2021 ANNUAL REPORT

Prepared for the WARF and Morgridge Trustees and friends of the institute.

MORGRIDGE
INSTITUTE FOR RESEARCH

Attracting a new wave of talent to the Morgridge Institute

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.

Jamie and his team have been a big part of our identity. We will be wise to aim for the same level of excellence and accomplishment as we search for new talent.

Along with Jamie's pending departure, two other Morgridge investigators have recently taken new positions and a number of long-planned new hires are in the pipeline. All told, we will be hiring no fewer than six new investigators in the next two years. That's a lot of change for an institute of our size. Those folks 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? Is this an opportunity to redefine ourselves, or forge entirely new research directions? Or do we lean more strongly into the traits we honor today, such as encouraging bold questions, taking advisable risks and following the science wherever it may lead us?

To answer that question, we have undertaken a comprehensive plan in 2021 involving the Morgridge Board of Trustees, the Morgridge Scientific Advisory Board, and most importantly, our scientists. In our interviews with investigators, the take-home message was unambiguous: Focus on the people, rather than any specific frontier in science. We should continue to focus on finding the best available scientific talent who also combine curiosity, creativity, collegiality, and a strong desire to work with and learn from others.

We recognize that to achieve this lofty goal of hiring the absolute best, we 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.

This, after all, is what society expects of us.

Sincerely,

Brad Schwartz
CEO, Morgridge Institute for Research

Morgridge investigators share their vision for the institute

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

— JING FAN

"What science do we want in the future? We want something that we can't currently imagine."

— PAUL AHLQUIST

"Somebody's approach to the scientific process, how they get ideas, and pursue ideas, is more important than the specific scientific niche. Somebody who has their eye on the future and is always looking for big problems to solve or bringing creative approaches to old problems."

— TONY GITTER

"The opportunity is to create a scientific community where people are doing great science, but also actually care about the science that other people are doing. There's no magic phrasing or motto or theme. It's all about recruiting the right people."

— PHIL NEWMARK

"When I think of a research community, since we're an academic institution, I think of the trainees. It's our job to create an environment where they thrive. That means we create a culture of inquiry, where people are generally interested in multidisciplinary science — beyond what's just happening in their lab."

—MELISSA SKALA

"I think of my colleagues at Morgridge as being great people who I can bounce ideas off of, and interact with. Very collegial. I think of the culture as sort of, 'high-level people who are Midwestern nice.'"

— JOSH COON

A science trailblazer retires:

James Thomson's legacy changed the face of biology

"One of the things that stands out about Jamie Thomson is how much he cares. He has always been incredibly careful with his work, taking extra time if needed to make sure that his findings were trustworthy and reproducible. He cares about the betterment of the world and the special role that scientists have in achieving that. He cares about the people in his lab, which is why he has always been so careful about who he brings into his group. To see the fondness that Jamie and his team have for each other is remarkable, and has led to strong implicit trust that continues to make their work top-notch; nobody wants to let their colleagues down.

Jamie also cares about the environment that allowed his work to thrive, and that has fostered his somewhat unconventional career. He reminds us often about what it takes to do high-quality research, and how important it is that those of us at the Morgridge Institute and the University of Wisconsin actively strengthen the environment that allowed him to make his remarkable discoveries."

— BRAD SCHWARTZ, MORGRIDGE CEO

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 miraculous, shape-shifting stem cells that give rise to all of the building blocks of life, from skin and bone, to hearts and blood, to neurons and brains.

Thomson, after more than 30 years with the University of Wisconsin–Madison and 12 years with the Morgridge Institute for Research, has announced plans to retire in July 2022.

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 primates, the first time ever done in a species closely related to humans. 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. The third leap was in 2007, with the discovery of adult pluripotent stem cells — a way of coaxing adult skin cells back to their original blank state.

Since those landmark discoveries, stem cell science now employs tens of thousands of scientists globally in industry and academia. Many are working in promising frontiers such as stopping or reversing blindness, Parkinson's disease and diabetes. They 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.

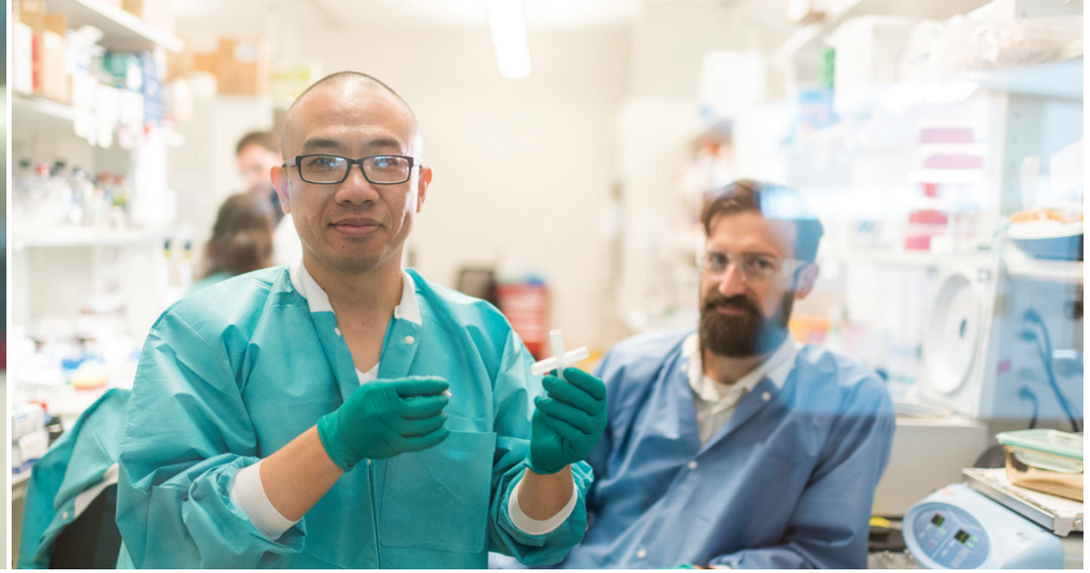
Thomson began his postdoctoral career in primate research in the early 1990s with an initial focus on species preservation. "At that time, about half of the 200 or so species of primates were threatened or endangered," Thomson says. "And by the time my children are older, a lot of them would likely be extinct. And I was interested in using reproductive technologies to at least maintain the germplasm if not maintain this species in the wild."

