RETURNING TO THE FOLD
EXAMINING PRIONS FROM NEW ANGLES.

STOWERS REPORT

NEWS AND INSIGHT FROM THE STOWERS INSTITUTE FOR MEDICAL RESEARCH FALL/WINTER 2016

STOWERS REPORT

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In perspective

BY DAVID CHAO, PHD
PRESIDENT AND CEO

Much scientific progress stems from new ways of seeing things. New knowledge and frameworks enable existing observations to be reinterpreted and connected in new ways while new technologies literally allow the unseen to become seen. Perhaps most importantly for institutions like the Stowers Institute, new people bring a fresh perspective and energy to the research enterprise.

New members who join us each year bring new approaches and perspectives to stimulate the Institute's research at all levels. For instance, the Institute has an ongoing commitment to recruit and invest in assistant investigators—those laboratory leaders who have just completed their training and are launching their independent careers. This issue of the Stowers Report introduces you to Sarah Zanders and Ariel Bazzini, our most recently recruited assistant investigators.

In addition, the Institute serves as the host institution for about 130 undergraduates, predoctoral researchers, and postdoctoral associates. These trainees come from many different backgrounds from around the world and each brings a distinctive perspective and expertise. The fresh perspective of a mind unclouded by experience often leads to unexpected scientific advances.

In a similar vein, this issue's cover story on prions serves as a case study of how new knowledge, frameworks, and technologies provide a novel way to look at and address a decades-old biological problem. Prions are a class of proteins involved in pathologies such as mad cow disease. Most infectious illnesses spread because a bacteria or virus moves from one host to another. However, in the case of prion-based conditions, disease spreads because proteins with pathological three-dimensional shape move to a new host and serve as templates for the new host's proteins to adopt the pathological shape.

For decades, the focus of prion research was on their role in disease. With the discovery that some prions are involved in normal cellular processes and not in disease, scientists looked at prions in a new light. One of these scientists was Investigator Kausik Si, who years ago saw a potential role for prions in maintaining memories in the nervous system. Another was Assistant Investigator Randal Halfmann, who saw a role for prions in normal yeast and mammalian physiology.

The change of perspective that prions might be helpful rather than harmful has opened up whole new areas of research. Not surprisingly, as pioneers in this new field, both investigators have also been developing new technologies for observing the molecular behavior of prions.

As you enjoy this issue of the *Stowers Report*, I hope you will be inspired by the many examples of how the Institute's research is often driven by new ways of seeing things.

RETURNING to the FOLD:

EXAMINING PRIONS FROM NEW ANGLES

By Nicholas Gerbis

They say that there's no such thing as bad press, but try telling that to prions.

When a protein folds properly, it carries out normal tasks without a hitch. But when it folds into the wrong conformation, as occurs in many prion diseases, the result not only poses a deadly hazard—it also spreads exponentially to impact sister proteins. While prion proteins can exist in alternative states, they have rarely made headlines except in accounts of their deadly role in brain-destroying disorders like Creutzfeldt-Jakob disease, or their links to the amyloid plaques of Alzheimer's disease.

Over the past few decades, however, the narrative has shifted to a more nuanced view, rewritten by research revealing that there appear to be normal, functional, even crucial, roles prions can play in cells. At the forefront of these advances stand two teams at the Stowers Institute, one led by Kausik Si, PhD, a pioneer in prion memory research for more than a decade, and the other led by Randal Halfmann, PhD, who brought his new prion model and quantitative methods to the Institute in 2015.

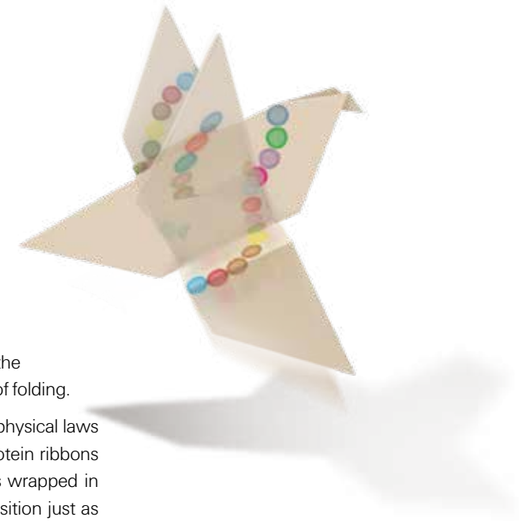
Their challenge lies in developing a clearer picture of how prions choose to adopt one state versus another, why they spread to nearby proteins, and what divides the functional from the dysfunctional. It's a tall order, but not quite as tall as overcoming the inertia of prevailing scientific wisdom.

A New Frontier

When Randal Halfmann first encountered prions in Susan Lindquist's lab at Massachusetts Institute of Technology (MIT), he saw a terrain ripe for pioneers.

"It was a wonderful time to get into that field because it was—and it's really still—a very Wild-West-y kind of a science," he says.

Halfmann, who grew up on a West Texas cattle ranch, knew a little something about untamed territory. But no run-in with mad cow disease set him on the prion research path. While at Texas A&M, his naturalist bent—which persists today in his hobbies of foraging for wild plants and mushrooms—initially steered him toward plant cytogenetics, the study of plant cells and chromosomes. Prions would wait until graduate school, when a chance meeting with a visiting lecturer lassoed his fancy with the protein folding problem.



Proteins, the building blocks of life, have mastered doing a lot with a little. Though they differ from species to species—even from organ to organ—all proteins draw from the same pool of around 20 amino acids, strung together in electron-sharing links called peptide bonds. This small cast fulfills a seemingly endless list of roles, from transcribing DNA to flexing muscles. This flexibility derives partly from the range of lengths these chains can reach, from a few amino acids to more than 27,000. But the real artistry of proteins, like that of origami, lies in the transformative power of folding.

Yet, even with a complete chemical blueprint and a thorough grasp of the physical laws that govern proteins, scientists often cannot predict how they will fold. Protein ribbons behave less like unwound springs and more like kinked-up garden hoses wrapped in magnets: Some parts repel, others attract and still others swing out of position just as neighboring sections settle into place. Even settling into a nice, low-energy bunch doesn't guarantee that a protein has reached its true minimum energy fold, or native state.

"This concept of the native state or the native fold can be really misleading," says Halfmann. "If you start playing around with it and pushing the boundaries, you start finding that there are multiple alternative states with even lower energy wells."

> "Nothing in biology is an accident."
> —Randal Halfmann

The protein folding problem, which some of the world's most powerful computers have tried in vain to solve, instantly captured Halfmann's imagination—and holds it still.

"It's still a major problem. It was so fascinating, and I just thought, 'Now there's a puzzle that is incredibly important.'"

Important is an understatement. Proteins build tissues, catalyze almost all cellular chemical reactions, and move key substances across cell walls. They form the basis of our immune system, hormones, and enzymes. Proteins even control how genes make more proteins.

Properly folded proteins perform these biological assignments successfully. But when proteins fold into the wrong conformation, they can have detrimental effects and may also propagate by forcing identical proteins to fold in their image. These newly minted prions then go and do likewise.

To researchers like Si and Halfmann, such a biological phenomenon seemed too useful for nature to limit it to destructive purposes. It would be like using oxidation-reduction reactions—the world's principal sources of energy—solely to rust car bumpers.

"Nothing in biology is an accident," says Halfmann. "Certainly, if it happens, cells find a way to take advantage of it."

Inspired by this biological adage, Halfmann set out to find more prions and found a lot of them, including examples responsible for aspects of cell signaling, differentiation, and evolution. His yeast studies have proven especially fruitful, turning up two dozen prion-forming proteins that help manage key cellular processes, from transcription (copying DNA data into messenger RNA) to translation (turning messenger RNA sequences into peptides or proteins).

A change in our view of prions was brewing, but new answers also inspired new questions. As Halfmann and his colleagues explored the margin separating functional prions from dysfunctional ones, another problem emerged.

> "How do prions help us form long-lasting memory?"
> —Kausik Si

"It was becoming clear that we in the field didn't have the right conceptual framework for understanding these proteins."

Fortunately, Halfmann had an idea in mind.

Transitioning to a New Phase

Elementary school science teaches that a phase transition is a shift from one state of matter to another, often involving the release or absorption of energy. It also defines 0°C as the temperature at which water shifts phases from liquid to solid.

In reality, though, the process occasionally requires a little help. Pure water can remain unfrozen even after its temperature drops past its freezing point. Its molecules slow down, wanting to fall into a cozy lattice formation, but can't quite find the right orientation. Then a tiny energy fluctuation orients some of them into the first microscopic ice crystal that kicks off the process. Once they have it, a wave of freezing sweeps through the liquid almost instantly.

