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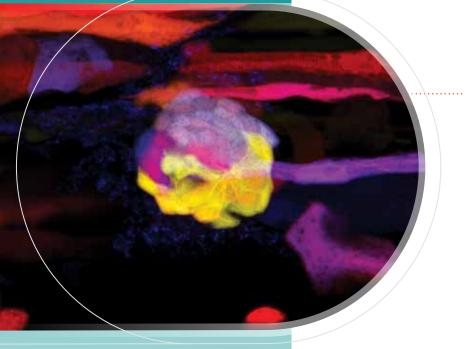




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# **OUR MISSION:**

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



THE SENSORY LATERAL LINE IN FISH CONSISTS OF HAIR CELLS, WHICH ARE GENETICALLY AND FUNCTIONALLY SIMILAR TO HAIR CELLS IN THE INNER EAR OF HIGHER VERTEBRATES. ASSOCIATE INVESTIGATOR TATJANA PIOTROWSKI, PHD, USES THE ZEBRAFISH LATERAL LINE AS A MODEL SYSTEM TO STUDY STEM CELL REGULATION AND HAIR CELL REGENERATION.

IMAGE: Sensory organ expressing distinct fluorescent proteins in individual cells. Courtesy of Andres Romero-Carvajal.



# STOWERS REPORT

NEWS AND INSIGHT FROM THE STOWERS INSTITUTE FOR MEDICAL RESEARCH









### STOWERS REPORT

PUBLISHED BY THE STOWERS INSTITUTE FOR MEDICAL RESEARCH



### MEET THE 2012 PREDOCTORAL RESEARCH SCHOLARS

Smart, enthusiastic and ready to emerge themselves in research

- BACK TO SCHOOL IN JUNE
  As foremost experts in their field, Stowers Investigators are regularly invited to teach students from all over the world.
- A DISCUSSION WITH ROBB KRUMLAUF
  The scientific director talks about his vision for the institute
- ON THE MOVE

  The constant remodeling of their internal skeleton propels cells forward
- RAUL DIAZ

  The enterprising reptile hunter forges his own academic path

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The future of biomedical research depends on instilling a passion for science and discovery in talented, driven students and on preparing them to serve as future leaders of the scientific enterprise.

Scientists learn their craft through a combination of formal training and informal apprenticeship. At first, undergraduate and graduate coursework provides young scientists with the conceptual frameworks and basic facts that form the foundation for a lifetime of learning. Later, as graduate students, postdoctoral researchers or even young independent investigators, junior scientists hone their skills and develop a wider understanding of science through their relationships with more senior mentors. Coached and motivated by their advisors, young researchers learn how to identify a significant and solvable question, how to design experiments and get them funded; how to write and publish a paper; how to grab and command an audience's attention and how to navigate critical junctures in their careers. Almost all successful scientists fondly recall the nurturing and care of at least one mentor who served as a continual source of wise counsel and inspiration.

Conversely, scientists leave a lasting legacy not only through the discoveries they have made but also, and perhaps more enduringly, through the protégés they have trained. Mentorship is such an important measure of success that scientific resumes (called *curriculum vitae*) list all of an investigator's protégés and their current positions. The legacy of investigators at the Institute will be defined as much by subsequent generations of scientists whose professional development they have guided and encouraged as by their scientific discoveries.

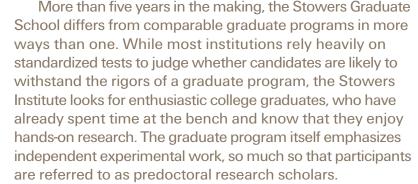
Investigators' long-term impact will reach far beyond the body of knowledge contributed over the years, no matter how significant their experimental results prove to be.

The dedication and commitment of senior scientists enable the Institute to offer training opportunities that attract young scientists from around the world. Currently, the Institute hosts about 180 undergraduates, predoctoral research fellows and postdoctoral researchers, recruited from over thirty countries. As part of the Stowers Summer Scholars program, undergraduates can try their hand at the bench, many for the first time. At the same time, predoctoral research scholars from the Open University, the University of Kansas and other institutions perform their dissertation research in the labs of Stowers investigators. The undergraduate and predoctoral scholars are joined by an international group of postdoctoral scientists, many of whom are taking the final step before launching an independent research career. This fall, we are especially pleased to welcome the first group of predoctoral researchers to the Institute's new graduate program.

