STOWERS INSTITUTE®
FOR MEDICAL RESEARCH

1000 E. 50th Street
Kansas City, Missouri 64110
Tel: (816) 926-4000
Fax: (816) 926-2000
www.stowers.org

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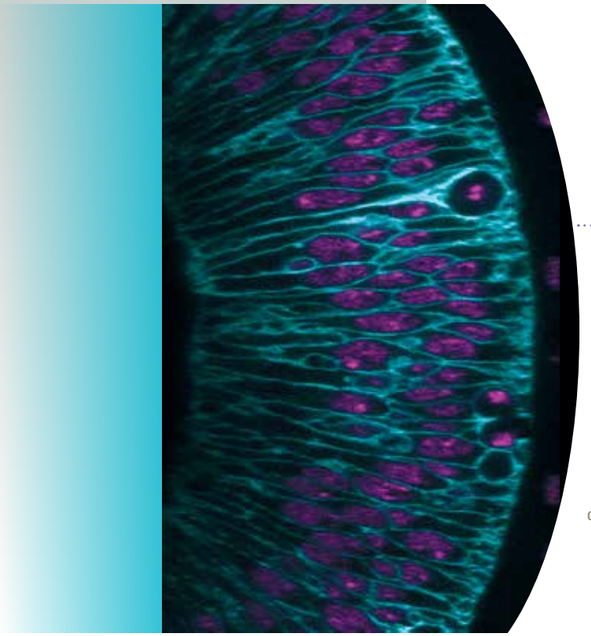
OUR MISSION:

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.



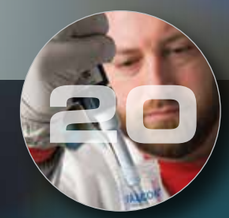
THE ORGANIZATION OF CELLS INTO EPITHELIAL SHEETS IS AN ESSENTIAL FEATURE OF ANIMAL DEVELOPMENT. THE GIBSON LAB USES LIVE IMAGING AND GENETICS TO STUDY THE DEVELOPMENT OF IMAGINAL DISCS – EPITHELIAL TISSUES FOUND IN INSECT LARVAE THAT DEVELOP INTO ADULT STRUCTURES SUCH AS THE LEG, WING AND EYE – TO GAIN NEW INSIGHTS INTO PROCESSES FUNDAMENTAL TO EPITHELIAL BIOLOGY.

Image: courtesy of Zachary Lee, Gibson Lab. A cross-section of the *Drosophila melanogaster* wing imaginal disc. Cell membranes are shown in blue and chromatin, composed of the protein-DNA-RNA complexes that form chromosomes, is shown in pink.

PROTEOMICS
A GLIMPSE INTO THE COMPLICATED INNER LIVES OF OUR CELLS.

STOWERS REPORT

NEWS AND INSIGHT FROM THE STOWERS INSTITUTE FOR MEDICAL RESEARCH SPRING/SUMMER 2016



STOWERS REPORT

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CONTRIBUTORS:

Editors
Kim Bland
Kristin Kessler

Copy editor
Emma Davis

Web content
Juan Carlos Grover
Philippe Noguera
Brian Swezy

Scientific Illustration
Mark Miller

Photography
Mark McDonald

Design and production
Trozzolo Communications Group

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In perspective

BY DAVID CHAO, PHD
PRESIDENT AND CEO

The British science fiction writer Arthur C. Clarke coined the famous adage: “Any sufficiently advanced technology is indistinguishable from magic.” At the Stowers Institute, magic happens every day.

Stowers scientists routinely use million-dollar microscopes to distinguish between objects that are separated by distances shorter than the wavelength of light. Others use mass spectrometers to measure the weight of molecules with enough precision to distinguish the presence or absence of a subatomic particle. Still others generate gigabytes of genomic data and apply advanced algorithms to identify and study interesting anomalies and patterns.

A centerpiece of the Institute’s strategy is investing heavily in expensive and wondrous technology and then pairing this technology with teams of experts in its use. A Stowers scientist in need of a magical assist need not spend weeks or months of apprenticeship to become an independent practitioner. Instead, the scientist can draw upon the support of teams of experts who are eager to apply cutting-edge technologies to solve the problem at hand.

The benefits of scientific teamwork at the Institute are very clear. Each year, the authorship of about two-thirds of the Institute’s publications reflects a collaborative effort among principal investigator and core technology laboratories. The productivity of this teamwork is impressive. Since opening its doors fifteen years ago, the Institute has published over 1000 papers, including collaborations with over 150 institutions around the world.

In this edition of the Stowers Report, the cover story explores the Institute’s work in proteomics, a field of rapid technological advancement epitomizing Clarke’s famous adage. Proteomics involves the large-scale study of proteins, including the measurement and detection of their abundance, modification, and interactions. Every day, the Stowers Proteomics Center uses a combination of hand-drawn chromatography columns, million-dollar mass spectrometers, and customized computer clusters to achieve amazing results. The central role of proteins in biology means that almost every research program at the Institute intersects in some way with the work of the Proteomics Center. Hundreds of researchers at the Institute have benefited from collaborations with experts in the Proteomics Center.

The Proteomics Center serves as an excellent example of the teamwork and expertise that make the Institute a special place to work. Jim and Virginia Stowers long ago recognized that collaboration and collegiality would be key ingredients for building a world-class research center. Sprinkling some technological magic on top of the Institute’s special culture has helped to inspire and support many creative new directions for the Institute’s research. I hope you enjoy reading more about proteomics and the magic of advanced technologies in the pages that follow.

By Marla Vacek Broadfoot

PROTEOMICS

A GLIMPSE INTO THE COMPLICATED INNER LIVES OF OUR CELLS

Proteins are the manifestation of what is written in our genomes—the blueprint of life brought to life. They give structure to cells and tissues, catalyze numerous activities within and between cells, and even control which sections of the DNA blueprint can be read at any given time.

Just as the human genome is the collection of all human genes, the proteome is the sum of all the genome's proteins. But that is where the similarity ends. While the genome locked within every cell remains relatively static, its protein output is constantly changing depending on the cell or tissue, time of day, or exposure to stress. "As a result, there is no single proteome to describe and understand. There are probably an infinite number," says Mike Washburn, PhD, director of the Stowers Proteomics Center.

Despite the daunting complexity of proteomics—or perhaps because of it—Washburn and his colleagues at the Stowers Institute are embracing the field. They believe that studying the proteins of the cell helps lay the foundation of understanding the mechanisms that drive human health and disease.

Tackling the infinite

Proteomics is loosely defined as the study of the structure, function, and interaction of all of the proteins in a particular cell or organism. For human cells, these proteins could number in the hundreds of thousands to over a million. What's more, they could undergo a myriad of modifications, take part in a variety of molecular pathways, or form complicated shapes with multiple protein partners.

The Stowers Proteomics Center is up to the task. Led by Washburn and Laurence Florens, PhD, the Center is staffed by a team of scientists with expertise in protein science, analytical

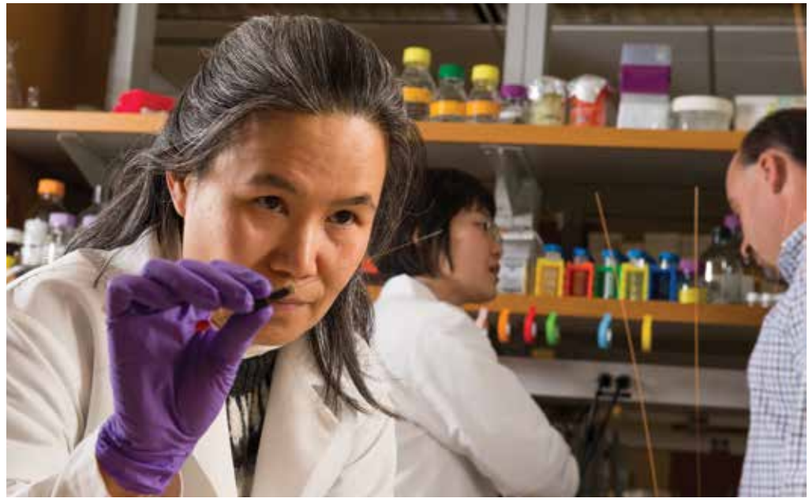
Proteomics is loosely defined as the study of the structure, function, and interaction of all of the proteins in a particular cell or organism

chemistry, biochemistry, computational biology, computer science, and molecular biology. This interdisciplinary design fosters collaboration, which starts with the proteomics team and then radiates out across the Institute and beyond.

"Everything we do is in the context of encouraging people to collaborate with each other and build strong teams around a particular scientific objective," says Washburn. "Our goal is to bring proteomics technologies to bear on important biological problems and stay on top of the technology enough that newer approaches can be introduced to get us there faster."

