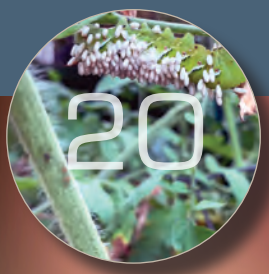
BRINGING A MISSION TO LIFE

THE STOWERS MISSION CONTINUES TO INSPIRE EMPLOYEES AND SHAPE GROWTH

STOWERS REPORT

NEWS AND INSIGHT FROM THE STOWERS INSTITUTE FOR MEDICAL RESEARCH

2021



STOWERS REPORT

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In perspective

BY ALEJANDRO SÁNCHEZ ALVARADO, PHD
EXECUTIVE DIRECTOR AND
CHIEF SCIENTIFIC OFFICER

As we enter the third decade of the Stowers Institute, I am honored and delighted to share my first letter to readers of the *Stowers Report*. Since taking the role of Executive Director and Chief Scientific Officer one year ago, I have spent many fruitful hours deeply contemplating and reflecting on the vision of Jim and Virginia Stowers, our mission to bring that vision to reality, and the Institute's first two decades of accomplishments.

Jim and Virginia articulated several key factors aimed at realizing their dreams for the Institute. They deliberately recognized the importance of the Institute's ability to attract the very best scientists, individuals who are adventurous and visionary with bold ideas and boundless creativity. They also envisioned a collegial environment where members are fundamentally motivated by the success of the Institute overall.

Since our research facility opened its doors in the fall of 2000, Stowers scientists have made discoveries that are transforming our understanding of human health and disease. Our researchers interrogate the most fundamental functions of living organisms. Jim and Virginia thought the most powerful contribution they could make to society was to enable the acquisition of this type of new knowledge, essential in the quest to generate understanding in order to improve human health and quality of life. I invite you to read this issue's cover story to learn more about our founders and how Stowers members are living the mission every day at our Institute.

As we begin 2022, after nearly two years of formidable challenges and uncertainties in our personal lives, our workplace, and all around the world, I'm reminded of the motivation and dedication of Stowers members who joined together to confront and overcome unimagined obstacles. A feature story in this issue describes the impact of the COVID-19 pandemic on the Institute and the many ways Stowers members rose to confront and surmount this challenge.

To start the new year, I wish to share the exciting news that The Graduate School of the Stowers Institute has received accreditation by the Higher Learning Commission, a recognition that our Graduate School has met national standards for quality and integrity in its programs. The path to accreditation has been an ongoing process since the Graduate School was established in 2011. We congratulate everyone associated with the Graduate School, past and present, on reaching this highly significant milestone.

I deeply appreciate your support for the Stowers Institute. When describing their vision, Jim and Virginia expressed their intent for everyone associated with the Institute to truly feel part of this great endeavor and to share their "hope for life"—hope for a better life for all of humanity. Together, let us champion audacious thinking, renew and intensify the cultivation of curiosity-driven research, engage in the vigorous debate of ideas, and share with each other and the world the impact of the scientific vision for the Institute. SI

BRINGING A MISSION TO LIFE

By Bonny Moseley

At the Stowers Institute, the mission set forth by founders Jim and Virginia Stowers continues to inspire employees and shape growth.

The story of the Stowers Institute's beginning may seem straightforward: Jim Stowers Jr. was going to be a doctor but changed course and started the company that became American Century Investments. After years of financial success, he and his wife Virginia used their vast wealth to found the Stowers Institute for Medical Research.

Dig a little deeper, though, and one discovers that our founding is rooted in generosity and a strong desire to make a difference to humanity.

In the 1990s, as Jim and Virginia Stowers sought to create the best biomedical research facility in the country, they encountered doubters and naysayers left and right. That didn't matter, though, not to Jim. He had full confidence in his dream and believed one could do whatever they set their mind to if they just had the determination and the drive.

We wanted to give back something more valuable than money to the millions of people who made our success possible, and we thought giving them a better life through science would be the best way to do that.

– Jim Stowers Jr.

Their determination was born in part from their own health issues. Jim had a bout with prostate cancer, which was found early and treated successfully. Several years later, Virginia had surgery after a breast cancer diagnosis. Facing cancer led them both to realize that they wanted to help others, and they had the assets to make a real difference. For Virginia, it was simple.

"When I found out I had cancer, I was very angry, I was very fearful, and I was very sad," Virginia shared in a 2000 interview. "I didn't want anyone else to go through that."

Making the dream a reality

Their initial vision—cancer research—soon broadened to foundational biomedical research to figure out the underlying mechanisms of health and disease, and the mission of the Stowers Institute was formed, carefully and thoughtfully written by Jim and Virginia: "Make a significant contribution to humanity through medical research by expanding our understanding of the secrets of life and by improving life's quality through innovative approaches to the causes, treatment, and prevention of diseases."

The first step was to build the best research institute in the world. They wanted to free scientists to follow their creative ideas and perform groundbreaking research and set up a model where labs received generous financial and technical support. It meant investing their fortune of nearly $2 billion, but it was well worth it to the Stowerses.

"We wanted to give back something more valuable than money to the millions of people who made our success possible, and we thought giving them a better life through science would be the best way to do that," said Jim in 2000.

Virginia had confidence in Jim's dream, and equally important, she had confidence in Jim. Just as he had made American Century a success, he would do the same with the Institute, but this time, they would do it together.

"When we decided to do something with science, I said I really want to be involved in this," Virginia said in an interview shortly after the Institute opened, and she was from day one.

Virginia's impact

In the beginning, her work revolved around planning the design of the Institute but in later years, she would often attend Institute events, celebrations, poster sessions, and more. Graduation ceremonies for the Graduate School were a particular highlight, marked on her calendar sometimes two years in advance. Virginia was a common sight at the Institute until her passing earlier this year, but "her imprint is on the Institute everywhere one looks," says Chair of the Board of Directors Richard Brown.

Jim and Virginia wanted the building to be impressive from the start, to offset any doubts top scientists might have about joining an upstart facility in Kansas City, away from the already-established research communities on the coasts. Virginia knew the environment was key, that it needed to be a place where people would want to come to work.

"When people walk in, whether it's their first time or their hundredth, they feel proud of being here, they feel invited into this facility that's state-of-the-art,"

says Judy Zimmerman, head of Research Services. "Not only are we doing fantastic science and research and fulfilling that piece of the mission, but we're doing it in an environment that is beautiful and warm and inviting and allows our members to be proud."

Virginia weighed in on layout and materials, selecting wood for paneling and furniture, fabric for chairs, and limestone and slate for flooring. She knew scientists needed good light, leading to the Institute's emphasis on open spaces and windows, allowing outdoor elements to shine through. The expansive ten-acre campus was filled with flowers, fountains, and walking trails. An art collection was cultivated so the scientists could enhance their workspaces with pieces that spoke to them.

If you build it, they will come

All of these elements came together to create what many visitors have called one of the most beautiful scientific laboratory campuses in the world.

Investigator Scott Hawley, PhD, filled one of those new labs in 2001. Many things appealed to him—Jim and Virginia's sense of family, their insistence that researchers be allowed to focus on what they do best—but he also appreciated the Institute itself and the lack of impersonal sterility common at so many other institutions.

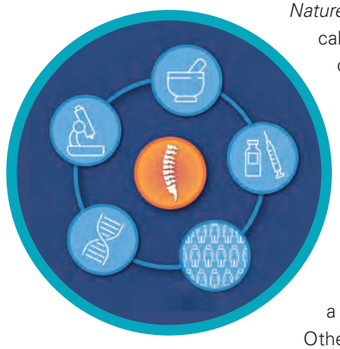
"Here, the beauty is everywhere and carries into each space," including the labs, says Hawley. "Creativity in thought really thrives under conditions of high aesthetic and beauty."

Within a few short years, those beautiful buildings housed top-notch, brilliant investigators, the most cutting-edge technology available, and expert support scientists to help the labs work quickly and efficiently. There was a synergy about the place, says Scientific Director Emeritus Robb Krumlauf, PhD, where growth snowballed as the creative, excited scientists at Stowers then recruited other excellent scientists.

Indeed, over the last twenty years, Stowers has been home to four National Academy of Sciences members, seven fellows of the American Academy of Arts and Sciences, and three Howard Hughes Medical Institute investigators. Researchers have been recognized with significant grants and awards, from prestigious National Institutes of Health and Pew grants to an American Cancer Society Professorship, as well as Searle Scholar and Basil O'Connor Scholar awards.

Institute makes an impact

All those achievements underscore the essential element of the Institute: the science. In 2003, Investigator Linheng Li, PhD, published a significant work in *Nature*, describing a part of stem cells called the niche. It was just one of the many groundbreaking publications and important discoveries to come out of the Stowers Institute.



In the years since, many more discoveries have been made. One such discovery, from the Krumlauf Lab, contributed to the creation of a new drug for osteoporosis. Other research is furthering our understanding of diabetes, congenital birth defects, infertility, Alzheimer's disease, blood cancers, and much more.

"The knowledge our Institute has generated during its first two decades has not only proven Jim and Virginia's detractors wrong but has also become a shining example of what living our mission means day in and out," says Executive Director and Chief Scientific Officer Alejandro Sánchez Alvarado, PhD.

Virginia once said, "I think I'd like to be remembered as having done something for humanity," and to Sánchez Alvarado, there is no doubt that both she and Jim will be remembered for just that.

"Jim and Virginia's vision and generosity have made a difference to the thousands of scientists around the globe who have cited the work of our scientists in their own work; to the hundreds of scientists we have trained and the hundreds they in turn are training," he says. "And that difference is both known and unknown, as the generation of knowledge always creates ripples in the fabric of history that are difficult to fathom but always help humankind better understand itself and the world around us."

Training future generations of scientists was vital to Jim and Virginia, which is why the creation of the Graduate School in 2012 could be considered one of the Institute's biggest milestones. Hawley, its founding dean, fondly remembers how much Virginia loved talking with the predoctoral researchers. Her passing this year has only strengthened his passion for teaching. For Hawley and other Grad School leaders, their work in the Grad School is a fundamental way they help fulfill the Stowers' vision.

> The knowledge our Institute has generated during its first two decades has not only proven Jim and Virginia's detractors wrong but has also become a shining example of what living our mission means day in and day out.
>
> *– Alejandro Sánchez Alvarado, PhD*

"I feel it is my job to do the best science possible and contribute to the mission of science outside my lab. I get to do both of those things as part of the Grad School," says Associate Investigator and Vice Dean Sarah Zanders, PhD. "It is also satisfying to know that Stowers trainees use skills they gained here to do great science when they leave."