In this issue of the *Stowers Report*, many of the Institute's scientists describe the joy and satisfaction of coaching and mentoring the next generation of scientific leaders. I hope you will enjoy reading about the various ways the Institute helps prepare young researchers for a career in science and will come to share my unwavering view that their passion, energy and talent bode well for the future of biomedical research.

MEET THE 2012 PREDOCTORAL

RESEARCH SCHOLARS



"The sole criterion for admission to the Stowers Graduate School is extensive, highly successful research experience," explains R. Scott Hawley, PhD, dean of the graduate school. Not surprisingly, all incoming predoctoral research scholars have, or soon will have, co-authored papers in scientific journals—indeed a number of them are the first author on manuscripts that are already published or are currently being written. "But more importantly, they all took intellectual

ownership of their projects and answered in-depth questions by a panel of Stowers investigators during the interview," he says. "That really attests to a high degree of independence."

During the first term, the predoctoral research scholars

participate in novel researchintensive modules in which they are introduced to and work closely with Stowers Institute investigators to become familiar with the latest research tools and acquire the necessary skills to analyze complex data. In January, they are at the bench full-time and get to know several research labs first hand during three consecutive two-month rotations. Come June, they join their dissertation lab and start tackling one of the big unsolved questions of life. Meet the next generation of scientists:

CORI CAHOON
University of California, Davis

It was love at first sight.

After spending many summers working at her father's animal clinic, Cori Cahoon was on the fast track to continue the family tradition and become a veterinarian until her first genetics class at the University of California, Davis, threw her off course.

Fascinated by the ever-present influence of genes on all aspects of life, Cahoon changed plans and graduated with a

bachelor's degree in genetics.

As an undergraduate, Cahoon worked in a lab studying the mustard weed Arabidopsis, the lab rat of plant biologists. But before she took the grad school plunge, she wanted to make sure that full-time, hands-on research actually resembled the glorified pursuit portrayed in books and memoirs. So after college she took a position as a research technician at UC Davis. There she found herself on what she describes as an exhilarating roller coaster ride, where the disappointment of failed experiments and the excitement of unexpected discoveries chase each other in quick succession. That "dry run" as a bench scientist convinced Cahoon that she was ready to embark on a research career.

Along the way she has discovered that scientists and veterinarians have more in common than lab coats: Each tries to solve a puzzle by collecting small pieces of information and putting them together, whether to understand a fundamental biological principle or what's ailing a dog.

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### KRISTI JENSEN University of Kansas, Lawrence

Pond scum, the green slimy muck that covers still waters the world over, has launched many a scientific career and Kristi Jensen's is no exception Since her first close-up of pond water teeming with microscopic organisms, she has been on a straight trajectory from amateur field biologist to research scientist. Jensen grew up on a family farm in rural Kansas and entertained herself during endless summer days by hunting for fossils and examining fresh water microbes. Soon she became fascinated by the simplicity of single-celled organisms and, not surprisingly, she graduated with a bachelor's degree in microbiology from the University of Kansas in Lawrence.

Throughout college she had worked full time as a certified nursing assistant and briefly considered enrolling in medical school. However, her firsthand experience with the lack of efficacious treatments for many of her patients reinforced her belief that she could have a bigger impact on people's lives as a scientist.

Despite her interest in microbiology, Jensen became enamored with neurobiology when she moved to Kansas City to join Stowers Associate Investigator Ron Yu's lab as a research technician. For the last year she has studied the effects of estrus pheromones on the behavior of female and male mice. Ready for more exploration, Jensen is excited about the prospect of doing lab rotations and learning about many other areas of research.

### MELVIN NOÉ GONZÁLEZ

National Autonomous University of Mexico, Cuernavaca Morelos

When Melvin Noé González considered his options for undergraduate studies at the National Autonomous University of Mexico, he gravitated toward biology. A traditional biology major, however, didn't seem like the right fit and he opted for medical school instead. But then he heard about a pioneering genomics degree offered by the university. It emphasized genetics and bioinformatics instead of botany and zoology and replaced

traditional lectures with talks by world-renowned scientists hosted by students. It was exactly what Noé González had been looking for. He sailed through the program's selective entry exam and made the switch to the Genomic Sciences program.

During one discussion, a visiting speaker told him about Stowers Investigator Alejandro Sánchez Alvarado's work on flatworms, those undisputed champions of regeneration. Noé González decided to travel to the Sánchez Alvarado lab to do undergraduate thesis work. Armed with unflagging enthusiasm but lacking hands-on lab experience Noé González immediately took to the bench and, by his own estimate, spent more time there than in his apartment, immersed in the study of epigenetic changes necessary for flatworms to reinvent themselves.