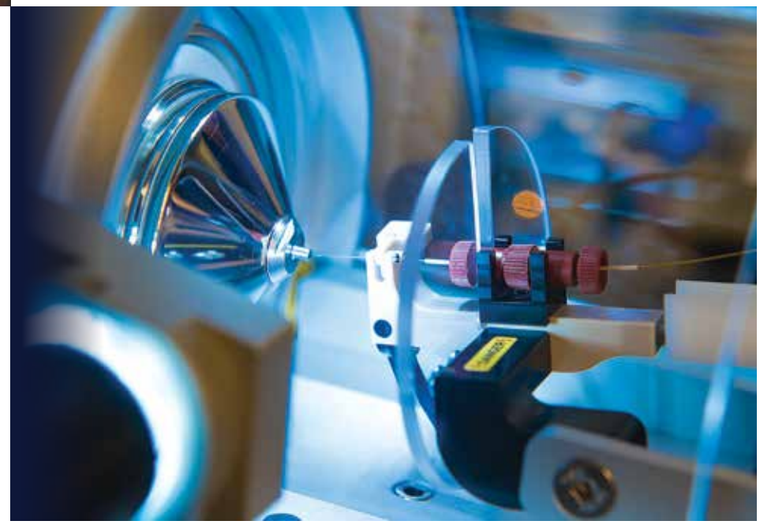
The proteomics pipeline

When Washburn and Florens, who are married, joined the Institute in 2003, the duo brought with them a powerful proteomics tool—called Multidimensional Protein Identification Technology or MudPIT—that gave Stowers investigators a competitive advantage over their peers. Since then, Washburn, Florens, and the proteomics team have used their technical expertise to adapt other technologies and develop new ones to study the levels of proteins and protein-protein interactions.



Most of these proteomics approaches follow the same basic recipe, with a few modifications. First, the researchers stick a tag on their protein of interest so they can extract it after they test a number of biological conditions. For example, they might want to know how the levels and interactions of a protein change in response to a specific anti-cancer drug. They can grow the protein in cells with and without the drug, and then use the tag to pull out the protein, like a magnet picking a needle out of a haystack. This purification step is particularly complicated, but Charles Banks, PhD, a research specialist in the Washburn Lab, has driven efforts to adopt and improve new purification methods that have become integral to the Proteomics Center and other labs at the Institute.

After purification, the scientists carefully break the proteins into fragments called peptides, turn the resulting concoction from a liquid into a gas, and run it through a high-tech piece of equipment called a mass spectrometer, which identifies the fragments based on mass and charge. These instruments are the cornerstone of proteomics experiments and enable researchers to detect, identify, and quantify tiny amounts of peptides.



In an ongoing effort to refine and improve proteomics strategies, Tim Wen, MS, a senior programmer analyst, and Ying Zhang, PhD, a senior proteomics scientist, have worked closely with Washburn and Florens to overcome technical obstacles and develop new capabilities in the Center. In a series of publications in *Analytical Chemistry*, they reported a number of new methods for acquiring, processing, and analyzing data, which make it possible to measure the levels of proteins in a sample more accurately and precisely.

Once each of these experimental steps is complete, a challenge still remains—making sense of all

"Proteomics is all about the power of discovery."

the data. Currently, seventy-three terabytes of data reside on the team's hard drive. That amount is roughly equivalent to the volume of information accessible online through the Library of Congress. Fortunately, the Institute has strong information management support to handle this massive amount of data, and the proteomics team includes expert analysts who can sift through data and present it in a way that enables researchers to generate meaningful insights and—in over 170 cases—highly regarded papers.

While Wen writes and maintains software to assemble large datasets rapidly, Gaye Hattem, a programmer analyst, helps researchers determine the biological pathways and functions of the proteins in the datasets, and Mihaela Sardiu, PhD, a senior proteomics scientist, conceptualizes innovative ways to understand and visualize protein interaction networks.

Discovery-driven research

Since its inception, the Proteomics Center has forged many valuable collaborations with other scientists at the Institute. Florens and Anita Saraf, PhD, a senior proteomics scientist, have worked closely with Associate Investigator Kausik Si, PhD, to study the proteomics of learning and memory in fruit flies. Selene Swanson, MA, a senior research specialist in the Proteomics Center, has collaborated frequently with investigators Joan Conaway, PhD, and Ron Conaway, PhD, to reveal insights about transcription, a key step in the process of constructing proteins from the genetic blueprint. Defective transcription can lead to health problems such as autoimmunity, cardiovascular disease, and cancer. The Conaway Lab has studied many proteins involved in transcription, including thirty individual proteins of a key protein complex called Mediator.

"Without proteomics, this work simply wouldn't be possible," says Joan Conaway. "The Proteomics Center is one of the best things that's happened to us in the last fifteen years."

One of the most frequent visitors to the Proteomics Center is Investigator Jerry Workman, PhD. His research involves histones, the protein spools responsible for wrapping yards of DNA into tight little coils called chromatin. The ability of histones to package DNA is dependent on a number of chemical tags that decorate their surface. The Workman Lab has identified several groups of proteins that are responsible for

modifying histones, either by attaching or removing these chemical tags or through some other means, and many of these proteins have been implicated in cancer.

A basic scientist at heart, Workman was interested in histones and chromatin remodeling long before their links to cancer brought them into the spotlight. But now, he uses proteomics technologies to see how these complexes are working in the cell, in the context of both health and disease.

"Proteomics is all about the power of discovery," says Workman. "There's a feeling in the life sciences that we have to focus on hypothesis-driven research, but with the Stowers Proteomics Center, we can do discovery-driven research. We might have an interesting protein that we think must be interacting with other proteins that are interesting. We don't know what they are, so we don't have a hypothesis, but we can use proteomics to find out. And more often than not, we will uncover interactions that we never could have predicted."

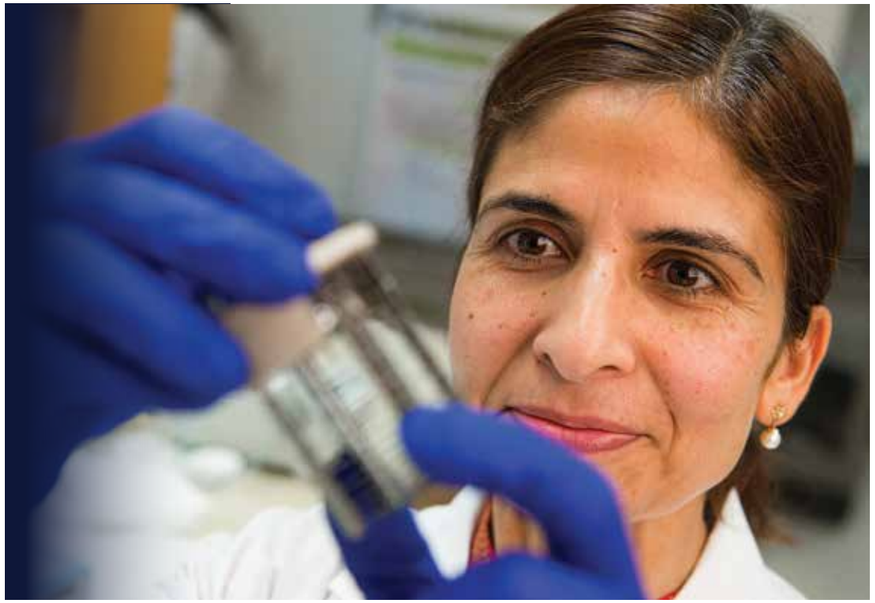
Recently, Workman was surprised to find a series of metabolic enzymes that are also involved in chromatin remodeling. One of these proteins, called pyruvate kinase M2 or PKM2, is overexpressed in human tumors and has been shown to reprogram metabolism in cancer cells. Workman and his colleagues purified the yeast version of the protein and used it to identify a handful of other metabolic enzymes that regulate histone modifications. They plan to use proteomics to characterize each of those proteins and determine how they manage to pull off their dual roles.

Workman's collaboration with the Proteomics Center has paid off in more ways than one. Their joint projects have produced over three dozen publications. One of their most successful projects formed the basis of a National Institutes of Health grant proposal, which was recently funded and will support a new line of research in Washburn's laboratory.

A broader impact

It all started with a conversation between Karen Smith, PhD, a former postdoc in the Workman Lab, and Sardiu in the Proteomics Center. Smith was trying to identify the members of Sin3/HDAC, a protein complex known to pop the acetyl groups off histones in order to silence genes. Histone deacetylases, or HDACs, often repress genes that would normally keep cells from growing out of control, and have become popular targets for cancer therapy. Sardiu, who was helping Smith take her protein inventory, suggested they take the project even further. She devised a way to determine statistically not only what was in the complex, but also how the entire complex was put together.

The researchers used the method to analyze Sin3/HDAC, both alone and in the presence of a histone deacetylase inhibitor called SAHA. This inhibitor is



currently approved for treatment of T-cell lymphoma and is being investigated in clinical trials for use in many other types of cancer, but its mode of action remains a mystery. Smith and Sardiu found that SAHA doesn't simply quench the activity of the histone deacetylase, but actually changes the architecture of the entire complex. Their results were published last year in the journal *Molecular & Cellular Proteomics*.

> "The Proteomics Center is one of the best things that's happened to us in the last fifteen years."

Washburn was recently awarded a five-year, $1.5 million grant from the NIH to expand the project. Together with Banks and Janet Thornton, a senior research technician, he will use proteomics technologies, as well as biochemical, computational, and genomic techniques, to tease apart further the mechanism of action of SAHA. In the end, Washburn hopes the research will yield a better understanding of how the inhibitor works, and perhaps even lead to the development of new HDAC inhibitors.

