MORGRIDGE
INSTITUTE FOR RESEARCH

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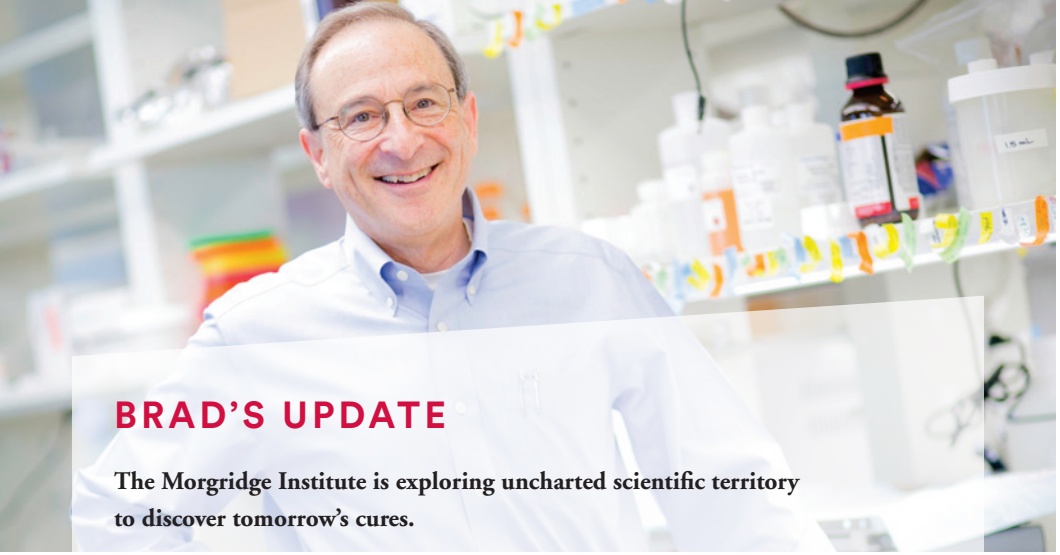
A SPECIAL REPORT FOR PARTNERS IN SCIENCE

INSIDE



BRAD'S UPDATE

The Morgridge Institute is exploring uncharted scientific territory to discover tomorrow's cures.

Basic science, the core of what we do, is all about the work. It's a fearless commitment to go where the science takes us. It is rigorous, determined and made stronger by a community of scientists and **supporters like you**, **our Partners in Science**.

As a member of Partners in Science, your philanthropic support provides critical resources: You make it possible to study promising areas of biomedicine that can lead to important discoveries and improve human health.

In this report, you will read about new research to tackle a deadly tropical disease and efforts to stop the spread of viruses like Zika, polio, dengue, SARS and hepatitis C. You'll also see how a community of supporters rallied to fund the Rural Summer Science Camp, an annual summer event that gives rural Wisconsin high school students and their teachers a hands-on experience exploring science.

But, there is always more scientific work ahead. Preventing and curing disease, stopping the spread of viruses, and improving the quality of human life won't happen tomorrow, next year or maybe even in ten years. It will take dedication, curiosity and integrity. We are committed because of your support.

Thank you for supporting the Morgridge Institute. I can't thank you enough for the trust you've placed in us.

Brad Schwartz, M.D.
CEO, Morgridge Institute

P.S. I am so thankful for your support as a Partner in Science. If you have any feedback about this new report, please email me at **brad.schwartz@morgridge.org**.

Thank you for being our partner

As a Partner in Science, you are helping explore uncharted scientific territory to discover tomorrow's cures. The partner community has doubled in one year. We can't thank you enough for your commitment to scientific discovery and outreach!

At the Morgridge Institute for Research, we explore uncharted research to go where the science takes us. By asking the right questions and following the highest standards of quality research, we will improve human health.

Thank you for supporting our research themes:

- VIROLOGY
- REGENERATIVE BIOLOGY
- METABOLISM
- HIGH THROUGHPUT COMPUTING
- MEDICAL ENGINEERING
- BIOETHICS

Learn more at
morgridge.org/partners

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Spark your imagination

Sign up for our monthly e-newsletter by visiting morgridge.org/spark to learn more about fearless scientists working to improve human health

COMMUNITY RALLIES

TO SUPPORT THE RURAL SUMMER SCIENCE CAMP

Thanks to your support, more than 50 donors joined together to help all 50 high school students in the 2018 Rural Summer Science Camp.

Private support from donors like you provides transportation scholarships and supports free and heavily-discounted science outreach programs like the Rural Summer Science Camp.

The camp, which celebrated its twelfth year, has brought more than 500 high academic achievers from across the state to spend a week learning from leaders in stem cell research. The high school students hail from some of the smallest high schools in Wisconsin and spend a week at the Morgridge Institute for Research exploring science.

This summer, 50 students from 10 rural communities conducted experiments about collagen, cancer, stem cells and more. Your support helped these students learn new, hands-on science and ignite a curiosity to explore future careers in science, engineering or technology.