His attention at the Wisconsin National Primate Research Center soon switched permanently to stem cells once that science started showing progress. Prior to that time, stem cells were only successfully isolated in rodents. "I wasn't really thinking that I'd be the one to drive the human cells, I figured that we would get the monkey advance and somebody else would drive it to humans. But for whatever reason, time was on our side."

The 1998 embryonic stem cell discovery would dominate headlines for years, both because of the cells' immense biomedical promise and the controversy surrounding their origins. The debate became closely entwined with the abortion debate and the question of when life begins. The controversy came to a head in summer 2001 when the George W. Bush administration, after literally months of intense lobbying on both sides of the issue, ultimately allowed research to continue only on the five cell lines that had been derived in the Thomson lab. Those lines are still used today in labs around the world.

Tommy Thompson, who cheered Thomson's discovery as governor of Wisconsin in 1998, ended up being a pivotal voice in the national debate when he became Bush's secretary of health and human services in 2001. His support of stem cell science proved to be a deciding

Vernella Vickerman Kelley, a biomedical engineer in the Thomson lab, focuses on developing model systems for the blood-brain barrier.



Jue Zhang (left) and Matthew Brown are part of the team working to generate tissue-engineered blood vessels for grafts.

Diana Marcela Tabima Martinez works on the bioreactor created to assist in the growth of engineered arteries.

factor for Bush. Sen. Orrin Hatch of Utah also became a surprising conservative advocate.

“I knew the controversy was going to be awful, but I figured in three to six months it would be gone,” Thomson says. “But once the Bush administration made it a top priority, the controversy lasted for 10 years rather than six months. That really surprised me.”

An intensely private person who doesn’t seek the limelight, Thomson nonetheless did dozens of speaking engagements in those early years to help educate decision-makers on stem cell science. “My best audiences would usually be comprised of predominantly white Republican businessmen, because I would explain the science and they would typically say, ‘Yeah, I get that. What’s the big deal?’”

Thomson recalled a meeting in Hollywood in 2001, where he spoke with a group of movie industry heavyweights, including film-makers David and Jerry Zucker, and actor Robert Klein. All of them had family connections to a disease that could be helped by stem cell research.

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 ten years,” he says. That fact is playing out today — now 23 years removed from the original science scientific breakthrough, many clinical trials are showing promising results. A fall 2021 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.

Some of the recent advances may have enormous potential to reduce human suffering. Doug Melton, a professor of developmental biology at Harvard University, has successfully developed an insulin-producing pancreatic cell line that could cure diabetes. It is being developed by a pharmaceutical company and appears to have fully cured its first patient, according to a November 2021 story in *The New York Times*.

On another front, Lorenz Studer, director of Memorial Sloan Kettering’s Center for Stem Cell Biology, is embarking on the first-ever human clinical trial using pluripotent stem cells to treat Parkinson’s disease. The treatment is being developed by BlueRock Therapeutics of Cambridge.

Other promising research has very close connections to the Thomson Lab. Dennis Clegg, a stem cell scientist at the University of California-Santa Barbara, where Thomson holds a faculty position, is using cells from one of Thomson’s original 1998 stem cell lines to treat macular degeneration. Phase one of the clinical trial is complete and, surprisingly, one-third of the patients with advanced macular degeneration showed noticeable improvement in their vision. This was a control group that clinicians thought would not get direct benefit.

“Two years ago I met one of the women who had the transplant,” Thomson says. “And she was saying how isolating macular degeneration is because you lose the center part of your vision. And you can’t go to a party and recognize people and talk to them, because your brain can’t process it. And she went from that condition to being able to read and actually recognize people again.”

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 three 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.

“This is a university with a medical school, a veterinary school, a primate center, the Morgridge Institute, and the Waisman Center cell manufacturing facility,” he says. “Nobody else has that combination of resources. So we can go from really basic science to actually making a clinical product without leaving campus.”

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* (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 the topic is still in development.

“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.”

Time to SHINE:

UW, Morgridge spinoff has great hopes for fusion's future

It's no secret that startups are on the rise. Economists point to the economic and social stressors brought by the pandemic as a big contributor. Startups are being spun up at such a high rate, odds are you might personally know someone who is starting one of their own.

Many Midwest companies are sharing in this trend. One such company is SHINE, a fusion energy company based in Janesville. Founded in 2010, SHINE has a journey that is emblematic of the heartland's tech entrepreneurial boom, particularly for Wisconsin.

SHINE's origins date back to 2005, when Greg Piefer was a Ph.D. student in the UW–Madison nuclear engineering program. At that time, Piefer took a medical imaging class from Thomas "Rock" Mackie, an imaging innovator who was creator and founder of Madison cancer imaging company Tomotherapy.

The Morgridge Institute and Mackie — who at the time was director of medical imaging for Morgridge — played a pivotal role in SHINE's early growth years. Mackie and Pfeifer worked together to land a $20.4 million grant from the Department of Energy in 2011, a time when SHINE only had two employees. SHINE was created as its own spinout to simplify the story and vision of attainable fusion energy solutions.

One of Piefer's big-picture goals as both an academic and entrepreneur is to "play a role in helping usher in the fusion age." He was particularly interested in trying to make fusion energy practical. At the time, it seemed that most people were just focused on the physics of getting it to work.

However, it turns out there are a lot more applications for fusion energy that are attainable in the shorter term, besides efficiently producing energy. In fact, SHINE is in the midst of a four-phase business plan to first perform non-destructive testing, such as neutron radiographs; second, produce isotopes for cancer treatment; third, recycle massive quantities of nuclear waste that is currently stored (though well-monitored) in pockets all over the globe; and fourth, create sustainable energy through nuclear fusion.

One of the exciting near-term technologies for SHINE is diagnosing and treating patients who have cancer. In particular, they are working to become a leading global supplier of an isotope called molybdenum-99, which is used in millions of medical procedures and is currently in short supply.

"We can turn uranium we might buy for $6 a gram into molybdenum-99, which costs $150 million a gram," Piefer says. "At SHINE, we can use neutrons to cause that change to occur. At this facility in Janesville, we also produce materials that are used to diagnose heart disease, diagnose cancer, and even treat cancer."

An interesting part of SHINE is it uses uranium that was once intended for nuclear weapons. The United States and Russia enriched a lot of uranium that would be suitable for nuclear bombs, but have recently signed treaties to de-enrich vast stocks of the element so it can no longer be used for weapons.