"We are in a position to ask and answer some questions about this cancer treatment that probably not a lot of people can," says Washburn. "Cancer is such a devastating illness, and seems to affect everyone at one point or another. If we can make a difference, it is certainly worthwhile."

In addition to working with nearly all the laboratories at the Stowers Institute, the Center has forged over a dozen collaborations with scientists around the world. One external collaboration focuses on decoding the malaria histone code and another involves uncovering interactions between the human immunodeficiency virus (HIV) and human immune cells. Both have generated insights into these persistent and deadly infections.

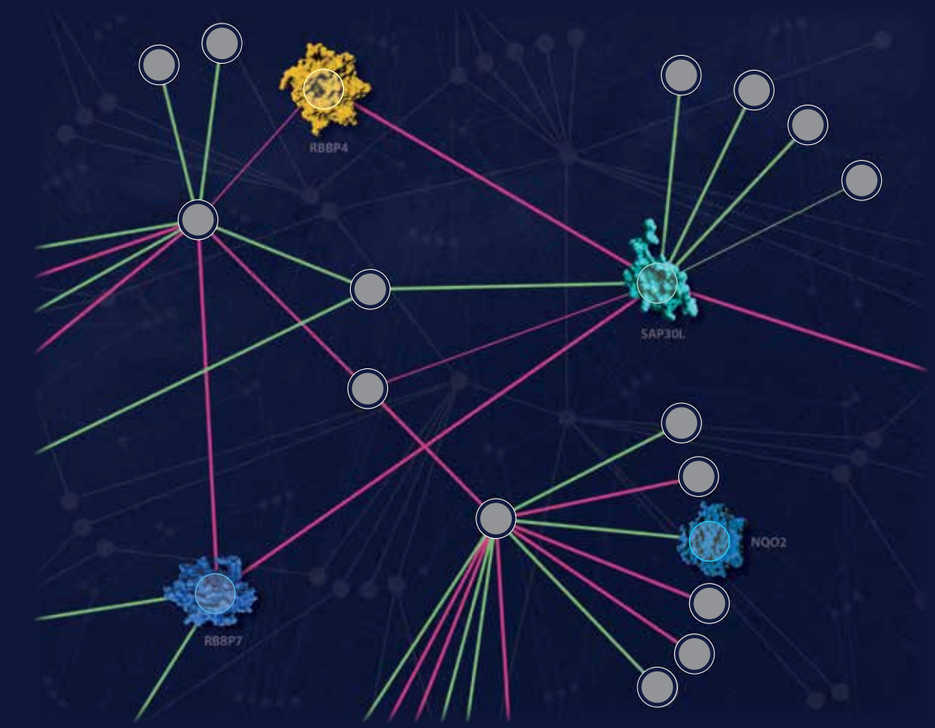
Concerted team efforts are key to advancing the complicated field of proteomics. Through multidisciplinary expertise and teamwork, scientists are gaining a better glimpse into the complicated inner lives of our cells and the proteins that make us tick.

"Proteomics enables us to ask basic questions about how things work and how things interact," says Washburn. "The answers this research generates could be applied to critical human health issues with a level of precision and detail that was never before possible."

See related story on page twenty-three.

BENEFITS OF NETWORKING

Proteomics research generates large amounts of data — how do scientists make sense of it? One way is by using network maps to visualize protein connections based on their physical interactions. Each node in the network represents an individual protein and interacting proteins are linked. Network maps can also show how protein interactions change over time or under different conditions.



The image above shows part of a protein network map from a study involving SAHA, a molecule used to treat certain cancers. The researchers analyzed protein interactions in cells from a human cell line before and after treatment with SAHA. Green links correspond to interactions that increased in abundance after SAHA treatment while magenta links represent interactions that decreased. The thickness of the lines corresponds to the degree of the effect. Structures are shown for some of the proteins in the network map.

How SAHA works against cancer is not completely understood, but studies like this help scientists glimpse changes in the protein network upon treatment. Researchers can get an idea of how widespread a molecule's effects are and may identify proteins in the network to investigate further.

Illustration adapted from Figure 3A of Sardiu ME et al, *Molecular & Cellular Proteomics* 13:3114-3125, 2014.

WEB EXTRA

To explore the shapes and features of some of the network map proteins, please visit our interactive web extra. **www.stowers.org/3D**

By Anissa Anderson Orr

HOW DOES THE NOSE KNOW?

The answer may be more complicated than you think

OF OUR FIVE traditionally recognized senses, we often take our sense of smell for granted.

Sure, we enjoy breathing in the perfume of fresh-cut flowers, and appreciate being able to sniff out a gallon of sour milk. But many people don't truly value this helpful sense until they lose it.

"For humans, losing your sense of smell can be devastating, because you pretty much lose all your sense of taste as well," says Stowers Investigator Ron Yu, PhD. "That's why when you have a severe cold or flu and can't smell, food tastes like cardboard and you often lose your appetite."

Not only is smell linked with taste and appetite—a large part of flavors we taste actually come from our sense of smell—a declining ability to smell is also an early sign of degenerative diseases such as Parkinson's and Alzheimer's. And in the animal world, smell is critical for survival as it helps animals detect food, find mates, and avoid predators.

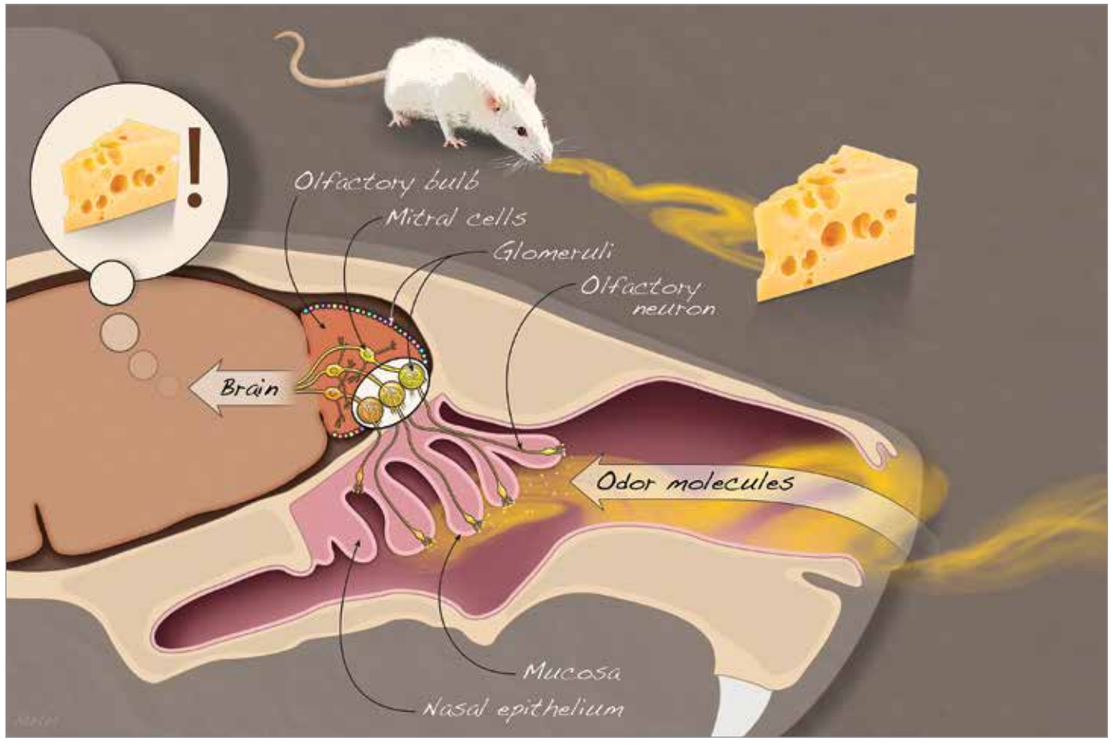
"We feel it's pretty important," explains Yu, whose lab focuses on identifying and mapping out the elaborate neural circuitry and processes involved in sensory systems. In particular, the Yu Lab studies the mouse olfactory system, which detects odors, and the related vomeronasal system, which detects pheromones.

Inside the olfactory system

At first glance, the olfactory system seems pretty straightforward. Odors are detected by proteins called receptors located on sensory neurons in the tissue that lines the inside of the nose. These neurons then pass information through their axons—the long, slender nerve fibers that conduct electrical impulses—on to the brain's olfactory bulb for further processing.

Then it gets more complicated. Humans have nearly 400 odorant receptors, and in mice, there are nearly 1,000. Neurons expressing these receptors are randomly distributed in the olfactory epithelia of the nasal lining, with each neuron expressing a single type of receptor.

From this seemingly disorganized jumble emerges an intricate neural network. Olfactory neurons with the same receptor reach out and connect to the same spot in the brain, called a glomerulus. This convergence forms an olfactory map, and it acts as a kind of a code book for the scents we encounter, helping us decide whether to respond by taking a big, juicy bite of an apple, or running for our lives from a hungry predator.



Glitches in the map's wiring affect how scents are perceived. Yu and his colleagues found that in mice, there's a brief window to fix problems—a window that lasts until about a week after mice are born, they reported in *Science* in 2014.