Halfmann says that a similar process might explain prions' cellular coup.

When cytoplasm, the viscous fluid that holds all of a cell's non-nuclear goodies, becomes supersaturated with prion-forming proteins, it grows unstable, like supercooled water. Drop in a prion, which is in effect a molecular crystal, and it kick-starts a prion formation cascade. The liquid has "frozen."

As the Halfmann Lab works to prove this hypothesis, it must also address vital limitations in customary prion research methods.

Our grasp of prion proteins has been hindered by a lack of quantitative methods, which rely on statistical analyses of key quantities. Lacking these measurements, early assays relied on color changes in yeast colonies, an indirect method that could only work after 30 or so generations of yeast. Halfmann says that such methods—really extensions of genetic tests used to study diseases—were limited in scope and prone to false positives, and "grossly obscured the real biology."

"I think that we're now emerging from that state, or beginning to," he says. "Now, you can really point at something and say, 'This is when it's happening, how much it's happening,' and so on."

Halfmann credits his colleagues for the new evidence, improved technologies, and emerging fields of study that have enabled him to conceive his new model and study it quantitatively.

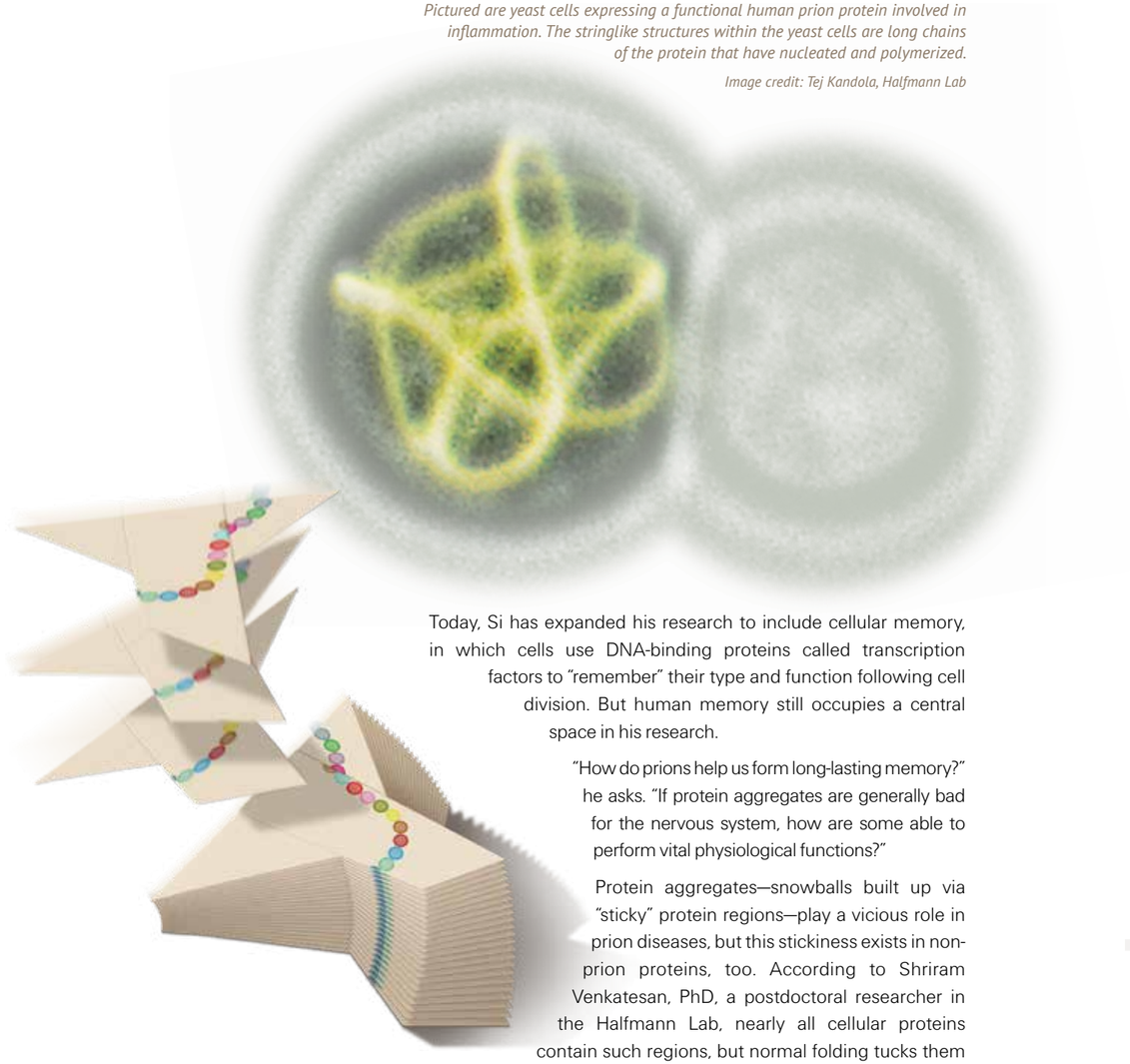
"The technology that makes the assay possible—robust photoconvertible fluorescent proteins—only recently became available. The timing coincides nicely with a recent frenzy of activity in biophysics and cell biology of liquid-liquid phase separation."

Thanks for the Memories

The questions these shifts could help answer include ones posed by Halfmann's Stowers colleague Kausik Si. Si first made a surprising discovery in the prion world in 2003, when he and Eric Kandel, MD, of Columbia University, put forth the idea that a prion protein called CPEB might have a normal role to help the brain form stable long-term memories. In response to a transient electrical signal, they argued, CPEB would switch to a prion state and spread that state to nearby proteins, thereby building neuron links vital to memory.

Pictured are yeast cells expressing a functional human prion protein involved in inflammation. The stringlike structures within the yeast cells are long chains of the protein that have nucleated and polymerized.

Image credit: Tej Kandola, Halfmann Lab



Today, Si has expanded his research to include cellular memory, in which cells use DNA-binding proteins called transcription factors to "remember" their type and function following cell division. But human memory still occupies a central space in his research.

"How do prions help us form long-lasting memory?" he asks. "If protein aggregates are generally bad for the nervous system, how are some able to perform vital physiological functions?"

Protein aggregates—snowballs built up via "sticky" protein regions—play a vicious role in prion diseases, but this stickiness exists in non-prion proteins, too. According to Shriram Venkatesan, PhD, a postdoctoral researcher in the Halfmann Lab, nearly all cellular proteins contain such regions, but normal folding tucks them away. Venkatesan studies how protein aggregates might help cells by sweeping up misplaced or harmfully plentiful proteins. The answers could support future cancer treatments.

"Cellular chaperones and protein degradation machinery act on them either to refold them and restore normalcy, or degrade them and restore normalcy by synthesizing new copies," Venkatesan explains.

The idea that an infectious agent linked to brain dysfunctions could prove crucial to cellular health or memory formation has stood the entire prion-brain relationship on its head. Not surprisingly, this emerging view has met with some resistance. If Halfmann's quantitative methods can help overcome that resistance, and help prove ideas like those under investigation in his and Si's labs, then he will have demonstrated their value.

"I think it's exciting, because Kausik has a new perspective on the biology, and we have a highly quantitative, rigorous manner for testing these behaviors," says Halfmann. "I think it could be a nice opportunity for synergy."

The Quest to Quantify

Bringing that perspective into practice requires measuring several telling traits of prion proteins, including how frequently they enter the prion phase (nucleation), how quickly the phase spreads (propagation), and how concentrated the protein must be for this chain reaction to kick off (critical concentration). The Halfmann Lab is also looking at a key indicator of prion functionality versus pathology called heterogeneity.

In the most general sense, heterogeneity refers to mixtures—of ingredients, of characteristics, and, in the case of cell biology, of causes. In the physics of phase transitions, heterogeneity gauges the degree to which extraneous factors can trigger nucleation. It also estimates the chances that those factors will themselves be influenced by a phase change. One such factor involves the surfaces of aggregates.

"What makes a protein aggregate toxic is, to a large extent, determined by what it binds to in the cell," says Halfmann. "The more heterogeneous the nucleation process, the more opportunities the protein has to interact with other things, and the more it will tend to cause problems for the cell."

Functional prions have very low heterogeneity. Like good cellular roommates, they respect everyone else's space and nucleate only at the proper time and place. Proteins that form disease-causing clumps, on the other hand, have a very heterogeneous nucleation process. They eat your food, wear your clothes, and steal your class notes.

