MORGRIDGE.ORG

MORGRIDGE INSTITUTE
for RESEARCH

—

Science moves.
It unlocks mysteries
in medicine and
opens new doors
in human health.

But science doesn't
thrive by asking
safe questions.
It moves when we
push fearlessly into
new frontiers.

You're holding a
new report that
explores science
with the promise
to move our lives.

MORGRIDGE INSTITUTE
for RESEARCH

FEAR LESS SCIENCE

FEARLESS SCIENCE

SPRING 2018

—

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

Our research themes:

REGENERATIVE BIOLOGY

METABOLISM

VIROLOGY

MEDICAL ENGINEERING

HIGH THROUGHPUT COMPUTING

BIOETHICS

—

MEET THE MORGRIDGE SCIENTIFIC TEAM

The quality of a successful research institute is ultimately defined by its people.

This publication will introduce you to outstanding Morgridge investigators, who are seeking a fundamental understanding of human biology to drive the next big advances in human health. Our team includes two Howard Hughes Medical Institute investigators, two National Academy of Sciences members, a National Institutes of Health Presidential Early Career scholar, two National Science Foundation CAREER winners, and investigators supported by the Max Planck Institute and Stand Up to Cancer.

Our scientists are driven by a curiosity about the mysteries of biology and a passion to alleviate human suffering from disease. You will read about some of the early influences that sparked their devotion to science and some of the dream outcomes that motivate them every day.

Morgridge uses its private status and streamlined organizational structure to respond nimbly to new opportunities, in partnership with the University of Wisconsin-Madison. In fact, this public-private synergy is our greatest asset: The ability to foster and accelerate new scientific opportunities with a world-class public university, making both entities more competitive in the process.

We remain the only such private biomedical institute of its kind in the Midwest. While only a decade old, we're building a national model for how this public-private partnership can amplify research excellence.

CEO BRAD SCHWARTZ

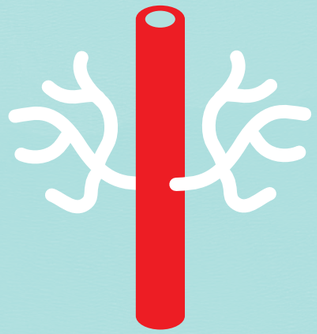
DISCOVERIES AT THE MORGRIDGE INSTITUTE

A better way to see inside the eye

The Melissa Skala lab has enhanced optical coherence tomography (OCT), a widely used tool for screening, diagnosis and treatment of eye diseases. OCT gives clinicians detailed 3D images of layers of the retina without using dyes. The Morgridge advance — called photothermal optical coherence tomography (PT-OCT) — provides greater functional contrast to see optical absorbers, such as melanin, naturally present in the eye.

Engineering functional arteries

The James Thomson regenerative biology lab perfected a method of growing arterial endothelial cells—a key step toward creating arteries for vascular surgery. The work offers further proof that scientists can create a reliable cellular source for arteries that perform and behave like the real thing.



Getting personal with pancreatic cancer

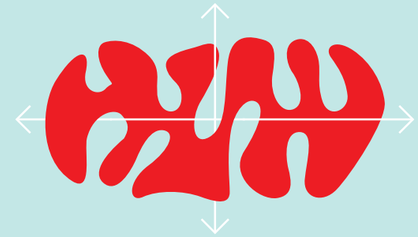
Survival rates remain bleak for pancreatic cancer, which kills more than 90 percent of people within the first five years of diagnosis. Medical engineer Melissa Skala has teamed with UW-Madison cancer researcher Dustin Deming to devise more patient-specific and precise treatment improvements, by measuring a tumor's metabolic response to different drugs.

Unmasking viral replication

The Morgridge Virology Team led by Paul Ahlquist published a landmark study illuminating, for the first time, the machinery that allows viruses to replicate rapidly inside cells and spread to new targets. The advance may open up new avenues to potentially disrupt, dismantle or redirect viral machinery.

Using stem cells to predict neural toxicity

Morgridge regenerative biologists created a faster, cheaper and more biologically relevant way to screen drugs and chemicals that could harm the developing brain. The team developed stem cell "organoids" in a dish that mimic human brain function, and can be used to test a wide range of compounds for neural toxicity — a process that currently costs millions and takes years with animal studies.



Mapping mitochondrial proteins

Mitochondria are the engines that drive cellular life, but hundreds of their component parts remain a mystery. Morgridge Metabolism Director Dave Pagliarini sheds light on the more than 200 proteins associated with mitochondria that currently have no defined function. The results will help scientists pinpoint the origins of more than 150 poorly understood diseases associated with mitochondria.

Redefining role of estrogen in cervical cancer

Scientists know the hormone estrogen plays a big role in cervical cancer growth, but a Morgridge virology study examining genetic profiles of 128 clinical cases shows estrogen thrives in the tumor micro-environment — not the tumor itself. The finding will help identify genetic signatures that predict what early stages of human papillomavirus infection are most likely to become cancerous.

Fast, powerful and gentle microscopes

Medical Engineering investigator Jan Huisken co-invented light sheet microscopy, which captures the sensitive biology of living specimens in their true functional state. Focused on the model organism zebrafish, light-sheet microscopy produces striking images of cellular movements, beating hearts and developing organs — all while keeping the specimen unaltered and "happy."

Identifying 'clockwork' genetic expression

Genes that turn on and off in precisely timed patterns, known as oscillatory genes, play an essential role in development functions like cell division and limb formation. But without a time-lapse view of genetic expression, these genes have gone largely undiscovered. An algorithm called Oscope, developed by Morgridge bioinformatics researchers, is helping scientists pinpoint oscillatory genes for the first time.