During that first week of life, the researchers showed that a scrambled olfactory map where neurons no longer converged onto the same glomeruli could be restored to the map's correct wiring. But, if they waited longer than seven days to attempt to restore order, the scrambled map could not be unscrambled.

This was a breakthrough discovery. A critical period was not thought to exist in the olfactory system. Unlike other sensory neurons, such as hair cells in the mammalian inner ear that can't be replaced once damaged, olfactory neurons regenerate and replace themselves throughout the life of an animal, and project their axons all the way to the brain to establish previous connections. Researchers thought that this lifelong regenerative ability of neurons coincided with the ability to re-establish correct connections.

"What this research indicates is that these maps are not maintained by a mechanism throughout the life of an animal," Yu says. "During that first week, whatever map is formed will last a lifetime." In other words, if the map doesn't get unscrambled during the critical period, the neurons are still able to regenerate but they connect to the wrong targets. This errant mapping alters odor perception.

Uncovering the mechanisms at work in olfactory map wiring could hold promise for regenerating and repairing olfactory neurons and neurons in other types of neural systems, such as those involved in spinal cord injury.

A closer look

Yu's research team is also testing how mice respond to scents emitted from a custom-designed device called an olfactometer, which can deliver 200 odors in one experiment. Depending on the scent, the reaction can be quite dramatic, Yu says.

"When the test mice sense predator-associated odors it can cause them to run away or even freeze," Yu says. "They will stop moving and become still for quite a long time—for minutes, sometimes perhaps half an hour, without moving at all."

When the olfactometer is coupled with a powerful microscope, the researchers can actually see what is happening in the mouse's brain as it reacts to the scent, and record how the neurons react to specific odors. Yu's team was among the first to capture these responses by establishing mice that express a genetically encoded sensor. These studies revealed important information about how the olfactory map's glomeruli are organized, and how the brain deciphers the response and creates a complex mental experience associated with different odors.

A product of the lab's collaborative atmosphere, the olfactometer was tweaked to perfection by a succession of lab members.

"The way my lab works is that we focus on a biological problem. Then we'll apply anything that is needed to try to solve it," he says. Yu also routinely utilizes experts from Stowers' core centers including Computational Biology, Molecular Biology, Microscopy, and Proteomics.

Next on his list is a tool that rapidly images the mouse brain, a project supported by a 2015 Neaves Award, which is presented to researchers pursuing innovative, high-risk research projects with the potential for broad impact.

Exploring the mysteries of pheromones

In mammals, the vomeronasal organ, located between the roof of the mouth and the nose, detects pheromones, the chemical signals that stimulate inborn social responses such as mating or attacking a threatening competitor. While humans don't have a functional vomeronasal system, the mechanisms that control our inborn behavior are similar to other mammals.

Yu and his team have identified two classes of pheromone receptors crucial for the mating process in mice, a landmark finding they reported in *eLife* in 2014. That study provides an important glimpse into the circuitry of the vomeronasal system, a sensory system just as complicated as the olfactory system.

"We are only scratching the surface at this moment," Yu says. "There are more than 300 receptors in the vomeronasal system, and we don't have a clue about most other receptors' function yet. We can identify many different pheromones and how they relate to specific behaviors."

Yu aims to trace the brain circuitry that passes sensory information from the vomeronasal organ all the way to behavior centers in the brain—from the moment a mouse first sniffs a pheromone to when it exhibits courtship responses.

Detailing the neural circuitry of both vomeronasal and olfactory systems is a monumental undertaking, but one Yu is well-equipped to pursue with backing from two National Institutes of Health RO1 grants and continuous support from the Stowers Institute.

"I've been very fortunate to have talented people working with me in the lab, and collaborating with experts in Stowers core centers," Yu says. "With the support researchers get from the Institute, we are free to explore a lot of ideas and conduct experiments in new territories without constantly worrying about funding. We are able to push our research forward in ways we hadn't previously imagined."

By Cathy Yarbrough

A DISCUSSION WITH

JOAN CONAWAY, PHD

When Joan Weliky Conaway, PhD, was a child growing up in Pittsburgh, she often accompanied her father, a scientist, to his lab on Saturday mornings. "I pretended to conduct experiments while my dad was busy with his work," she said. "Scientific labs became a very comfortable and familiar place for me."

Today Conaway is a Stowers investigator and member of one of science's most accomplished research teams, "The Conaways." The research of Conaway and her husband Ron Conaway, PhD, also a Stowers investigator, has advanced scientific knowledge about many of the mechanisms that underlie gene transcription. During this complicated biological process, a gene's DNA instructions for a specific protein are transcribed into a format (messenger RNA, or mRNA) that can be "read" by the cell's protein manufacturing machinery. In addition to revealing how gene transcription occurs at the molecular level, the Conaways' research has highlighted some of the steps in the process that may play a role in cancer and other diseases.

Gene transcription was a "black box" when Conaway graduated from Bryn Mawr College in 1979 with a bachelor's degree in chemistry and biology. She subsequently joined the lab of Roger Kornberg, PhD, at Stanford University as a graduate student. At the time, her future husband was conducting graduate studies in another lab at the university.

Kornberg, who would receive the 2006 Nobel Prize in Chemistry for his pioneering studies on gene transcription, encouraged the two talented young scientists to join forces to work to tackle a scientific mystery: the identity of the molecular factors that signal the RNA polymerase II to catalyze the transcription process.

Conaway, who was awarded a PhD in cell biology at Stanford, conducted her postdoctoral studies at the DNAX Research Institute in Palo Alto, California. Before joining the Stowers Institute in 2001, the Conaways were faculty members at the Oklahoma Medical Research Foundation. In 1997, they were honored with the American Society for Biochemistry and Molecular Biology/ Amgen Award and five years later were elected to the American Academy of Arts and Sciences.

In addition to her position as an investigator, Conaway holds the Helen Nelson Distinguished Chair at the Institute and is a professor in the Department of Biochemistry and Molecular Biology at the University of Kansas School of Medicine.

DID YOUR PARENTS PLAY A ROLE IN YOUR DECISION TO BECOME A SCIENTIST?

They had a big influence. I was born when my parents were both in graduate school. Although my mother stopped being an active researcher so that she could be a stay-at-home mom, she certainly talked about science as one of those fields that I might want to consider.

DID YOU DECIDE TO BECOME A SCIENTIST WHEN YOU WERE A CHILD PRETENDING TO CONDUCT EXPERIMENTS IN YOUR DAD'S LAB?

I made that decision in college. When I was in high school, I became interested in other subjects. So when I arrived as a freshman at Bryn Mawr, I was unsure whether I would major in political science or biomedical science. During the summer after my freshman year, I worked in a pharmaceutical company immunology lab and saw the connections between what I had been learning about cells in the classroom and what happens in real cells in the lab. That's when I decided to become a scientist.

DID YOU AND RON EVER WORK INDEPENDENTLY OF EACH OTHER AFTER YOU BOTH HAD EARNED PHD DEGREES?

Early in our careers when Ron was a postdoctoral researcher and I was a graduate student and subsequently when we were both postdocs, we spent long hours in the lab. We found that we enjoyed conducting research together. And, because we have different strengths, Ron and I realized that we complemented each other's skills.

Several successful senior female scientists told me that if I continued to work with Ron, my career would be subsumed under his. That did not happen.

WHY?

Ron's attitude was that the work that we did together was a team effort, and both the responsibility and credit should be shared by us independent of our formal positions. We took turns on being senior author when we published scientific papers.

Another reason that our relationship works so well is that we don't compete with one other. We take pleasure in each other's success. But, that's how it should be with any group of colleagues. Scientific collaborations are more effective when researchers who work together don't compete with each other but celebrate their colleagues' successes.

WHAT DO YOU SAY TO STUDENTS WHO ASK YOUR ADVICE ABOUT WHETHER THEY SHOULD BECOME A SCIENTIST?

Being a scientist is hard work but can be an incredibly rewarding and fun career for individuals who have a passion for science, enjoy thinking about how to solve problems, are curious, have a stick-to-itiveness, and are willing to fail once in a while. When you take a creative approach to solving scientific problems, sometimes it doesn't work out. But when it does, it's very exciting.

HOW DO YOU RELAX?

Soon after moving to Kansas City, Ron and I discovered the great pleasure of the local jazz community here. We enjoy hearing live music in small settings, eating out in restaurants, and just being at home.

WHY DID YOU AND RON JOIN THE STOWERS INSTITUTE?

Soon after the Institute opened, we visited and were very impressed. We found that the Institute's facilities were beautiful, but more important to us was the vision for the Institute. Before our visit, we were not that serious about joining. But after talking with Bill Neaves who was then president and CEO, Robb Krumlauf who is scientific director, and Jim and Virginia Stowers, the Institute's co-founders, Ron and I wanted to come here.

And we're so glad that we did. Everything has turned out better than we could have imagined. The Institute has made an enormous investment in technology and has recruited spectacular researchers with whom we enjoy collaborating. We could not have accomplished what we have if not for our colleagues here. However, I must say that throughout our career, wherever we've been, we've had the opportunity to work with terrific people. We've been very lucky.

WHY DOES TRANSCRIPTION STILL FASCINATE YOU?

