MORGRIDGE
INSTITUTE FOR RESEARCH

SPRING 2022

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A SPECIAL REPORT FOR SUPPORTERS OF THE MORGRIDGE INSTITUTE FOR RESEARCH

INSIDE

BRAD'S UPDATE

Attracting a new wave of talent

If there is a central premise behind *Fearless Science* — the aspirational theme we live by here at the Morgridge Institute — it would be to embrace the unknown.

This year, we'll be doing that in more ways than one. We will be seeing very significant changes to our scientific team.

As you will read in our lead story, Jamie Thomson — the inaugural investigator at Morgridge and arguably Wisconsin's most famous contemporary scientist — will be retiring this summer. As the researcher who put stem cell science on the map 23 years ago, Jamie embodies the kind of scientific discovery we strive for at Morgridge: Born from basic curiosity, capable of changing our fundamental understanding of biology, and replete with great societal benefit.

Along with Jamie's departure, two other Morgridge investigators have recently taken new positions and a number of long-planned new hires are in the pipeline.

Our new hires will have a major impact on our identity and our success moving forward. So the question on our minds lately is: What do we want the Morgridge Institute to be in the future?

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

To answer that question, we have undertaken a comprehensive plan. In our work, the take-home message was unambiguous: Focus on the people, rather than any specific frontier in science. We should find the best available scientific talent who combines curiosity, creativity, collegiality, and a strong desire to work with and learn from others.

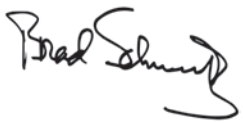
That means have to get the best people from all aspects of society, including those who have been traditionally underrepresented in science. So an integral part of our searching, recruitment, and retention strategy will be to ensure that we are reaching the widest range of talent.

We also want to ensure that we have a culture of excellence and inclusiveness and a place where people care for one another. We are not going to make this process about accumulating prestige or status. We want not only the best possible scientist but the person most likely to make major advances because they are here instead of somewhere else.

That leads to a triple-win: A win for the new recruit, whose career will thrive; a win for the Morgridge community, as a place that offers fertile ground for discovery; and importantly, a win for the scientific enterprise, because we're genuinely improving research, not just competing with other places.

As I look ahead, I want to thank you — our donors. Your support is critical to attracting a new wave of talent here. I cannot thank you enough for the trust you've placed in us.

I hope you are inspired by reading this report. We depend on a community of supporters like you. Thank you for making a difference.



Brad Schwartz, M.D.
Chief Executive Officer
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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

A SCIENCE TRAILBLAZER RETIRES

STEM CELL RESEARCHER JAMES THOMSON'S LEGACY CHANGED THE FUTURE OF BIOLOGY

The developing human body will eventually grow from a tiny two-celled zygote to a massively complex system comprising more than 37 trillion cells. If a single cell represented one second in time, all of our cells combined would span 1.8 million years.

James Thomson helped the scientific world turn its attention to the shape-shifting stem cells that give rise to all of the building blocks of complex living organisms, from skin and bone, to hearts and blood, to neurons and brains.

After more than 30 years with the University of Wisconsin–Madison and 15 years with the Morgridge Institute, Thomson announced plans to retire in July 2022.

"There are few scientists in the world, across all of history, with the ability to translate their deep curiosity about life into discoveries that fundamentally change what's possible for humanity," says UW–Madison Chancellor Rebecca Blank. "We are all fortunate that Jamie Thomson dedicated his own life and career to such pursuits, and we are especially grateful he did so at UW–Madison. His work has influenced generations of our students and scholars."

Thomson will always be best known, as the cover of *TIME* Magazine trumpeted in summer 2001, as "the man who brought you stem cells." His life's work contains three quantum leaps in regenerative biology.

The first was in 1995, when he derived stem cells from non-human primates, the first time ever done in a species closely related to people. Then in 1998, he isolated five stem cell lines from human embryos, work that enabled stem cell discovery in thousands of labs around the world and spawned a prolonged, high-stakes bioethical debate in the U.S.

The third leap was in 2007, with the discovery of adult pluripotent stem cells, which offered a way of coaxing adult skin cells back to an original blank state.

Stem cell science now employs tens of thousands of scientists globally in industry and academia. Many are

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working in promising frontiers such as stopping or reversing blindness, and treating or preventing Parkinson's disease and diabetes.