MORGRIDGE

CONNECTIONS ACROSS UW-MADISON

Our collaborations seek to enhance and accelerate groundbreaking work across the university.

OUR
INVESTIGATORS

FRONTIERS OF BIOLOGY

REGENERATIVE BIOLOGY
METABOLISM
VIROLOGY

I see tremendous parallels between the early days of recombinant DNA technology in the 1970s and the early days of stem cell research. Both created a social uproar over whether we should be doing the work, followed by a compromise and then getting on with the research.

Recombinant DNA essentially gave us unlimited access to all the genes in the body — and pluripotent stem cells provide the same thing, except for cells. For the first time, pluripotent stem cells give biomedical science access to all of the cellular building blocks of the human body.

"It's the insights we get from stem cells on how the human body works that will change the face of medicine."

Today, our lab focuses on two topics: blood vessels and developmental clocks. On clocks, we'd like to understand what controls the wide variation in gestation rates across species — or why it takes 9 months for a human to develop and three weeks for a mouse. This is important because human stem cells repeat this timing in a culture dish. Growing some types of cells, like neural cells, takes several months, making stem cell therapies difficult. If we can find a way to control developmental timing, we can make those cells available faster to treat disease.

We also decided to focus on blood vessels because any advanced engineered tissue will require a blood supply, and cardiovascular disease is a major cause of death worldwide. In the U.S., for example, heart disease and stroke are the No. 1 and No. 3 killers, respectively. A better understanding of vasculature will have an impact on the majority of conditions that kill us.

We are already seeing clinical trials based on stem cell therapies, including trials for macular degeneration, a leading cause of blindness. And multiple groups are gearing up for clinical trials for Parkinson's disease. However, the insights we get from stem cells on how the human body works will ultimately change the face of medicine.

Parkinson's is a good example. While I am hopeful that stem cell-based transplantation therapies will work for Parkinson's, in the long term, it will be much more important to understand why those cells are dying, so we can prevent their death from occurring in the first place.

THE BUILDING BLOCKS OF BIOLOGY

—

JAMES THOMSON

DIRECTOR,
REGENERATIVE
BIOLOGY

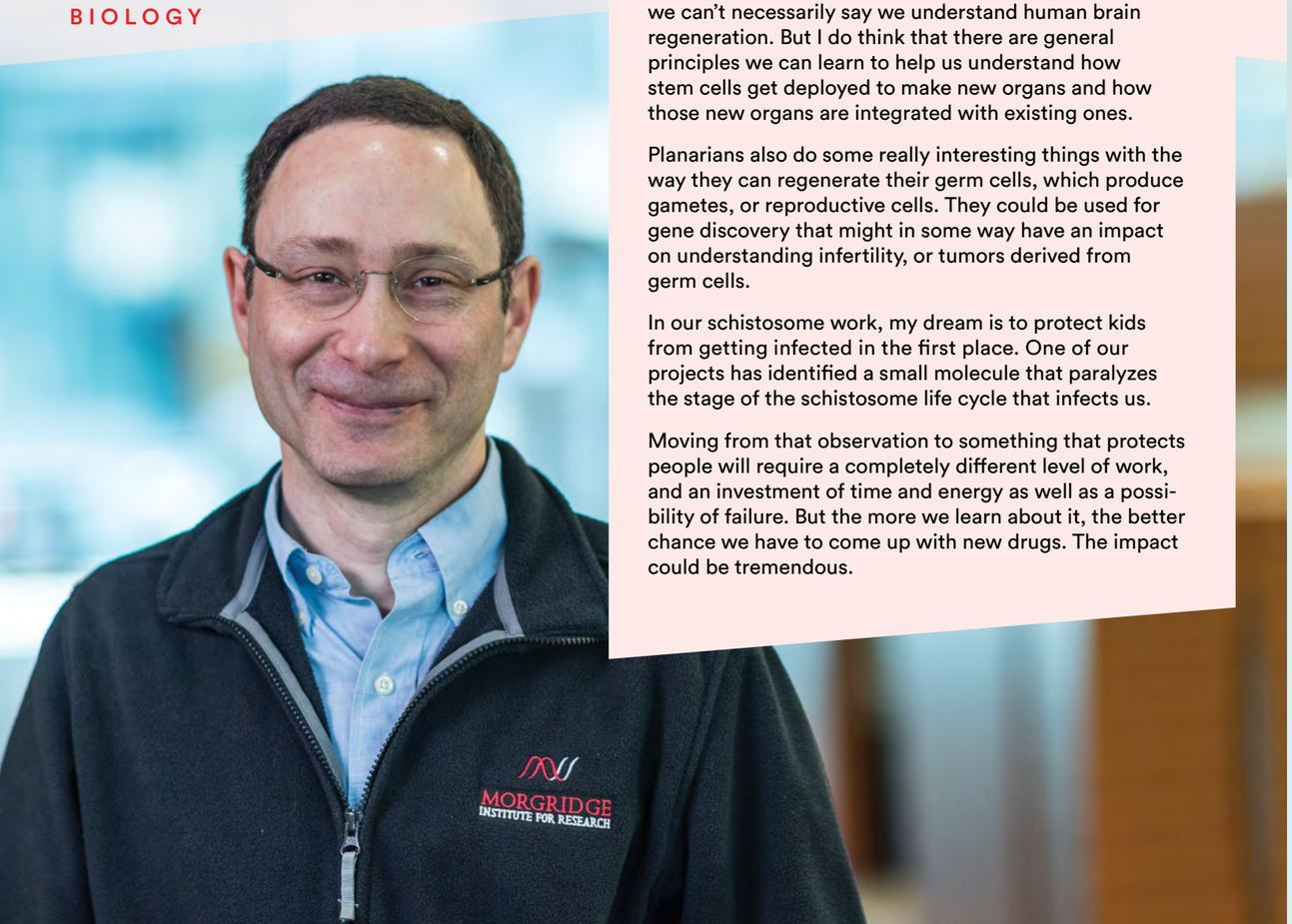
THE RULES OF INFINITE REGENERATION

—

PHIL
NEWMARK

BURNELL R. ROBERTS
CHAIR `

REGENERATIVE
BIOLOGY



In my lab we study flatworms, known as planarians, because their stem cells can regenerate entire new animals from tiny fragments of the body. We hope to understand how stem cells are regulated and why some animals can regenerate missing or damaged organs.