When Ron and I began studying it thirty years ago, transcription was a "black box." In principle, the copying of a gene's DNA into mRNA should be a simple process, but it's not. Our lab and scientists at other institutions have shown that almost forty individual proteins are needed just to initiate transcription. And beyond that, there are many additional proteins involved in regulating how much RNA is made during transcription. It's quite remarkable.

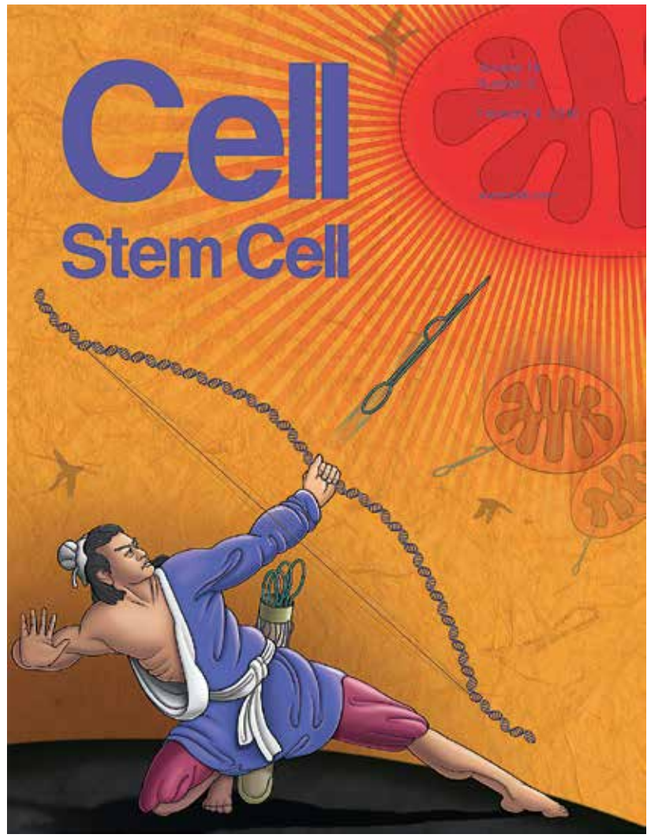
The Conaways enjoying an evening at one of their favorite local restaurants, Julian.

HOW A GENETIC LOCUS PROTECTS ADULT BLOOD-FORMING STEM CELLS

Hematopoietic, or blood-forming, stems cells are essential to the healthy functioning of the human body.

These cells renew themselves and differentiate into other cells, including white blood cells, red blood cells, and platelets, and constantly renew the body's blood supply.

The creation of new blood cells in the body requires a delicate metabolic balance that is not well understood. Investigator Linheng Li, PhD, and colleagues found that a particular location in DNA, called the Dlk1-Gtl2 locus, plays a critical role in protecting hematopoietic cells by restricting metabolic activity in the cells' mitochondria. This discovery suggests that Gtl2 may be useful clinically as a biomarker to determine if cells are normal or potentially cancerous. The locus's tumor suppression qualities also may lead to future treatments targeting cancer.



This research was published in *Cell Stem Cell* in February 2016.

The journal *Cell Stem Cell* that published the research results also featured cover art conceived and designed by Li, Postdoctoral Research Associate Pengxu Qian, PhD, and Scientific Illustrator Mark M. Miller. The cover illustration depicts a parallel between a story from Chinese mythology and the researchers' findings.

The Chinese myth holds that ten suns once flooded the earth with excessive energy, causing crops to shrivel, rivers to dry, and life to collapse. Houyi, the god of archery, shot down all but one of these suns, restoring energy balance and allowing life to flourish.

As represented in the illustration, the imprinted Dlk1-Gtl2 locus (Houyi with bow) protects and preserves hematopoietic stem cells (earth) from apoptosis by expressing multiple miRNAs (arrows) to suppress excessive reactive oxygen species production, a byproduct of energy (heat) generation from mitochondria (suns).

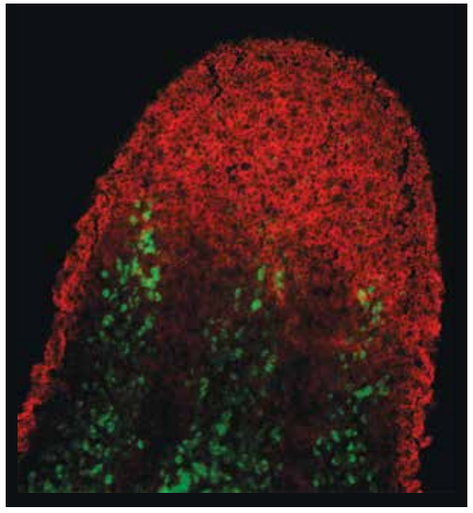
THE WORM HAS TURNED

New research uncovers processes driving planarian stem cell differentiation in living tissues.

Planaria are tiny (about the size of a toenail clipping) aquatic flatworms, most often found in standing water. Though humble in size and appearance, they are one of nature's wonders. Planaria have the ability to regenerate from a small scrap of tissue, and have an abundance of adult stem cells, called neoblasts, that can specialize, or differentiate, into other cell types. Two studies from the Sánchez Alvarado Lab shed light on some of the intricate processes at work when planarian neoblasts differentiate into skin cells.

In one study, the researchers identified how the enzyme MLL1/2 affects the development of planarian cilia, the microscopic, hairlike structures on the organism's skin that help it swim. Without the enzyme, planaria lose their cilia and stop swimming. The discovery suggests that defects in the process of building cilia may begin earlier than thought, a finding that has potential implications for the detection of a broad range of human health conditions.

The other study found that a gene called egr-5 is important and plays a key role in helping neoblasts differentiate into skin cells. When the activity of egr-5 was reduced, it blocked neoblast daughter cells from differentiating properly, and they did not make mature skin cells. The findings uncover the critical role of egr-5 in the development of skin cells, and illustrate the complexity of this seemingly simple organism.



These studies were published respectively in the December 2015 online issue of *Cell Reports* and the October 2015 issue of the online journal *eLife*.

USING A MOUSE MODEL TO STUDY CRANIOFACIAL DEVELOPMENT

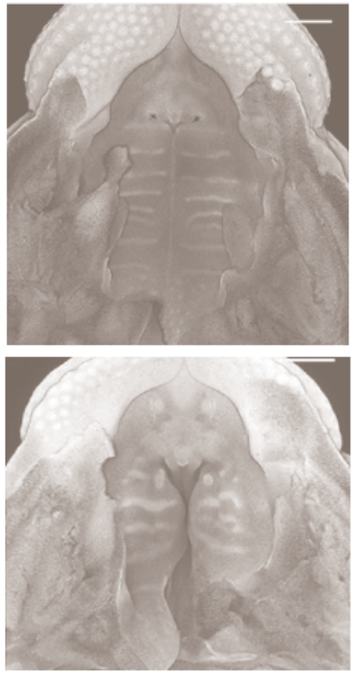
Researchers from the laboratory of Paul Trainor, PhD, have found a way to use mice to study high-arched palate, a disorder in which the roof of the mouth is oddly high and steep.

The mice mimic Treacher Collins syndrome (TCS) in humans, of which high-arched palate is a feature. To help move this research forward, scientists needed to come up with a consistent, measurement-based definition of high-arched palate, one they could use across all mouse models.

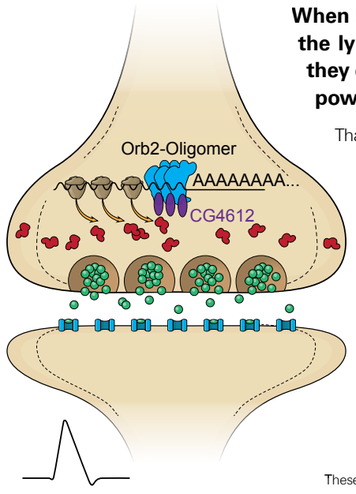
Trainor and his collaborators used a 3-D imaging technique to measure the palates of the offspring to see which of their attributes—palate shelf length, shelf width, arch height, or arch angle—were significantly different. They found that TCS mice had much higher arched palates, in terms of shelf height and angle, than the normal mice.

Recent related work from the Trainor Lab and their collaborators showed that TCS mice born to mothers who had received antioxidant supplements exhibited fewer craniofacial abnormalities than control group mice. This observation suggests that a dietary supplementation approach may provide a way to protect against TCS.

This work was published in recent issues of *Nature Communications* and *Developmental Biology*.



POTENTIAL BIOCHEMICAL MECHANISM UNDERLYING LONG-TERM MEMORIES IDENTIFIED



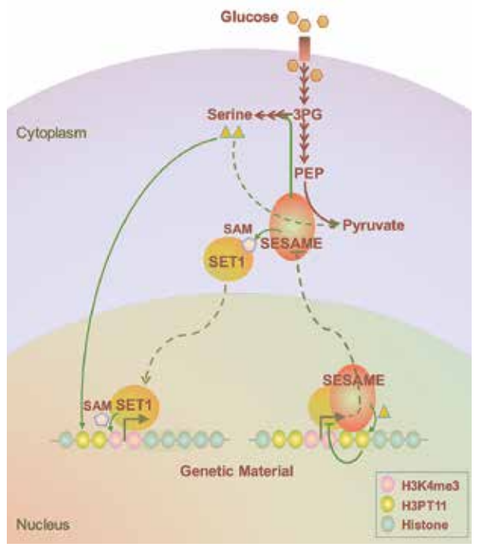
When Dean Martin and other crooners in the 1950s and 1960s sang the lyrics to the then popular song, "Memories Are Made of This," they described the types of romantic experiences that can generate powerful, long-lasting memories.