More than science

The mission of the Stowers Institute is rooted in science but encompasses much more, such as maintaining balance. For Hawley it is about balancing priorities in both work and personal life. "Jim and Virginia recognized that we all had lives and it was important to them that we be able to fully live those lives," he says. Hawley aims to create that same level of support in his lab.

Executive Vice President of Administration George Satterlee does the same on a bigger scale, creating an environment of support, inclusion, and equity for the Institute through the efforts of his team. Satterlee worked closely with Virginia and believes that to create great science, you must create great scientists.

"Virginia had such a beautiful humility about her, and such tremendous wisdom about what it is to be human," says Satterlee. "Our goal is to create an environment that understands all those challenges that come with what it is to be human."

To that end, in the last several years the Institute has increased its training opportunities, established a program to provide seminars and support for all facets of home and work life, and created an executive role to strengthen diversity and inclusion.

"When you lose a founder, and now we've lost both, it's a good time to reroot ourselves in the values and mission that those founders espoused, and recommit ourselves to the vision they had," says Satterlee.

Zimmerman does that by making decisions with the knowledge that she is working with endowment funds and a desire to be a good steward of that gift. In balancing Virginia's original vision with changing needs, decisions like repurposing an original piece of furniture are rewarding for Zimmerman, as they preserve the history and move it into the future, allowing the Institute to keep manifestations of the decisions made by Virginia.

For Zanders, that means being a good steward of the endowment. "I am always acutely aware that the Stowers money spent in my lab is not mine," Zanders says. "It shapes the decisions we make in the lab each day and

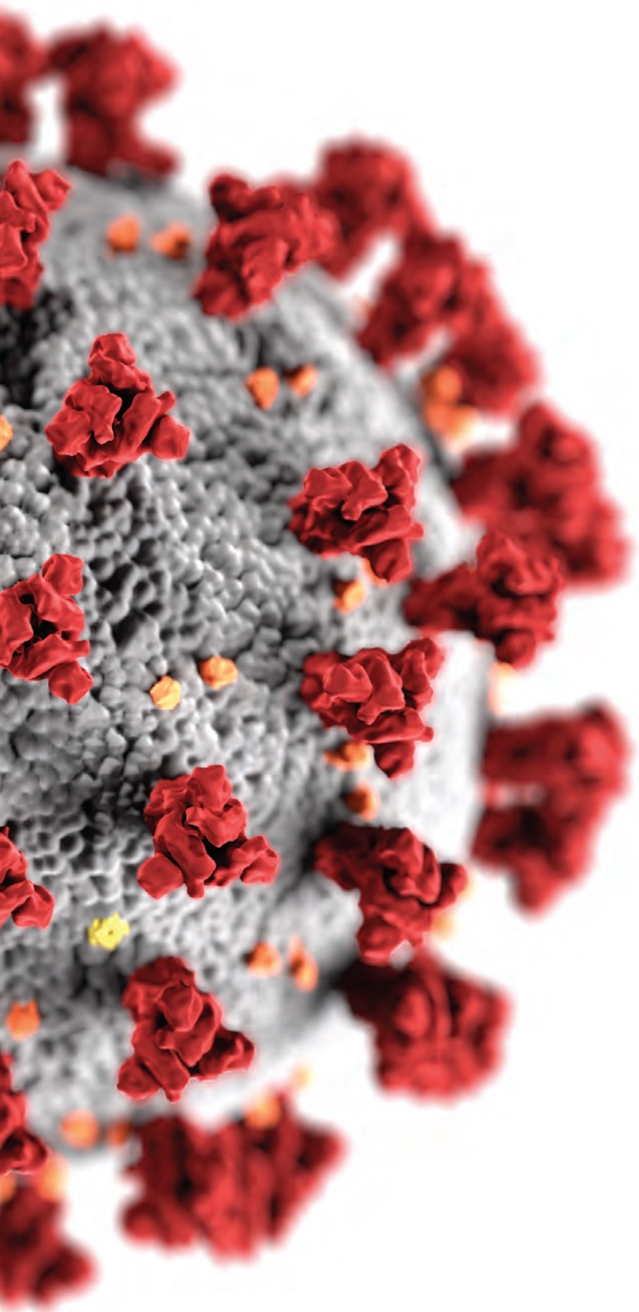
helps me manage the money in a way that maximizes our contribution to science. We ask if 'the juice is worth the squeeze' for each experiment."

Stowerses' gifts resonate with community

The impacts of Jim and Virginia's actions are vast and far-reaching. Kansas City has benefited from the creation of three successful enterprises, American Century Investments, the Stowers Institute, and BioMed Valley Discoveries, a clinical stage biotechnology company established to translate basic research findings into potential treatments. Students have benefited from the educational programs offered by the Graduate School. Employees from all over the world have enriched the nearby communities. But for some, like Susan Weigel, the impact is personal. Weigel joined the Institute early on and has witnessed the tremendous growth from fewer than thirty employees to more than 500.

"What an impact they've had on everyone who's worked here, to help us support our families. What a gift that has been," says Weigel, associate dean for administration and registrar of the Graduate School. "They've given a gift to humanity with the research that's being done, but everyone here has been given a gift, too."

Jim passed away in 2014, Virginia in 2021. The losses are felt personally by so many, but the science has continued without pause. Twenty years after its founding, the mission of the Stowers Institute remains unchanged, with memories of its founders continuing to resonate.



Using science to keep Stowers safe—and keep science going

On March 7, 2020, Stowers Investigator Jennifer Gerton, PhD, took her family to see a major league soccer game at Children's Mercy Field. The air was electric, but as Gerton scanned the full-capacity crowd—18,467 smiling faces—she felt a growing sense of apprehension.

Every day, she had been following the numbers as more people in the US and around the world were infected with SARS-CoV-2. That day 118 new cases of COVID-19 had been reported in the US, bringing the total number of cases stateside to 400. As part of the then newly commissioned Stowers COVID-19 Task Force, Gerton was immersed in discussions about the Institute's response to the unfolding crisis. That night, though, she was trying to cling to some remaining sense of normalcy.

"I remember telling my family to look around, to enjoy the game because it is going to be your last one for a long time," says Gerton. "They called me crazy and said you're just thinking about it too much." It didn't take long for her to be proven right. The COVID-19 pandemic has affected everyone, forcing people to adapt in ways they never envisioned. At the Stowers Institute, a combination of foresight, ingenuity, and determination averted some of its most distressing impacts. For example, not a single outbreak of COVID-19 occurred on campus. There were zero losses of research organisms due to the pandemic. And scientists were safely back at the bench months earlier than their peers. As we head into the end of another calendar year of the pandemic, members across the Institute are looking back at how they managed the worst public health crisis in a century, and what lessons they will take into the future.

By Marla Broadfoot

PUTTING A PLAN IN PLACE

In January 2020, the Institute's chief operating officer, Brent Kreider, PhD, noticed reports of a mysterious coronavirus-related pneumonia in Wuhan, China. At the time, his office was next to the office of David Chao, PhD, then president and CEO of the Institute. Their conversations centered on one topic as they watched SARS-CoV-2 spread throughout Asia and Europe and arrive in the US. In February, after the US declared a public health emergency, Kreider and Chao prepared for the worst—largely shutting down Stowers.

"We thought, how could we pull this off?" recalls Kreider. "There is so much interconnectivity across the Institute. Every single lab works with multiple technology centers every single day; if those shut down, the labs shut down, and the science shuts down. And we have thousands of research organisms on-site; we can't just shut them down."

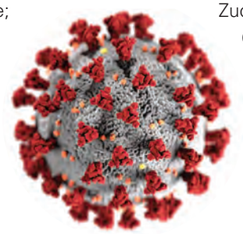
Together they created a COVID-19 Task Force made up of administrative and operational members and scientists to advise them on how to shift operations and keep the Institute and its people safe. They set up a variety of different conditions for members and for research, such as "research with mitigation measures" and "research with limited people on-site." They warned scientists to shorten the length of their experiments so they could end them with only a few days' notice. And they grouped the lab technicians into pods to limit any potential COVID-19 transmission and reduce the number of people who might have to isolate or quarantine.

When Kansas City's stay-at-home order was issued on March 21, 2020, the Task Force had established a detailed plan for an orderly shutdown just the week before. Almost everyone was sent home to work remotely, except for a skeleton crew. "It was ironic because one of my staff called the next day and said, how did you guys know we would need to shut down, and when?" says Kreider. "We really had no idea what day we'd need to transition to remote work—but had been planning for it all first quarter 2020."

With the Institute in a reduced operating mode, unrest within the financial markets, and COVID-19 uncertainty all around us, the Institute also created the Strategic Management Committee. Composed of members representing all functions across the Institute, this group met—and continues to meet—daily to discuss both internal and external developments that could impact the Institute or its members.

DEVELOPING A TEST

Many Institute leaders believed any hopes of returning to campus safely hinged on widespread SARS-CoV-2 testing to quickly identify positive cases and prevent larger outbreaks. But the Centers for Disease Control (CDC) had created testing kits that were contaminated. Many labs across the country began devising their own, homegrown coronavirus tests, and Gerton and other members of the COVID-19 Task Force suggested that the Institute do the same. On April 1, 2020, Gerton, Kreider, and Chao met via Zoom with one of Gerton's longtime collaborators who had set up a viral testing program at the Chan Zuckerberg Biohub in California. Even though Gerton had studied virology as an undergrad and has a PhD in microbiology, she had a lot to learn about diagnostic testing, new technologies, and FDA guidelines. "It was a landslide of work from that point on—I was living and breathing and sleeping this stuff," she says.



To get Emergency Use Authorization (EUA) from the FDA, the team had to run their test on paired sets of saliva and nasal swabs, thirty positive for SARS-CoV-2 and thirty negative. Gerton says it was easy to find negative clinical samples but collecting positive ones "proved to be a bridge too far." The team was ten samples away when the FDA announced they were no longer granting EUAs for viral testing. In the end, the scientists gave all their data and protocols to MRIGlobal, a neighboring translational and scientific research organization and a certified clinical testing laboratory, to run the viral testing program. But because the Institute's team had designed the test to be fully automated, they also had to pass along their giant sample-testing robot.

After MRIGlobal looked at the specs for the robot, they told Gerton it wouldn't fit in the elevator. "I thought, we're dead in the water because you could not for love or money order any of the automation equipment needed to run the test." She asked about the size of the windows, envisioning a pulley system like one used to hoist a piano into a walk-up apartment. There were no windows in the lab. The team had already packed the robot onto the truck, and Gerton didn't have the heart to tell them to bring it back in. So, she let them drive off. And somehow it fit.