Insights from this research have also led us to study parasitic flatworms like schistosomes, which harm hundreds of millions of people in developing countries. As we learn more about how they infect people and reproduce inside them, we hope to devise new strategies to control these devastating parasites.

I first encountered planarians in freshman biology and was completely mesmerized. As a postdoc, I went to the University of Barcelona to study at the only lab in the world I was aware of that was actively trying to do molecular biology on these animals.

“I first encountered planarians in freshman biology and was completely mesmerized.”

If we understand how a planarian regenerates its brain, we can’t necessarily say we understand human brain regeneration. But I do think that there are general principles we can learn to help us understand how stem cells get deployed to make new organs and how those new organs are integrated with existing ones.

Planarians also do some really interesting things with the way they can regenerate their germ cells, which produce gametes, or reproductive cells. They could be used for gene discovery that might in some way have an impact on understanding infertility, or tumors derived from germ cells.

In our schistosome work, my dream is to protect kids from getting infected in the first place. One of our projects has identified a small molecule that paralyzes the stage of the schistosome life cycle that infects us.

Moving from that observation to something that protects people will require a completely different level of work, and an investment of time and energy as well as a possibility of failure. But the more we learn about it, the better chance we have to come up with new drugs. The impact could be tremendous.

THE MYSTERIES OF MITOCHONDRIA

—

DAVE
PAGLIARINI

DIRECTOR

METABOLISM

As happens in science, my path to metabolic and mitochondrial research came from an unexpected discovery. Not knowing what to do next in my thesis work, I decided to determine where the protein I was studying “lived” in the cell. The strange, bright green pattern I stared at was unrecognizable to me then, but is now unmistakable—mitochondria!

“Mitochondria dysfunction is a component of some 150 diseases.”

Mitochondrial biology has undergone transformations unforeseen by the scientist that unlocked the mysteries of “oxidative phosphorylation” decades ago. While it is certainly still true that the ten million billion mitochondria throughout our bodies (about 10 percent of our mass) produce nearly all of our cellular energy in the form of a molecule called ATP, the simplistic concept of these organelles as discrete, kidney bean-shaped energy factories has given way to that of a cell-specific, dynamic network that fuses, divides and directs a vast array of functions central to cellular life and death.

It has also become clear that mitochondrial dysfunction underlies more than 50 inborn errors of metabolism, strongly contributes to a growing list of disorders including type II diabetes, Parkinson’s and cancer, and is central to the aging process. Yet hundreds of mitochondrial genes remain mere database entries with no known function, and an even greater number of patients live with mitochondrial disorders with no available treatment, or no known cause.

Since that fateful moment at the microscope, I have become a bona fide “mitochondriac.” At Harvard Medical School, I led an interdisciplinary study aimed at answering an open question: What are mitochondria made of? Using powerful technology, high-powered computing and old-fashioned biochemistry, we identified hundreds of new mitochondrial proteins to reveal how these organelles differ in tissues throughout our bodies, and discover new mitochondrial proteins that are mutated in human disease.

The resource we developed, which we call the MitoCarta, is now the foundation for our work at Morgridge. My group is driven to understand the biochemical underpinnings of mitochondrial dysfunction in human diseases. If we can arrive at a clear, fundamental understanding of the obscure, disease-related processes that still elude our grasp, we have the potential to contribute to real cures.

NAVIGATING METABOLISM ROAD MAPS

—

JING FAN
DIRECTOR

METABOLISM

“I want to figure out what cancer cells use that is different from normal cells.”

I study the metabolism of cancer cells to understand why they grow fast and how we might be able to stop them.

Metabolism is basically a set of chemical reactions that takes nutrients and converts them into the different things cells need. I want to figure out what cancer cells use that is different from the normal cells. By knowing that, we could potentially target the specific pathways and starve cancer cells or inhibit their growth without hurting the normal cells.

If you think of the map of a city, the map is the genes, defined in your genome. Metabolic pathways are like the ways in which cities control roadways. What I’m really interested in is the traffic flow. Even if you have the same exact road structure, you can use it so differently. Sometimes the whole thing is boring. At other times, the city has a lot of factories running and you have an influx of material for the product you’re making.

Cancer cells differ from normal cells because they grow so much, and to double your cells you need to double all the contents. There’s also environmental factors that drives the cancer metabolism to be different. We are asking whether we can specifically inhibit how the cancer uses the nutrients.

I’m also collaborating with Melissa Skala, a medical engineer, to try to see the metabolism of immune cells through imagery. We are activating the immune cells, and we can take an image when the metabolism changes to see which pathway is making the cell light up.

Metabolism is a fundamental process that every cell in every organism is doing. Even though a lot of my research focuses on cancer cells and immune cells, understanding metabolism in specific systems will give us insights into general metabolic regulation. It is an underlying problem in many different health issues, like diabetes, or conditions of aging. That’s why I like metabolism so much.

“By unlocking the magic of self-renewal, I think within two years we’ll have a pretty cool working model of a human artery.”

My current research is focused on two core biological questions. We want to know how stem cells reproduce and how they organize themselves into a tissue or organ.