"We like to say over the lifetime of our factory here in Janesville, we should be able to take material that was meant to potentially kill billions of people and turn it into over a billion doses of medicine," Piefer says.

About ten years ago, many people in the U.S. were driving conversations away from nuclear energy. But now, things may be changing. What have those conversations looked like over the course of SHINE's journey with investors?

"Leading the charge are some of the most vocal environmental activists who in the past didn't like nuclear energy options," Piefer says. "But I think everything in life is a trade-off and there are no perfect options. Nuclear energy generates about 10 million times as much energy per kilogram of fuel burned versus fossil fuels, so you just have a lot less waste — millions of times less waste."

"We have a real problem right now that nuclear fission can help solve," Piefer adds. "It's not perfect, but it's better than global warming running amok and destroying all our coastal cities."

Piefer offered some advice for people thinking about starting a company of their own, especially those who are academics.

"One of my favorite questions for entrepreneurs is 'does it make sense?'" Piefer says. "Ask yourself that all the time. You're already an entrepreneur if you want to change the way things are done."

Kevin Eliceiri, a Morgridge biomedical imaging investigator and director of the Morgridge Fab Lab, also played an important role in SHINE's technology development at Morgridge. Eliceiri says SHINE is a great example of the role basic research plays in enhancing quality of life.

"A lot of people don't realize that companies often have academic sparks, and are 'spinoff' companies from scientific research," says Eliceiri. "Universities and places like Morgridge can play the role of catalysts where academics take on the risk of new ideas."

"Academics can jump out early before the big money is there, where a company can help develop an idea to a big payoff," Eliceiri adds. "Companies see an idea all the way through large-scale production. For SHINE and other companies, Morgridge was the collaborative catalyst that helped the transition to happen."

SHINE Medical is a classic example of how curiosity-driven science helps society, often in ways we can't predict.

While SHINE was founded in 2005, a discovery made 29 years earlier proved to be a vital contributor to the company's success. UW-Madison medical physicist Paul DeLuca developed and patented a fusion acceleration process in 1976 that demonstrated proof of concept that medical-grade isotopes could be developed with small-scale devices.

That patent remained dormant until an enterprising nuclear engineering Ph.D. student, Greg Piefer, began a personal quest to bring fusion energy to the marketplace. Building on DeLuca's work, Piefer developed his own patented technologies that now form the basis for SHINE's approach to creating medical isotopes without the need for enriched uranium.

Piefer's development is now poised to address a potential worldwide shortage in the life-saving medical isotopes, now that several nuclear power plants that once provided the material have been decommissioned.

"The SHINE story beautifully illustrates why we have to take the long view in scientific research," says Morgridge CEO Brad Schwartz. "Many fundamental discoveries in science advance knowledge of how the world works, but don't have immediate applications. It can take years or even decades of additional research before that initial discovery yields a product that improves the world."

"We like to say over the lifetime of our factory here in Janesville, we should be able to take material that was meant to potentially kill billions of people and turn it into over a billion doses of medicine."

– SHINE CEO GREG PIEFER

Resilience:

How COVID-19 changed how we do science

"We need a 'space race' against viruses. We simply need to understand them better," Ahlquist says. "We have a crucial need. We have clear pathways to address that need. The final step is: let's get going."

– PAUL AHLQUIST, DIRECTOR OF THE JOHN W. AND JEANNE M. ROWE CENTER FOR RESEARCH IN VIROLOGY

The COVID-19 pandemic isn't the first time that humanity has faced a major public health challenge, and it certainly won't be the last.

From day one, our scientists quickly responded to the rapidly growing burden of this disease from a relatively unknown virus — embracing the unknown and continuing to follow the science, fearlessly, to make the discoveries that benefit human health.

"Here you have all of these people who are basic researchers who made a change in what they were doing, because they knew society needed it," says Brad Schwartz, chief executive officer at the Morgridge Institute. "To me, this was a huge win. It demonstrated their commitment: 'here's a chance for me to do something good, and I'm going to do it.'"

The great pivot: the desire to make a difference

How can a biomedical research institute devoted to the long view of science — big questions that may take decades to solve — make contributions to fighting the disease that suddenly upended the world?

Morgridge Investigator Josh Coon wrestled with this question early in the pandemic.

"We're not virologists. This is not our thing. But we're all thinking, 'How do you pivot to contribute?'" Coon remembers.

What Coon did have was a state-of-the-art mass spectrometry lab equipped by major technology investments from the National Institutes of Health (NIH). This innovative technology helps scientists understand disease, metabolism, and the intricate complexity of our body's proteins, lipids, and molecules.

Coon partnered with fellow Morgridge Investigator and bioinformatics expert Ron Stewart, and Dr. Ariel Jaitovich, a pulmonary and critical care physician at Albany Medical Center in New York — one of the major hotspots during the first wave of the COVID-19 pandemic.

Together, they tackled the question: Why do some COVID-19 patients get really sick and die, while others only have mild symptoms?

The team produced an interactive, public web tool to help researchers navigate the unknowns of the disease. The Coon Lab estimates that about 1,700 users have accessed the resource, demonstrating the desire for data accessibility and transparency to advance COVID-19 research.

Finding order in the chaos

The COVID-19 pandemic served as a great motivator to make science more open, transparent, and accessible.

"We're in a crisis, let's use the tools and knowledge we have to actually make progress," says Tony Gitter, a Morgridge investigator specializing in research computing and machine learning applications for virology. "That's the primary, and maybe the only goal. Openness really helped accelerate things."

Gitter leveraged his expertise with the Manubot software tool he codeveloped to chronicle the pandemic in real-time. The scientific literature surrounding COVID-19 was exploding — more than 50,000 papers in PubMed in the course of a year — and researchers needed a tool to quickly parse through vast amounts of COVID-19 data.

"Scientists were very, very eager to contribute and help, and we were all desperate to learn anything that might help with treatment — but there wasn't amazing coordination there," says Gitter. "There's this parallel to Wikipedia, just continually updating entries that massive teams can collaborate on."

Fifty scientists and researchers made contributions to the Manubot collaboration. The developmental journey of the entire project will be published as a special issue of *mSystems*, to showcase the power of collaboration and how new approaches to science must evolve.

Little things have big impacts

Basic research is fundamental to advancing human health. Morgridge scientists have been working to understand the depths of biology to help fight deadly diseases like cancer, HIV/AIDS, and now COVID-19.