DATA DRIVEN

When MRIGlobal ran the new test, they showed it could detect as few as six copies of SARS-CoV-2 per milliliter of saliva—on par with the best tests available on the market. Stowers Institute Co-Director of Microscopy, Imaging, and Big Data Jay Unruh, PhD, who had helped manage many of the logistical challenges associated with the task, estimated that the Institute could prevent an internal outbreak if they identified 90% of positive cases and tested twice a week. The Institute's test sensitivity ended up being 98%, allowing them to test just once a week. But Unruh and others were not completely satisfied. In addition to identifying people with an active viral infection, they were also interested in investigating who had COVID-19 in the past and now had antibodies against the virus.

Former Investigators Joan and Ron Conaway's lab and the Institute's Cytometry Facility had already purified a large amount of synthetic spike protein, which adorns the surface of the coronavirus like a crown. The Stowers Institute Screening Facility and the Conaway Lab then developed a test that could detect antibodies to the spike, indicating a previous infection. Eventually, they had a test they could use to track antibody levels in 200 members and family members. "The results were crystal clear: anyone with strong COVID-19 antibodies had a positive viral test," says Unruh. When they did antibody testing on over 100 volunteers who had not had a positive viral test, not a single one had a strong antibody signal. "We knew then that our population was still naïve, or largely unexposed." At the time, only the small handful of people who had tested positive for the virus actually had antibodies.

Later, after members had been vaccinated against SARS-CoV-2, the researchers started used the antibody test to monitor how well the vaccines were working. Their preliminary results indicated that all three vaccines—those from Moderna, Pfizer, and Johnson & Johnson—elicited a clear antibody response. "But the biggest surprise was how low the J&J antibody response was," says Unruh. That response, on average, was less than the other vaccines and that of people who had not been vaccinated at all but had recovered from COVID-19. Unruh and the team plan to submit their results for publication later this year.

There is so much interconnectivity across the Institute. Every single lab works with multiple technology centers every single day; if those shut down, the labs shut down, and the science shuts down. And we have thousands of research organisms on-site; we can't just shut them down.

– Brent Kreider, PhD

KEEPING COUNT

22,464
COVID-19 saliva tests administered

603
COVID-19 vaccines administered at the Institute

263
Antibody study participants

1,465
Blood samples provided by members enrolled in antibody study

95
Members assisted with Institute COVID response

INTO THE FIRE

Laura Remy had just finished her PhD in nursing from the University of Missouri-Columbia in the spring of 2020 when she heard that Stowers was looking for a nurse with infectious disease experience to help guide its infection control policy. Remy, who had worked on infectious disease prevention campaigns in Africa, China, and India, interviewed and was hired on the spot. "Once I learned that Virginia Stowers had been a nurse, but that the Institute had never hired a nurse, I was in," she recalls.

Shortly after joining Stowers, Remy was given less than 48 hours to set up drive-through testing so that Institute scientists and other members could return. "It didn't seem doable, but we pulled it off," she says. "We managed to test 500 people a week with very little waiting time." Remy facilitated more than 22,277 viral tests and more than 1,094 antibody tests overall. While the testing program had been an administrative success, it also took an emotional toll when she had to tell members they had COVID-19. "It's never gotten easier," she says. Like others in the health care profession, Remy found herself fielding not just concerns about health but also frustrations over policies related to testing, mask mandates, and vaccines.

At one point, Remy hosted an Institute-wide webinar on compassion fatigue, encouraging people to care for each other and take care of themselves. When not wearing scrubs, Remy was often seen in a T-shirt emblazoned with *Be Kind* or *We're all in this together.*

CARING FOR COLLEAGUES

"Even before the pandemic, mental health was a huge priority for the Institute," says Jennifer Herbers, human resources manager at the Institute. "When we sent everyone home except for operationally essential personnel, we started recognizing that it was truly isolating. We were putting the testing in place to protect our members' physical safety, so what could we do to support physical and mental wellness to combat the isolation?"

The Institute already had two popular wellness initiatives, InBalance and Stowers Connection, and could shift the programming to a virtual format. Through InBalance, the Institute created a two-part webinar with a parenting expert to help members working from home with children. Through Stowers Connection, the wellness team held a webinar on mindfully managing stress. They also offered several Mental Health First Aid courses, which taught members how to help coworkers struggling with a mental health issue. Other programs tackled different aspects of wellness. A work-from-home session covered the basics of ergonomics and technology. The fitness center offered virtual exercise classes and yoga recordings. And a new segment called Kitchen-to-Kitchen live-streamed café chefs as they made nutritious meals while Stowers members followed along at home. "What we've learned throughout this time is that mental health, and overall well-being, is so important," says Herbers. "I think there's a lot to learn, and even more we can do to support our members once we get back to whatever that new normal looks like."

REDEFINING NORMAL

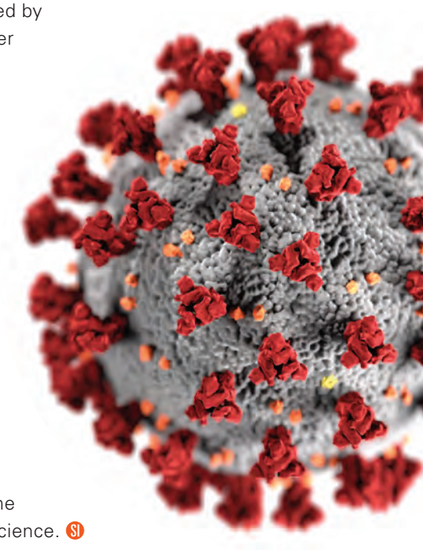
Recognizing that many are still grappling with a world changed by COVID-19, the Graduate School of the Stowers Institute has worked over the last year to expand its mental health offerings. "Graduate students in general have higher levels of anxiety, and that only gets worse in the context of the pandemic," says Jinelle Wint, PhD, the assistant dean of academic affairs. Through various mental health partnerships, the Graduate School and the Institute offer counseling resources to those who need them. But Wint wanted to do more, so she facilitated efforts to provide in-person therapy to the Institute's predoctoral researchers through the Counseling Center at the University of Missouri-Kansas City and provided connections to other mental health resources in the community.

As the Institute headed into the fall, all were eager to make up for lost time. In conversations with other research institutes, Kreider has realized that the Institute, in many ways, fared much better than its peers. "In many ways we feel we were way ahead," he notes. "We had all our services up and running when researchers elsewhere weren't even allowed back on their campuses."

"Since the beginning of the pandemic, we have closely followed CDC and local governmental guidelines to inform our decisions," says Alejandro Sánchez Alvarado, PhD, executive director and chief scientific officer of the Institute. "As the pandemic has shifted with the multiple variants, we do our very best to provide our members with a safe environment in which to do our very important work."

Gerton and others on the COVID-19 Task Force—which still meets—are focused on keeping the science going, even amidst the emergence of new coronavirus variants like Delta. That means employing evidence-based policies, such as maintaining widespread COVID-19 testing, embracing a hybrid model to reduce the number of people on campus, putting masking in place when community transmission is high, and perhaps the biggest one of all: vaccines.

Despite the difficulties presented by the pandemic, there is a silver lining—scientists around the world were inspired by the pandemic to work together in unprecedented ways. At one count over ninety-three Institute members assisted with testing efforts. The Institute pivoted from its typical activities to create two high-quality and high-throughput COVID-19 tests that helped both the Institute and the community respond to the virus. The very fact that three safe and effective vaccines are widely available in our community a year and a half after the start of the pandemic is a testament to the resilience and innovation of science.



A CONVERSATION WITH AMERICAN CENTURY INVESTMENTS' JONATHAN THOMAS

By Bonny Moseley

The Stowers Institute and American Century Investments were both created from the vision of one man, James E. Stowers Jr., and the two organizations continue to work toward a shared mission. Put simply, that mission is to help people, says American Century President and CEO Jonathan Thomas.

Jim Stowers founded American Century to help people become financially independent, while Jim and Virginia Stowers created the Stowers Institute to drive breakthrough biomedical research for treatments and cures of devastating diseases. The Institute is the controlling owner of American Century, which means that more than 40% of American Century's profits are directed to the Institute. The Institute is also often named the official charity for the American Century Championship, an annual celebrity golf tournament that has raised millions of dollars for charity.

Jonathan joined American Century in 2005 as chief financial officer and executive vice president, and in 2007 was named president and CEO. Prior to that, he spent over two decades on the East Coast working in investment and wealth management industries. He's a Kansas City native, though, having lived here through high school. Jonathan says his "best business decision" was returning to Kansas City to lead American Century, calling it an exceptional place to live, work, and raise his three children with his wife, Cyndi.

Jonathan has a BA in economics from the University of Massachusetts and an MBA from Boston College. He is a member of the board of governors at the Investment Company Institute and serves on the Stowers Institute for Medical Research and BioMed Valley Discoveries' boards of directors.

AMERICAN CENTURY INVESTMENTS AND THE STOWERS INSTITUTE FOR MEDICAL RESEARCH HAVE A SHARED FOUNDER IN JIM STOWERS JR. WHAT DID YOU LEARN FROM HIM THAT INSPIRES YOUR WORK?

When Jim started American Century, he was working in a basement office with two funds, three employees, twenty-four clients, and $100,000 in assets under management. Today, American Century is one of the top global money managers, serving individuals, financial advisors, and institutional investors in over thirty countries.

A well-known, cherished company adage is what Jim said when he started the firm in 1958: Making clients successful would make American Century successful. Turning the focus outward to help people was the right concept, and truly ahead of its time. Upholding a client-centric culture is something we've been doing sincerely for sixty-three years and is absolutely how we still run our business today. It continues to inspire me.

WHAT KIND OF IMPACT DOES THE UNIQUE RELATIONSHIP BETWEEN AMERICAN CENTURY AND THE STOWERS INSTITUTE HAVE ON YOUR CLIENTS AND EMPLOYEES?

It's profound and it's personal. Every day our employees are motivated by knowing that they are making a larger difference in the world. Almost everyone knows a friend or family member touched by a disease like cancer, Alzheimer's, diabetes, cardiac disease, or birth defects. I often hear from employees and clients that *this* is why they choose to work for us or with us. They want to support a greater purpose through research that has the potential to impact the lives of millions.

Pictured left to right: Patrick Bannigan, Executive Vice President and Chief Financial Officer; Ashley Thornton, Product Owner – Client Business Management; and Jonathan Thomas, President and CEO, gathered at a pre-Covid American Century Investments all-employee meeting.

WHAT DO YOU LOVE ABOUT THE AMERICAN CENTURY CHAMPIONSHIP CELEBRITY GOLF EVENT?