Stem cells have become ubiquitous tools in the world of drug development and testing. They sparked Proposition 71, a California referendum in 2004 that led to the investment of $5.5 billion in state funds to support stem cell-based medical advances.

And they've opened up wide basic science frontiers, permitting researchers across the globe to explore vast new questions about how biology works. The Wisconsin Alumni Research Foundation (WARF), a vital long-term supporter of Thomson's research, created the organization WiCell in 1999 to enable the distribution of Thomson's original stem cell lines to scientists across the world.

Today, WiCell's repository holds more than 1,500 stem cell lines, and more than 7,300 distributions have been made to more than 2,300 laboratories at 956 institutions across 43 countries globally.

In hindsight, Thomson says the excitement over potential stem cell therapies and disease cures led people to unrealistic expectations. "The timeline for human therapies was always wrong, it was never going to happen in 10 years."

That fact is playing out today. Now 23 years removed from the original finding, many clinical trials are showing promising results. A fall 2020 paper in the journal *Nature* estimates there are more than 130 current clinical trials involving pluripotent stem cells, which are defined by their capacity for indefinite self-renewal and ability to differentiate into any cell in the body.

Thomson's own lab at the Morgridge Institute has been singularly focused on a project that could greatly improve health prospects of people with cardiovascular disease, which accounts for one in every four deaths annually in the United States.

Now in its 10th year, the project is developing functional stem cell-derived arteries for use in vascular surgery. The lab has developed scaffolds from synthetic materials that give form and shape to the artery. They then use a bioreactor that enables endothelial and smooth muscle cells to grow naturally around the scaffolding.

The need for alternatives is great. People with advanced cardiovascular disease often have blockage in the main arteries in their legs, a debilitating condition that can lead to amputation or death. The ultimate goal would be to provide clinicians with a "bank" of arteries that could be used for all kinds of peripheral artery disease treatment.

The project is in the final two years of a seven-year grant from the National Institutes of Health. Igor Slukvin, a professor of pathology and laboratory medicine who is leading the clinical trials, will be the lead investigator of the artery project after Thomson retires.

Thomson says the unique landscape at UW–Madison really helped stem cell science thrive in ways that aren't possible at most universities. Today, an estimated 600 UW–Madison researchers are working in stem cell science in some capacity.

Thomson's work also led to a highly successful spinoff company at University Research Park. Cellular Dynamics International, formed in 2007, was purchased in 2015 by FujiFilm for $307 million. Still based in Madison and employing nearly 300 people, the company manufactures cell lines derived from pluripotent stem cells for myriad applications across scientific research and health care.

Thomson's discoveries led to two "Breakthrough of the Year" honors from the journal *Science*, in 1998 and 2007; cover-story coverage in *TIME*, which named him one of the "World's 100 Most Influential People" in 2008; and receipt in 2011 of the Albany Medical Center Prize in Medicine and Biomedical Research, known as "America's Nobel."

Before retiring, Thomson is planning to give a valedictory talk to the university community. He says he's still developing the topic.

"My preference would be to just go 'whoosh' through this puff of smoke," Thomson jokes. "But of course, I am very grateful for what the university and the Morgridge Institute has done for my research, so I want to give back on my way out."

YOUR SUPPORT MATTERS

Research milestones made possible by YOU

Thanks to private support from donors like you, the Morgridge Institute is pushing science and engagement forward. We can't do this work without you — THANK YOU.

Here's a look at some of the milestones made possible by you.

Optical imaging highlights metabolic interactions that make pancreatic tumor cells grow

Pancreatic cancer is a rare, yet elusive and deadly cancer, with a five-year survival rate of about 10%. If the cancer has metastasized, that rate lowers to 3%. And treatment options are extremely limited.

> **"It's one of the scarier cancers because once you discover that a person has pancreatic cancer, it's often too late because there are no symptoms," says Rupsa Datta, an assistant scientist in the Skala Lab. "The survival rate is so low because, at that point, you can't really do anything."**

The Skala Lab uses advanced optical imaging to study the metabolic activity that leads to tumor growth, in hopes that a better understanding of the tumor microenvironment can lead to new therapies and treatments.

Their findings, published in the journal *Science Advances*, describe how cancer cells can hijack the metabolic activity of certain non-cancer cells in the pancreas to fuel tumor growth.

Open wide: Detecting links between what's in your mouth and illness

Using tiny specks of dental plaque, Morgridge scientists Katherine Overmyer and Josh Coon compiled a sophisticated analysis that opens the door to using the trove of micro-organisms in your mouth as an indicator of other health issues.