Through its quantification process, the Halfmann Lab tracks prion formation in unmatched detail. They also screen for other proteins that show nucleated phase transitions—the key to crystallizing proteins into a new state and, thus, making prions such potent cellular switches.

"Our lab has the unique capability to measure this property in a systematic manner. Now, for any protein, in principle, we can say, 'How prion-like is it?' or, 'How good a prion is it, and when is it doing this, and what's regulating it?' and so on."

Beyond memory creation or protein-sweeping, prion-based switching could occupy a key slot in our immune signaling and response machinery. Research suggests that an infection-fighting protein called MAVS boosts immune response by undergoing a prion-like change. As the cell dies, it prompts an uptick in interferon, which dampens virus replication, and in macrophages, which consume infectious agents. The Halfmann Lab has turned again to yeast to probe this process and the delicate balance it requires.

"If a cell is too quick on the trigger, it dies needlessly and inflames surrounding tissue," says Ellen Bruner, a Halfmann Lab research technician. "This dysfunction may be a heretofore unexplored factor in the initiation and progression of all autoimmune diseases, including multiple sclerosis and arthritis."

Halfmann looks forward to the future and the discoveries it holds, but also remembers his path over the years—when he left that West Texas ranch, attended graduate school at MIT, and went straight into research at The University of Texas Southwestern Medical Center. What has endured in him is a desire to look past established models and perceive puzzles in biology from new angles. After Si, who knew him through his MIT mentor Lindquist, asked Halfmann to give a guest lecture at the Stowers Institute, Halfmann knew he'd found a place that would support that longing.

"The Stowers Institute has been great because it's just so accepting and the people are fantastic. The message I hear is, 'We believe you. You understand your research better than anyone else, and we have confidence that good things will come of it. We want you to drive it forward.'"

> "Our lab has the unique capability to measure this property in a systematic manner."
> —Randal Halfmann

By Cathy Yarbrough

A DISCUSSION WITH

NICOLAS ROHNER, PHD

Nicolas Rohner, PhD, has been thinking about science since his childhood in Southern Germany.

"I learned everything I could about the plants, fungi, and animals in the forests near my home," he said.

At the Friedrich-Alexander University (FAU) in Erlangen, Germany, Rohner majored in biology. Having decided on a career as an academic scientist, he earned an MSc degree at FAU and a PhD degree at the Max Planck Institute for Developmental Biology in Tübingen, Germany.

His mentor at Max Planck, the Nobel laureate Christiane Nüsslein-Volhard, PhD, introduced Rohner to fish as a model system for basic research in developmental biology. Rohner's current research on the genetics of adaptation takes advantage of the attributes of an unusual species of fish, *Astyanax mexicanus*, commonly known as the Mexican cavefish. His postdoctoral studies of *Astyanax* in the laboratory of the renowned developmental biologist Cliff Tabin, PhD, at Harvard University have established this cavefish as an emerging model for studying comparative physiology and as an entry point for probing the genetic basis of metabolic disorders.

Mexican cavefish, which represent one of the most striking examples of adaptation in the animal kingdom, are the descendants of river fish that millions of years ago were swept by floods into dark underground caves. Because vision is useless in such environments, cavefish over time lost their eyesight. To survive long periods without food between the unpredictable floods that contain their only source of nutrients, cavefish developed a dramatically slower metabolism. They also developed the ability to feed to excess and accumulate large reserves of body fat—ten times more body fat than fish that live in the rivers near the caves, according to Rohner's research at Harvard.

Rohner and his collaborators found that cavefish are able to live long and healthy lives even though they have high body fat levels, are insulin-resistant, and have unstable blood glucose levels—a condition similar to fatty liver disease and diabetes in humans. They also determined that the cavefish's increase in appetite is due to a mutation in their melanocortin 4 receptor (MC4R) gene. This mutation is the most common single-gene cause of inherited obesity in people.

In 2015, Rohner completed his postdoctoral research at Harvard and joined the Stowers Institute, where he continues to use cavefish in research to provide insights into metabolic processes and diseases.

Q A

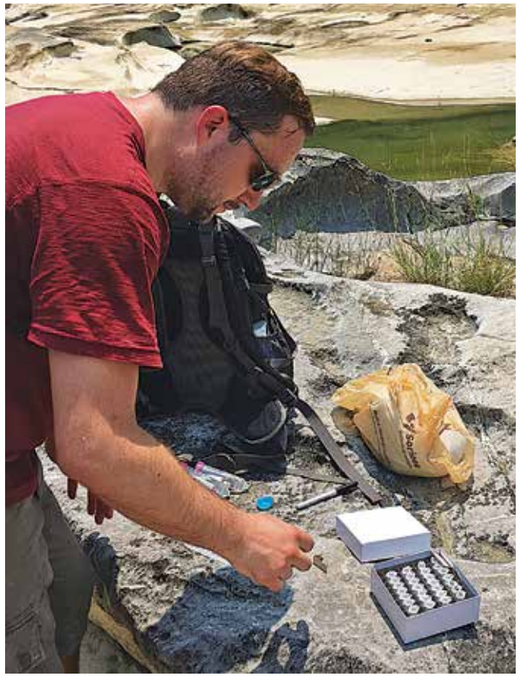
HOW COULD THE RESULTS OF YOUR LAB'S BASIC RESEARCH WITH CAVEFISH PROVE RELEVANT TO HUMAN HEALTH?

In humans, diseases such as diabetes, allergies, and some types of cancer can result from a mismatch between our traits and biological processes and our current environment. In some ways, changes in our biology have not been able to keep pace with relatively rapid changes in our environment and lifestyle. By studying how cavefish have adapted successfully to their cave environment, we hope to identify the molecular mechanisms or genes that have evolved in these fish to allow them to survive and even thrive in extreme conditions. These genes and pathways that provide a protective function in cavefish may suggest therapies that could limit the impact of some diseases on human health.

WHAT ARE THE ADVANTAGES OF USING CAVEFISH OVER MORE ESTABLISHED LABORATORY MODELS SUCH AS FRUIT FLIES AND MICE?

Cavefish are a natural model whose metabolic changes are adaptive, not pathological. They occurred in such a way that other physiological changes happened to compensate for any detrimental consequences of the metabolic changes.

Studies with a natural model can complement research that focuses on laboratory animals with impaired metabolic responses. To understand the complex network regulating energy metabolism, both approaches are needed.



HOW OFTEN DO YOU AND YOUR LAB CONDUCT FIELD WORK IN THE CAVEFISH'S NATURAL ENVIRONMENT?

Through field work, laboratory scientists can obtain a better understanding of the role of environment in evolution and adaptation. Each year we try to spend about two weeks at a Mexican cave. It can be very challenging to visit—on our last trip, we spent four hours en route to the cave and occasionally had to use a machete to clear a path in the jungle. We used ropes to descend into the cave. At one point, we were attacked by killer bees, but finally getting to the fish was rewarding.

YOU HAVE AN APPOINTMENT AS AN ASSISTANT PROFESSOR AT THE UNIVERSITY OF KANSAS MEDICAL CENTER (KUMC). ARE YOU WORKING WITH THE CLINICAL RESEARCHERS AT KUMC?

Soon after I arrived at the Institute, I established research collaborations with leading diabetes researchers in the Department of Molecular and Integrative Physiology at KUMC. Through these collaborations, I am able to gain access to clinical studies and patient samples, which will facilitate the translational value of our work. I thrive from discussions with our KUMC collaborators—their expertise is absolutely crucial for my research.

HOW HAVE YOU ADAPTED TO LIVING IN KANSAS CITY?

Very well. Kansas City is a very easy city to live in and navigate—traffic here is like living in the 1950s but with modern cars. My wife, who is a lab manager in another lab, and I live just ten minutes away from the Institute.

Since I'm half French, I really enjoy good food and wine. Surprisingly, there is more authentic German and French food in Kansas City than there is in Boston.

WHY DO YOU PARTICIPATE IN SOCIAL MEDIA?

It's important for my lab and me to have an online presence by using social media platforms such as Facebook and Twitter so that scientists and students who are interested in our research can connect with us. In particular, Twitter provides a platform that is connecting me with my peers and keeps me up to date about the latest research, discussions, and controversies in the field, important conferences, and recent papers—and everything is pre-digested into 140 characters or less.

SEVERAL SCIENTIFIC INSTITUTIONS IN THE US, EUROPE, AND ASIA OFFERED YOU A FACULTY POSITION. WHY DID YOU PICK THE STOWERS INSTITUTE?