The American Century Championship is an incredible venue to increase awareness of who we are, what we do and how we make a difference in the world. Last year, the event's eighty-plus players included Justin Timberlake, Tony Romo, Charles Barkley, Annika Sörenstam, and Patrick Mahomes. I love the opportunity to tell people about our story of delivering investment results while benefiting life-changing medical research. The Championship gives us that opportunity.

HOW HAS THE PANDEMIC AFFECTED AMERICAN CENTURY? WHAT LESSONS DID THE COMPANY LEARN?

I am tremendously proud of how the American Century team came together to support our clients and one another in the face of extreme economic, social, professional, and personal challenges over the last year and a half. We learned that our culture and legacy of being client-centric and performance focused was an even greater asset than we imagined. The pandemic proved the value of being a trustworthy partner and the importance of adhering to a long-term, disciplined investment plan.

HOW DO YOU HOPE TO CONTINUE JIM'S LEGACY?

Most directly, through American Century's profits supporting the Stowers Institute's research. This was Jim's vision. But if we take it back to how it all started, people are entrusting American Century with their hard-earned life savings, which is a massive responsibility. The team works relentlessly every day to provide value to people and help them establish financial independence. We're living Jim's original inspiration.

On a personal level, it is my honor to serve on the board of directors for both American Century and the Stowers Institute to shepherd the continued success of these outstanding organizations and help align our activities and goals.

SMALL DIFFERENCES, BIG IMPACT

Tiny differences in a key protein sequence can have an important impact on how species evolve. This breakthrough discovery sheds light on the evolution of the gene regulatory networks that drive diversity among organisms.

Researchers in the laboratory of Robb Krumlauf, PhD, used modern gene editing technologies to replace a HOX gene in the fruit fly with the three related genes from the mouse. The researchers found that only one of the replacement genes restores original function in the fruit fly, suggesting that this gene retains an ancestral function that has survived 600 million years of evolution, while the other genes have diverged in function.

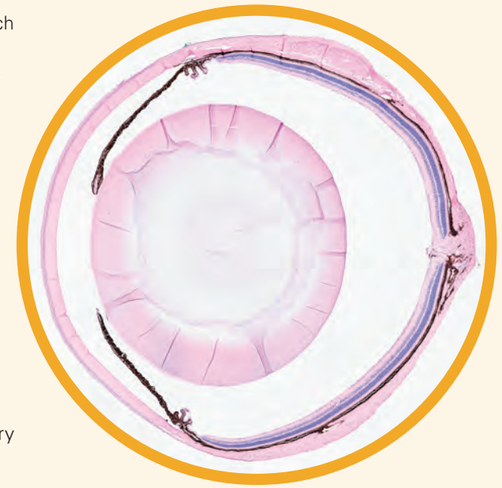
Additionally, they pinpointed a six-amino acid sequence critical for the ancestral function of the gene, which is important for modulating interactions with other proteins. Surprisingly, this sequence makes up only 2% of total amino acids in the protein, suggesting that tiny differences in certain key regions can have a big impact on protein function.

This study was published online in Genes and Development, *November 12, 2020.*

A NICHE FOR THE EYE

One of the leading causes of glaucoma is high intraocular pressure, which can cause blindness due to damage of the optic nerve. Intraocular pressure is largely maintained by the ciliary body, a specialized tissue in the eye of animals that secretes fluids. It also functions to maintain structural integrity of the eye, but detailed mechanisms of how it does so had not been determined.

Researchers from the laboratory of Ting Xie, PhD, and collaborators recently discovered how the Notch molecular pathway regulates the secretion of proteins important for supporting eye structure, and also how this pathway controls the expression of certain proteins to promote the normal structural development of the ciliary body, a part of the middle layer of the eye just below the iris. They found that Nectin proteins, which are cellular proteins that help cells adhere to one another, modulate expression of another protein, Connexin43, which functions to ensure proper fluid secretion. This work highlights the broad role of the ciliary body in maintenance of eye health and implicates the ciliary body in various degenerative eye diseases.

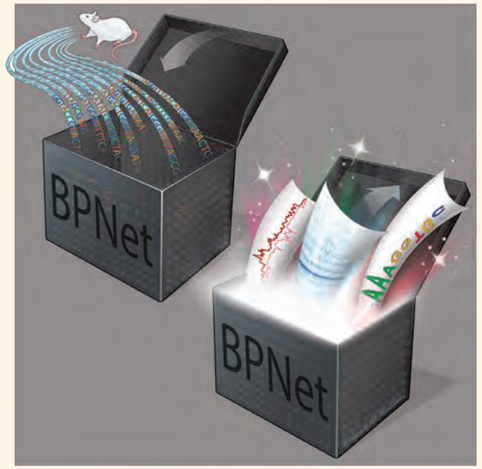


This work was first featured online in Cell Reports, *January 12, 2021.*

EXPLAINABLE AI FOR DECODING GENOME BIOLOGY

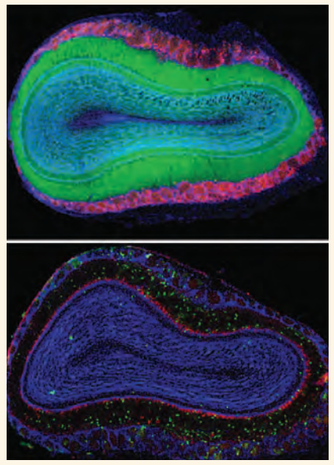
DNA is well known for encoding proteins. It also contains another code—a regulatory code—that directs when and where to make proteins in an organism. Earlier this year, Stowers Institute researchers from the lab of Julia Zeitlinger, PhD, and collaborators from Stanford University and Technical University of Munich reported how they have used explainable artificial intelligence to help decipher the genome's regulatory code.

The researchers developed a neural network whose inner workings can be uncovered to reveal regulatory DNA sequence patterns and their higher-level organizing principles from genomics data. The Zeitlinger Lab anticipates that the predictive models, rules, and maps generated using this type of approach will lead to a better understanding of natural and disease-associated genetic variation in regulatory regions of DNA.



This report was published online in Nature Genetics, *February 18, 2021.*

DECODING THE SENSE OF SMELL



Animals possess an inborn ability to recognize certain odors to avoid predators, seek food, and find mates. Two studies from the lab of Investigator Ron Yu, PhD, have uncovered details about how this ability—known as innate valence—is encoded in the nervous system of mice.

In the first study, the team showed that whether a particular odor is attractive or aversive is communicated through a complicated computational code, in which different olfactory neurons are activated to varying degrees to spell out the odor's valence. In a separate study, the team found that this coding for innate valence is not hardwired at birth, but rather is malleable and can be shaped by exposure to different odors during a critical period early in life.

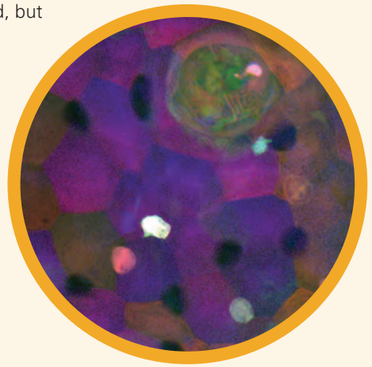
Though COVID-19 has warped the sense of smell in millions of people, Yu does not predict that it will have significant implications for most adults who recover from the disease. However, he thinks this altered sensory experience could have a major impact on affected infants and children, especially considering the role that many odors play in social connections and mental health.

These studies were published online in the journal Current Biology, *March 1, 2021, and in the journal* eLife, *March 26, 2021.*

DISCOVERY OF AN ELUSIVE CELL TYPE IN FISH SENSORY ORGANS

Humans cannot regenerate inner ear hair cells, which are responsible for detecting sound, but non-mammalian vertebrates can readily regenerate sensory hair cells that are similar in function. During the quest to understand zebrafish hair cell regeneration, researchers from the lab of Investigator Tatjana Piotrowski, PhD, discovered the existence of a cell type not previously described in the process.

The research team found newly differentiated, migratory, and invasive ionocytes, which are mitochondrian-rich cells, located in the sensory organs that house the cells giving rise to new hair cells in larval and adult fish. Normal invasive, or non-metastatic, behavior of cells after embryonic development is not often observed. Future research by the team will focus on identifying triggers for such behavior and the function of such cells, including how this process may relate to hair cell regeneration. Advances in this area may make it possible to develop medical therapies to restore hearing through the regeneration of hair cells.



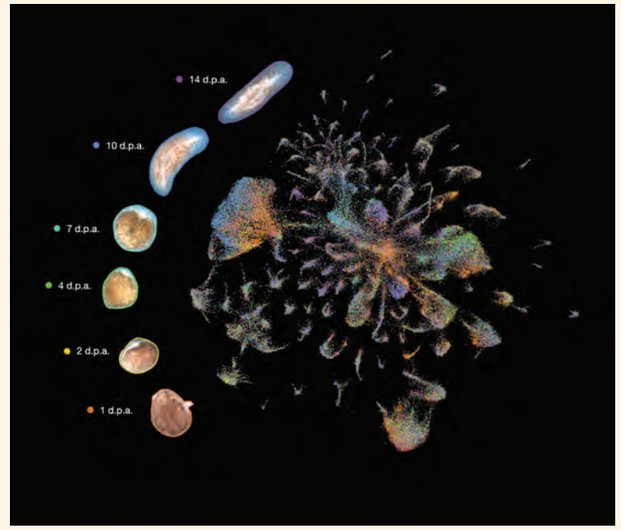
This research was published online in Developmental Cell, *April 19, 2021.*

CREATING A CELLULAR ATLAS FOR FLATWORM REGENERATION

The free-living planarian *Schmidtea mediterranea*—a type of flatworm—is capable of regenerating an entire body from a tiny portion of tissue. How it accomplishes this has largely been a mystery. But members from the lab of Alejandro Sánchez Alvarado, PhD, have now described an atlas of cell identity and cellular behavior over time in worms that are healthy, beginning the process of regeneration, and completing regeneration.

The study is the first to definitively show that whole-body regeneration involves transcriptional changes in cells from all three germ layers—muscle, epidermis, and intestine—of the body, and that tissue in areas distant from, as well as nearby, the site of injury contribute to the process of regeneration.

Overall, this work provides a global look at what type of cells throughout the organism need to be activated to stimulate stem cells to create new tissue and replace missing tissue.



This report was published in Nature Cell Biology, *September 2, 2021.*

A DISCUSSION WITH

SARAH ZANDERS, PHD

By Samantha Costa

Oftentimes scientists will share a groundbreaking experience or a specific moment in time that led to their love of science. For Assistant Investigator and Vice Dean of the Graduate School Sarah Zanders, it was simply her first undergraduate genetics course at the University of Iowa.