The ability of stem cells to reproduce, a process called self-renewal, is key to generating and regenerating tissues and organs. Through self-renewal, stem cells are able to produce enormous quantities of daughter cells, which are the raw materials used to make all the parts of our bodies. In particular, we are studying self-renewal in the cardiovascular system, because cardiovascular diseases are the number one killer worldwide.

Producing enormous quantities of cells through self-renewal is the first step toward making tissues or organs, but it’s not the only step. A second, equally important step involves organization. Simply throwing a bunch of cells together won’t turn them into a tissue. They have to come together at the right time and in an organized way.

It’s like making cookies. You first combine butter, sugar, flour, and eggs to form a dough, then you bake the dough, and then ta-da! Fresh warm cookies. But now suppose you do things out of order. You bake each of those raw ingredients separately and then combine them together. The result isn’t a cookie. It’s scrambled eggs with sugar on top.

In the same way, during development our cells come together at the right time as raw ingredients and then mature or “bake” into functional tissues and organs.

In our group, we’re trying to figure out the right time and method to put blood vessel cells together so that they form a functional vessel.

With a little luck, I think our studies of self-renewal and tissue organization will yield some pretty cool working models of human arteries within several years. We will use the models to answer questions about cardiovascular diseases, as well as discover and test novel therapies to treat those diseases.

Looking even further ahead, we hope to ultimately grow healthy arteries to replace ones that are diseased or clogged.

THE RIGHT ‘RECIPE’ FOR FUNCTIONAL TISSUES

—

DAVID VEREIDE
MORGRIDGE FELLOW

REGENERATIVE BIOLOGY

A NEW GAME TO UNDERMINE VIRUSES

—

PAUL AHLQUIST

DIRECTOR

VIROLOGY

We're trying to understand big-picture questions about how viruses work.

Viruses have a remarkable capacity to appropriate a cell's own functions, much like guerilla warfare, that keeps the virus thriving and changing in the body and transmitting to other people.

On the academic side, this knowledge will improve our understanding of evolution and biology. On the practical side, it will help us develop better ways – vaccines and medicines -- to prevent or disrupt the ability of viruses to hijack healthy cells.

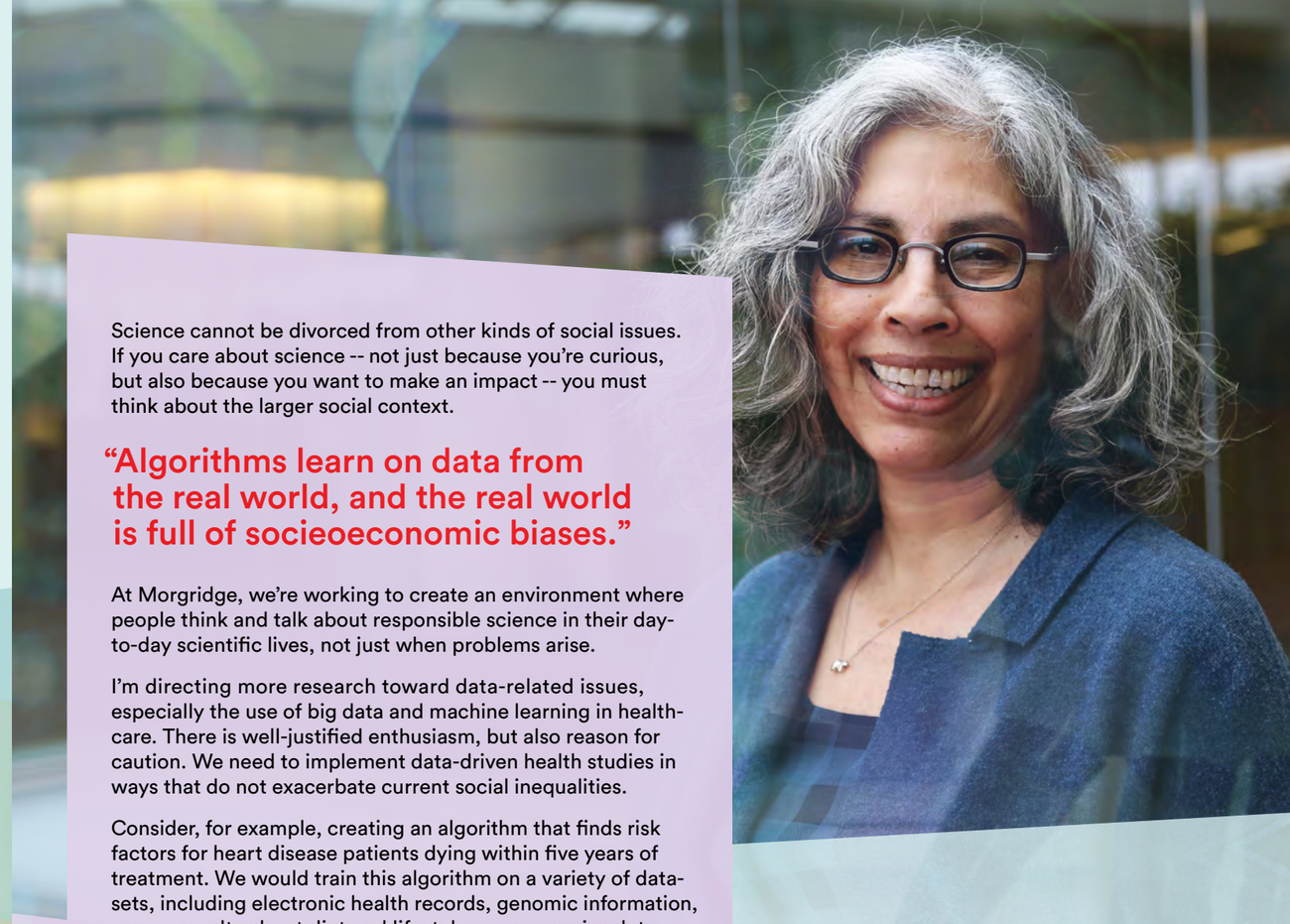
Our research includes viruses that can lead to cancer. Liver cancer is caused by hepatitis B or hepatitis C virus, and human papilloma virus causes essentially all cervical cancers in women. The beauty is that if you control the virus, through vaccines or antiviral drugs, you're going to eliminate these cancers.

