition to the lab experience, SURF mentees also have the opportunity to present their research at the SCRMC Fall Conference. This helps mentees to learn how to prepare a poster and give an oral presentation.

“These programs are extremely important for the next generation of scientists,” says Herman. “They provide an opportunity for students to really understand what the research of a graduate student looks like. You’re there for all the literature searches, lab meetings, and experiments.”

Thank you to the SURF sponsors WiCell and the National Science Foundation Engineering Research Center for Cell Manufacturing Technologies (CMaT).

Join SURF in 2024!

Applications for the next round of SURF will open in February 2024 with a deadline of March 22, 2024.

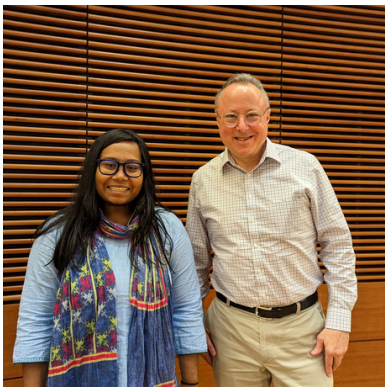
To learn more visit stemcells.wisc.edu/.

2023 Research Training Awards

The SCRMC Research Training Awards were established in 2008 to recognize and provide support for promising graduate students and postdoctoral fellows of all citizenships conducting stem cell and regenerative medicine research at the University of Wisconsin-Madison. The 2023 SCRMC Research Training Awards Program provides unique, interdisciplinary training for four future leaders in stem cell and regenerative medicine research. Additionally, this program will foster interdisciplinary collaborations among campus investigators. To learn more, please visit https://bit.ly/49fwFJR.

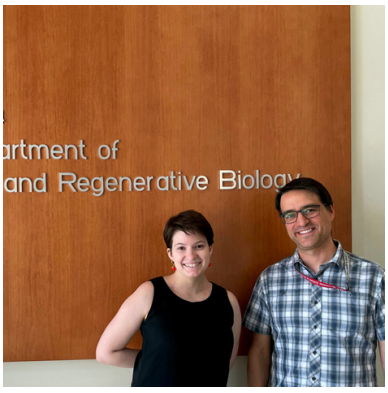
The SCRMC and the awardees would like to thank those who philanthropically support the SCRMC and make these awards possible.

Meet the 2023 Winners



Rodsy Modhurima
Emery Bresnick Lab
Research project title: Role of GATA factor-regulated signaling networks in maintaining hematopoietic progenitor cells

Kwangdeok Shin
Junsu Kang Lab
Research project title: Dissecting roles of il11a as a pro-regenerative and fibrotic factor in zebrafish heart regeneration



Nicole M. Woodhead
Owen Tamplin Lab
Research project title: Integrin alpha 4 (itga4)-mediated lodging in the fetal liver niche triggers programmed quiescence of hematopoietic stem and progenitor cells (HSPCs)

Eliana F. Torres-Zelada
Melissa Harrison Lab
Research project title: Identifying limitations to pioneer factor-mediated reprogramming

News & Awards

FROM SCRMC MEMBERS

Engin

Mahmoud

Two SCRMC members receive the 2023-2024 Vilas Associates Award

Feyza Engin and Ahmed Mahmoud have received the 2023-2024 University of Wisconsin-Madison Vilas Associates Award. This honor recognizes new and on-going research of the highest quality and significance. Those who are selected receive research salary support for summers 2023 and 2024, as well as a flexible research fund in each of the two fiscal years.

Audhya

Bement

Two SCRMC members elected as American Society of Cell Biology Fellows

Anjon Audhya and William Bement are two of only nineteen distinguished scientists recognized as 2023 ASCB Fellows. This honor, which is voted on by peers, recognizes Audhya and Bement for their "meritorious efforts to advance cell biology and/or its applications, and for their service to the Society."

SCRMC member receives a UW–Madison Award for Mentoring Undergraduates in Research, Scholarly and Creative Activities

Marina Emborg has been recognized for her important role in fostering undergraduates' intellectual, personal, and professional growth through participation in high-impact practices including research, scholarly and creative endeavors.