"Genetics just makes sense to me. At the core are very simple rules that govern everything. But at the same time, there are some complex mechanisms required to transmit DNA between generations," explains Zanders. "I have always loved learning about those mechanisms."

And just like that, a passion was ignited that has continued to radiate throughout her career and all that she does at the Stowers Institute. This fascination with what's passed on from one generation to the next continues to drive her lab's research.

After graduating with a BS in biology, this Midwesterner moved from one coast of the US to the other as she pursued her PhD at Cornell in New York and a postdoctoral fellowship at the Fred Hutchison Cancer Research Center in Washington state. However, an opportunity at Stowers to build her own lab with generous and stable funding while having the freedom to further pursue her interest in parasitic genes and their role in the evolution of genomes was all it took to re-root Zanders back in the Midwest.

Since joining the Institute in 2016, Zanders has been busy expanding upon the work she started during her fellowship. Together with her colleagues at the Fred Hutchinson Cancer Research Center, Zanders discovered meiotic drive genes and identified the parasitic selfish gene *S. kambucha* wtf4, which acts as both a poison and an antidote to eliminate its genetic competition and ensure its transmission into the next generation. Zanders' work in these areas earned her widespread recognition in 2018, as she received three highly competitive and sought-after scientific awards. And in 2020, *Science News* magazine named Zanders one of the SN10 Scientists to Watch. This award recognizes early- to middle-career researchers who have already made big contributions in their fields.

Undoubtedly, since accepting the role of the vice dean of the Graduate School of the Stowers Institute in 2019, Zanders has become busier, but she prioritizes the time she spends mentoring young researchers. Crediting her own mentors for teaching her how to "do science," she strives to instill the same critical thinking, communication, and research skills that she learned from them. And someday, if not Zanders herself, perhaps one of her mentees will build upon her work to uncover the strategies used by selfish genes to affect genome evolution.

YOU ARE CURRENTLY STUDYING GENETIC PARASITES AND HOW THEY CAUSE INFERTILITY. CAN YOU SHARE ANY NEW OR RECENT PROJECTS?

We mostly focus on genetic parasites, but we also study other aspects of biology beyond that, like how meiosis works and how it evolves. We identify new factors that are required for meiosis—the cell division process giving rise to reproductive cells like sperm and eggs—and that are independent of the parasites. The pathways of those projects will likely intersect again in the future. In addition, we are now studying centromeres, which are specialized regions of chromosomes important for proper segregation during cell division, in collaboration with Jennifer Gerton's lab here at Stowers. We work on a broad range of things, but what we've published so far is focused on those parasites.

WHAT IS SOMETHING ABOUT YOU PERHAPS YOUR COLLEAGUES OR PEERS DON'T KNOW?

I'm interested in gardening. I grow all sorts of stuff, including vegetables, herbs, fruit, and flowers. I got into composting during the pandemic. It's kind of my zen place now—to go and watch the progress of it. I think it's a very fascinating process watching all of the microbes and insects do their thing and basically turn food and plant scraps into compost.

WHAT PUTS YOU IN THE RIGHT STATE OF MIND TO COME INTO THE LAB AND BE PRODUCTIVE? DO YOU HAVE A PLAYLIST OR PODCAST YOU LISTEN TO?

I used to listen to music while I worked but I don't really do that anymore. It's not a hard transition for me. Just physically being in my lab puts me into scientist mode.

HOW HAVE YOU ELEVATED YOUR PASSION FOR TEACHING IN YOUR TIME AT STOWERS?

Prior to coming here, I was a postdoc, so I didn't get a lot of opportunities to formally teach. I would mentor interns and new technicians in the lab. I still get to do that but also get to teach in the genetics modules of the Grad School here, which I very much enjoy. I get to mentor other students outside of my lab, being part of their thesis committees and things like that.

CAN YOU TELL ME MORE ABOUT YOUR INTEREST IN PROMOTING DIVERSITY, EQUITY, AND INCLUSION?

I see it as an extension of our research in a way. It's the same kind of thinking. Our research looks at what our parasites do, and how they get an unfair transmission advantage into the next generation. They basically cheat the process that is supposed to be fair and supposed to be a merit-based process or natural selection. I feel like society with systemic racism is very similar. We have a system of advancement that's supposed to be fair and merit-based but it's really not. As part of this society, we aren't doing the best science we can, and we should try to fix that.

WHAT ARE SOME OF YOUR GOALS?

An overarching goal of mine is to try to talk about science in the simplest terms possible to broaden accessibility. Sometimes, science is discussed in very highfalutin terms, and I feel like it is exclusionary. I try to reject fancy words whenever possible. I am very informal.

Joseph Varberg, PhD

Postdoc magnifies protein research in yeast

For Postdoctoral Research Associate Joseph Varberg, researching proteins in yeast is more fascinating through the lens of a microscope, and he's noticed it's true for others too.

"There's just something about being able to see it all that makes it that much more interesting," he says. "If I'm talking about my project with my friends or family, they may not follow, but I can show them images, and it clicks. Oftentimes, when they see the images, they ask some of the same questions that we, the scientists, are interested in."

Since starting his postdoc at the Stowers Institute in 2017, Varberg has used imaging techniques as a focus for his research on proteins in the fission yeast *Schizosaccharomyces pombe*. Yeast is a valuable tool for studying fundamental cellular processes shared by many organisms, including humans. And fission yeast cells, which grow exclusively through their tips and divide across the middle to create two daughter cells of equal size, are particularly useful for studying mechanisms of cell growth and division. Understanding how the cells accomplish these biological feats normally is critical for determining what happens when they malfunction, which can lead to a wide spectrum of human diseases, including cancer and birth defects.

Each cell's genetic material is surrounded by a protective barrier called the nuclear envelope, and this is where Varberg's research lies. He studies a specialized set of proteins in the nuclear envelope that help maintain the shape and function of the nucleus—thus protecting the instructions for life contained within—and also influence chromatin organization and gene expression.

In 2019, Varberg was awarded a fellowship from the National Institutes of Health, and he set out to screen a library of *S. pombe* membrane proteins and develop imaging and analysis methods to characterize the organization of the yeast nucleus. As he's specifically interested in studying proteins at the inner membrane of the nuclear envelope—and previous tools for looking at protein-protein interactions don't work with membrane proteins—he used a special approach for this project called the "membrane yeast two-hybrid" system, or MYTH, to perform high-throughput screening and identify network interactions for three nuclear envelope proteins of diverse structure and function.

"By building a list of proteins and complexes present at the inner nuclear membrane, we hope to expand our current understanding of how these proteins interface with the genome as well as how they perform essential functions" of the nucleus, says Varberg.

The results of his research were published in December 2020 in the journal *G3*, providing a tool for studying membrane protein interactions for the *S. pombe* community. This will support further studies of nuclear envelope proteins in fission yeast as well as comparative studies in other research systems.

Varberg began his postdoc career in the Jaspersen Lab but recently moved to the Gerton Lab, which has a similar focus on the biology of the nucleus. He's developing new ideas with the team but imaging will still feature heavily in his research, and he hopes to continue to work closely with the Microscopy Center team.

"That's been one of my major focuses—utilizing various microscopy techniques and developing tools to analyze the resulting data," Varberg says, adding that "with the technology, resources, and training available from the Microscopy Center, you can quickly move from having a hypothesis to having data in hand."

Varberg's fascination with biology developed gradually. In high school Varberg focused on literature, history, and music. But during a chemistry class in his sophomore year of college, he realized he had a knack for the subject. He switched his major to chemistry and began working on a collaborative research project conducting computational modeling of new polymer materials for solar devices.

During a summer internship at the University of Kansas, he delved deeper into experimental work, using ultrafast spectroscopy to study the properties of compounds being developed for use in next-generation ultra-high-density data storage devices.

While finishing his bachelor's degree, he began working as a technician in a lab at the Stowers Institute, where he pursued molecular and cell biology. He enjoyed the pace of laboratory bench work, and his doctoral plans shifted from chemistry to biology. At the Indiana University School of Medicine, he was co-mentored by two investigators working on the parasite *Toxoplasma gondii*.

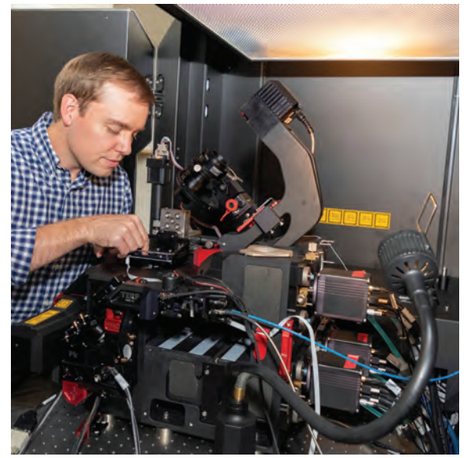
During his doctoral research Varberg focused on understanding the machinery used by the parasite to sense and respond to cellular stresses, and how misregulation could make the parasites die, with the aim of identifying potential new drug targets for treatment of toxoplasmosis and other pathogenic diseases.

Going forward, Varberg will continue to hone his coding skills, and he's also doing more live-cell imaging. In the Gerton Lab, he'll work on identifying the functional significance of the interactions for proteins present in the inner nuclear membrane. Historically, even identifying proteins on the inside of the nuclear envelope, versus what's on the outside, has been a challenge, he says.

"Now that we've identified these proteins, we can begin to study how they impact nuclear organization and function using our imaging approaches," Varberg says. "The next step is to continue to develop those imaging and analysis tools to be able to test our hypotheses in a quantitative way."

That's been one of my major focuses—utilizing various microscopy techniques and developing tools to analyze the resulting data. With the technology, resources, and training available from the Microscopy Center, you can quickly move from having a hypothesis to having data in hand.

– Joseph Varberg



NIH, National Science Foundation announce funding for trainees

Alexandria Cockrell received an F30 Ruth L. Kirschstein National Research Service Award from the National Institute of General Medical Sciences of the National Institutes of Health (NIH). This award provides support of $119,000 over three years for her research on ribosomal DNA and nucleolar organization in fission yeast. Cockrell is a predoctoral researcher with the University of Kansas Medical Center, doing her thesis work in the Gerton Lab.

The National Science Foundation announced fellowships for two Stowers postdoctoral researchers in 2021. These Postdoctoral Research Fellowships in Biology (PRFB) are offered only to early-career postdocs, with the expectation of active mentorship from the postdoc's sponsoring scientist. The two-year awards grant a total of $138,000 to support the postdoc's research project.

From left to right: Alexandria Cockrell, Curtis Bacon, Jasmin Camacho.