The Institute has unmatched core facilities and remarkable, brilliant faculty with complementary interests in genetics, developmental biology, and evolution. I also admire the American way of doing science. Here, the science often comes first, and the infrastructure surrounding it is designed to help achieve the scientific goals.

SEARCHING FOR A CREATIVE WAY TO PREVENT TREACHER COLLINS SYNDROME

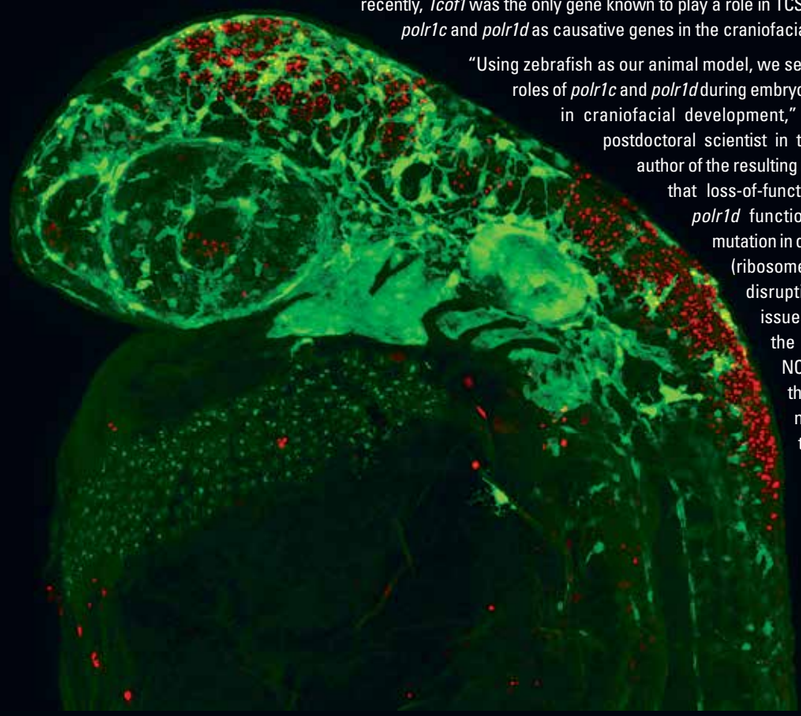
Children who are born with the rare craniofacial defect Treacher Collins syndrome (TCS) often have facial deformities and other physical defects related to the disorder.

These children often undergo multiple surgeries in an attempt to repair the physical defects caused by TCS. Improved scientific understanding of how TCS begins at the most basic level—in the neural crest cells (NCCs) that give rise to the cartilage, bone and connective tissue of the head and face—is critical.

Investigator Paul Trainor, PhD, has been dedicated to generating that knowledge. He and his team have used mouse models to define how the loss-of-function mutation in the gene *Tcof1* disrupts NCCs to cause TCS. Until recently, *Tcof1* was the only gene known to play a role in TCS, but a recent study implicated *polr1c* and *polr1d* as causative genes in the craniofacial development disorder.

"Using zebrafish as our animal model, we set out to explore the functional roles of *polr1c* and *polr1d* during embryogenesis and more specifically in craniofacial development," explains Kristin Watt, PhD, postdoctoral scientist in the Trainor Lab. Watt is lead author of the resulting research paper, which reports that loss-of-function mutations in *polr1c* and *polr1d* functioned similarly to the *Tcof1* mutation in disrupting a crucial component (ribosome biogenesis) of NCCs. The disruption of ribosome biogenesis issues a distress call that compels the *p53* cell death gene to kill NCCs. With the death of NCCs, the body no longer has sufficient numbers of cells to construct the craniofacial skeleton.

The Trainor Lab also determined that TCS, at least in the animal model, is reversible by experimentally blocking the actions of the *p53* gene. In doing so, the population of NCCs was restored to its normal level, and TCS did not occur.



A developing zebrafish that harbors a genetic mutation implicated in Treacher Collins syndrome has a reduced number of neural crest cells (green). Some precursors of the neural crest cell population are undergoing cell death (red).

These results were published in the July 22, 2016, issue of *PLoS Genetics*.

RESEARCHERS GENERATE WHOLE-GENOME MAP OF FRUIT FLY GENETIC RECOMBINATION

Meiosis is the process of cell division that gives rise to reproductive cells. During this process, chromosomes are copied and paired up to swap bits of their DNA before being separated to create eggs and sperm.

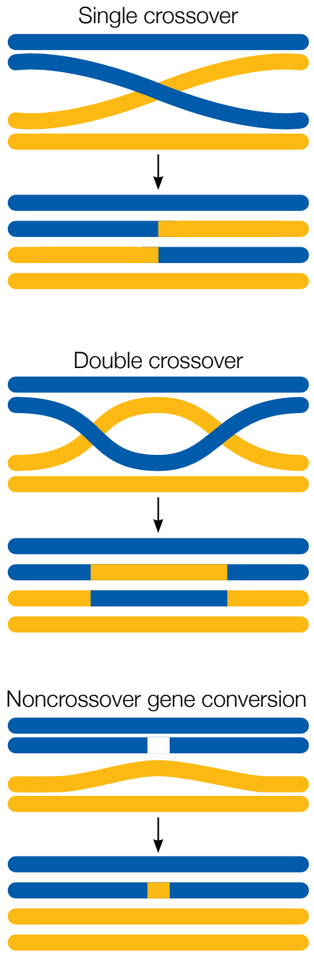
This process, called recombination, is an important driving force behind genetic variability and evolution, but most importantly, it ensures that chromosomes move properly during the subsequent divisions that form these eggs and sperm. When the recombination doesn't go smoothly, it can cause a number of problems in humans, including miscarriages and birth defects.

For the first time, Stowers researchers in the Hawley Lab have mapped where recombination occurs across the whole genome of the fruit fly *Drosophila melanogaster* after a single round of meiosis. Their results indicate that separate mechanisms position the two main kinds of recombination events, crossovers and noncrossovers.

The Stowers researchers wanted to determine how both crossovers and noncrossovers are distributed across the chromosomes of fruit flies. Crossovers are relatively easy to identify because they involve large sections of chromosomes that encompass thousands of base pairs, the A's, C's, T's, and G's that make up DNA. But noncrossovers are tougher to spot, because they only involve a few hundred of those letters. So, Danny Miller, an MD-PhD student at the University of Kansas Medical Center who conducted his doctoral research in the Hawley lab, had to rely on whole genome sequencing and new computer algorithms to pinpoint the locations of both kinds of events.

"It is amazing to me that more than 100 years after the discovery of genetic recombination in flies, we are only starting to understand just how these events are distributed," says Investigator Scott Hawley, PhD.

This research was published in the May 2016 issue of the journal *Genetics*.



PLANARIA ARE PROVING TO BE AN INFORMATIVE ANIMAL MODEL SYSTEM

WITH AMAZING REGENERATIVE CAPABILITIES, THE FRESHWATER FLATWORM PLANARIA IS A FAVORITE ANIMAL MODEL SYSTEM IN THE SÁNCHEZ ALVARADO LAB AT THE STOWERS INSTITUTE. SCIENTISTS USE IT TO STUDY THE MOLECULAR AND CELLULAR MECHANISMS THAT DRIVE REGENERATION AND RESTORATION OF BODY PARTS. NEW STUDIES FROM THE SÁNCHEZ ALVARADO LAB UTILIZING THESE CURIOUS CREATURES HIGHLIGHT TWO PROJECTS WITH INTRIGUING FINDINGS.

SHIFTS IN THE MICROBIOME IMPACT TISSUE REPAIR AND REGENERATION

Shifts in the balance of the human microbiome—the microbial communities that call our bodies home—underlie persistent inflammatory disorders, chronic nonhealing wounds, and scar formation. In a recently published paper, Stowers scientists in the Sánchez Alvarado Lab explore the interplay between the microbiome, host immunity, tissue repair, and regeneration in planaria.

Postdoctoral Research Associate Chris Arnold, PhD, and collaborators find that ailing flatworms experience a dramatic expansion of pathogenic Proteobacteria that closely mirrors changes associated with human ailments. This bacterial infection stimulated the flatworms' immune response, impeding their regeneration capabilities. The study provides a valuable animal model for understanding host-microbiome interactions and for designing therapies that may enhance healing in humans.

"This is the first animal model to link pathological shifts in endogenous bacteria with the inhibition of regeneration," says Sánchez Alvarado. "We know that some kinds of bacteria are critical to our health, and that other kinds of bacteria can make it very difficult for us to recover from illness. Now we can study how the changing nature of the microbiome—and the way the immune system responds to those changes—impacts the natural execution of regenerative processes."