For Paul Ahlquist, this work centers on the question — how do viruses replicate and interact with their hosts?

Ahlquist, the director of the John W. and Jeanne M. Rowe Center for Research in Virology, has spent much of the last decade revealing the molecular structures of important viral "protein machines" inside of virus-infected cells.

His team used revolutionary cryo-EM approaches to first reveal and now produce increasingly detailed structural images of a crown-like viral RNA replication complex responsible for genome replication in the class of viruses that includes SARS-CoV-2.

Morgridge Investigator Tim Grant says that near atomic-level details reveal valuable insights into how the replication complex assembles and functions — a foundational discovery needed to develop antiviral approaches.

"There are hundreds of structures, different parts of the coronavirus, that have been solved by cryo-EM in the last year," says Grant. "As a field, cryo-EM has really provided a lot of coronavirus knowledge."

Endgame: the space race against viruses

The COVID-19 pandemic has highlighted that we need to double down on basic research to better understand, prevent, and stop the next deadly outbreak from an unknown foe.

"We are often asked, 'Why don't you just work on the important viruses?' But the lesson of the last 100 years is: everything is important," says Ahlquist. "Nearly every time the world has been hit with a new viral plague, it's been from a class of viruses that had not previously been linked to serious human disease."

Investment in basic research could help understand the extent, diversity and function of viruses out there. It could advance rational approaches to control them — and improve upon existing approaches, like the mRNA technologies used in COVID-19 vaccines.

"We need a 'space race' against viruses. We simply need to understand them better," Ahlquist says. "We have a crucial need. We have clear pathways to address that need. The final step is: let's get going."

2021 MILESTONES

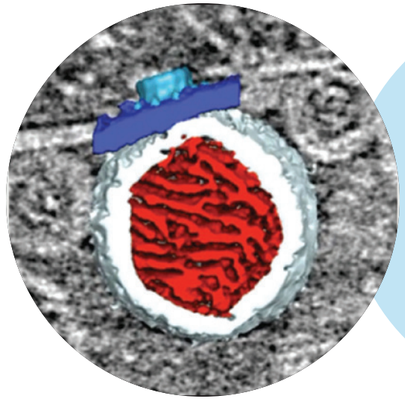
The COVID-19 pandemic took everyone by surprise, but teams at the Morgridge Institute continued pushing science and engagement forward through collaboration and innovation.

Giving middle school students a glimpse into the 'invisible world' of viruses

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, highlights the Morgridge Institute virology research team.

Morgridge scientists join forces with Genentech to soup up Cryo-EM imaging

A partnership with Genentech is helping Morgridge Investigator Tim Grant improve software that helps scientists harness the incredible power of cryo-EM microscopes for drug discovery.



Imaging method predicts how well stem cells can differentiate into cardiac muscle cells

Morgridge researchers developed an imaging technique that can predict the efficiency of cardiac muscle cell differentiation from stem cells as a method of quality control for potential regenerative therapies.

Imaging technique sheds light on a notoriously slow-growing cancer

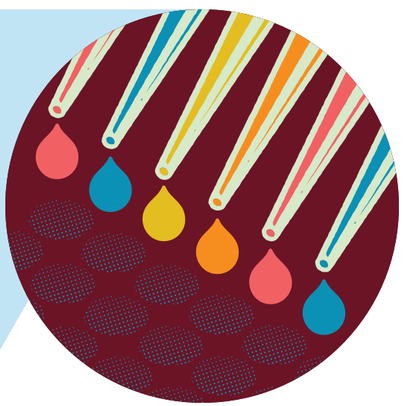
Neuroendocrine cancers grow so slowly they often evade detection before it's too late. By mimicking that slow growth in the lab, the Melissa Skala Lab hopes to speed up the creation of more effective treatments.

Building a better bioimaging community: Chan Zuckerberg Initiative supports international partnership

Investigator Kevin Eliceiri is leading the creation of BioImaging North America, helping hundreds of imaging innovators connect to resources and learn from each other.

Hunting viral variants across Wisconsin, powered by high-throughput computing

When dangerous COVID viral variants were sweeping the globe, UW-Madison researcher David O'Connor was busy tracking their spread in Wisconsin. He turned to Morgridge high-throughput computing to make sense of the results. This was just one of hundreds of HTC-facilitated projects in 2021.



The (cell) medium is the message: A new tool for studying cell biology in a dish

Morgridge Investigator Jason Cantor is partnering with Thermo Fisher Scientific to give biologists a new medium to study human cells in their most natural state.

Alumni Profile:

Anji Trujillo

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 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. We are constantly getting messages of gratitude from Pfizer leaders, highlighting the dedication and hard work Pfizer colleagues put towards the science that enables the delivery of drugs to patients around the world. For the COVID-19 efforts, it is a privilege and an honor to get an insight into the clinical trials — if it involves pediatrics, or the COVID anti-viral pill (PAXLOVID) — I am part of the team that ensures the highest quality and efficacy during the developmental and manufacturing stages. 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. It was there she got to work with a professor on building a mass spec device to figure out what's in that pristine air.

"I never got to use it, but it fueled my interest in mass spec. I also realized I was really good with my hands — a skillset that has allowed me to fix and run mass spectrometers," she says.

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. It was a big decision, but she accepted the challenge and was open to the new opportunities she couldn't quite see ahead.

"For a first-generation college student, obtaining your bachelor's degree is typically the ultimate goal," she says. "That bachelor's degree represents the end of a windy and tiring journey. What comes after is a whole other ball game."

Where are they now? Catching up with recent alumni in their new careers

Morgridge Institute alumni are making their mark on the world.

A few Morgridge graduates shared thoughts on how their research experience at the institute prepared them for their careers, and gave shoutouts to some instrumental people who helped them along the way.

NURUDDIN UNCHWANIWALA
Ahlquist Lab

In the Ahlquist Lab, Unchwaniwala studied how positive-strand RNA viruses manipulate host cells to produce a vast excess of new infectious virions.

"Leading this project was instrumental in honing my scientific skills while at the same time developing new skill sets," he says.

Currently, Unchwaniwala works as a research scientist at Assembly Biosciences, a clinical-stage biotechnology company in San Francisco. His projects advance small molecule drugs to block Hepatitis B Virus (HBV) replication and cure chronic HBV infections, a leading cause of liver cancer.