After a steep learning curve and a few failed experiments, he got his project off the ground and graduated with a bachelor's degree in genomics from the National Autonomous University. Noé González was so impressed by the supportive Stowers community that he applied to and was accepted into the Stowers graduate program.

### SOON KEAT OOI National University of Malaysia, Bangi

Before Soon Keat Ooi ever set foot on US
soil he was already intimately familiar with the Stowers
Institute. An Internet search for "histone modifications"—
which are an integral part of the regulatory network
that controls whether genes are on or off—had led
him straight to Stowers Investigator Jerry
Workman's research. Equally impressed by the
rest of the world-renowned investigators who call
Stowers their intellectual home, Ooi applied to the
institute's graduate program.

Although he found Stowers through virtual means, his scientific curiosity was sparked in a hands-on manner. In high school biology class, his classmates refused to even touch a frog during a dissection, but Ooi leaped at the opportunity to disassemble the frog and then spent hours studying it. Afterwards, Ooi felt increasingly compelled

to learn about the molecular origins of disease, particularly after his grandmother succumbed to cancer.

After graduating from the National University of Malaysia with a degree in molecular biology, Ooi took a position as a research assistant and started working on the bacterium *Burkholderia pseudomallei*, which causes a life-threatening disease endemic to Malaysia and parts of Australia. Throughout his training, mentors had emphasized the importance of understanding how biological processes are regulated, kindling Ooi's interest in the epigenome. Little did he know that in his quest to learn more, a simple Internet search would take him from Kuala Lumpur to Kansas City.

### RYAN RICKELS

University of Tennessee, Knoxville

Reading changes lives. This has never been truer than in the case of Ryan Rickels, who was well on his way to a bachelor's degree in fine arts when a stray copy of *Scientific American* stopped him in his tracks. Mesmerized by an article about sensors that could read movement-generating brain waves, Rickels abandoned media arts and set his sights on biology. Any lingering doubts about switching majors just one year before graduation disappeared as soon as he hit the bench. He had so much fun he knew he had made the right choice.

Growing up, Rickels had been interested in all things science fiction and couldn't get enough of the movie Jurassic Park. But once he entered high school, his interest in music took over and he became busy playing guitar and bass in bands and planning a future as an artist. When he read the fateful magazine article, it sounded as futuristic as the science fiction books of his childhood and rechanneled his interest toward science.

Four years later, Rickels graduated with a bachelor's degree in biochemistry, cell and molecular biology from the University of Tennessee. He was working as a research technician at UT when an essay on regeneration in flatworms—authored by Stowers Investigator Alejandro Sánchez Alvarado—piqued his interest. From there it was only a short step to submitting an official application to the Stowers graduate program.

### WANQING SHAO

Wuhan University, China

Hearing a presentation given at Wuhan University by Stowers Associate Investigator Ron Yu was all that it took to convince Wanqing Shao that her future was at the Stowers Institute. Participation in the Stowers Summer Scholars program—an intense ten-week, hands-on research experience—seemed like a natural first step in getting there, but the application deadline had passed. With Yu's encouragement, she nevertheless pursued a position in the program. Her tenacity paid off and she joined the Summer Scholars class in 2011.

During that summer, Shao's abilities so impressed Stowers Assistant Investigator Julia Zeitlinger that at the completion of the program, Zeitlinger offered her the opportunity to remain in Kansas City as a short-term Stowers International Scholar. Shao stayed on and completed her undergraduate biology degree requirements at Wuhan University while working on transcription in *Drosophila* embryos in the Zeitlinger lab. Last year Shao applied and was accepted for a position in the Stowers graduate program.

As a child, Shao's desire to pursue science was initially sparked by watching programs on the Discovery Channel. Her mother, an accountant, and her father, a police officer, encouraged her interest in biology by always reminding her that scientific knowledge is power. That family support, plus her natural curiosity, will likely drive Shao to pursue her dissertation research with the same gusto she brings to solving crossword or sudoku puzzles.

## CHRISTINE SMOYER University of Kansas, Overland Park

Christine Smoyer was an intellectual nomad before her inquisitive mind found a home among fellow scientists journeying to the uncharted depths of life itself. Waitressing, road paving crew, retail management—Smoyer did it all before she embarked on a short but



successful career as a banker. When she grew increasingly bored with crunching lifeless numbers, she started taking science classes at her local community college in Overland Park, Kansas. From there she quickly moved on to the Molecular Biosciences Program at the University of Kansas and quit banking for good.