The study was published July 21, 2016, in the journal *eLife*.

A KEY MOLECULAR SIGNAL SHAPES REGENERATION IN PLANARIAN STEM CELLS

Like a magician, planaria can survive decapitation or even being cut into many pieces. But the flatworm does not need to rely on trickery.

Its remarkable ability to fully regenerate from tiny remnants of tissue is due to a special population of adult stem cells known as neoblasts. In recently published work, Stowers scientists explore the precise mechanisms shaping the population dynamics of neoblasts.

Postdoctoral Research Associate Kai Lei, PhD, and collaborators have discovered that a molecule called EGFR-3 is part of a cascade of signals necessary for neoblasts to regenerate, and might control the way these cells divide and differentiate in response to otherwise lethal doses of radiation.

The finding has important implications for advancing regenerative medicine and for developing more effective cancer therapies. Sánchez Alvarado explains, "Anything that perturbs our body—aging, injury, even a spicy meal—can affect our stem cell functions. If we understand better how planarians regulate the population dynamics of their stem cells, it may provide a clue for addressing our own pathologies."

These results were published online August 11, 2016, in the journal *Developmental Cell*.

By Jessica Johns Pool

DETERMINED TO RESEARCH

Kansas native Christina Ward wanted a summer internship where she could expand her lab experience between her bachelor's and master's programs. She was delighted to find the Summer Scholars Program at the Stowers Institute practically in her back yard.

After graduating with a BS in biology from the University of Saint Mary in Leavenworth, Kansas, Ward spent nearly a year working in a lab at the University of Southern California in Los Angeles, where she performed various experiments in plasmid design and cloning for amyotrophic lateral sclerosis (ALS) research. She then joined the Stowers Institute for the summer, and worked on a joint project between the Linheng Li Lab and the Stowers Microscopy Center.

"I learned so much from my mentors—things I'd not even considered before," enthuses Ward. "In the past I'd done a lot of biochemistry bench work, and at the Stowers Institute I was able to dive into bioinformatics and *in vivo* work with mice. It was exciting to try new things and new techniques, and become more versatile."

This fall Ward begins a one-year master's program in biomedical sciences at the Kansas City University of Medicine and Biosciences. This determined young woman has her sights set on eventually becoming an MD-PhD physician scientist with her own lab working on clinical trials and translational medicine.

"The dual program would offer more time to develop fully a research focus extended from my medical specialty," explains Ward. "It would also allow exponentially more time in laboratory training. During my master's program, I plan to consider both the options of becoming a physician scientist as an MD or DO only versus an MD-PhD, with the input from knowledgeable advisors and professors."

Growing up, Ward didn't want to be a scientist, though she was always good in math. An ankle surgery in high school exposed her to physical therapy (PT) and she thought PT work was her passion. However, after shadowing some physical therapists, she realized she wasn't interested in that particular career.

Her college professors helped her realize that her mastery of her lab classes might translate well for a career in medical research. Her passion for science also grew during a biochemistry internship at Kansas State University during her senior year where she purified proteins.

At the Institute, Ward joined the Li Lab where she worked with Postdoctoral Research Associate Meng Zhao, PhD, and Research Specialist Sarah Smith, PhD, on a project to investigate the hematopoietic stem cell (HSC) niche in adult mouse bone marrow. Distribution analysis of two HSC populations within bone marrow may help determine what molecular signals emitted by niche cells contribute to controlling whether the stem cells are primed and readily enter the cell cycle, or remain in a relatively quiescent state.

HSC activity is essential for daily maintenance of healthy blood, for immune response, and for repopulating blood cells following an injury. Meanwhile, quiescence helps maintain a reserve of healthy HSCs throughout life, and is thought to play a role in resistance to chemotherapy.

"Christina was very quick to grasp the goal of the project and how the daily experiments contributed to the goal. Despite having had very little experience with microscopes, she took to imaging right away and was able to run samples completely independently within the first two weeks, and was similarly quick to master other techniques," says Smith. "She asked thoughtful questions and, being familiar with both sample preparation and imaging, was able to make tweaks to the procedure to improve efficiency. She's a very hard worker, ambitious, kind, friendly—she has a very bright future."

Ward predicts that her time at the Stowers Institute will make a lasting impact on her career.

"My experience at the Stowers Institute was a memorable one," says Ward. "It helped solidify my decision to incorporate research into my career path, and the laboratory techniques I learned increased my versatility. I was drawn to the Institute because it fit geographically, but then I found this beautiful facility with amazing resources."

EIGHT BUDDING SCIENTISTS

Growing the Stowers Graduate School

In August, eight new predoctoral researchers joined the Stowers Institute Graduate School program. Over the next four to five years they will be instructed and mentored by some of the most accomplished scientists in the world and will have access to cutting-edge technologies and equipment. They have the opportunity to acquire a wealth of knowledge to help prepare them for a career in research while earning a PhD degree.

WEB EXTRA

Hear more about these promising scientists in their own words.

www.stowers.org/stowers-report/audiocast2016

José (Fibo) López Hernández

National Autonomous University of Mexico

Center for Research and Advanced Studies of the National Polytechnic Institute (CINVESTAV)

Jose (Fibo) López Hernández studied genomic sciences and earned a BS degree, then completed his master's program in bioinformatics, biostatistics, and cellular differentiation. He thought his next step was a PhD in biology and math, but his experience as a Summer Scholar at the Stowers Institute changed that plan. He found himself amazed by the beauty and power of experiments—the power to test a hypothesis and establish new knowledge.

Sirma User

Middle East Technical University

During her childhood, Sirma User's parents bought her science magazines geared toward kids. Her favorite parts of the magazines were the posters and cards about animals, star maps, and planets. She credits those magazines with her fascination of the scientific world.

Today, her interests focus on the biological sciences as she explores and solves complex questions in biology.

Alejandro (Alex) Rodríguez Gama

National Autonomous University of Mexico

Complexity of cellular processes and molecular structures fascinates Alejandro (Alex) Rodríguez Gama. His interests range from cellular biology and biochemistry to synthetic biology and proteomics.

An experience that furthered his interest and shaped his scientific education was his participation in his college's team effort in the 2015 International Genetically Engineered Machine (iGEM) competition. Rodríguez Gama led his team's experiments as they created a bacterial glucose sensor that would respond to glucose concentrations during insulin production.

Todd Gallagher

Humboldt State University

A high school biotechnology class exposed Todd Gallagher to various technologies and the theories behind experimental techniques, and provided visits to labs and biotech companies. He also got to try his hand at laboratory skills, learning restriction enzyme digestions, bacterial transformation, PCR, and some protein analysis.

Gallagher knew then that he wanted to pursue a career in this fast-paced branch of research. He is endlessly fascinated by "the ways people have figured out how to view and understand processes we cannot directly see with our eyes."

Augusto Ortega Granillo

National Autonomous University of Mexico

Adventures, whether of the mind or the body, captivate Augusto Ortega Granillo.

As a former Stowers Summer Scholar in the Jaspersen Lab, Ortega Granillo enjoyed the Institute's balance of creativity, collaboration, efficiency, and hard work. He is glad to return to pursue his passion for hands-on research and bioinformatics as he earns a PhD. He finds the idea of "making experiments with my own hands" and exploring the "what ifs" deeply exciting.

Qiushuang Wu

Wuhan University

Qiushuang Wu hopes to understand nothing less than the nature of life, on a genetic level, and to change the world. That interest may explain her two loves, biology and cooking.

Wu takes great pleasure in cooking, especially Chinese dishes. She finds the creativity in cooking similar to conducting scientific experiments. "You follow the protocol and get the normal result, but if you add something new, chances are you will get a surprise." When she isn't cooking, Wu wants to research the general mechanisms for transcription regulation.

Soham Karmakar

University of Calcutta

A lifelong love of science fiction novels and movies stoked Soham Karmakar's passion for real-world science and ultimately led to his decision to become a research scientist.

In high school, Karmakar says the "absurd ideas and technologies" depicted in science fiction inspired him to read about different areas of science. His reading made him even more curious as he earned a BS in microbiology and an MS in biotechnology. Following his master's training, Karmakar interned in the lab of Associate Investigator Kausik Si. He considers the Stowers Institute a dream location as he continues his education.

Wei-Ting Yueh

National Taiwan University

Deep-seated curiosity has driven Wei-Ting Yueh for as long as he can remember. As a child he wanted to know "why," especially when it came to the mystery of what makes living things do what they do.