Rohner Lab Postdoc Jasmin Camacho, PhD, received her PRFB award in July 2021. Camacho's research involves the study of nectarivory, or the eating of nectar, which she believes is an ideal system to investigate the mechanisms of how traits become adapted by natural selection. Specifically, her project aims to discover the beneficial genetic mechanisms necessary for excessive sugar consumption in bats, including how they avoid and/or repair DNA and cellular damage from the harmful byproducts of sugar metabolism. Camacho believes using an uncommon research organism with extreme adaptive traits, such as a bat, is a significant tool for communicating biological concepts.

In the Zeitlinger Lab, Curtis Bacon, PhD, received a fellowship that will begin January 1, 2022. His project focuses on understanding how transcription factors interpret DNA sequence. He and another lab member aim to develop and implement a sequencing method that will reduce the amount of starting material necessary to obtain transcription factor binding locations and collect chromatin accessibility information from a single experiment. He will also utilize a deep learning model developed in the Zeitlinger Lab that could advance knowledge of how variations in DNA sequence lead to observable phenotypes in development.

Postdocs pick up prestigious honors

Kristin Watt, PhD, received a Pathway to Independence grant from the NIH in August 2021. The award is designed to provide transitional support from a postdoctoral position to an independent faculty position and provides $200,000 over two years at the postdoctoral level with the opportunity for an additional three years of funding at the researcher's next institution.

Watt, a postdoc in the Trainor Lab, is studying transcription in neural crest cells (NCC) and craniofacial development. Neural crest cells give rise to the majority of craniofacial bone, cartilage, and connective tissue, and understanding their development is crucial for advancing the prevention of craniofacial birth defects. Disruptions in NCC development are known to underlie several craniofacial disorders that account for one-third of all birth defects and are a significant cause of infant mortality.

Another Trainor Lab postdoc, Soma Dash, PhD, was awarded a fellowship from the American Association for Anatomy in early 2021. The award supports her research into the etiology of Hirschsprung disease, a birth defect in which nerve cells are missing from a segment of the bowel in an infant. Building upon previous studies published by the Trainor Lab related to cranial neural crest cell function and Treacher Collins syndrome, this new research has a high potential impact for therapeutic studies of Hirschsprung disease.

From left to right: Blair Benham-Pyle, Soma Dash, Kristin Watt.

Postdoc Blair Benham-Pyle, PhD, was recognized by the American Society for Cell Biology (ASCB) with the Merton Bernfield Memorial Award. The ASCB recognizes contributions that people have made to science across many career stages, as well as to the pursuit of science for the benefit of humanity. Benham-Pyle's award for postdocs and graduate students was established in memory of pediatrician and cell biologist Merton Bernfield.

Benham-Pyle, a postdoc in the Sánchez Alvarado Lab, uses a combination of sequencing and imaging techniques to identify the cell types and tissue structures required for complete regeneration and accurate scaling of planarian worms. Through this work, she hopes to reveal mechanisms regulating self-organization and growth in some adult tissues, which may expand our ability to improve human regenerative capacity and treat human cancers that arise from aging tissues.

Hats off to the graduates

Having adjusted to the challenges of the pandemic, the predoctoral researchers of the Graduate School of the Stowers Institute for Medical Research continued to make progress toward their degrees, with several predocs defending their theses in 2021. While the Graduate School was unable to hold a graduation ceremony in 2021, plans are being made to celebrate all the recent graduates in spring of 2022.

Cheng-Yi Chen and Darrick Hansen both had their PhD degrees conferred this year, after defending in late December of 2020. Chen did his thesis work on germline development in the starlet sea anemone, *Nematostella vectensis*, in the Gibson Lab. He is now a postdoctoral researcher in the Farrell Lab at the National Institute of Child Health and Human Development. Hansen, who was in the Si Lab, worked on characterization of the stem cells dedicated to regenerating the intestinal epithelium.

Irina Pushel presented the first thesis defense of 2021 in March. Her research in the Krumlauf Lab focused on the roles Hox genes play in the gene regulatory network controlling mouse cranial neural crest cell formation, migration, and differentiation. Later that month, Pushel joined Children's Mercy Hospital in Kansas City, Missouri, as a senior bioinformatic scientist.

Three predocs defended in May, beginning with Zachary Lee. In the Gibson Lab, Lee studied phosphorylation dynamics during epithelial cell division in the fruit fly, *Drosophila*. He is now a biologics scientist at Catalent in Kansas City. Soon-Keat Ooi presented his research on the structure-function analysis of the human INO80 chromatin remodeling complex, done in the Conaway Lab. He has moved to the Fox Chase Cancer Center in Philadelphia, Pennsylvania, as a postdoctoral researcher.

Wrapping up the month was Shuonan He, another Gibson Lab predoc, whose project focused on the functional analysis of Hox genes in the sea anemone, *Nematostella vectensis*. His next position as a postdoctoral researcher at the Howard Hughes Medical Institute and Harvard University began in late summer.

In August, Yanfeng He, a member of the Conaway Lab, defended his thesis expounding on the mechanisms of transcriptional regulation by enhancers. In September, he joined the Dana-Farber Cancer Institute in Boston, Massachusetts, as a postdoctoral researcher. Karla Terrazas-Falcon did her predoctoral research in the Trainor Lab, and her September defense described her research investigating the tissue-specific roles of Tcof1, Polr1c and Polr1d during ribosome biogenesis. In December, Wei-Ting Yueh will be the final predoc of 2021 to defend, sharing his research from the Gerton Lab.

Top row left to right:
Cheng-Yi Chen, Darrick Hansen, Irina Pushel

Middle row left to right:
Zachary Lee, Soon-Keat Ooi, and Shuonan He

Bottom row left to right:
Yanfeng He, Karla Terrazas-Falcon, Wei-Ting Yueh

New program aims to add diversity in science training

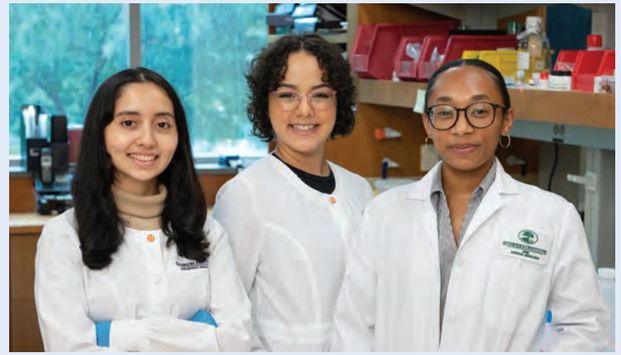
The Graduate School of the Stowers Institute for Medical Research is committed to preparing young scientists whose innovative approaches to research will revolutionize twenty-first-century biology. With that goal in mind, this year the Graduate School introduced the Stowers Research Scholars postbaccalaureate program.

The Stowers Research Scholars program is a one-year mentored fellowship for recent undergraduates that was developed to increase diversity. Participation is open to US citizens or permanent residents with an undergraduate degree in a STEM field who are interested in pursuing an advanced research degree, and preference is given to members of communities traditionally underrepresented in STEM.

Creation of the program was led by Dean of the Graduate School Matt Gibson, PhD. His goal was to create a program that provides an important steppingstone for students from underrepresented backgrounds to get lab experience and discover whether they want to pursue further education in science.

The key component of the program is full-time research in the lab of their choice. Along with benchwork, the Scholars participate in Graduate School events and can audit some of the Graduate School coursework. Benefits include a competitive stipend, a relocation stipend, and a travel allowance. Participants will attend workshops, seminars, and panel discussions to prepare for applying to graduate school and have regular meetings with Assistant Dean for Academic Affairs Jinelle Wint, PhD. With a background in DEI programs, Wint is uniquely suited for the career coaching and guidance that the Scholars receive during their fellowship.

"The mission and aim of the Stowers Research Scholars program are to train underrepresented students in basic biomedical research and have them apply and get into their graduate school of choice," says Wint. "I am really excited about launching the program this year and I can't wait to see what the future holds."



From left to right: Brenda Sanchez, Shanaika Vargas Rivera, Enya Dewars

Scholars return to the Institute for a summer of science

The Stowers Summer Scholars program resumed this year after a hiatus in 2020 due to COVID-19, with nineteen students selected to participate. The research internship ran June 7 through July 30, giving the students eight weeks to immerse themselves in an independent research project of their choosing under the guidance of a senior scientist.

The program began in 2004 as an intensive research internship for undergrads interested in a research career. The advantages of the Institute are unique, says Assistant Dean for Academic Affairs Jinelle Wint, PhD, with Summer Scholars fortunate to work closely with world-class investigators and state-of-the-art facilities not found at many other institutions.

"I first learned about the Stowers Institute when I visited the Institute to attend a BIG IDEAS lecture in high school, and ever since then, it has been a goal of mine to apply for the Summer Scholars program," says Calvin Winkler, an undergrad at the University of Missouri-Columbia. "I never fully realized the caliber of science going on here. It has been very exciting to be surrounded by it."

For undergraduate researchers, a summer spent in the research-focused environment of the Institute can help foster passion and commitment for research, motivating students to pursue science-related careers. Along with their benchwork, the students attend seminars, meet for weekly lunches, and present their work at an all-Institute poster session.

"I get to experience tons of different subjects in biology that I would otherwise never see, and learn how scientists present their data to their audience. Hopefully I'll pick up on how to show the world my science here," says University of Missouri-Kansas City undergrad Olivia Rippee. "What better place to kick-start a research career than the Stowers Institute, a well-supported facility for innovating science just across the street from my college campus?"

The Stowers Summer Scholars program is supported by generous funding from the Stowers Foundation, a philanthropic foundation established by the Stowers family.

Five new faces

After a challenging year finding ways to adjust the PhD program to COVID-19 restrictions and precautions, the Graduate School of the Stowers Institute welcomed five new predoctoral researchers for its ninth year. Read about what inspired these junior scientists to pursue the study of biology.

María José ("Majo") Blanco Salazar

National Autonomous University of Mexico

María José Blanco Salazar has been doing research since high school, when she joined a summer research program at the National Autonomous University of Mexico. That experience sparked a fascination with the mechanisms regulating gene expression, especially the idea that understanding gene expression can have an impact on human health.

Anna Galligos

Rockhurst University

Anna Galligos grew up listening to her father tell her kid-friendly stories about cells and enzymes, with characters like Ernie the Enzyme and Sal the Stem Cell. The more stories she heard, the more questions she had. Though she eventually outgrew the stories her father told her, she never outgrew the science, and she credits her father for encouraging her to take the initiative to find answers on her own.