Shoutout: "It would be unfair to point at a single individual, because what made Morgridge special was the feeling that you are a part of a larger integrated team—and various individuals were making a significant impact at different stages of my scientific career."

TIFFANY HEASTER
Skala Lab

Heaster's work in the Skala lab involved characterizing metabolic autofluorescence as a biomarker of immune response in cancer.

"My exposure to multi-disciplinary areas of research, both in the Skala lab and across Morgridge, broadened my horizons to diverse scientific concepts," reflects Heaster.

Heaster is now a principal scientific researcher at Genentech, focused on establishing and validating imaging techniques to study disease progression and expedite drug discovery and development. These projects intersect between the fields of oncology, neuroscience, ophthalmology and more.

Shoutout: Melissa Skala. "Melissa always cultivated a very collaborative research environment, constantly establishing connections to provide unique and essential expertise to guide our projects. She was also very supportive of exploring new research directions in her lab."

JUSTIN MCKETNEY
Coon Lab

McKetney is currently an assistant researcher in the Nevan Krogan Lab at the University of California-San Francisco where he applies MS-based proteomics to a variety of cell and tissue types to better understand the molecular effects of disease.

"The Morgridge Institute helped me by supplying a venue where I could present my work to a wider scientific audience," says McKetney. "This helped with both my scientific communication skills and my ability to place my specific projects in a wider disease context."

Shoutout: Josh Coon, Katie Overmeyer, and Evgenia Shishkova. "Professor Coon was a significant mentor to me as my PI," McKetney says. "But I also learned many lessons from staff scientists in our lab, such as Katie and Evgenia."

Other recent alumni:

DANIEL GIL
Skala Lab
Following his time at Morgridge, Gil began a postdoctoral fellowship with the University of Texas-Austin.

JAYHUN LEE
Newmark Lab
Lee is an assistant professor at the University of Texas Medical School in the Department of Microbiology and Medical Genetics.

TANIA ROZARIO
Newmark Lab
Rozario is an assistant professor at the University of Georgia in the Department of Genetics, working in their Center for Tropical Global Diseases.

ANDREA REBOLLEDO VIVEROS
Ahlquist Lab
Rebolledo Viveros is pursuing a Ph.D. in Molecular Microbiology at Tufts University in Boston, Mass.

ALEXANDRA WALSH
Skala Lab
After her time in the Skala Lab, Walsh joined Texas A&M University as a faculty member in the Department of Biomedical Engineering.

Outreach and education

Morgridge scientific teams found many ways to adapt during the pandemic. For the Discovery Outreach Team, it meant recreating the world of hands-on science instruction for online audiences — and keeping it relevant, fresh and fun.

The Wisconsin Science Festival celebrates 11 years

The 11th annual Wisconsin Science Festival offered more than 170 events virtually and in-person across the state for people of all ages to dive into science topics.

A focused theme was fungi. UW–Madison has one of the strongest fungi research communities in the nation, if not the world. The festival featured a range of events in person, on panels, through asynchronous content, and through our partnership with the Badger Talks Live series.

This year's festival featured several new elements:

- The team debuted a new platform: Science in a Bag. These STEM activity kits were prepared by several UW–Madison units, and some new items were created altogether, to help give a hands-on element to participants. Approximately 2,500 kits were distributed to libraries across the state.
- Science on the Square was back! This popular event is a partnership with the Business Improvement District in Madison. It featured hands-on exploration stations ad vendors on State Street and the Capital Square. New this year, the event also coincided with the popular Night Market.
- We are continuing our engagement with UW–Extension's Upham Woods facility to host the Wisconsin Science Festival bioblitz. The bioblitz is also being featured at a number of community organizations. Last year's debut bioblitz resulted in more than 1,000 new recorded observations from hundreds of participants statewide.
- The 2021 Big Ideas for Busy People panel focused on the importance of evidence in advancing understanding. The event featured Phil Newmark, a Morgridge investigator in regenerative biology.

New partnership with Madison schools

A newly expanded partnership with the Madison Metropolitan School District (MMSD) will help bring science, research, and discovery into the hands of more students in our area. These students will be a part of the district's Personalized Pathways Program on one of two tracks: Health Services or Information Technology.

Working with MMSD, the institute has designed a program to create a biotechnology and professional skills "bootcamp" course for high school students seeking youth apprenticeship or internship opportunities.

With the support of MMSD's leadership, we are now seeking grant funding to allow co-design of the curriculum with science teachers, followed by implementation with the next available cohort of apprentices. In addition, the institute is in the early stages of planning STEM career events at Madison West High School that will link students with Morgridge researchers through informational interviews, career fairs, and job shadowing.

Serving up summer science

For the second year, the Summer Science Workshop Series helped students and teachers.

The virtual workshop was a six-week online course where high school students (and a small group of middle school students) and science teachers logged on weekly to meet with scientists from the Morgridge Institute and UW–Madison.

The workshop was created last year during the COVID-19 pandemic to create a safe, digital alternative to explore science.

Twenty-one schools in the Wisconsin Rural Schools Alliance and seven sites in the Upward Bound program, which focuses on underrepresented and first-generation precollege students, joined the workshop.

Together, the students met with scientists and researchers who illustrated their diverse paths to scientific careers. Since 2007, the summer science experiences have helped nearly 500 students from nearly 80 state high schools.

Online Field Trips bring science to the state

For more than ten years, the Field Trip Program has brought students and teachers to Madison for a day of activity and exploration. But when the COVID-19 pandemic shuttered on-campus activity, the Discovery Outreach Team got creative.

They honed an online approach that is engaging, inspiring, and fun. And over the spring, they welcomed 28 Field Trips from nine school districts across Wisconsin.

"If students can actually meet a scientist and hear what their favorite color is, or where they went to school — and maybe they're from your same rural hometown — that's the impact that we are so proud to make," says Val Blair, senior outreach coordinator.

Everyone is quick to point out that in-person Field Trips to campus are the most impactful experience for students — the trip itself, the hands-on experience, and the lab spaces always bring a 'wow' factor.

This year's field trips included workshops for K–12 students of all ages with activities like the triboelectric nanogenerators, but also "Finding Buried Treasure" with a fossil activity led by the UW Geology Museum, and "Meet the Lab: Cancer Detectives — Superpowered by Laser Microscopes" led by the Melissa Skala Lab at the Morgridge Institute where students uncover some of the patterns researchers use to find new cancer treatments.