This is an exciting time in virology. As sequencing technology gets more sensitive and powerful, it's become possible to sequence very small amounts of material. This has led to an explosion of new virus sequences that are greatly expanding our understanding of what's out there.

"We're proposing antiviral agents that have much broader effects against whole classes of viruses. We need a new game."

When you apply an over-the-counter antibiotic cream to your child's scraped knee, it works without having to know exactly what bacteria you're fighting. We don't have anything like that for viruses; our vaccines and drugs are virus-specific. We need a new game. We're proposing to come up with antiviral agents that instead have much broader effects against whole classes of viruses.

To do this, we are working to identify the genes in people that viruses exploit to carry out their infection and replication. We want to figure out how to modulate them in ways that deny the virus what it needs. When we find a gene that many viruses use, we should be able to develop a drug that inhibits a broad spectrum of viruses.



A CULTURE OF RESPONSIBLE SCIENCE

—

PILAR OSSORIO

BIOETHICS SCHOLAR IN RESIDENCE

Science cannot be divorced from other kinds of social issues. If you care about science -- not just because you're curious, but also because you want to make an impact -- you must think about the larger social context.

"Algorithms learn on data from the real world, and the real world is full of socieoeconomic biases."

At Morgridge, we're working to create an environment where people think and talk about responsible science in their day-to-day scientific lives, not just when problems arise.

I'm directing more research toward data-related issues, especially the use of big data and machine learning in healthcare. There is well-justified enthusiasm, but also reason for caution. We need to implement data-driven health studies in ways that do not exacerbate current social inequalities.

Consider, for example, creating an algorithm that finds risk factors for heart disease patients dying within five years of treatment. We would train this algorithm on a variety of datasets, including electronic health records, genomic information, survey results about diet and lifestyle, even exercise data from fitbits.

But problems may lurk in the information itself. These datasets are not precisely curated for big studies. The algorithms learn on data from the real world, and the real world incorporates all kinds of socioeconomic biases. They're essentially baked in.

Heart disease is a good example. We know from recent studies that women are diagnosed for heart disease much later than men. And they often don't get the same treatment recommendations, even when health conditions are similar. Unfortunately, the data reflects these biases. The algorithm learns something we don't want it to learn.

Under any measure of fairness used to analyze healthcare delivery, we cannot develop tools and treatments that result in much better healthcare for some groups over others. What can we do? We need to understand how generalizable big data studies are, and for whom they will be medically useful. We also need to build enough tools to help people from all demographics, so we create precision medicine that is relevant across race, gender and socioeconomic status.

This is just one example from this fresh and demanding field. I encounter and address all sorts of interesting issues, from the security implications of gene editing to privacy of genetic information. I have one of the greatest jobs in the world.

OUR
INVESTIGATORS

TOOLS OF DISCOVERY

MEDICAL ENGINEERING
FAB LAB

I like to work with my hands and build things and was drawn to optical engineering for that reason. I loved optics because I wanted to work with light, and I decided to build new instruments that use light to sense the body.

Now I am a biomedical engineer working on cancer, especially pancreatic cancer, one of the biggest killers. We take samples from tumors and test different chemotherapy combinations on them. I've developed imaging technology that is sensitive enough to quickly test and measure how the cancer cells are responding to treatment.

"I want to impact the quality of life and survival of cancer patients."

Collaboration is vital to this work. I don't treat patients. I don't prescribe them treatment. I work very closely with surgeons and oncologists to develop a technology that will be useful and also fit within the clinical workflow so it can be used with current clinical practices.

Biomedical engineers serve as a bridge between technology and clinical practice. It takes a lot of time and a lot of interactions to learn how to speak the language of clinicians when you're an engineer.

Right now, we're taking tissues from patients and seeing if we can predict how they will respond to treatment, but we're not yet informing the physicians how to treat patients. If it turns out the technology is effective, it will be used to help physicians decide what combinations of drugs to use on their patients in a personalized way.

Metabolism is important to our work. It's going to tell us not only whether the cells are responding, but maybe why and if they aren't, how they are circumventing the drug. We do this at the single-cell level, so we can understand the dynamics of cells and whether a subset might be driving resistance.

I want to impact the quality of life and survival of cancer patients. If I can make anything that improves treatment so patients receive less toxicity and live longer, that's a grand slam homerun for me.

TAILORING CANCER TREATMENTS TO THE INDIVIDUAL

—

MELISSA SKALA

PRINCIPAL INVESTIGATOR

MEDICAL ENGINEERING

I build smarter, cheaper microscopes because I want to help people use technology to see biology in ways they've never seen it before. It's important to me that the data I produce is appealing and revealing. Looking at something that is behaving, something that's alive, made me interested in working on concepts that go beyond what people have achieved so far.

During my PhD work we were looking for an instrument that would allow us to collect data from different sides of one sample and then combine this data. We came up with this idea of illuminating the sample from the side with a sheet of laser light.

Now we combine this light sheet microscopy with new techniques where you can make tissue samples more or less transparent and then image them at high resolution.

Our strength is that we always develop a microscope together with a biologist and demonstrate the performance of the instrument with a particular biological question. We are best known for imaging the developing beating heart in an intact zebrafish. The microscope enabled us to record multidimensional data sets that were impossible before.