When Smoyer had the opportunity to work in Stowers Investigator Scott Hawley's lab as an undergraduate, she knew she had found her calling. Textbooks had left her with the impression that all the important questions in biology had been answered. As soon as she started working in the lab she realized how much of life's complexity is still unexplored, sparking her desire to learn more.

After graduating from the University of Kansas,
Smoyer took a position as a research technician with
Stowers Assistant Investigator Sue Jaspersen and threw
herself into the challenge of understanding cell division.
Occasionally she considered going to graduate school but
found it difficult to let go of her projects. Encouraged by
Jaspersen and inspired by an exhilarating teaching stint at
a Cold Spring Harbor summer course, the banker-turnedscientist is ready for the next leg of her journey.

### AMANDA WILSON University of Kansas, Overland Park

If passion and perseverance are what it takes to succeed as a predoctoral research scholar, Amanda Wilson is well equipped to tackle the challenges ahead. When her son was ready for kindergarten, she decided to go back to school herself. She started taking classes at the University of Kansas while working full-time as a lab assistant in the microbiology department of Quest Diagnostics, a clinical lab test provider.

Wilson, who had always had a penchant for math and science, enjoyed her work at Quest but quickly realized that what she really wanted to do was research. Inspired by a genetics course she took, taught by Stowers Investigator Scott Hawley, she decided to sacrifice even more of her sleep and added an internship in Hawley's lab at the Stowers Institute to her already crammed schedule. Working in a research lab gave her a first taste of the rush of discovery and reinforced her decision to become a scientist.

Despite sixty-hour workweeks—not counting study time—Wilson tenaciously kept her focus on the ultimate prize and graduated from the University of Kansas with a bachelor's degree in molecular biosciences in 2010. Since then, she has been working in Hawley's lab as a research technician. For the time being, she enjoys working only one job and holding increasingly sophisticated discussions with her son, who has apparently inherited her scientific bent.

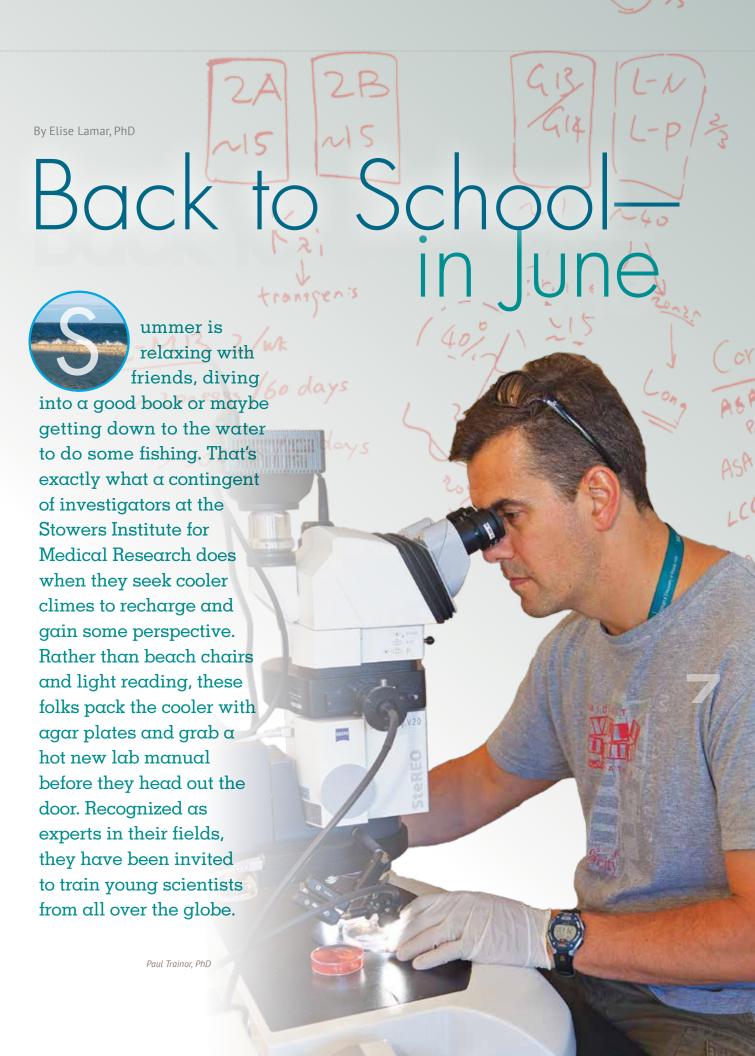
### KOBE YUEN

Chinese University of Hong Kong, Hong Kong

Why is lemon juice sour? Why do people look like their parents? Why do things fall down and not up? Even the most insistent children stop barraging their parents with constant questions at some point, but Kobe Yuen never tired of looking for an explanation and started experimenting to find out the "why".