2021 Participating School Districts:

- Gibraltar School District in Fish Creek
- KM Global in the Kettle Moraine School District in Wales
- The LUMIN Online School with locations in Milwaukee, Racine, and Beloit
- Muskego Middle School in Muskego
- Oconto Middle School and Bayshore Community Academy in Oconto
- Olson, Leopold, Cherokee Heights and Capital High in the Madison Metropolitan School District
- The Taylor/Price County 4H in Medford
- Thoreau Elementary in the Milwaukee Public School District
- The Upward Bound/Forward Service Corporation with locations statewide

Pregnancy project advances

NIH has chosen UW-Madison as one of 25 sites to implement the HEALthy Brain and Child Development Study, and Pilar Ossorio will co-chair the national working group on ethics, law and policy. Her team will help develop procedures for consent, confidentiality, return of findings and reporting of legally reportable issues. The project aims to begin recruiting pregnant women to the study in May 2022.

Wisconsin bioethics project chronicles pregnancy, substance use disorder and the law

The National Institutes of Health (NIH) is embarking on a massive research project to shed light on early child development, including the health and developmental implications of opioid use during pregnancy. The very first task is to ensure the study — the HEALthy Brain and Child Development study (HBCD) — is on solid legal and ethical ground.

A team of Wisconsin law and bioethics scholars are supporting HBCD with a 50-state analysis of the surprisingly diverse range of laws that address substance use during pregnancy — ranging from court-ordered treatment, to loss of child custody, to possible imprisonment.

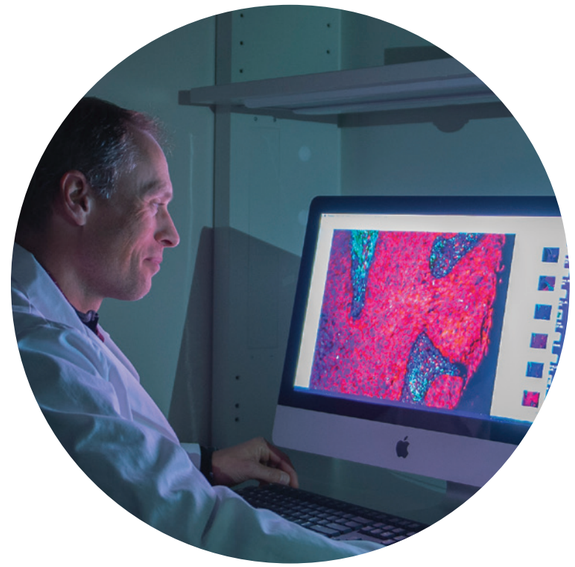
Pilar Ossorio, professor of law and bioethics at the University of Wisconsin-Madison and bioethicist-in-residence at the Morgridge Institute for Research, says the 50-state analysis is critical to protecting both research participants and researchers so this important work can move forward. Biomedical science does not have a firm grasp on all of the downstream child health impacts of substance use during pregnancy, Ossorio says, an issue made more pressing by the widespread opioid epidemic.

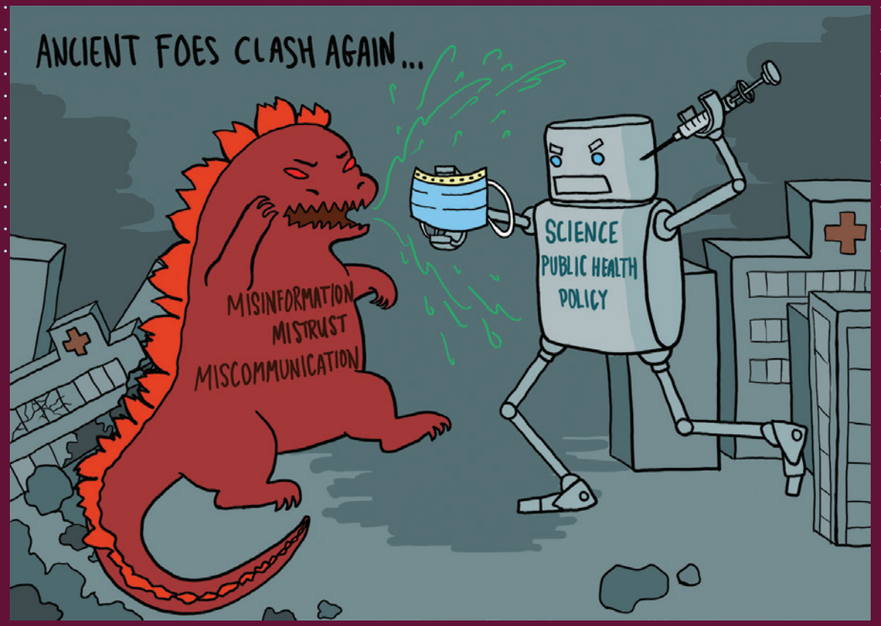
The Department of Health and Human Services estimated that 1.6 million U.S. citizens had an opioid use disorder in 2019. More than 48,000 deaths between June 2019 and June 2020 were attributed to opioid overdoses. In a Centers for Disease Control study, about 7 percent of women in 2019 self-reported using prescription opioid pain relievers during pregnancy, and polysubstance use during pregnancy is increasingly common.

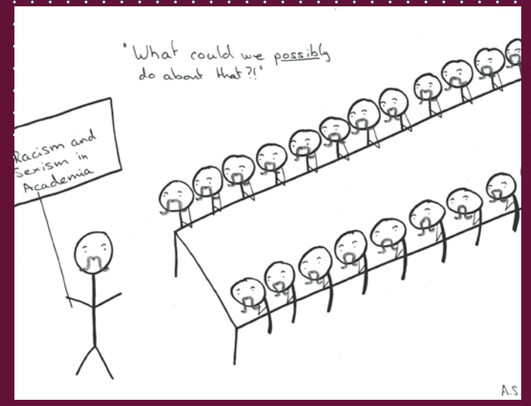
The HBCD study will recruit around 10,000 pregnant women, follow them through their pregnancies, and study their children through age 10. Some portion of the pregnant participants will have reported using substances (particularly opioids) at some point during their pregnancy. One goal of the HBCD will be to identify the impacts of such exposures on child development and to suggest strategies to improve health and potentially save lives.