Yueh believes the most important aspect of basic science is to ask good questions. He hopes to learn how the researchers at the Institute find and solve interesting scientific problems, from the design of experiments to the analysis of data.

Where science and art collide

The natural world is inherently beautiful. Artists frequently capture the beauty of the ocean or sunset or a majestic tree. But what we cannot see with the naked eye often goes unobserved and unappreciated. With advances in microscopy and imaging, scientists are now able to reveal and interpret the beauty of the microscopic world around us. Enjoy a dazzling artistic display of Stowers scientific research.

WEB EXTRA

Please visit our scientific image gallery.

www.stowers.org/stowers-report/yisr2016

By Jessica Johns Pool

Catching Up with RAYMOND CAMAHORT, PHD

With his restless curiosity, Ray Camahort fits right in with many others who have been predoctoral researchers at the Stowers Institute. What has not been so typical is his career path after graduation.

During his graduate training, Camahort had an inkling a professorship was not in his future and he started to explore possible careers outside of academia. While enrolled in the doctoral program at the University of Kansas and completing degree requirements in the lab of Jennifer Gerton, PhD, he interned at the Kansas City Police Department Crime Lab. As he recalls, DNA testing was not nearly as thrilling as portrayed on the television show CSI: Crime Scene Investigation.

After completing the PhD program, Camahort moved to Harvard University to pursue postdoctoral training. During this time, he was a teaching fellow for a couple of semesters, and although he enjoyed teaching, Camahort felt he still hadn't found his niche.

While completing a National Institutes of Health postdoctoral fellowship in medicine at Harvard, Camahort did an internship in embryology at the Fertility Center of New England, and an internship in business development at Partners HealthCare Research Ventures and Licensing, which commercializes inventions and treatments developed in labs at Brigham and Women's Hospital and Massachusetts General Hospital. The business development internship gave Camahort a window into the commercial side of science and it intrigued him.

In 2013, Camahort took a full-time position in business development at the Harvard University Office of Technology Development, where he worked to commercialize the innovative science coming out of the departments of chemistry and of stem cell and regenerative biology. This experience kindled his passion for the business side of science.

"Moving out of academia and into the commercial side of science isn't unusual in the Boston area," says Camahort. "At the Stowers Institute, I was frequently thinking outside the academic box. All of those internships helped me hone what I really liked about a career in science."

Camahort joined Novo Ventures (US) Inc., a life sciences venture capital firm in Cambridge, Massachusetts, in 2015. Now, he uses his ten-plus years of combined research and business development experience to assess the potential of companies bringing new drugs or medical devices to the market.

"I perform diligence for new investments for companies trying to raise money for clinical trials or to launch a new treatment," says Camahort. "I read more papers now than I ever did as a predoc or postdoc. In a nutshell, when you're in a lab, you are digging deeply into one topic. Now it's much more broad. I dig into many things."

Camahort stays in touch with his former colleagues at the Institute including his mentor, Investigator Jennifer Gerton, PhD, and Stowers alumni who pass through Boston. In fact, he recently helped a former Stowers colleague move into a new Boston-area home.

Camahort credits the Institute with deepening his love of science and his desire to stay in the field, even if he didn't remain in basic science research.

"The Stowers Institute doesn't put any limits on your creativity or your scientific pursuit," recalls Camahort. "They have the resources to allow you to do what it takes for top-notch work. That kind of freedom and the collaborative environment is unique."

For young scientists just beginning their career journey, Camahort recommends they consider career options outside the research lab. "Every day I use what I learned in the lab. The scientific context of my work now is translational and commercial, rather than basic discovery, but it's just as interesting."

A champion of HOPE

In May, Stowers Institute Co-Founder Virginia Stowers was recognized by the Center for Practical Bioethics with the 2016 Vision to Action Award presented at their annual dinner. The award honors individuals who encourage and exhibit the highest ethical standards of conduct in their leadership, vision, and commitment.

Virginia was selected for her lifelong commitment to her family, her community, and the fields of healthcare, nursing, and biomedical research. She has approached all of these commitments with humility and integrity, which, according to John Carney, president and CEO of the Center for Practical Bioethics, are reflective of the core values of the Center.

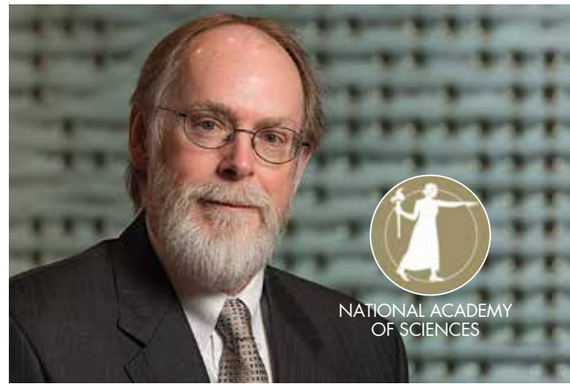
At the event, Virginia's son, Jim Stowers III, spoke of her selfless devotion to her family while she maintained a thirty-year career as a nurse anesthetist. He lauded her for her years of service to many community organizations, including the Center, and for the vision and tenacity that led to her co-founding the Stowers Institute with his father, Jim Stowers Jr.

The Center for Practical Bioethics is a nonprofit organization nationally recognized for its work in practical bioethics.

NATIONAL ACADEMY HONOR GOES TO KRUMLAUF

In May, Scientific Director and Investigator Robert Krumlauf, PhD, was elected to the National Academy of Sciences (NAS) for his distinguished and continuing achievements in original scientific research. Membership in the NAS is considered one of the highest honors given to a scientist in the United States. Krumlauf will be inducted into the NAS next April during its 154th annual meeting in Washington, DC.

Krumlauf is the second Stowers investigator elected to the society of distinguished scholars. Scott Hawley, PhD, was elected in 2011.



A world-renowned developmental biologist, Krumlauf was among the first to insert genes into the mouse genome to create "transgenic" mice that mimic human development. Today, he also studies the molecular and cellular pathways that govern the patterning of the nervous system, the establishment of the basic body plan, and craniofacial development of vertebrate embryos, particularly how these processes are altered or affected in human diseases.

"The Stowers Institute is proud of Robb's accomplishments not only as a world-class researcher but also as our scientific director," says David Chao, Stowers president and CEO. "We are delighted that the members of the esteemed National Academy of Sciences have now honored Robb with election to its membership."

NIH R00 AWARD ALLOWS ZANDERS TO PROBE THE CONSEQUENCES OF RAPID GENOME EVOLUTION

Shortly after her arrival this summer, Stowers Assistant Investigator Sarah Zanders, PhD, was awarded an R00 grant from the National Institute of General Medical Sciences of the National Institutes of Health. The R00 is the second phase of a two-phase Pathway to Independence Award, also known by its NIH activity codes K99/R00.

The Pathway to Independence Award is intended to support scientists as they make career and research transitions. The first-phase K99 grant was awarded to Zanders while she was a postdoc at Fred Hutchinson Cancer Research Center. The R00 grant is awarded after a K99 recipient secures an independent research or faculty position as well as institutional commitment to provide research support and professional development opportunities.

With three years of R00 funding, Zanders plans to study how genetic conflicts affect the rapid evolution of essential cellular processes and how they may contribute to human health problems such as infertility and cancer. Understanding the details of how genetic elements exert their effects in fission yeast may allow a better understanding of the causes of infertility in other organisms including humans.

STOWERS INVESTIGATOR KICKS OFF THE 2016 TEDxKC TALKS

TED talks are a popular forum for sharing worthwhile ideas. The TED organization invites the world's leading thinkers and doers to speak on topics ranging from ecology to technology to political policy.

Kansas City is one of many communities that organize and host a local TED-like event called TEDx that is designed to help spark conversation and connections at the local level.

Howard Hughes Medical Institute and Stowers Investigator Alejandro Sánchez Alvarado, PhD, was invited to participate in the eighth annual TEDxKC event. He opened the event by introducing guests to their jellyfish "cousin" *Thalia democratica* and explained the extensive genomic ancestry they share with humans. He used this curious example to highlight the importance of basic, curiosity-driven research in a wide variety of intriguing and new model organisms.

Sánchez Alvarado also introduced guests to *Schmidtea mediterranea,* a freshwater flatworm that can be cut into multiple pieces that will each regenerate into a complete animal. He revealed that the flatworm does not conform to some of the biological "rules" that scientists have derived from the seven most common species used to study biological function. Those seven species, which include humans, mice, and fruit flies, make up only 0.00009% of all known animal species.