Thank you for supporting science education for children and families across Wisconsin.

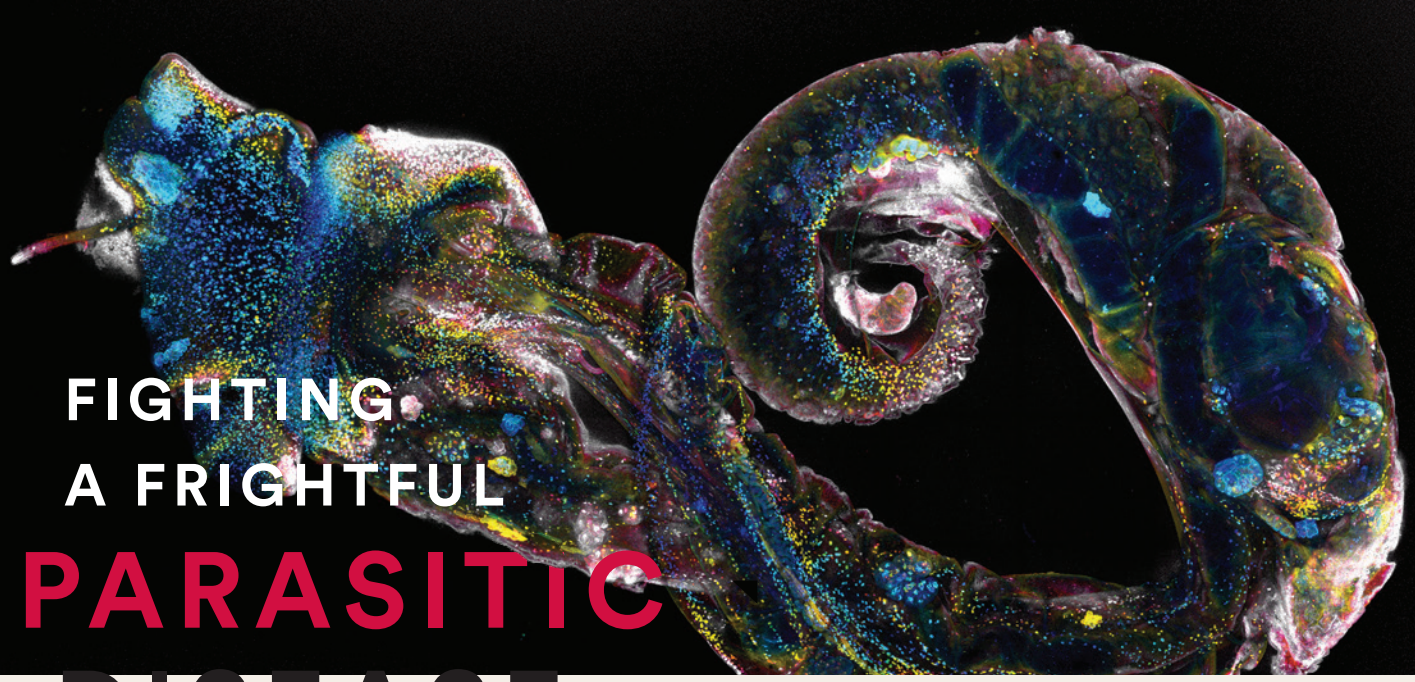
"Being from such a small town, I thought it was awesome that students were able to talk to UW–Madison and Morgridge scientists."

- Hailey Enders, 2016 graduate of Prentice High School and 2015 Rural Summer Science Camper

MEET THE KIDS' SCIENCE COUNCIL

The Morgridge Institute Kids' Science Council is a group of 20 elementary and middle school children who engage in fun, hands-on research adventures with scientists three times a year in the Discovery Building.

Your support provides funding for the Kids' Science Council and many more outreach programs that bring the wonder of science to children, families and students across Wisconsin!



FIGHTING A FRIGHTFUL PARASITIC DISEASE

JAYHUN LEE

PHIL NEWMARK

The parasitic disease schistosomiasis is one of the developing world's worst public health scourges, affecting hundreds of millions of people. Yet, only a single, limited treatment exists to combat the disease.

Scientists at the Morgridge Institute are searching for potential new targets by probing the cellular and developmental biology of the parasitic flatworm *Schistosoma*.

A team led by Phil Newmark, a Howard Hughes Medical Institute investigator, has shed light on the essential stages in the life cycle of this parasitic flatworm. They characterized several different types of stem cells that govern the parasite's complex life cycle and also identified a gene associated with the earliest development of the germline, from which reproductive cells form.

"Understanding how these stem cells drive the development of each life-cycle stage may ultimately help prevent disease transmission," says Newmark, the Burnell R. Roberts Chair of Regenerative Biology.

More than 250 million people, mostly in Africa and Asia, have schistosomiasis. The World Health Organization classifies it as the deadliest neglected tropical disease, killing an estimated 280,000 people each year. Children with the disease are often ravaged by anemia, malnutrition and pervasive learning disabilities.