Jacques Galipeau named to the 2023 class of Harrington Scholar-Innovators

Recipients are recognized as "outstanding physician-scientists whose work has the potential to advance standard of care."

Amish Raval wins 2023 UW Health Physician Excellence Award

This award recognizes individuals who demonstrate exceptional skills in clinical practice, education and leadership.

Wisconsin Stem Cell Symposium

On April 19, more than 300 students, researchers, and industry professionals gathered for the 17th annual Wisconsin Stem Cell Symposium at the Biopharmaceutical Technology Center (BTC) on the Promega Corporation Campus in Fitchburg, Wis.

The event entitled, Stem Cell Innovations in Building and Rebuilding the Nervous System included a poster session and competition as well as presentations from scientific leaders who discussed recent advancements, promising strategies, and clinical trials in regenerative technologies related to neurological disorders.

SCRMC Director Tim Kamp welcomes attendees to the 2023 WI Stem Cell Symposium. Photo credit: Bekah McBride

Congratulations to the poster competition award winners!
1st Place: Yunlong Tao, UW-Madison, Zhang Lab
2nd Place: Aaron Simmons, UW-Madison, Palecek Lab
3rd place: Bo Peng, UW-Madison, Moore Lab

SAVE THE DATE

18th Wisconsin Stem Cell Symposium

BLOOD STEM CELLS: MECHANISMS, PATHOGENESIS, AND GENOME EDITING

April 17, 2024

BioPharmaceutical Technology Center Institute

Madison, WI

Look for more information coming soon at btci.org/events-symposia/wisconsin-stem-cell-symposium/

Want to learn more about the research happening at the SCRMC?

ANNOUNCEMENTS
Stem Cell & Regenerative Medicine Center
UNIVERSITY OF WISCONSIN-MADISON
NEWSLETTER

Sign up at:
stemcells.wisc.edu/subscribe-to-scrmc-announcements/

FALL CONFERENCE

On September 8, nearly 100 students and researchers gathered for the annual SCRMC Fall Conference. The event included a blitz talk competition, a poster session, and a cool image competition as well as keynote talks from renowned researchers Cheng-Yu Lee (University of Michigan) and Fei Zhao (University of Wisconsin-Madison). This event, which is organized by SCRMC trainees, is an opportunity to network, present, and learn from top biomedical and biotechnology researchers.

A special thank you to the trainees Rodsy Modhurima, Nicole Woodhead, Eliana Torres-Zelada, and Kwangdeok Shin (left to right in photo above) for their leadership in planning this event. Photo credit: Hollie Thompson

Award winners (left to right) Elsa Salido, Ian Begeman, Ana Caroline Gandara, and Matthew R. Wagner. Photo credit: Hollie Thompson

Thank you to our sponsors!

MORGRIDGE INSTITUTE FOR RESEARCH · WARF · WiCell

Congratulations to the Fall Conference Award Winners!

Cool Image Award (cover image):
Ana Caroline Gandara won for the image of drosophila melanogaster testis filled with individualizing GFP-labeled sperm.

Blitz Talk Award:
Elsa Salido in the Valentina Lo Sardo Laboratory won for the presentation: 9p21.3 Coronary Artery Disease Risk Locus Regulates Cell Fate in Vascular Smooth Muscle Cells.

Poster Awards:

- Ian Begeman, Junsu Kang's Lab : Identifying novel cardiac regeneration enhancers via computational analyses and transgenic assays
- Matthew R. Wagner, Barak Blum's Lab: Roundabout receptors are required for maintaining islet architecture during acute pancreatitis

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THE FUTURE OF MEDICINE

We invite you to invest in the future of medicine through a donation to the SCRMC. Your gift will foster breakthroughs in regenerative medicine by supporting research and training, academic education, and faculty collaboration.

Learn more and donate through the enclosed envelope or online at:
stemcells.wisc.edu/make-a-gift-2/

Or contact Pete Schmeling if you would like more information on how to give.

Pete.Schmeling@supportuw.org
608-354-9388

Photo Credits: University of Wisconsin-Madison

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