He suggested that research specialization "is beginning to impede our progress at best, and at worst leading us astray." He argued that a renewed sense of exploration, by asking better questions, is in order and that support of basic research institutions like the Stowers Institute is necessary.

Listen to Sánchez Alvarado's entire motivating talk at
www.youtube.com/watch?v=_Wj_KTraw7c

FIVE-YEAR PILOT GRANT AWARDED TO WORKMAN

The Workman Laboratory received grant funding through a newly established award called Maximizing Investigators' Research Award (MIRA) from the National Institute of General Medical Sciences. The intent of a MIRA grant is to consolidate multiple project grants into one unified grant that supports the investigators' overall research program, thus providing greater stability and flexibility. MIRA grants are awarded for five years. The MIRA grant awarded to the Workman Lab consolidated previous grants held by Jerry Workman, PhD, and his colleague Susan Abmayr, PhD.

The Workman Lab was awarded a MIRA based on the lab's research strategy of chromatin modifying complexes that includes a focus on the multi-subunit complexes SAGA and SWI/SNF. Mutations in these and other complexes have been implicated in cancer and other diseases.

While chromatin modifying complexes can contain as many as 10-20 subunits, an overall view of the assembly and organization of the subunits within the complexes is critical to understanding the effects of mutations. And because mutations of different subunits often do not have the same effects on specific cancers, it is important to understand the individual subunit interactions and how they impact chromatin modifying activity.

27TH ANNUAL AMERICAN CENTURY CHAMPIONSHIP GOLF TOURNAMENT

Every summer, sports and entertainment celebrities converge in beautiful Lake Tahoe, Nevada, for a week of golf at the American Century Championship. This premier celebrity golf tournament is sponsored by American Century Investments (ACI). And, while there are fun and games to be enjoyed, there is also serious business occurring off the course.

This golf tournament serves as an annual gathering for many ACI clients and provides the firm an important opportunity to inform and educate them on the health of their investments and provide a window into the scientific discoveries being made at the Stowers Institute due, in part, to their clients' investments with ACI.

When Jim and Virginia Stowers founded the Stowers Institute for Medical Research, they wanted to provide for the long-term, stable funding of its basic research programs. They understood that scientific advances are not made overnight, but instead can span decades. With that wisdom, they endowed the Institute with roughly 40 percent ownership of American Century Investments, which provides the Institute a steady flow of dividends for its research programs.

Since the founding of the Institute, Stowers researchers have accelerated understanding of biological processes in both health and disease. Some of the landmark findings by Stowers scientists have included identifying biological mechanisms that cause a severe birth defect called Treacher Collins syndrome, discovering a new target for drugs to treat a childhood leukemia, determining that a prion-like protein plays a key role in storing long-term memories, and discovering the molecular basis for an osteoporosis treatment now in late-stage human clinical trials.

These are the kinds of discoveries and advancements that inspire hope for a better tomorrow. *Prosper With Purpose* is at the heart of a new marketing and sales initiative, launched by ACI at this year's golf tournament. *Prosper With Purpose* aims to target individuals and companies that seek to not only invest for their own future, but also to make a difference with their money. *Prosper With Purpose* shares the story of how ACI investors have the potential to create positive change in the world through basic research.

Scientific Dynamos

New members join the Stowers faculty

Sarah Zanders, PhD

Assistant Investigator

Coming to the Stowers Institute and settling in to life in Kansas City is a little like coming home for Sarah Zanders, PhD. Zanders grew up in the neighboring state of Iowa, where she got her start in science with a BS in biology at the University of Iowa. From there she moved from one coast to the other as she completed her PhD at Cornell University in Ithaca, New York, and a postdoctoral fellowship at Fred Hutchinson Cancer Research Center (FHCRC) in Seattle, Washington.

Zanders' research focuses on a set of genes called selfish genes. Unlike genes that encode for proteins crucial to healthy function of an organism, such as insulin or collagen, selfish genes "have no apparent redeeming features," Zanders says. Their sole function appears to be to promote their own survival by ensuring their presence in the genomes of the offspring of an organism.

While investigating meiotic recombination, a critical step in the formation of gametes, as a graduate student at Cornell University, Zanders noticed something fascinating. "I was puzzled that the genes responsible for meiosis were rapidly evolving," she says. "The fact that the meiosis field of researchers had no satisfying explanation for their rapid evolution suggested that there was something important about meiosis that we were missing."

When Zanders moved to FHCRC she began exploring, under the tutelage of Harmit Malik, PhD, and Gerry Smith, PhD, the possibility that selfish genes could drive the evolution of genes, including those required for meiosis. Ultimately, Zanders' findings, published in 2014 in *eLife*, suggest that selfish genes play a role not only in the evolution of genes, but in the evolutionary process of speciation.

Here at the Institute, Zanders plans to continue her research of selfish genes to gain a better understanding of their impact on fertility and thus genome evolution and speciation.

Ariel Bazzini, PhD

Assistant Investigator

If he couldn't become a professional soccer player, he would do what he thought was the next best thing and become a scientist. And by age 15, Ariel Bazzini, PhD, had set his sights on pursuing science. His dreams were instilled and encouraged by his middle school biology teacher's lectures on the Human Genome Project.

Those early lessons fed a curiosity that led him to the University of Buenos Aires for master's and doctoral degrees in molecular biology. He pursued his doctoral studies in plant genetics in the laboratory of Sebastian Asurmendi, PhD, at the Institute of Biotechnology in Argentina's National Institute of Agricultural Technology (INTA).

Bazzini continued his training as a postdoctoral fellow and subsequently an associate research scientist in the laboratory of Antonio J. Giraldez, PhD, in the Department of Genetics at Yale University. Bazzini's current focus on the regulation of gene expression in vertebrates originated during his time there.

One of Bazzini's early findings, reported in the journal *Science* in 2012, provided important evidence that "at a certain point of development and cell differentiation, very strong gene regulation can occur at the level of translation without any change of the mRNA level," Bazzini says. This suggested that using mRNA levels during embryogenesis as the sole indicator of gene regulation was not reliable. While the cellular processes of transcription and translation are very complicated and many questions about these processes remain, Bazzini looks forward to using the resources available at the Institute to tackle them in hopes of discovery.

Read more about these interesting individuals at www.stowers.org/research/scientists

Promotions and Renewal

Concluding a lengthy and in-depth review of three scientific research programs, the Stowers Scientific Advisory Board recommends promotion and renewal.

Matt Gibson, PhD – *promoted to Investigator*

Matt Gibson, PhD, researches how dividing cells become regimented into highly organized layers known as epithelia. Epithelial tissue covers multiple surfaces, lines cavities, and provides a variety of functions for an organism. He seeks to understand the mechanisms that coordinate this tissue's architecture.

Gibson's research is a comparative analysis of epithelial morphogenesis, architecture and growth control in fruit flies and the sea anemone *Nematostella vectensis,* whose genome exhibits a surprising degree of complexity and similarity to the vertebrate genome. Gibson's epithelia research is likely to produce broad phylogenetic significance as well as direct relevance to epithelial cancers and other forms of proliferative disease.

Kausik Si, PhD – *promoted to Investigator*

What are the biochemical mechanisms that create long-term memory and produce a persistent change in behavior? This question forms the basis of the research programs of Kausik Si, PhD. What Si currently knows is that a messenger RNA (mRNA) binding protein called cytoplasmic polyadenylation element binding (CPEB) is involved in the persistence and recall of long-term memory. The CPEB protein also forms stable aggregates similar to prion-like proteins.

Si's research program utilizes the fruit fly version of CPEB to interrogate how and specifically where these proteins form into a prion-like aggregate that facilitates synaptic changes associated with memory storage, yet without the destructive results of true prions. He is also exploring what happens to these protein aggregates when memory is forgotten or decayed.

Ting Xie, PhD – *renewed as Investigator*

When Investigator Ting Xie, PhD, joined the Stowers Institute in 2000 he established a research program that examines the mechanisms by which stem cells differentiate to become specialized cells. Xie has continued his exploration of stem cell communities called niches and the relationships of stem cells within the niche.

Much like siblings in a family, sometimes stem cells cooperate and at other times they compete for attention. Cancer stem cells, which drive tumor growth, take advantage of competition to push "good" stem cells out of the niche, leading to tissue destruction. Xie's quest is to enable future therapies by revealing key aspects of stem cell regulation in animal model systems and determining what's similar in humans.

HR leader with a unique interest in basic research joins the Institute

Autumn arrives at the Institute with the addition of George Satterlee as the vice president of human resources. He will oversee the Institute's programs related to human resources, including staffing, member relations, immigration, compensation, compliance, policy development, and strategic planning.