The research — conducted in collaboration with the Marshfield Clinic Research Institute — has the potential to help break down barriers between dentists and physicians and help patients by diagnosing diseases outside of the mouth earlier while reducing the cost of their disease management.

The team used multi-omics — an integrated approach to viewing multiple levels of biology — to analyze dental plaque from nearly 100 Marshfield Clinic patients.

The research confirmed previous findings that the dental plaques of patients with diabetes and pre-diabetes — who show a much higher incidence of periodontal disease — are clearly different from those of healthy individuals. But it went further, measuring in vast detail what happens in the complex and changing biome of the human mouth.

Building better proteins with machine learning

Neural networks and machine learning once seemed like far-fetched futuristic concepts but are now proven successful tools that can help scientists approach big problems (and big datasets).

In a new study in the journal *Proceedings of the National Academy of Sciences*, Morgridge Investigator Anthony Gitter and his lab demonstrated that a machine learning model could predict new protein sequences that could improve protein function.

The Gitter Lab's proof-of-concept for protein engineering has a huge potential in biomedical research.

Proteins are made up of a sequence of up to thousands of characters long — a combination of the 20 different amino acids that serve as building blocks. The sequence determines how the protein folds into a three-dimensional shape, and the shape determines its function. Changing even a single amino acid in the sequence could drastically alter the shape and function of a protein.

"We actually came up with a new version of a protein that works much better than anything that's been observed naturally before or anything that's been engineered before," says Gitter.

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.

Morgridge community earns awards and honors

Skala to develop new imaging approach for retinal diseases

Morgridge Investigator **Melissa Skala** has landed a grant from the National Eye Institute to develop a new imaging method that could allow for earlier disease detection, monitoring and treatment evaluation for retinal diseases.

New collaborative research center to provide a clearer image of tumor microenvironment

Morgridge Investigator **Kevin Eliceiri** and collaborators at the University of Minnesota will develop and test an integrated toolkit of imaging and data analysis technologies for immunotherapies, funded by the National Cancer Institute.

Cantor wins ACS award to continue investigating human cancer cells

Morgridge Investigator **Jason Cantor** was recently granted an award from the American Cancer Society to continue his investigation into conditionally essential genes in human cancer cells. Utilizing CRISPR, a revolutionary DNA-editing technology, Cantor and his team will make large-scale screens to possibly identify what genes are essential for the survival and growth of human cells.

GIVING MIDDLE SCHOOL STUDENTS A GLIMPSE INTO THE 'INVISIBLE WORLD' OF VIRUSES

COVID-19 may have tested humanity's strength over the past two years, but a group of 5th-grade students at Notre Dame School of Milwaukee is discovering that the science of virology can be a new superpower.

The students are among the first users of a new digital learning resource developed by PBS Wisconsin called "Meet the Lab," which gives middle school-aged students a glimpse into high-powered research labs and the scientists who run them. The resource debuted in fall 2021 and features the work of the John W. and Jeanne M. Rowe Center for Research in Virology at the Morgridge Institute.

The modules are designed to plug into regular middle school sciences classes and give students a deeper appreciation of how research impacts our lives. For "Virus Investigators," that begins with a video featuring Madison firefighter and EMT Adam Perez, who describes how the COVID 19 pandemic affected every corner of his professional and personal life.

Then the program shifts to UW–Madison professor and Morgridge Investigator Paul Ahlquist and his team, who describe the tools of virology, what questions motivate them and their own "superpowers," like perseverance, curiosity and risk-taking. The last element is an in-depth activity where students get to search for viral particles inside an infected cell and figure out how the virus replicates itself.

Kathy Biernat, Grades 5-8 science teacher at Notre Dame, used Virus Investigators on November 3 with her 5th-grade students, and she says she noticed impressive before-and-after results about what the students knew about viruses.

"Prior to this, talking about COVID was really relegated to prevention — six feet apart, masks, etc. — and not really on how the virus works," Biernat says. "So, yesterday we talked about how it actually is affecting the cell. They knew it affected the body — they mostly thought the lungs — but by the end, they realized that the reason people get sick is because of the damage to the cell, but more importantly because viruses use the energy of the cell to replicate."

The scientists describe their research in highly relatable ways. Scientist Megan Bracken describes microscopy as a pathway to an "invisible world."