Olivia Lawler

John Brown University

Olivia Lawler fell in love with science over a centrifuge. In high school, she shadowed a biochemist studying the effects of drugs on liver cells and became fascinated by the idea of contributing to the knowledge of human health through lab work. Lawler's long-term goal is to research Parkinson's disease at the cellular/molecular level with the hopes of understanding what factors lead to its onset.

Amruta Swaminathan

Indian Institute of Science Education and Research

Amruta Swaminathan fell into her love for science in high school. Finding her textbooks inadequate, she turned to college textbooks to get a better understanding of subjects like physics and found "a passion for devouring these excellently written texts that helped me see the beauty and elegance in all the sciences."

Dung Vuu

University of Science, Ho Chi Minh City

In high school, Dung Vuu became curious about how scientists develop new medical treatments for diseases. This curiosity led her to the University of Science in Ho Chi Minh City. She believes that discoveries made in molecular and developmental biology can help answer fundamental questions in life sciences, which can then lead to a better understanding of human diseases.

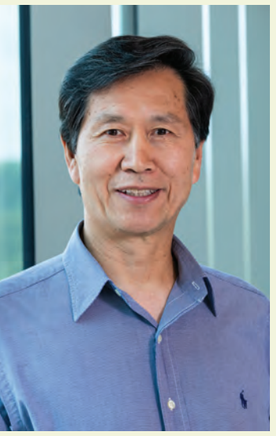
GRANT ANNOUNCEMENTS FOR STOWERS INVESTIGATORS

Several Stowers investigators have received external National Institutes of Health (NIH) funding notifications during 2021.

Director of Imaging Paul Kulesa, PhD, was awarded an R03 grant from the Eunice Kennedy Shriver National Institute of Child Health and Human Development of the NIH. This award provides $330,000 over two years for Kulesa's research into outcome prediction of pediatric neuroblastoma. The project, led by Jennifer Kasemeier, PhD, aims to develop a predictive artificial intelligence algorithm (PredictNeuroB) based on embryonic signals. By using a large set of patient-derived data from the Gabriella Miller Kids First genomic database, they anticipate the model will prove highly predictive for a broad class of neuroblastoma patients and support clinical decision-making in disease treatment and targeted drug therapies.

Associate Scientific Director and Investigator Kausik Si, PhD, was awarded an NIH R01 grant in January 2021 from the National Institute on Aging. The R01 provides $2 million over five years. For Si, the funding will support his research to identify the biochemical substrates of long-lasting memories in mammals and gain a better understanding of the relationship between amyloids that support memory and amyloids that disrupt memory. Results of this research could aid in the development of treatments for neurodegenerative diseases such as Alzheimer's disease.

KUCC PILOT GRANTS AWARDED TO TWO AT STOWERS



Investigators Linheng Li, PhD, and Jennifer Gerton, PhD, have received grant funding from the Kansas University Cancer Center (KUCC).

For the past decade, immunotherapy has revolutionized cancer treatment. However, it is mostly only effective with limited solid cancer types including melanoma, lung, and renal cancers. Li's award will support preclinical research and proof-of-principle for the use of antibodies to break through the immune barrier of microenvironments of other cancerous tumors.

Centromeres, the region of a chromosome that separates it into a short arm and a long arm, play an essential role in segregation of chromosomes and have the potential to cause problems with chromosomal structure and copy number in cancer. However, centromeric stability has not been examined in cancer. The Gerton Lab will use samples from a clinical trial for acute lymphoblastic leukemia to assess whether centromere instability is a useful biomarker to identify patients early in therapy who are at high risk of relapse.

SÁNCHEZ ALVARADO NAMED PRISCILLA WOOD NEAVES ENDOWED CHAIR IN THE BIOMEDICAL SCIENCES

Executive Director and Chief Scientific Officer Alejandro Sánchez Alvarado, PhD, has been named the Priscilla Wood Neaves Endowed Chair in the Biomedical Sciences at the Stowers Institute. Priscilla Wood Neaves was the wife of the Institute's first president and CEO, William B. Neaves, PhD. The Neaveses believed strongly in the Institute's mission as defined by Jim and Virginia Stowers, and the endowed chair was created to honor Priscilla when she was diagnosed with a neurodegenerative disease. Priscilla passed away in 2019.

"Knowing that Alejandro Sánchez Alvarado is now formally the Priscilla Wood Neaves Endowed Chair in the Biomedical Sciences at the Stowers Institute for Medical Research gives me great satisfaction and is the most comforting event since Priscilla's death," says Neaves.

Prior to joining the Institute, from 2002 to 2011 Sánchez Alvarado was a faculty member in the Department of Neurobiology and Anatomy at the University of Utah School of Medicine, where he held the H.A. and Edna Benning Presidential Endowed Chair. In 2005, he was named an Investigator of the Howard Hughes Medical Institute (HHMI). Sánchez Alvarado joined the Stowers Institute in 2011.

Sánchez Alvarado's distinguished and continuing achievements in original research have been recognized by his election to the National Academy of Sciences, the American Academy of Arts and Sciences, and the Academia de Ciencias de América Latina. He has served as president of the Society for Developmental Biology and is a fellow of the Marine Biological Laboratory in Woods Hole, Massachusetts.

TRAINOR HONORED FOR CONTRIBUTIONS TO CRANIOFACIAL SCIENCES

Investigator Paul Trainor, PhD, was named the recipient of the 2021 David Bixler Distinguished Scientist Award from the Society for Craniofacial Genetics and Developmental Biology (SCGDB). The award is named after the first president of the SCGDB and is the Society's highest honor. It was created to recognize long-term distinguished leadership and meritorious contributions to the craniofacial sciences by a senior-level SCGDB member.

Trainor joined the Stowers Institute in 2001. His research focuses on understanding neural crest cells and craniofacial development, concentrating on mechanisms that regulate neural crest cell formation, migration, and differentiation. As part of the award, Trainor delivered a plenary lecture on his research at the 44th Annual SCGDB Meeting in October.

Leadership team undergoes changes and welcomes two new members

During 2021, the executive team at Stowers has seen several changes, with two additions, one promotion, and the retirement of the Institute's first CFO, Roderick Sturgeon. Sturgeon joined Stowers in 2007, coming from an executive role at Hallmark Cards Inc.

Stepping into his role is Penny Spence, who was named the executive vice president and chief financial officer for the Stowers Group of Companies, including the Institute, BioMed Valley Discoveries, and Stowers Resource Management. Spence joined the Institute in 2019 as vice president of finance and treasurer. In her new role, she will continue to build on the financial strength of the organization, drive innovation to support the scientific strategy, and help guide the mission of the Institute. Spence worked closely with Sturgeon before his retirement, which was effective in April 2021.

Joining Stowers in September 2021 was Kim Chee, who was named vice president of finance. Prior to joining the Institute, Chee held a variety of finance and accounting roles in multiple large corporations in Kansas City, most recently at Corbion. While at Corbion, Chee was a finance director, responsible for the financial and accounting aspects of Corbion North America as well as Risk Management and Corporate Tax. Chee received a BS in Accounting from Kansas State University and an MBA with a finance concentration from University of Missouri-Kansas City.

Also new to the Institute is Jennifer Pawlosky, who was named vice president of communications in August 2021. Pawlosky will direct the communications efforts for the organization with an emphasis on branding and marketing efforts to support the scientific strategy and mission of the Institute through various communications platforms.

Prior to joining the Institute, Pawlosky worked at the Allen Institute in Seattle, Washington, as the executive director of communications. Before that, she worked at Fred Hutchinson Cancer Research Center and at Arthur Andersen. Pawlosky received a bachelor of arts in English literature and economics from the University of Virginia in Charlottesville. She is a board member and co-program chair for the Association of Independent Research Institutes.

Advisory board recommends promotions, renewals

In 2021, the Scientific Advisory Board (SAB) recommended promotion and renewal of four of our investigators, effective January 1, 2022. Investigators Jerry Workman and Ron Yu have been renewed for seven-year terms. Assistant Investigators Sarah Zanders, PhD, and Ariel Bazzini, PhD, have both been promoted to associate investigators and reappointed for seven-year terms.

The Workman Lab studies how large protein complexes modify chromatin and control gene expression, and the role of these processes in health and disease. Yu's research investigates the complex connections between neurons that link sensation to behavior, specifically in the mouse olfactory system, which detects odors.

Bazzini is interested in how genes are regulated to impact development, physiology, and disease. His lab is exploring how mRNA stability and translation are regulated. Zanders' research focuses on selfish genes in gametogenesis, a process that produces reproductive cells such as eggs and sperm. Her lab uses fission yeast to study the survival strategies used by "selfish" genes and how they have affected genome evolution.

The SAB, composed of members of the National Academy of Sciences, provides independent advice and guidance on the scientific direction of the Institute.

For this BIG IDEAS lecturer nothing is *Impossible*

Without a conscious career plan, Patrick O. Brown, MD, PhD, CEO and founder of Impossible Foods, bounced from graduate school to medical school and eventually to entrepreneurship business.

Brown, who was the featured speaker for the April BIG IDEAS @ScienceStowers lecture, shared his ideas on how developing a technology to make meat without the use of animals can have a significant impact on reversing climate change and the loss of biodiversity.

The idea for the company came to him while on sabbatical from his position as an HHMI investigator and professor of biochemistry at the Stanford University School of Medicine. Brown began to consider what the most important problem facing the world—that he could contribute to solving—might be. He quickly determined that the use of animals as food causes significant destruction to and is, in his opinion, the greatest threat to our planet. He immediately went to work looking for ways to change that.

It was then that Brown founded Impossible Foods. With his experience and background in research and medicine, he set out to produce delicious, nutritious, affordable, and sustainable meat, fish, and dairy foods from plants.

Due to COVID-19 restrictions, the lecture was presented online; however, that allowed for record-breaking attendance. More than 275 viewers joined to listen and pose questions.

Brown is a member of the National Academy of Sciences and the Institute of Medicine and recipient of the American Cancer Society Medal of Honor.

The BIG IDEAS lectures are open to the public and bring cutting-edge and provocative scientific ideas in an engaging and accessible way to the greater Kansas City community.

Outreach springs into action

Spring of 2021 kicked off a busy year of outreach efforts, with multiple activities involving local science enthusiasts of all ages. Activity was up this year partly due to the development of Ampli-Sci, a community of Stowers Institute volunteers with a goal to amplify Stowers research.

This year, volunteers delivered virtual high school classroom sessions, engaged teachers in science training, inspired young scientists at career fairs, and served as undergraduate research and high school project mentors. Eighteen Stowers members served as judges for the high school Project Lead the Way biomedical competition.

Institute researchers partnered with the KC STEM Alliance to create an "Explore Microscopy" project kit for Remake Learning Days, a nationwide festival of engaging educational events hosted by organizations such as schools, museums, and libraries. The free kit included a paper microscope that can be assembled at home and a code that linked to an interactive website with how-to videos and activities.