Thanks to the research of Associate Investigator Kausik Si, PhD, and other scientists, we now know more about how these powerful memories are created and maintained in the brain. An individual's experiences—a major source of memories—induce changes in brain cells and in the synapses, or junctions that separate the cells. Thus, even a transient experience is capable of producing an enduring physical change in the brain.

Si and his team recently discovered a possible biochemical mechanism by which the specialized brain cells known as neurons create and maintain memories that endure and do not fade away. Using a fruit fly model system, they found that the synaptic connections where memories are stored are kept strong by the transformation of the Orb2 protein from one physical state to another. The transformation changes Orb2's function so that it solidifies and strengthens the memory connections in the brain.

These research findings were reported in the December 2015 issue of the journal *Cell*.

PROTEIN COMPLEX LINKS CELLULAR METABOLISM TO GENE EXPRESSION



Researchers in the Workman Lab have found a new link between a cell's basic life functions and its genetic operations.

The connection involves a protein complex named SESAME, which uses enzymes responsible for glycolysis to activate proteins that regulate genetic material. Glycolysis is the first stage of cellular metabolism, the chain of biochemical reactions by which cells break down food, build proteins and amino acids, and produce energy.

"It has been suggested that chromatin regulation and gene expression might link to cellular metabolism," says Tamaki Suganuma, PhD, a Stowers research scientist who directed the study. "However, SESAME is the first example of a protein complex that directly regulates cellular metabolism and chromatin modification by utilizing its own enzyme subunits."

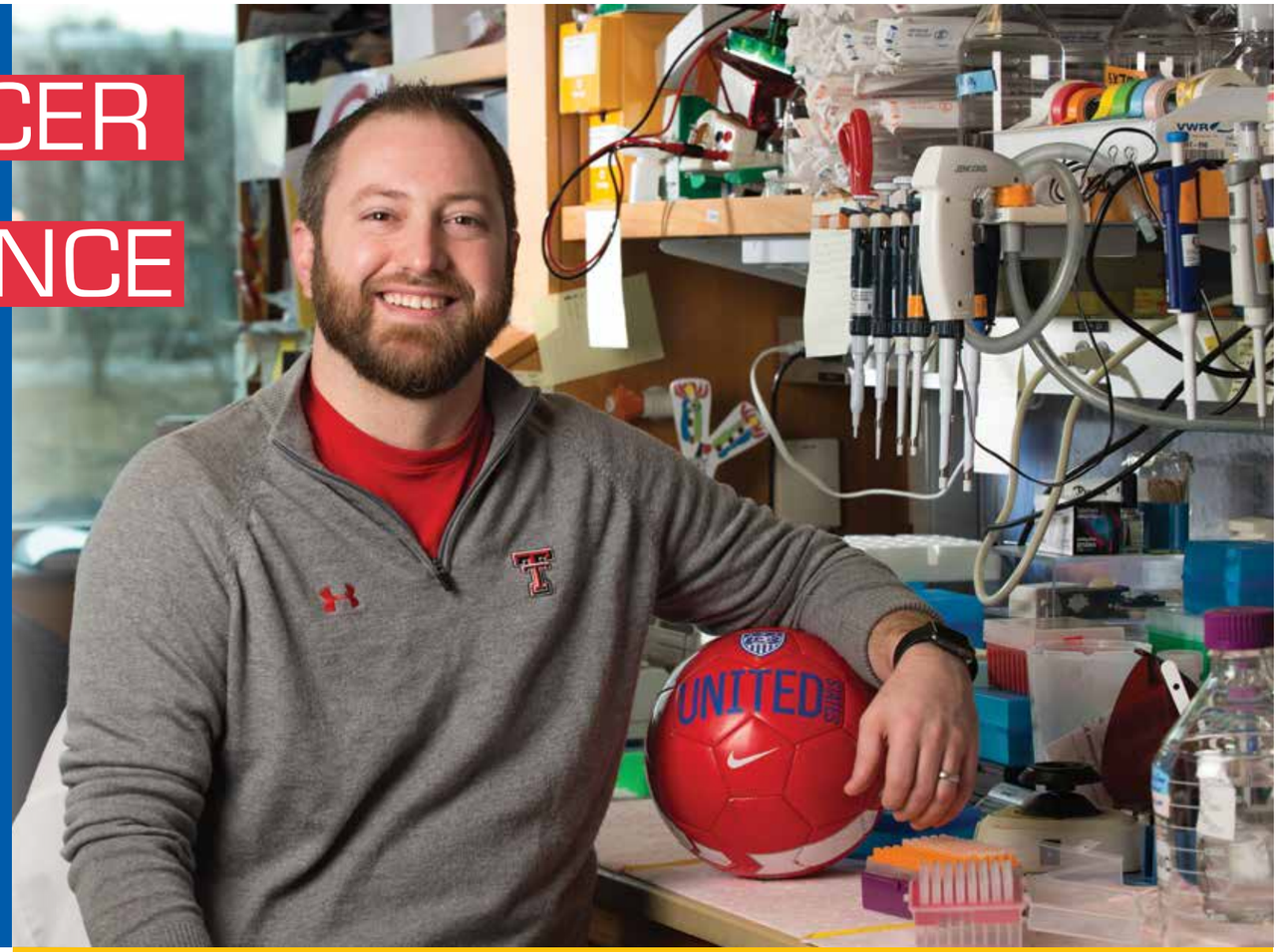
Although their research involved yeast, the authors say the link may hold true in humans. If a SESAME equivalent in humans is found, it could offer insight to enable novel approaches for cancer risk prediction and treatment.

The study was published in October 2015 in the journal *Molecular Cell*.

By Anissa Anderson Orr

FROM SOCCER TO SCIENCE

As a sports nut growing up in Lubbock, Texas, Juston Weems clearly remembers the hassle of being a kid with asthma. Wheezing and out of breath, he often pondered the condition when sidelined from a soccer game.



"By the time my mom would get me to the doctor, the worst of it was already over," Weems says. "They had me run on a treadmill so they could actually see the symptoms and signs. I went in quite frequently."

His early struggles with asthma sparked scores of questions he hoped to answer with a career in medicine, but once in college, scientific research had a stronger pull on him. Now he works as a postdoc in the lab of Stowers Investigators Joan Conaway, PhD, and Ron Conaway, PhD, and has recently published a major scientific paper based on his research at the Institute.

But before the test tubes, petri dishes, and microscopes, there was soccer. Weems loved the sport and stuck with it throughout high school and into college. His commitment earned him a soccer scholarship to Oklahoma City University and entry into the lab of diabetes researcher Ann Louise Olson, PhD, at the University of Oklahoma Health Sciences Center, where a fellow soccer player leaving his position as a lab tech encouraged Weems to take his place.

"While I was there, I got a firsthand look at what research in biology and biochemistry actually looked like," Weems says. "I just absolutely loved it and really felt like I wanted to be on the discovery side of things as opposed to the diagnosing and treating side. It's really what helped me make the switch (from medicine), and that's actually the lab where I completed by PhD."

Weems spent the next several years investigating the glucose metabolism of type 2 diabetes, and, along the way, uncovered a novel role for the histone deacetylase HDAC5, one of the enzymes responsible for controlling the expression of the glucose transporter GLUT4.

"Figuring out what's going on when a normal cell expresses GLUT4 helps us better understand what goes wrong in the diabetic, when the insulin-resistant cell is not expressing it," Weems says. "Ultimately we believe our discovery will lead to breakthroughs and actual therapeutic targets."

As he neared the completion of his PhD in 2010, Olson introduced him to Stowers Investigators Ron and Joan Conaway, who were in town for a lecture. An invitation to interview for a Stowers postdoc position followed, and Weems was won over by the facilities, research mission, and unwavering support of its scientists.

"It seemed like the Stowers Institute was the best possible place to get the most research done, and where I could make the most impact," he says.

At the Institute, Research Advisors Brian Slaughter, PhD, and Jay Unruh, PhD, gave Weems a crash course in microscopy to help him master the intensive imaging work the Conaway lab's research required. Weems began investigating elongin A, a molecule that aids in the speed of transcription, the first step in gene expression.

He tracked the formation of a protein complex called elongin A ubiquitin ligase by fluorescently tagging its proteins. He and his colleagues found that when cells were under stress, the complex rapidly accumulated and halted the transcription process—breakthrough results published last June in the *Journal of Biological Chemistry*.

Building on the elongin study, Weems is investigating whether ligase assembles not only during times of stress, but also when large changes in gene activation occur. Understanding the mechanisms at work could provide insight into human diseases such as cancer, where transcription errors may contribute to deadly cell mutations.