Our microscopes are much more powerful than any commercial instrument, because we can customize them. That gives us the advantage that we, and our collaborators, can do experiments that nobody else can do because we address every single aspect in a modern biological experiment.

I want to open up the market so that biologists get their hands on cutting edge technology built in an engineering lab and don't have to wait for the commercialization to happen. Once we develop a new microscope that we can easily make, the idea is to build several and send them out to many labs, collect their feedback and improve the technology. It would change the microscopy landscape quite dramatically.

NATURAL-STATE MICROSCOPY

—

JAN HUISKEN

DIRECTOR

MEDICAL ENGINEERING

"I want to open up the market so that biologists can get their hands on cutting edge technology built in an engineering lab."

My interest is in collaborative science, where people play their different roles but come together to delineate a problem. Our main focus is on multi-scale imaging.

It's a great time to be in the imaging field. The last 40 years has largely been the age of genetics, when we figured out the parts list for most organisms. But it's like knowing the parts to your car without actually knowing what the car does. Imaging allows you to drive that car, and figure out what all the components do. I want to see how the components — particularly cells — function, both in normal and abnormal development, like cancer.

"We want to shatter the silos."

Cancer is a multi-scale disease. It starts off as a single cell phenomenon, becomes multi-cellular in terms of a tumor, but then can become single-cell again. The thing that kills you are cells that are metastasized and break off from the tumor. If we can see a cell become a tumor mass of many cells, and then track the cell movement, we might be able to stop or delay cancer progression.

We are too often stratified by scale. Scientists like myself who have spent most of their career in the sub-micron world, peering into parts of cells, can lose sight of the tumor when it becomes metastasizing in an organ and spreads.

Right now in biology there is also a spatial gap, as if there were a room in your house you couldn't see. We're blind in certain aspects of our ability to see cancers. We want to develop new methods that could offer views in between the sub-cellular world and the tissue organ level world. We are interested in building instruments that can cross spatial scales including combining imaging modes that not typically combined.

We want to shatter the silos so that researchers combine their expertise with other collaborators to study a biological phenomenon. And our dream is to have projects that are across scales, recognizing that the biology doesn't stop at a spatial scale.

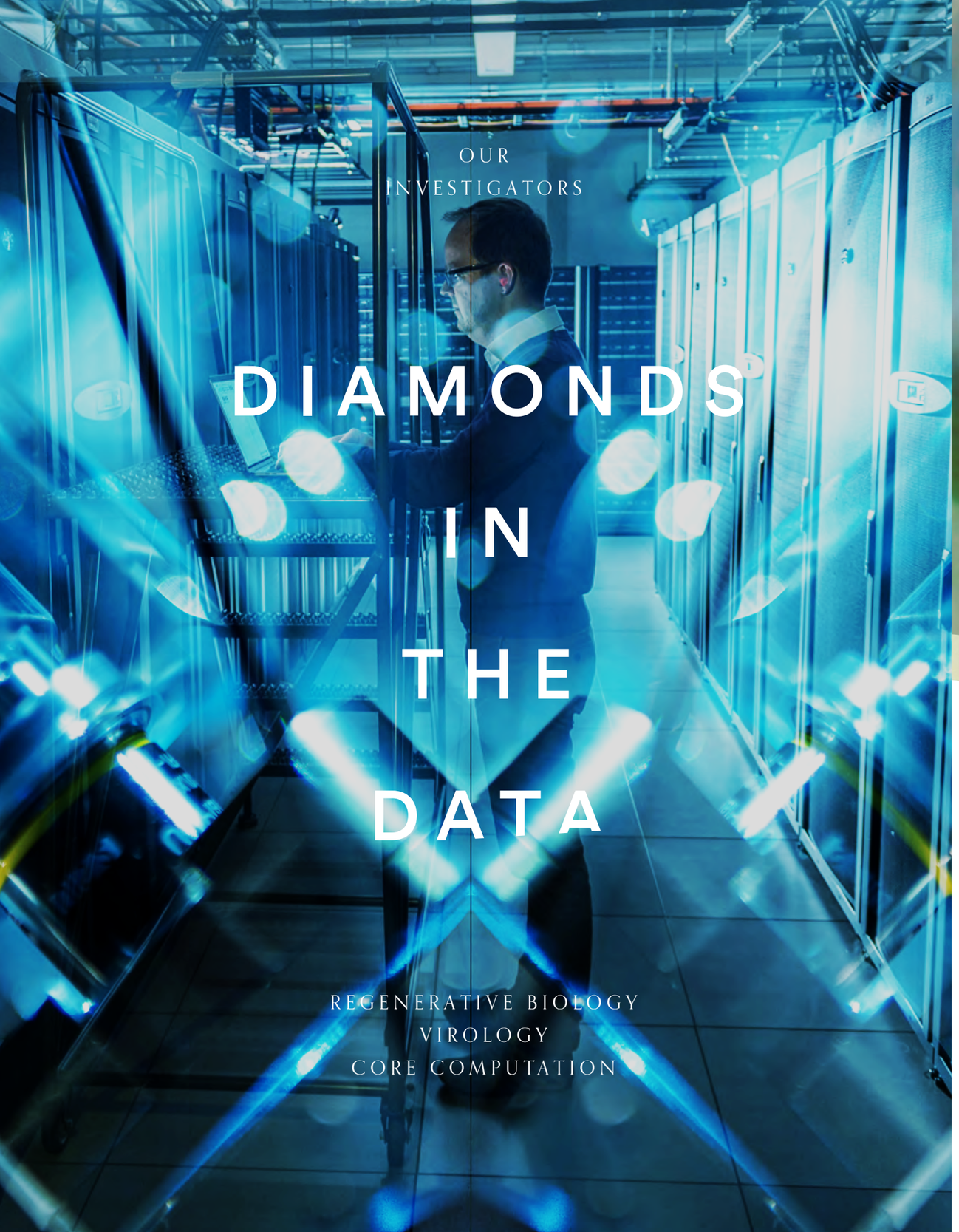
ELIMINATING IMAGING BLIND SPOTS

—

KEVIN ELICEIRI

DIRECTOR + INVESTIGATOR

FAB LAB + MEDICAL ENGINEERING



I use computational methods to help us make sense of very large biological datasets.