The Institute also welcomed an excursion of delegates from the National Consortium of Secondary STEM Schools (NCSSS). The goal of special events like this is to share the excitement of innovative research in Kansas City and provide educators with information on our training opportunities.

Leadership Fellows program offers executive-level training

The Stowers Institute is well known for the exceptional training and resources it provides to early-career scientists, but now it is extending a similar opportunity to nonscientific professionals. Launched in January 2021, the Stowers Institute for Medical Research Leadership Fellows Program aims to provide leadership and governance experience and training to early-career professionals from diverse and underrepresented backgrounds.

With an abundance of nonscientific organizational resources in areas like legal and governance, human resources, finance and accounting, operations, and community outreach, the Institute is fertile ground for fellows who want to gain a deep understanding of functional management and leadership in an organization.

The six-month program was developed for postgraduate professional degreed individuals who are ready for advanced training. Vice President of Human Resources, Diversity, Equity, and Inclusion Patrick Mitchell shares, "Our target candidates for the program are postgrads, on a similar level as our scientific postdocs, who have earned a higher education degree and are ready to do some advanced training."

The Institute's first Leadership Fellow, Mirjana Gacanich, is a graduate of the University of Missouri-Kansas City School of Law who was eager to take on a role allowing her to engage in the corporate side of a science organization.

Mitchell says he sees the variety of opportunities within the program as a way for early-career professionals to gain credentials that often take years to develop. Not only will this expand the Institute's Diversity, Equity, and Inclusion efforts, it brings new ideas and perspectives to the organization.

While these underrepresented professionals gain valuable knowledge, exposure, and experience from the Leadership Fellows Program, Mitchell recognizes the future value that these individuals can have as ambassadors and community partners. "It's a win-win situation for Stowers and these early-career professionals."

Investigators step away from the bench to embark on new roles

> I find that the most fulfilling and rewarding part of my job is to watch those individuals go off and have an impact in science.
>
> *– Sue Jaspersen, PhD*

After nearly twenty years at Stowers, Joan and Ron Conaway closed their lab in late summer of 2021. While Ron retired, Joan began a new role as the vice provost and dean of basic research at the University of Texas Southwestern Medical Center. She was also appointed professor of Molecular Biology and holds the Cecil H. Green Distinguished Chair in Cellular and Molecular Biology.

The Conaways arrived at the Institute in 2001, soon after it opened. They are regarded as one of science's most accomplished research teams that have advanced scientific knowledge about many of the mechanisms that underlie gene transcription.

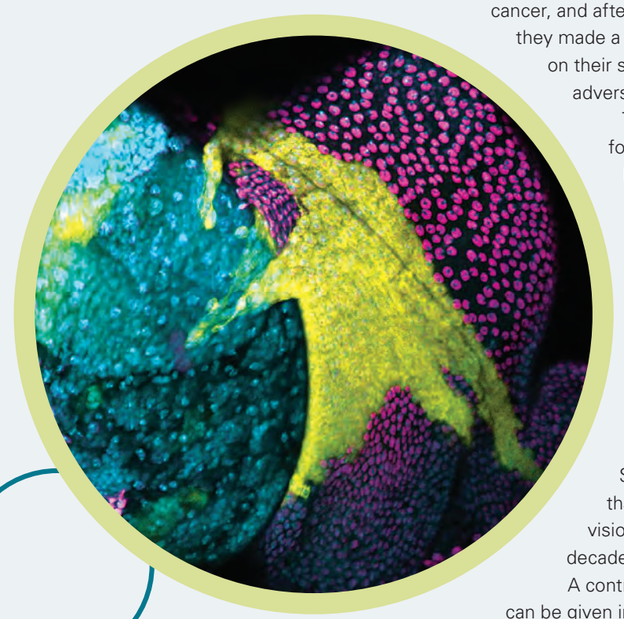
Another Stowers investigator, Ting Xie, PhD, accepted a position as the head of the Division of Life Science at Hong Kong University. Though he began transitioning to his new role in mid-2021, he will remain an adjunct principal investigator at the Stowers Institute throughout 2021.

Xie was one of the first investigators to join the Institute in June of 1999. The next year he published his first Stowers-affiliated paper in *Science*, describing a special cellular microenvironment capable of controlling stem cell behavior, microenvironments now referred to as "niches." Xie's research has continued to shed light on the molecular regulatory mechanisms underpinning how niches function in regulating stem cells.

After fifteen years at Stowers, Associate Investigator Sue Jaspersen, PhD, also closed her lab this year. Jaspersen joined Stowers in 2005 and led a team that focused on the complex processes that guide cell division in yeast. She received multiple awards for her scientific achievements while at Stowers but is proudest of the scientists who went through her lab and launched successful careers in science. Jaspersen mentored over seventy trainees in her lab and served on the faculty of the Graduate School. "I find that the most fulfilling and rewarding part of my job is to watch those individuals go off and have an impact in science," she said. Jaspersen is stepping away from benchwork to pursue new endeavors.

We are grateful for the impact these investigators have had on the innovative research coming out of the Stowers Institute, as well as on the many junior scientists who have gone on to research careers of their own.

INVESTING IN TOMORROW'S CURES:
The Hope Shares® Endowment



Cancer. Alzheimer's disease. Diabetes. Cardiovascular disease. Birth defects. Chances are, you or someone you know has been affected by at least one of these conditions, which are all too common in our society.

For Jim and Virginia Stowers, the challenge was cancer, and after successful treatment and recovery, they made a momentous decision: They would draw on their substantial fortune to transform their own adversity into Hope for Life® for millions.

Today, Stowers scientists are at the forefront of unraveling the mechanisms behind health and disease and preparing the groundwork for novel treatments and cures. Their work is made possible by the Hope Shares Endowment—the lifeblood of the Stowers Institute.

Unlike most research programs at universities, which immediately spend their donors' contributions, the Institute uses every gift, no matter how big or small, to add to its endowment. As the capital invested in the Hope Shares Endowment grows, it ensures that Jim and Virginia Stowers' extraordinary vision continues to gain momentum for decades to come.

A contribution to the Hope Shares Endowment can be given in the donor's name or in memory or honor of someone they love.

We are fortunate to have the support of many loyal donors who know their generous contributions to the Hope Shares Endowment help secure the Institute's future and accelerate our researchers' life-changing contributions to human health. It's an investment that will pay dividends in improved health and well-being for decades to come.

The following pages pay homage to all the visionary men and women who believe in our mission and are convinced that an investment in the Stowers Institute is the best way to advance knowledge and provide Hope for Life®.

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Pamela Stowers

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BACKSTAGE PASS

While our planet is home to over thirty million species of animals that look very different on the outside, our biology is often more similar than different, especially at the level of cells and genes. Studying the biological processes of animals allows researchers to find answers to fundamental questions that in turn contribute to our biological knowledge base and provide insight to human and animal health and disease.

The Stowers Reptile and Aquatics Facility provides the Institute's scientists with the technical support for its non-mammalian research organisms. The technicians are specially trained to assist researchers with colony management, animal identification, breeding, tissue sampling, technical services, and cryopreservation. Whether it is self-regenerating flatworms, fluorescent sea anemones, or blind cavefish, it takes the attention of many dedicated individuals to provide the exemplary care for these research animals.

REPTILE AND AQUATICS BY THE NUMBERS

421,000
Crickets used as feed for the reptile colonies annually

>373,000
Fertilized cavefish eggs collected in the past year

>35,600
Zebrafish

30,000
Planaria flatworms shipped from Stowers to other research institutions annually

>9,500
Sea anemones

>5,600
Cavefish

2,134
Reptile eggs produced last year

2,000
Zebrafish tanks in use

>900
Apple snails

48
Lizards

31
Team members

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FOR MEDICAL RESEARCH

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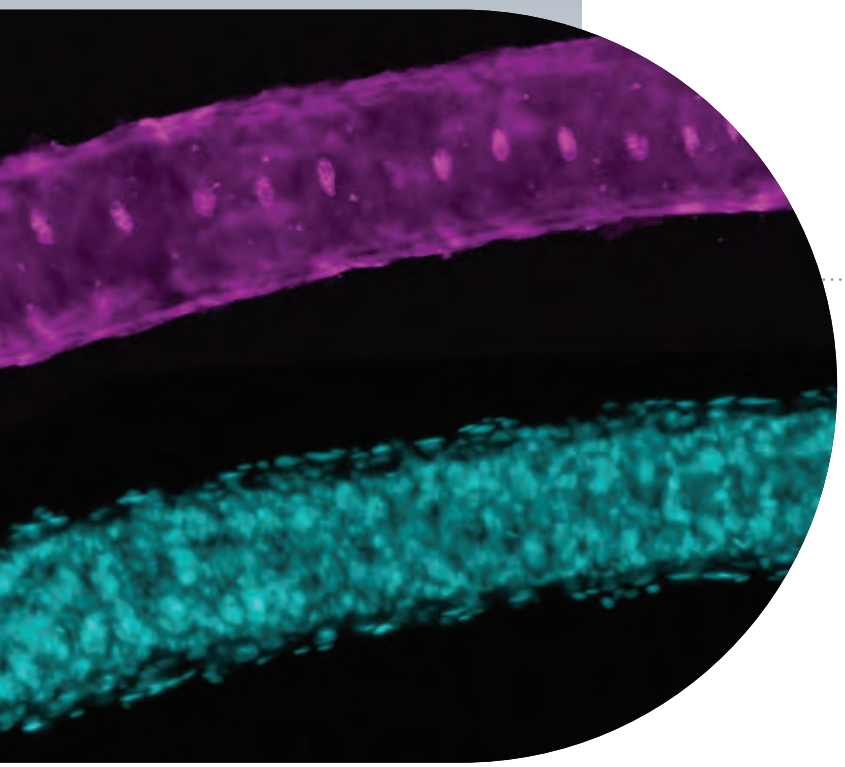
OUR MISSION

TO MAKE A SIGNIFICANT CONTRIBUTION TO HUMANITY THROUGH MEDICAL RESEARCH BY EXPANDING OUR UNDERSTANDING OF THE SECRETS OF LIFE AND BY IMPROVING LIFE'S QUALITY THROUGH INNOVATIVE APPROACHES TO THE CAUSES, TREATMENT, AND PREVENTION OF DISEASES.



Stowers researchers study chromosome recombination and segregation in the silkworm, *Bombyx mori*. Top image shows part of an ovary stained for a protein important in meiosis, a type of cell division that gives rise to egg cells. Bottom image shows the same region stained for DNA.

Image courtesy of Hawley Lab