"It's like a tiny parallel universe that is existing alongside us or even inside of us," Bracken says.

Biernat says that's the real superpower of the project. "This resource gave students a way to visualize what we cannot see," she says. "And instead of

just saying viruses are 'really small,' they compared it to trying to find an M&M on a football field, making it something students could relate to."

Ahlquist says the project really has two-way benefits, since translating their group's research for non-scientist audiences really forces them to consider what matters most to the general public.

"It challenges us to think about what's fundamentally important about what we're doing. At some level, it gets us to reevaluate the priorities we should have."

SUMMER SCIENCE CAMPS RETURN IN 2022

The annual Summer Science Camp will return to a residential, on-campus program this summer. The in-person camps were temporarily paused during the COVID-19 pandemic.

There will be three camps running through June and July 2022 that invite high school students and a teacher from 15 school districts to participate in a four-day immersive experience at UW–Madison.

The summer camps give high school students from rural Wisconsin communities the experience of rigorous academic excellence and cultural adventures provided by UW–Madison.

In addition, the Discovery Outreach team will also provide a third year of the Summer Science Camp Online Workshop Series. The program debuted during the pandemic and is a six-week program where high school students meet weekly with scientists to explore STEM careers. Students receive hands-on kits and digital resources that accompany their webinars and lectures.

YOUR SUPPORT HELPS HIGH SCHOOL STUDENTS EXPLORE SCIENCE

ALUMNI SPOTLIGHT:

MEET ANJI TRUJILLO

MORGRIDGE, UW ALUM 'DIVING INTO THE DEEP END' OF VACCINE DEVELOPMENT

Anji Trujillo's introduction to analytical chemistry came as an undergraduate at Humboldt State University, where she helped build a device to measure how ancient redwood forests surrounding the northern California campus influence air quality.

It began an odyssey that would lead Trujillo to a 2021 Chemistry Ph.D. from UW–Madison, a vast working knowledge of mass spectrometry, and a coveted job working on the frontlines of drug development at Pfizer in St. Louis.

Trujillo worked in the lab of UW–Madison and Morgridge Investigator Josh Coon, who uses mass spectrometry to explore a wide range of biological and medical questions.

Mass spec is one of the essential tools of modern biochemistry, helping scientists precisely measure the mass of different molecules in a sample. Rather than study the atmosphere, Trujillo analyzed molecular compounds that yield clues on everything from Alzheimer's and Parkinson's disease to the COVID-19 virus.

Today, Trujillo is about six months into a job as a senior scientist at Pfizer's Chesterfield, Mo., facility, which is ground zero for the company's massive mRNA vaccine rollout to fight the COVID-19 pandemic. She says her facility manufactures the very first step of the vaccine process — the development of DNA templates — and ensures safety testing of vaccine doses. All told, the facility has had a hand in producing nearly 3 billion vaccine doses.

"It's a very exciting time to be here," Trujillo says. "We celebrate together not just from the vaccine point of view, but all of the other drugs that are in the pipeline. I get to see the breakthrough moments, courage, and excellence that permeates at Pfizer and this is extremely motivating."

Trujillo, a first-generation college student, grew up in Santa Barbara, Cal., where her parents immigrated from Mexico when they were teenagers, seeking a better life.

She started her undergraduate work at Santa Barbara Community College, where she fell in love with anything involving chemistry and research. She later transferred to Humboldt State University to complete her bachelor's degree in chemistry.

Trujillo's journey 2,300 miles east to the Midwest started with the National Science Foundation's Research for Undergraduates (REU) program, which connects research-minded juniors with a network of labs around the country. She had five offers but chose UW–Madison, working in the lab of chemical biologist Laura L. Kiessling.

She was then accepted to the master's program at UW–Madison and joined the Coon lab in May 2015. While at UW–Madison, she also minored in research communication and contributed to science outreach in the Discovery building in programs like Science Café and Saturday Science.

"In hindsight, I didn't realize when working in Josh's group that we were considered national leaders in the mass spec field," she says. "I didn't realize the impact until I came to Pfizer and they were talking about me coming from a world-renowned lab. And I'm like, 'OK, you're right about that.'"

THANK YOU
Your support helps young scientists launch their careers.

“One analogy would be that Morgridge scientists can be like the stem cells of the research world. We have the flexibility and potential to become almost anything.”

– JING FAN, MORGRIDGE METABOLISM INVESTIGATOR

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