As a Kansas City native, Satterlee had been aware of the Stowers Institute since its beginnings. When his son, Andrew Satterlee, spent two summers pursuing research in Investigator Ron Yu's lab, he became more closely acquainted with the Institute's work and mission. However, it was an earlier, more personal experience that originally ignited Satterlee's interest and appreciation for the kind of basic research pursued by Stowers scientists. After his son was diagnosed with a germ cell brain tumor, Satterlee immersed himself in scientific and medical research. Seeking to help guide his son's treatment and find expert answers to his questions, he read scientific journal articles and medical textbooks. He even sought advice from basic researchers working in the field of germ cell tumorigenesis.

"I give great credit for Andrew's health to the many national and international experts who were doing both basic and translational research on germ cell tumors," said Satterlee. "I'll be forever grateful to the many scientists and physicians who devote their lives to solving complex problems that either directly or indirectly impact human life. The important work being done at the Institute isn't lost on me. I'm honored to serve an organization with such an important mission."

Satterlee joins the Institute from Missouri Bank, where he was responsible for the company's human resources, organizational development and effectiveness, marketing and public relations, strategic planning, and crisis management. Prior to his 17 years at Missouri Bank, Satterlee spent 15 years at Hallmark Cards, where he held a variety of human resource positions. In addition, he has been extensively involved with civic and nonprofit organizations such as the Greater Kansas City Chamber of Commerce and Children's Center for the Visually Impaired. He also serves as a mayoral appointee on the board of directors of KC Workforce Investment Board/Full Employment Council.

"George Satterlee's wealth of experience in human resource management, organizational leadership, and strategic thinking, along with managing personal challenges, makes him uniquely qualified for a role at the Institute," said Stowers Vice President for Administration Abby Freeman. "He has an appreciation for the Institute's culture and recognizes the exceptional talent of our workforce. I know George will serve our members well and help ensure they maximize their contributions to achieving the Institute's goals."

Satterlee earned an undergraduate degree from Westminster College in Fulton, Missouri, with an emphasis in business administration and political science. He has a Master of Liberal Arts degree in philosophy from Baker University in Baldwin City, Kansas, and attended a three-year program in the Graduate School of Banking and in Executive Leadership at the Wharton School of the University of Pennsylvania in Philadelphia.

Satterlee lives in Overland Park with his wife, Susan, and their dog, Maggie. Their daughter, Sarah, lives in Michigan. Andrew recently received a PhD in biomedical engineering from the University of North Carolina (UNC) and is preparing to begin a postdoc experience working on the problem of partially resected glioblastoma brain tumors, also at UNC.

SUSAN LINDQUIST, PHD

1949-2016

Susan Lindquist, PhD, a highly accomplished scientific leader and member of the Stowers Institute's Scientific Advisory Board from 2000 to 2011, passed away on October 27, 2016.

Lindquist was a pioneering scientist in the area of protein folding in health and disease, and was well known for the creativity of her research, the strength of her leadership, and her ability to unify others in a common pursuit of unconventional ideas. She was a member of the Whitehead Institute in Cambridge, Massachusetts, where she was a Howard Hughes Medical Institute investigator and professor of biology at Massachusetts Institute of Technology (MIT).

"Susan was a truly exceptional scientist who made landmark discoveries of broad significance, and she combined this with a passion for mentoring and developing the careers of young scientists," said Stowers Scientific Director Robb Krumlauf, PhD. "Her impact on the Stowers Institute was enormous."

Lindquist served a key role on the Institute's Scientific Advisory Board throughout its first decade to help place it on a successful trajectory. "Of particular note, Susan enthusiastically embraced the Institute's determination to make a cordial home for women investigators as well as men," said Stowers President Emeritus Bill Neaves, PhD. "Susan contributed immensely to the fulfillment of Jim and Virginia Stowers' vision for the Institute."

"Susan was by far the most formative scientific influence in my life," said Stowers Assistant Investigator Randal Halfmann, PhD, who was a graduate student in Lindquist's lab at MIT. "She believed that passion, versatility, and breadth of vision are the keys to long-term success. These values have strongly shaped my own thinking."

Stowers Assistant Investigator Nick Rohner, PhD, considers himself fortunate to have had the opportunity to collaborate scientifically with Lindquist and discuss ideas that seemed unlikely at first but often turned out to be game-changing. Stowers Investigator Kausik Si, PhD, agrees, "Susan was in the truest sense of the word an 'original thinker' and had the vision to see beyond the obvious."

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

Our founders, Jim and Virginia Stowers, had one vision for the institute they established. They wanted to give people "Hope for Life"—hope for a better life. Their unwavering determination to help make the lives of others better resulted in a scientific institution that is a nucleus of innovative research.

With state-of-the-art laboratories, cutting-edge technologies, and trailblazing researchers, the Institute is positioned at the forefront to unravel the complex mechanisms behind health and disease and to lay the groundwork for novel treatments and cures.

This formula for scientific excellence is made possible by the Hope Shares Endowment. We are fortunate to have the support of many loyal donors who know their generous investment in science helps to secure the Institute's future and accelerates our researchers' path of discovery that leads to improved human health.

As the Hope Shares Endowment grows, it ensures that Jim and Virginia's extraordinary vision endures for generations to come. We encourage you to consider a gift to the Stowers Institute that will continue our progress in advancing knowledge and providing Hope for Life.

BACKSTAGE PASS

The sights, sounds, and smells of a traditional library are distinct—stack upon stack of books, the smell of aging paper and bookbinding glue, the squeak of wooden chairs, and the hushed whispers of library patrons. But at the Stowers Institute one will find a vastly different library environment—soaring panes of glass, inviting furniture, and the click-clack of a computer keyboard during the workday or the gentle music of a string quartet during an evening reception.

Instead of large physical collections of books and journals, most library information at the Institute is now housed and maintained digitally by two library specialists who provide an array of assistance to the Institute's researchers.

LIBRARY SERVICES BY THE NUMBERS

1,000,000+
Laboratory notebook pages scanned for digital archiving

58,860
Citations of publications with Stowers Institute affiliations

16,000
Book or journal requests filled via interlibrary loans

1791
Year of publication of the oldest paper requested and obtained

1,753
Library archived documents and records

1,382
Documents, including books and scientific papers with Stowers Institute affiliations

1,358
Scientific posters printed for research presentations

450+
Print books in the Stowers Library Catalog

300
Electronic journal subscriptions

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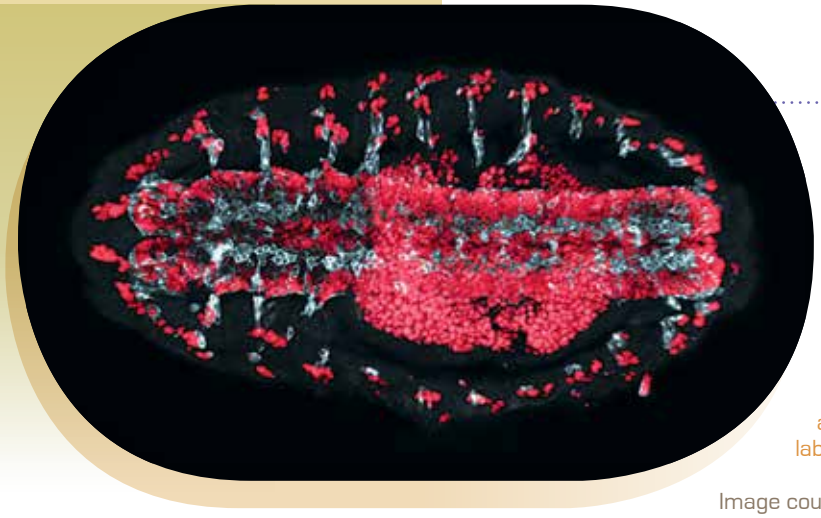
OUR MISSION:

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.



How cells of an organism acquire their individual identities and functions is a long-standing question in biology. During this process, each cell type generates its own gene expression programs by reading DNA in a context-specific manner. The Zeitlinger Lab develops genomics tools to examine and understand gene expression programs on a genome-wide level and uses the well-studied fruit fly as a model system.

The image shows a ventral view of a *Drosophila melanogaster* embryo in which several cell types are highlighted. Neurons are stained in red (by anti-Elav antibody) and glial cells are labeled in white (by repo-GAL4, UAS-GFP).

Image courtesy of Bjoern Gaertner, Zeitlinger Lab.