Today, biologists can generate billions of data points overnight. Our first goal is to help scientists understand the large datasets they create or download from the public domain. A second goal is to help them decide which future experiments are most likely to deliver results.

"My dream is to build tools that allow scientists to do their work faster and easier."

An example of the first goal is in processing and understanding high-throughput data from DNA sequencers. The data can represent many things, such as genes expressed in cells or tissues, or regions of the genome that regulate gene expression. We create new algorithms for processing and understanding the data so that we can partner with biologists to make discoveries to improve human health. We have used these methods to help Morgridge scientists investigate questions in regenerative and vascular biology and other collaborations on eye diseases, blood diseases and heart health.

An example of the second goal is an algorithm we developed called "KinderMiner." This simple yet powerful algorithm computationally "reads" all 30 million papers available in the PubMed dataset, and provides suggestions to scientists about which targets to explore in their next set of experiments.

Experiments are expensive, and it is impossible for scientists to investigate all potential targets. For instance, for cellular reprogramming, genes are turned on in a cell to reprogram it into another cell type that might be useful for therapy. But reprogramming usually requires a combination of genes, and combinatorial problems become difficult fast.

A typical reprogramming task might require performing about 2 million experiments to cover all the combinations. KinderMining can help prioritize the genes to only require about 200 experiments. This narrows the playing field, making infeasible experiments possible.

We are currently expanding KinderMiner using machine learning and other methods to consider context, synonyms and distinguishing a negative from a positive hit. We are also building a web application so anyone can use it.

We aim to build tools that allow biologists or anybody in related fields to do their work faster and easier.

MAKING SENSE OF LARGE DATASETS

—

RON STEWART

ASSOCIATE DIRECTOR OF BIOINFORMATICS

REGENERATIVE BIOLOGY

I use computers to help researchers save time and money as they study diseases or experiment on new drugs to fight them.

First, we need to understand what is happening inside a diseased cell. Cells have information processing channels and communication mechanisms that help them decide what to do when they are stimulated or threatened and need to react to survive. Modern techniques in genomics are used to measure what's going on inside cells. My group then builds computational models to make sense of and predict all this cellular activity, and we recommend which experiments to take forward in a lab.

"My group tries to build computational models to better understand and predict cellular activity."

In the short term, we want a much better understanding of certain aspects of human disease, such as how HIV-infected cells actively attack and transmit viral particles to uninfected cells. In the long term, my group will continue to improve our computational ideas so that we get more powerful, accurate models and gain confidence in what's really going on inside extremely complex diseased cells.

I'm also getting more interested in the therapeutic possibilities. If our cellular modeling works, it will suggest specific genes and proteins that are behaving abnormally and will give us candidate proteins to look at when creating drugs and other treatments.

My newest interest is in chemical modeling. Once we identify a new protein that's potentially relevant to a disease, we want to use computational techniques to guide a search for treatment options. A typical academic lab can afford to test tens of thousands of chemicals experimentally, but there are millions if not billions of chemicals to consider as potential drugs for this protein.

We're trying to use a new generation of Netflix-like computational techniques to make this search ultra-efficient. Netflix has a huge amount of information on what films, genres or actors people collectively like. There's a class of computational models that uses these preferences to suggest new things for any individual movie buff. With a similar recommender system, we hope to narrow in on a limited number of chemicals to screen and achieve the same results as a massive and costly chemical screen.

DECODING THE LANGUAGE OF DISEASED CELLS

—

TONY GITTER

INVESTIGATOR

VIROLOGY

"There are no limits to the kinds of problems we can tackle."

I specialize in distributed computing and work with researchers around the world to advance data-intensive science.

The problem I'm trying to solve with distributed computing is simple, but not completely solvable. I use the metaphor of being stuck in a seemingly endless line of customers at a local bank. What if someone whispers that there's a branch of the bank just a block away with no lines and idle tellers? Would you decide to run across the block, hoping you were the only one who heard the whisper? Or would you use some kind of rationale to stay put?

With distributed computing, where questions run in parallel across thousands of computers, making the right decisions to avoid the queue is essential.

Our major contribution is HTCondor, which first went online in 1985. It's a high-throughput computing network that harnesses thousands of computers across partner institutions to achieve computational power that dwarfs a supercomputer. HTCondor is providing the horsepower to do great research by removing the bottlenecks from big data.

With a big boost in infrastructure from the Morgridge Institute, we are enabling more science than ever, from every corner of the UW-Madison campus. In 2016, we provided facilitation support for 189 projects, which altogether logged 265 million computing hours.

Some of the largest research projects in history have benefited from HTCondor. The technology served as a backbone for the massive LIGO physics project, which set out to confirm the existence of million-year-old gravitational waves. They found their proof in 2016, confirming a century-old prediction by Albert Einstein. HTCondor helped process data being generated from 15 different countries, and more than 1,000 scientific team members.

We have used HTCondor to optimize Wisconsin corn varieties and to track invasive species in the Mississippi River. We've used it to study brain patterns in people who have been diagnosed as psychopaths. Boeing has used HTCondor for airplane materials research and Pixar uses it to optimize its animated films.