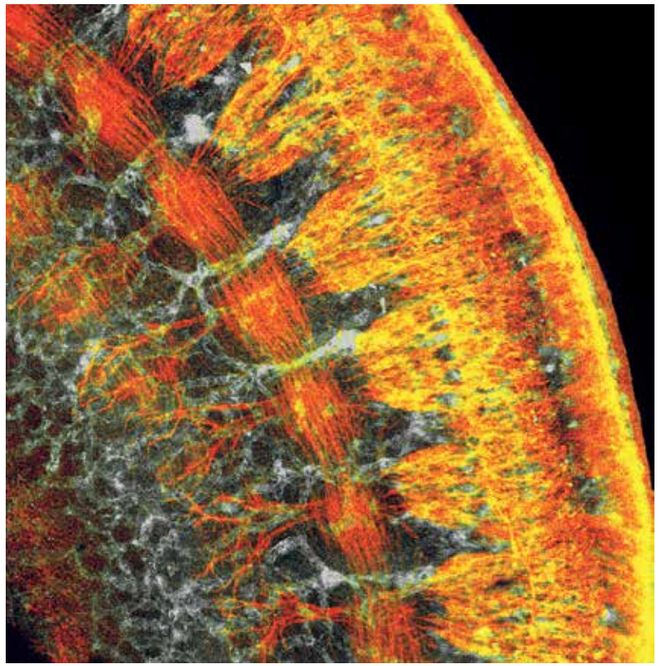
Currently, Weems is sidelined once again from soccer, this time the result of a benign tumor on his femur. Now when he's not in the lab, Weems plays golf, takes his cocker spaniels Skyler and Sophie on walks, and hangs out with his wife, Lauren, a research technician in the Stowers screening facility. Before coming to the Institute, they had worked in the same lab where Weems completed his PhD.

"We drive in every day about the same time. We eat lunch together most of the time if we can, and then we leave roughly at the same time depending on how our days go. And she's not tired of me yet," jokes Weems.

As his postdoc winds to a close, Weems is planning his next step—ideally a faculty position at an academic institution that will allow him to continue pursuing the elongin project. He appreciates the support and training he's found at the Institute, and in the Conaway Lab.

"As a postdoc, you're almost like an independent contractor," Weems says. "My mentors helped me branch out to where I can work within their general research scope, but also push the science out further in certain places. It's a great experience."

BIOLOGICAL ART BURSTING WITH COLOR



Science imagery is having a heyday. It is no longer just instructional material found in school textbooks, but is showing up in places like airports, art museums, and breweries as artwork. And some of the work of Stowers scientists is among the most stunning bioart on display.

Recently, Trainor Lab Postdoctoral Researcher Shachi Bhatt submitted a scientific image that she had produced in her research of neural, vascular, and craniofacial development to an image competition sponsored by the Federation of American Societies for Experimental Biology (FASEB). Her image was one of eleven images and two videos selected from a multitude of entries as winners of the fourth annual BioArt competition.

Bhatt's image, along with other winning images, will be on display throughout the next year at the National Institutes of Health Visitor Center in Bethesda, Maryland.

Bhatt's winning image illuminates blood vessels and nerve cells of the trunk region of a developing mouse. Her research focuses on the pathways of these nerves and blood vessels, and how they follow similar routes in early development. The blood vessels are highlighted in gray, the nerve cells in red, and where they appear in yellow is where they overlap one another.

The image was captured on a confocal microscope in the Microscopy Center at the Institute. Bhatt explains that imaging normal neural and vasculature development provides a critical foundation to further understand how these processes may go awry resulting in birth defects and other diseases, and can provide a basis for therapeutic interference.

WASHBURN SCORES GRANT TO ADVANCE UNDERSTANDING OF CANCER THERAPY

Director of the Proteomics Center Michael Washburn, PhD, has been awarded a $ 1.5 million multiyear competitive grant by the National Institute of General Medical Sciences (NIGMS) of the National Institutes of Health (NIH). Washburn was awarded the grant to further explore the mechanism of action of suberoylanilide hydroxamic acid (SAHA). This molecule inhibits enzymes called histone deacetylases (HDACs), which have been directly linked to cancer. SAHA is used in the treatment of certain lymphomas and is being evaluated in clinical trials for other cancers.

Specifically, SAHA inhibits the catalytic activity of HDAC enzymes. Inhibition of HDAC activity results in changes to gene expression that can block cell growth and increase cell death. Recent research suggests that SAHA has additional, noncatalytic effects that involve the HDAC protein network more broadly, thus suggesting other possible mechanisms of action. Washburn and his team hope to gain a deeper understanding of how SAHA achieves its pharmacological effects and provide a framework for the development of more specific and effective HDAC inhibitor therapies.

Washburn insists that this grant was possible only because of the quality of collaborative work at the Institute. Previous HDAC inhibitor studies by Stowers colleagues contributed to the breadth of knowledge that underlies his hypothesis that SAHA induces a dynamic rearrangement of an entire protein interaction network that plays a key role in how SAHA produces its pharmacological effects.

"We have collaborated with Jerry Workman, PhD, and his team for many years, and this project is the direct result of an excellent collaboration between Mihaela Sardiu, PhD in the Proteomics Center and Karen Smith, PhD formerly in the Workman group. Without Mihaela and Karen's efforts, this grant would not have been possible."

MUNOZ AWARDED FELLOWSHIP

The American Association of Anatomists has awarded Trainor Lab Postdoc William Munoz, PhD, a one-year, $20,000 fellowship grant to further his exploration of the timing of neural crest cell specification.

Neural crest cells are a vertebrate cell population that gives rise to a variety of other cell types and tissues. Defects that occur during neural crest cell formation, migration, or maturation can result in a variety of birth defects called neurocristopathies.

Previously, scientists thought that in mouse models the formation of neural crest cells occurred at about eight and a half days into development. Recently, Munoz has found that this formation can occur as much as two days earlier. Munoz hopes to identify the timing of neural crest cell development more precisely and learn more about the underlying mechanisms.

Specifically, Munoz will focus on the nuclear receptor called germ cell nuclear factor *(Gcnf),* which is essential for neural crest cell formation in mammals. He will investigate the gene and protein networks that are regulated by *Gcnf*. He hopes his research will provide new insight on this step of vertebrate development and the possible causes of congenital neurocristopathies.

BEYOND THE BENCH

Last fall, nearly 100 Stowers researchers attended a full day of presentations about a topic almost as important as their science—writing successful grant applications.

Most of the attendees at the "Write Winning Grant Proposals" workshop were predoctoral or postdoctoral researchers. "The Institute actively supports the professional development of trainees," explains Michelle Lewallen, PhD, grants information manager. "Our trainees will be with us for only a few years. When they take their next career step, many of them will have to compete for research funding. We want them to know how to write a successful grant application."

The Institute encourages postdocs to apply for fellowships in order to gain valuable grant writing experience with the benefit of having a mentor to provide guidance. In addition, obtaining a competitive fellowship award is a mark of distinction and an important step toward independence for young scientists.

The Stowers Institute is one of a few scientific institutions that uses its endowment as primary support for its research programs. However, faculty members are free to apply for external funding if they wish to expand their research programs beyond the support provided by the Institute. Thus, Lewallen was not surprised that several investigators attended the workshop.

Stowers researchers who attended the workshop applauded the presentations and the speaker, David Morrison, PhD. "I found the workshop very helpful, particularly since I am in the process of writing my first grants," says Assistant Investigator Nicolas Rohner, PhD. "The presentations specifically addressed every step in the process and highlighted the 'do's and don'ts' with many distinct and detailed examples."

Postdoctoral Researcher Stacey Hanlon, PhD, reveals that the workshop "gave me insight on how to structure a grant as well as submit it to the funding agency to maximize its chance of success."

"The instruction provided in the presentations and the information in the handouts and workbook are invaluable," Hanlon adds. "I will be able to immediately use what I learned for my postdoctoral grant submissions. My career goal is to become a research professor. To support a lab, I will likely need to write grants several times a year."

By supporting the professional development of its scientists, the Stowers Institute is helping to develop the next generation of successful scientists—an investment with long-lasting and far-reaching benefits.

CORE CENTERS KEEP THEIR SIGHTS ON THE FUTURE

Philip E. Hockberger, PhD, had a lot to say about the Stowers Institute when he returned to Evanston, Illinois, after attending the Midwest Association of Core Directors (MWACD)'s sixth annual meeting in Kansas City.

"I've been telling everyone at Northwestern about the Stowers core facilities, which do their jobs exceptionally well," says Hockberger, executive director of research facilities at Northwestern University. A co-founder of MWACD, Hockberger was one of over 100 core facility leaders from about two dozen research institutions who attended the organization's annual meeting last October.

Organizations such as MWACD help bring together core facility leaders, managers, and staff from different institutions to discuss the latest research methods and instrumentation, share insight about operational matters, and establish networks and interest groups. A number of Stowers core facility members participate in these organizations through conferences, study groups, discussion forums, and collaborative projects.

Another attendee at the MWACD meeting was Paula B. Turpen, PhD, director of research resources at the University of Nebraska Medical Center in Omaha. "I was most impressed with the high level of education and training as well as the expertise of the leaders and staff of Stowers core facilities," she says.

In addition to tours of Stowers core facilities, the three-day meeting featured plenary talks and discussions on topics ranging from new technologies to facility management, says Karen Staehling, PhD, head of the Institute's molecular biology core and MWACD's president and co-founder.