“There is clearly a huge demand in the medical and research community for more knowledge and help in this area,” Ossorio says. “NIH has completed a very successful study looking at adolescent brain cognitive development from ages 9-10. But obviously a lot of brain, cognitive, behavioral and emotional development happens before that time.”

A longitudinal study starting with pregnant women is fraught with challenges — not the least of which are widely divergent and fast-changing state-by-state laws related to pregnancy and drug usage. “The law doesn’t look at prenatal substance exposure as a unitary kind of a thing,” Ossorio says. “Instead it has particular pieces of evidence that are used legally to define prenatal substance exposure as a kind of child abuse or neglect.”







Top prizes in ethics cartooning contest address COVID-19 and more

Five prizes were awarded in the fourth annual Morgridge Institute for Research Ethics Cartooning Contest, which invites participants to make a cartoon on any ethical issue related to biomedical research.

The competition drew 56 entrants from 35 different departments and programs at UW–Madison and affiliated research institutions.

Alyssa Wiener, a first-year postdoctoral research fellow and general surgery resident at UW–Madison School of Medicine and Public Health, took the top prize.

“Bioethics comes up a lot in my day-to-day work,” says Wiener, who does human subjects research in her postdoc. “Being involved clinically also demands bioethical consideration, because what is ‘right’ for a patient, population, or system is often not straightforward.”

Wiener’s winning cartoon explores the ethical and existential challenge of communicating scientific findings to society at large in order to effect practical change.

“This challenge can sometimes escalate to the proportions of an ‘epic battle’ with tremendous collateral damage, as I think is the case with the COVID-19 pandemic response,” says Wiener. “Just as comics function on both an emotional and intellectual level, I hope we can communicate the scientific process and research findings in an impactful but accurate manner.”

The COVID-19 pandemic served as a major influence on the competition this year, with many submissions focused on COVID-related topics. Many researchers needed to reassess their day-to-day engagement with ethics issues as they worked remotely away from colleagues and the university research environment.

The Morgridge Ethics Cartooning Competition, developed by Pilar Ossorio, a Morgridge investigator in bioethics, encourages scientists to shed light on timely or recurring issues that arise in scientific research.

“Ethical issues are all around us,” says Ossorio. “An event like the competition encourages people to identify some of those issues, perhaps talk about them with friends and colleagues, and think about how to communicate about those issues with a broader community of people.”

Each year, a panel of judges review each cartoon’s depiction and analysis of a research ethics issue, humor, and artistry. A popular vote by the public also contributes to the final awards.

2021 ETHICS CARTOONING CONTEST WINNERS

FIRST PRIZE
Alyssa Wiener,
School of Medicine and Public Health

SECOND PRIZE
Vivian Hsiao and Madhuri Nishtala,
School of Medicine and Public Health

THIRD PRIZE
Anjalie Schlaeppi, Morgridge Institute for Research

HONORABLE MENTIONS
Da-Inn Lee, Wisconsin Institute for Discovery;
Noah Trapp, School of Medicine and Public Health

NEWS & HIGHLIGHTS FROM 2021

Morgridge community earns awards and honors

Morgridge alumna receives one of the most elite young investigator awards

Tania Rozario, a 2020 alumna of the Phil Newmark Lab at Morgridge, received a National Institutes of Health Director's New Innovator Award for high-risk, high-reward research she is pursuing. The $2 million award will help Rozario, an assistant professor at the University of Georgia, continue studying the remarkable regenerative capacity of flatworms that cause parasitic diseases.

Honoring Ernie Micek: 'always doing the right thing'

Ernest 'Ernie' Micek was a global trade leader and entrepreneur who brought decades of experience to the Morgridge Institute. He was a founding member of the Morgridge Board of Trustees and served as chair from 2011–14. Micek, who had a 42-year career at Cargill, Inc., and led global trade efforts under Presidents Bush and Clinton, passed away in Oct. 2020 but his legacy lives on today.

Fan pens Career installment in *Nature Metabolism*

Jing Fan, a Morgridge metabolism investigator, wrote about the challenges and opportunities facing young investigators in the Career Pathways installment of *Nature Metabolism*. Fan writes about her 'risky' decision to pursue metabolism, a new research direction for her — a turn that many young investigators would be hesitant to tackle when the 'clock' for tenure has started.

But with support and encouragement from Morgridge leadership, Fan continued her research direction into metabolism and to "do research that has real impact," she writes.

"I am very grateful to have had great support on this journey. A value at my institution that I embrace is to pursue 'fearless science' — to do our best to generate real meaningful knowledge instead of overfocusing on small-minded merits," she writes.

Raja awarded the 'Women Scientist Award' for achievements in bioinformatics

Kalpana Raja, a postdoctoral research associate in the Ron Stewart Computational Biology Group, received the 2019 Women Scientist Award for her meritorious and significantly outstanding scientific contributions. The annual award comes from the Society for Bioinformatics and Biological Sciences, a non-profit professional society based in India, that supports the advancement and development of bioinformatics across interdisciplinary science fields.

Beckman Foundation will spur smart light sheet technology development

Morgridge investigators Jan Huisken and Kevin Eliceiri are leading an initiative to advance light sheet microscopy through a grant funded by the Arnold and Mabel Beckman Foundation. As one of eight awardees, the team will receive $1.2 million to support this cutting-edge, fast-imaging technique that creates a comprehensive 3D view with less phototoxic effects.

Investigators

Paul Ahlquist, John W. and Jeanne M. Rowe Center for Research in Virology

Brian Bockelman, Research Computing

Jason Cantor, Metabolism

Joshua Coon, Metabolism

Kevin Eliceiri, Biomedical Imaging

Jing Fan, Metabolism

Anthony Gitter, John W. and Jeanne M. Rowe Center for Research in Virology

Tim Grant, John W. and Jeanne M. Rowe Center for Research in Virology

Laura Heisler, Discovery Outreach

Miron Livny, Research Computing

Phil Newmark, Regenerative Biology

Pilar Ossorio, Bioethics Scholar in Residence

Melissa Skala, Biomedical Imaging

Ron Stewart, Regenerative Biology

James Thomson, Regenerative Biology

Morgridge Affiliates

Dominique Brossard, Discovery Outreach

Matthew Brown, Regenerative Biology

John Denu, Metabolism

Rick Eisenstein, Metabolism Research

Jan Huisken, Biomedical Imaging

Anna Huttenlocher, Biomedical Imaging

Laura Knoll, Metabolism

Elizabeth Meyerand, Biomedical Imaging

Deane Mosher, Metabolism

Dave Pagliarini, Metabolism

Chad Reinstra, Metabolism

Dietram Scheufele, Discovery Outreach

Igor Slukvin, Regenerative Biology

Andreas Velten, Biomedical Imaging

Justin Williams, Biomedical Imaging

Elizabeth Wright, John W. and Jeanne M. Rowe Center for Research in Virology

Ming Yuan, Virology

Board of Trustees

Carl E. Gulbrandsen, Ph.D, J.D. Morgridge Board Chair, Emeritus Managing Director of Wisconsin Alumni Research Foundation