There are no limits to the kind of problems we can tackle.

BEYOND THE DATA BOTTLENECK

—

MIRON LIVNY

DIRECTOR

CORE COMPUTATIONAL TECHNOLOGY

INSPIRING THE NEXT GENERATION

—

Discovery Outreach sparks scientific curiosity in thousands of children, families and educators across Wisconsin. Cutting-edge, hands-on science programs and events introduce vibrant UW-Madison science to an eager public looking to expand their creativity and imagination.

750,000

Annual visitors to the Discovery Building

250,000

Annual participants in Discovery Outreach programs

400

Summer stem cell campers from 70 rural high schools

37,000

Average statewide participants in the annual Wisconsin Science Festival

600

UW-Madison contributors to outreach programs since inception

12

Unique science outreach programs for the public

LET'S DISCOVER TOMORROW'S CURES

"There's been a real push away from asking fundamental questions in science. And yet all of the breakthroughs that impact people ultimately come from asking questions about how the world works."

PHIL NEWMARK
BURNELL R. ROBERTS CHAIR IN REGENERATIVE BIOLOGY

IMPROVING HUMAN HEALTH STARTS WITH YOU.

Financial gifts help scientists exploring new frontiers in health and medicine.

We can match your passion to the areas of greatest promise in human health. Private gifts from individuals, families, and corporate and industry sponsors are one of the most critical ways to deepen our understanding of the natural world and improve human health.

TO LEARN MORE, VISIT:
MORGRIDGE.ORG/GIVE

WAYS YOU CAN MAKE A DIFFERENCE

01 –

IMPROVING HUMAN HEALTH

We believe that a deep understanding of biology will drive tomorrow's cures. With a discretionary gift to the Morgridge Institute, you help improve human health by igniting new scientific partnerships, retaining outstanding scientists, and supporting the next generation of research talent.

02 –

INSPIRING FUTURE SCIENTISTS

In a rural state like Wisconsin, many students have few opportunities to learn new, hands-on science or work with scientists on the job. But we believe any student, no matter their economic background, should have the opportunity to learn about science.

03 –

BECOMING A PARTNER

Science must be pursued fearlessly. That's why we depend a growing community of supporters in the Partners in Science society. With an annual gift of $1,000, our partners drive new science and participate in exclusive learning opportunities to see the impact of their support.

MORGRIDGE.ORG

THE FOUNDING VISION

The vision for the Morgridge Institute for Research began in 2005, when we sought to create an outstanding private biomedical research organization that could catalyze, amplify and enhance research at UW-Madison.

Private research institutes previously of this kind existed almost exclusively on the East and West Coasts. We envisioned the Morgridge Institute reinforcing the tremendous quality of research happening in the Midwest — particularly Wisconsin — and making our alma mater even more globally competitive. Our partnership with the university and the Wisconsin Alumni Research Foundation (WARF) made this vision a reality.

The institute is now a tremendously exciting place focused on some of the great biomedical challenges of our time, including life-threatening viruses, vascular disease and metabolic disorders. The Morgridge Institute also has cultivated a unique science outreach platform where experts engage curious minds to help enhance the public's understanding of science.

Our institute's personality is reflected in the phrase "fearless science." We recognize that science cannot thrive by asking safe questions, and some risk-taking is needed to truly make progress. We are emboldened by high bioethical standards that enable us to address difficult biomedical

challenges. And we are empowered to take the long view of research, which may yield unexpected rewards to human health.

Support for fundamental biomedical research may be more important today than at any point in our generation. We are in an era where curiosity-driven, basic science receives less mainstream support, in favor of safer questions that promise more predictable results in a shorter time frame.

But basic research is where transformational discoveries happen — and our public-private model here in Wisconsin is helping basic research thrive.

JOHN & TASHIA MORGRIDGE

MORGRIDGE INSTITUTE CO-FOUNDERS AND MEMBERS
BOARD OF TRUSTEES

BOARD OF TRUSTEES

Fred Robertson, MBA, M.D. - Board Chair
Venture Partner with Baird Capital
Clinical Assistant Professor, School of Medicine and Public Health, University of Wisconsin
Retired CEO, Director, TomoTherapy

James Berbee, M.S., MBA, M.D.
Clinical Assistant Professor, Department of Emergency Medicine, University of Wisconsin
Founder, Berbee Information Networks Corporation

Mary Burke, MBA
CEO and Founder, Building Brave

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

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

James Dahlberg, Ph.D.
Former Interim Chief Executive Officer, Morgridge Institute for Research
Professor Emeritus, Department of Biomolecular Chemistry, University of Wisconsin
Founder, Third Wave Technologies

Carl E. Gulbrandsen, Ph.D., J.D.
Former Managing Director, Wisconsin Alumni Research Foundation

Erik Iverson, JD, LLM
Managing Director, Wisconsin Alumni Research Foundation

Thomas M. Krummel, M.D.
Emile Holman Professor and Chair Emeritus, Department of Surgery
Co-Director, Stanford Byers Center for Biodesign

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

Terri L. Potter, MHA
Retired Chief Executive Officer, Meriter Health Services
President, Potter Consulting

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

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

Brad Schwartz, M.D.
Chief Executive Officer, Morgridge Institute for Research
Professor, Departments of Medicine and Biomolecular Chemistry, University of Wisconsin

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

SCIENTIFIC ADVISORY BOARD

Teresa Compton, Ph.D.
Biopharma Executive and Academic Advisor

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

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

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

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

William L. Murphy, Ph.D.
Harvey D. Spangler Professor, Biomedical Engineering and Orthopedics
Co-Director, Stem Cell and Regenerative Medicine Center, University of Wisconsin