"We don't get that many ah-ha moments in our lives as scientists. This was one of them."

- Phil Newmark

Schistosomes have a complicated life cycle, switching through many different body forms as they move from snails to water to humans. The cycle begins in tainted freshwater lakes and ponds, where parasite eggs released from human waste hatch into tiny creatures whose sole task is to infect a specific type of snail.

The Newmark team examined the poorly understood early stages after infection through an ingenious experiment designed by co-author Jayhun "Jay" Lee, a Morgridge Postdoctoral Researcher. The next research step will be to follow these five stem cells as they continue to differentiate and form tissues.

"We don't get that many ah-ha moments in our lives as scientists," Newmark says. "This was one of them."

It's a case where model organism research may help provide answers for a human health tragedy.

"This provides another example of how curiosity-driven basic research can lead to unanticipated outcomes and why it is important to support such work," Newmark says.

AN ACHILLES HEEL IN VIRUSES?

Scientists at the Morgridge Institute for Research have discovered a promising new target to fight a class of viruses responsible for health threats such as Zika, polio, dengue, SARS and hepatitis C.

MASAKI NISHIKIORI

PAUL AHLQUIST

Masaki Nishikiori, a researcher in the Morgridge Institute John W. and Jeanne M. Rowe Center for Research in Virology, showed for the first time that, in replicating their genomes, viruses create pores inside parts of the cell that are normally walled off. This process of "punching through cellular walls" allows the virus to operate across different parts of the cell to activate and regulate its replication.

This could be big news in the quest to develop broad-spectrum antivirals, which are vaccines or drugs that target entire families of viruses. There are hundreds of viruses that threaten human health, but today the only way to combat them is by targeting each individual strain separately, rather than finding a common weakness.

The study, published in the journal *Science Advances*, looks at a class known as positive-strand RNA viruses, which make up one-third of all known viruses (including the common cold). It appears that this pore-creating mechanism could be common across many or most members of this family of viruses.

"One exciting aspect of these results is that pores of different kinds in membranes are very important for many biological processes, and there are established drugs that interfere with them," says Nishikiori. "We now recognize that this virus, and based on conserved features, likely most viruses in this class, depend on similar types of pores to replicate. This is a target we know how to interfere with."

Current pore-blocking drugs, also referred to as channel blockers, are used in treating high blood pressure, certain neurological or psychiatric disorders, including Alzheimer's disease, and other maladies.

Basic research on the mechanisms of viral replication is essential to the larger quest to find broad-spectrum antivirals, one of the holy grails of virology, Ahlquist says.

"When you apply an over-the-counter anti-bacterial cream to a child's scraped knee, it works even though you don't know exactly which bacteria you're fighting," he says. "We don't have anything like that for viruses; most of our antiviral vaccines and drugs are virus-specific. We need new approaches that target broadly conserved viral features to simultaneously inhibit many viruses."

PUSHING TOWARD PERSONALIZED PANCREATIC CANCER TREATMENT

Survival rates remain bleak for pancreatic cancer, which kills more than 90 percent of people within the first five years of diagnosis.

"It is the most lethal cancer because we have no really effective way to treat it," says Melissa Skala, a principal investigator in medical engineering at the Morgridge Institute for Research.

Skala and Paul Campagnola, a professor of biomedical engineering at UW-Madison, hope to make inroads toward improved drug therapies through a two-year National Institutes of Health Exploratory/Developmental Research Grant.

MELISSA SKALA

They plan to use Campagnola's novel imaging and micropatterning techniques to create a 3D model of pancreatic ductal adenocarcinoma, which will improve their ability to identify effective drugs.

Current testing relies either on mouse models, which don't match the human disease in aggressiveness or the start of tumor development, or on two-dimensional cultures that generally fail to account for interactions between cancer cells and those in the stroma, the tumor's hefty supportive tissue. That's a key missing ingredient, because the stroma protects the cancer cells from drugs while also encouraging tumor growth.

To build their model, the engineers will take high-resolution images of cancerous tissue using second-harmonic generation microscopy, then print small-scale 3D replicas of the tissue's extracellular matrix, part of the stroma that creates structure. By bringing together cancer cells and support cells in that realistic environment, they'll see how the cancer cells move, divide and produce energy—and which drugs stop them.

WELCOMING JASON CANTOR

Jason Cantor could describe himself as an engineer, biologist and biochemist, but don't try to put his expertise into one box.

Cantor, a scientist exploring the environmental influences on cancer cell metabolism, is launching a new lab in the Metabolism Theme at the Morgridge Institute for Research. His lab is exploring how environmental factors influence cell biology from a fundamental aspect and from a translational aspect.

"To take risks in science and move the field forward in meaningful ways, you need resources and personnel and the support to do that," Cantor says, "and Morgridge, with the university, exemplified this vision of doing big things. The exciting part for my work is we actually don't know what we're going to find because we're studying these systems, whether it's cancer or otherwise, in a way that no one has before."

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