Mary Burke, MBA, CEO and Founder, Building Brave

John Burris, Ph.D. President Emeritus, Burroughs Wellcome Fund

Harvey Cohen, M.D., Ph.D. Professor, Department of Pediatrics, Stanford University School of Medicine

James Dahlberg, Ph.D. Former Interim CEO, Morgridge Institute for Research; Professor Emeritus, Department of Biomolecular Chemistry, University of Wisconsin

Jacquelyn Fredrick, MBA. Former President and CEO of BloodCenter of Wisconsin and the BloodCenter Research Institute; Former President and CEO of Versiti, Inc.

Erik Iverson, JD, LLM. CEO, Wisconsin Alumni Research Foundation

Deborah Keller, MBA. Retired, CEO of Covance Drug Development

Thomas M. Krummel, M.D. Emile Holman Professor and Chair Emeritus; Department of Surgery, Stanford University School of Medicine

Patricia Lipton, M.S. Retired Executive Director, State of Wisconsin Investment Board

John Morgridge, MBA. Chairman Emeritus, Cisco Systems

Tashia Morgridge, M.S. Author and Retired Educator

John Neis, CFA. Managing Director, Venture Investors

Thomas F. Pyle Jr., MBA. Chairman, The Pyle Group LLC; Retired Chairman, President, CEO and Principal Owner, Rayovac Corporation

Fred Robertson, MBA, M.D. Venture Partner, Baird Capital; Clinical Assistant Professor, School of Medicine and Public Health, University of Wisconsin

Winslow L. Sargeant, Ph.D. Managing Director, S&T LLC

Brad Schwartz, M.D. CEO, Morgridge Institute for Research

Emeritus Trustees

James Berbee, M.S., MBA, M.D. Clinical Assistant Professor, BerbeeWalsh Department of Emergency Medicine, University of Wisconsin

Terri L. Potter, MHA. Retired CEO, Meriter Health Services; President, Potter Consulting

Carol Skornicka, M.A., J.D. Retired Senior Vice President, Secretary and General Counsel, Midwest Airlines

Joan Spero, M.A., Ph.D. Retired President, Doris Duke Charitable Foundation

Burnell Roberts, MBA. Retired CEO, Mead Corp.

John Rowe, J.D. Chairman Emeritus, Exelon Corporation

Jan Ver Hagen, B.S. Retired, Emerson Electric

David Whitwam, B.S. Retired CEO, Whirlpool Corp.

Scientific Advisory Board

John Durant, MA, Ph.D., Board Chair MIT Museum Director and Adjunct Professor in the Science, Technology & Society Program

Andrew Dillin, Ph.D. Thomas and Stacey Siebel Distinguished Chair in Stem Cell Research, Howard Hughes Medical Institute Investigator, Professor, Department of Molecular and Cell Biology, University of California, Berkeley

Lynn Enquist, Ph.D. Henry L. Hillman Professor in Molecular Biology and Professor in the Princeton Neuroscience Institute at Princeton University

Xavier Darzacq, Ph.D. Associate Professor of Genetics, Genomics and Development, University of California, Berkeley

Ian Fisk, Ph.D. Scientific Computing Core Co-Director, Simon Foundation, Flatiron Institute

Scott E. Fraser, Ph.D. Provost, Professor of Biology and Bioengineering, Elizabeth Garrett Professor of Convergent Biosciences, Director of Science Initiatives, Co-Director Bridge Institute, Translational Imaging Center, Michelson Center for Convergent Bioscience, University of Southern California

Christina Kendziorski, Ph.D. Professor, UW Biostatistics and Medical Informatics, University of Wisconsin

Christina Leslie, Ph.D. Principal Investigator, Computational and Systems Biology Program of the Sloan Kettering Institute at Memorial Sloan Kettering Cancer Center

Erika Matunis, Ph.D. Professor, Principal Investigator, Department of Cell Biology, Johns Hopkins University

Amy McGuire, J.D., Ph.D. Leon Jaworski Professor of Biomedical Ethics and Director, Baylor College of Medicine

Robert F. Murphy, Ph.D. Ray and Stephanie Lane Professor of Computational Biology and, Professor of Biological Sciences, Biomedical Engineering and Machine Learning, Head, Computational Biology Department, Carnegie Mellon University

Clodagh O'Shea, Ph.D. Professor, Molecular and Cell Biology Laboratory, Howard Hughes Medical Institute Faculty Scholar, Wicklow Chair, Salk Institute for Biological Studies

"It took courage for Jamie to pursue the discovery of human embryonic stem cells. He knew it would be controversial but before he started he sought advice from Alta Charo and other bioethicists so that it could be done in an ethical, responsible manner. Even so, his personal safety was at risk, but he persisted and ultimately succeeded where others had failed. He did it not for personal fame or status but because he knew it was a valuable research tool and would ultimately improve lives. As a research tool, his discovery is being used by researchers all over the globe who are using HES cells to better understand human biology and discover ways to improve lives; and now, less than 20 years later the therapeutic uses of HES cells are becoming a reality.

I think it is safe to say that without Jamie, there would not be a Morgridge Institute for Research. He was the first scientist at Morgridge and the Institute has been honored to be his research home."

— CARL GULBRANDSEN, EMERITUS MANAGING DIRECTOR, WARF;
CHAIR OF MORGRIDGE BOARD OF TRUSTEES

MORGRIDGE
INSTITUTE FOR RESEARCH

WISCONSIN
UNIVERSITY OF WISCONSIN–MADISON

WARF
Wisconsin Alumni Research Foundation

MORGRIDGE
INSTITUTE FOR RESEARCH

THE DISCOVERY BUILDING / 330 N. ORCHARD STREET, MADISON WI 53715

608.316.4100 / MORGRIDGE.ORG