"Because the meeting was held in Kansas City," Staehling explains, "our core facility staff had an opportunity to showcase the collaborative environment at the Institute. Faculty and core center staff work together in highly collaborative ways that may not be as readily achievable at other research universities and institutes." Stowers faculty regard members of the Institute's core facilities as their technology partners, Staehling explains.

Scott Hawley, PhD, a Stowers investigator who collaborates heavily with the core facilities and often includes core facility staff as co-authors of his lab's papers, spoke about his groundbreaking research on meiosis, which is a type of cell division, at the MWACD annual meeting. Hawley "showed convincingly how Stowers core facilities were instrumental in helping him discover new elements in the meiotic process," Hockberger says.

"I was most impressed with the high level of education and training as well as the expertise of the leaders and staff of Stowers core facilities."

Because the core centers are funded by the Institute, core leaders and managers do not have to devote a lot of their time on cost recovery—billing faculty for services in order to obtain funds to cover core salaries and other expenses.

Andrew Box, laboratory manager of the Cytometry Facility, says, "Instead we can focus on finding the technology solutions that will generate the type and quality of data that Stowers scientists need."

In addition to providing routine services, core center members often modify existing equipment to accommodate specific research needs. "And, we occasionally have the opportunity to custom-design technologies," Box adds. One example involved custom-designing and using a 3-D printer to manufacture small parts and adapters that allow researchers to do cell sorting into nonstandard tubes and containers. The Stowers cytometry team has also custom-designed fluidics and sorting nozzle assemblies that can be autoclaved for use with sterile cell sorting work.

During her tour of the Stowers core centers, Chris Wright, PhD, assistant director of DNA services at the University of Illinois at Urbana-Champaign, noted the "many custom-built robotics used throughout the Institute to meet laboratory needs." She also noted that the core facilities are stocked with the latest equipment and experts who know how to use it. "I've had the opportunity to visit core centers throughout industry and university settings. Stowers core centers are anything but normal," Wright says.

2005-2015 10 YEAR RECOGNITION

In January, twenty-five individuals were honored for reaching a milestone ten years of service to the Institute.

Front row, left to right: Jay Casillas, Jennifer Tuttle, Jennifer Gardner, Mark Hembree, Sarah Smith. Second row: Erin Hamilton, Lacey Ellington, Mihaela Sardiu, Brandy Lewis, Madelaine Gogol, Karen Staehling. Third row: Richard Kupronis, Kausik Si, Brian Slaughter, Ron Yu, Sharon Beckham, Dan Bradford. Back row-David Jewell, Rodney McKay, Limei Ma, Michael Durnin, Christof Nolte, William McDowell, Judy Foye. Not pictured: Sue Jaspersen.

Investing in tomorrow's cures: THE HOPE SHARES® ENDOWMENT

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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.

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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. Hope Shares donors receive updates on the progress our researchers have made.

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®.

LIFETIME CONTRIBUTIONS

The information listed below represents contributions from, in memory of, or in honor of the following as of December 31, 2015.

$10 Million+

Pamela Stowers

$1 Million+

American Century Investments Foundation

William Neaves for the "Priscilla Wood Neaves Endowed Chair in Biomedical Sciences"

Helen Nelson Medical Research Fund for the "Helen Nelson Distinguished Chair"

Pamela Stowers in Memory of Laura S Stowers

$500,000+

Dunn Family Foundation

Barnett and Shirley Helzberg, *including*
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Margaret Lichtenauer Estate

Frederick and Mary McCoy

$100,000+

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In Memory of Mary T and Andrew T Goodyear

Richard and Jeanette Brown, *including*
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Fowler Family Fund II

Frederick and Louise Hartwig Family Fund

Felix and Helen Juda Foundation

Tom and Nancy Juda Foundation

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In Memory of Steve Sturgeon

Jonathan and Cyndi Thomas, *including*
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David and Wendy Welte, *including*
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Hank Young (*Gameface* book proceeds)

$50,000+

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John and Shirley Wagner

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In Memory of Virginia Wimberly

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In Memory of Wendell and Irene Smith
In Memory of James E Stowers Jr.

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Richard and Jeanette Brown for the "James Stowers Memorial Lecture Fund"

David Chao and Julia Zeitlinger for the "James Stowers Memorial Lecture Fund"

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Roger Hanaway in Memory of Gloria Hanaway

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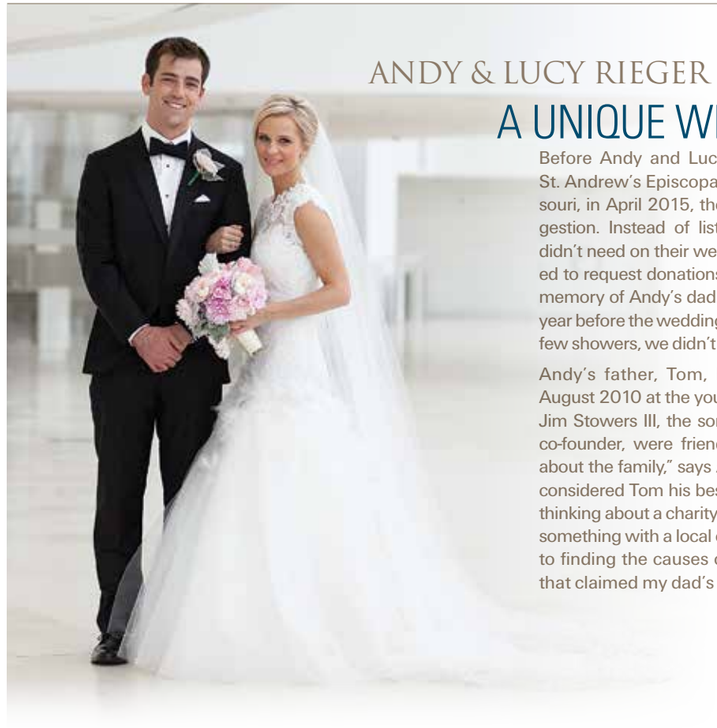

ANDY & LUCY RIEGER

A UNIQUE WEDDING GIFT

Before Andy and Lucy Rieger were married at St. Andrew's Episcopal Church, Kansas City, Missouri, in April 2015, they had an unusual gift suggestion. Instead of listing household items they didn't need on their wedding registries, they decided to request donations to the Stowers Institute in memory of Andy's dad. "We'd bought our house a year before the wedding," says Lucy, 27, "and after a few showers, we didn't really need much else."

Andy's father, Tom, had died from cancer in August 2010 at the young age of 55. "My dad and Jim Stowers III, the son of the Stowers Institute's co-founder, were friends, so I grew up knowing about the family," says Andy who, as an only child, considered Tom his best friend. "When we started thinking about a charity gift, it seemed natural to do something with a local connection that's dedicated to finding the causes of diseases like the cancer that claimed my dad's life."

Andy, 28, had grown up in Kansas City, but met Lucy in Dallas where he was working as an investment banker after graduating from Southern Methodist University. On a trip home, Andy called on Ryan Maybee, owner of the speakeasy-style bar Manifesto and the newly opened Rieger Hotel Grill & Exchange in the historic Rieger Hotel. "My family hadn't owned the hotel in years, but my dad had suggested I offer some family memorabilia," says Andy. "This guy started talking to me about relaunching the Rieger Distillery, which didn't interest me at all. But I started helping him with various things and before we knew it, we were business partners."

The distillery was originally conceived by Andy's great-great-great grandfather, Jacob Rieger, in 1887. His son Alexander Rieger took over the distillery in 1900 and built the hotel in 1915 to capitalize on passengers arriving in the newly opened Union Station who might be thirsty for one of Rieger's beverages. Only four years later, however, both Rieger businesses closed because of Prohibition and Alexander went on to found a Kansas City bank.

Newly reopened in 2014, the distillery J. Rieger & Co., located in Kansas City's East Bottoms, now crafts whiskey, vodka, and gin. Through the distillery's involvement with fundraisers, Andy and Lucy, a University of Missouri communications grad who works in AMC Theatres' corporate headquarters, have grown much more aware of charitable giving.

Establishing a means for their wedding guests to donate to the Institute was relatively simple. The Riegers set up an account with an online fundraising site for charitable and personal causes, and received a notification every time one of their 200 guests contributed. "Our guests loved it," says Andy. "Some of my dad's friends even cried when they heard about it. Our friends were a little more hesitant. They still wanted to give us tangible gifts, but many of them got it."

For Andy and Lucy, the Stowers Institute gift was the start of something big. "It was great to give in my dad's memory," says Andy, "and it just made us want to do more." Lucy adds, "We've actually talked a lot about this being the first step for us going forward. We hope to lead by example within our generation in regards to philanthropy."

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Armed with a thorough understanding of drive belts, o-rings, bearings, and couplings, the technical services team provides critical maintenance, repair, and troubleshooting on numerous small and large lab instruments and equipment.

TECHNICAL SERVICES BY THE NUMBERS

>$65,600,000
Amount spent on scientific equipment since 2000

>$1,200,000
Cost to support scientific equipment in 2015

5,829
Number of pieces of scientific equipment supported

1,371
Number of pipettes that require calibration

1,200
Average number of equipment repair and maintenance requests fulfilled annually

346
Number of microscopes

230
Freezers that require defrosting

3
Biomedical and scientific equipment technicians