His first scientific project involved the conversion of coconut shells into activated carbon in his school's chemistry lab. Albeit technically successful, the acrid fumes produced during the process had people gasping for fresh air. Creation of a gas-driven seatbelt, which reduced the impact force on the driver by 40 percent, was not only less offensive to bystanders' throats and noses; it also earned Yuen and his science fair team a trip from Hong Kong to the Shanghai International Youth Science and Technology Expo 2005, where they won in the category of Best Demonstration.

Gradually, Yuen's scientific curiosity turned to biomedical science and he enrolled at the Chinese University of Hong Kong. There, he delighted in spending time at the bench and co-authored two scientific papers. After graduating with a bachelor's degree in molecular biotechnology, he took a position as a graduate research associate in a developmental biology lab, an area of biological research he is particularly drawn to. Not surprisingly, he cites Stowers' strong program in developmental biology as the main reason he applied to the Stowers graduate program. §§



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Each year, several Stowers investigators team up with colleagues from academic institutions worldwide to organize or teach renowned summer courses at two world-class seaside laboratories: the Marine Biological Laboratory located at Woods Hole in Cape Cod, Massachusetts, and at the Cold Spring Harbor Laboratory (CSHL), a research institute on Long Island, New York.

These are picture-postcard spots. But instead of picnicking on the beach, faculty and students put in twelve- to fourteen-hour days crammed with lab and lectures, with maybe a Sunday off. They may be intense, but for most participants, CSHL and Woods Hole training courses are life-changing and career-altering experiences.

### Kicking back at Cold Spring Harbor

Stowers Assistant Investigator Sue Jaspersen, PhD, was one of three instructors who ran this summer's CSHL Yeast Genetics & Genomics course. Long

before flying east, she planned labs, invited distinguished yeast geneticists as guest speakers, wrote experimental protocols, shipped boxloads of Stowers-made agar plates to

Long Island and devised free-time activities for sixteen graduate students and postdocs.

Once there, Jaspersen and her colleagues worked around the clock to teach students how to conduct, and think about, yeast genetics experiments. A typical day during the three-week course started off with "Marching Orders" for the day, followed by lectures until lunch, and continued with lab work that could last until midnight and was interrupted only by dinner and a guest speaker late in the afternoon.

Jaspersen herself ran five experiments,

among them, "Characterization of Auxotrophic,
Temperature-sensitive and Osmotic-sensitive
Mutants"—a genetics classic that has been taught
every year since the CSHL yeast course premiered in 1970.

Others sounded more intuitive, such as "Looking at Yeast Cells" (an imaging experiment) and "Dr. Evil," in which students were tasked with deducing the mystery gene damaged in mutant yeast.

Why would Jaspersen—in the early years of a demanding career—devote such energy to tasks that won't form the basis for her next paper? Simple. "Teaching is one of my greatest responsibilities," she says. "By training students to conduct well-designed experiments and address important questions, I make sure the next generation will continue doing rigorous science."

#### Crepidula, cerebratulus and squid

Over in Woods Hole, Stowers
Investigator Alejandro Sánchez Alvarado,
PhD, co-directed the Embryology course
along with his colleague Richard Behringer,
PhD, from the MD Anderson Cancer
Center in Houston, Texas. Every year, this
six-week course gathers twenty-four young
developmental biologists who learn to



Alejandro Sánchez Alvarado, PhD

manipulate classic model systems such as fruit flies, frogs, zebrafish and mice, and explore new ones, such as Sánchez Alvarado's specialty, the flatworm planaria.

The Embryology course has a deep history: It was first taught in 1893, a mere five years after the establishment of the Marine Biological Laboratory in Woods Hole. And it is no accident that this grandfather of summer biology schools began by the sea. Many of the first animal models studied, like sea urchins and jellyfish, were not ordered from a biological supply company but pulled right out of the sound.

This summer—119 years later—was no different. For the marine model organism module (on the syllabus: "crepidula, cerebratulus and squid," aka slipper limpets, ribbon worms and, well, squids), student volunteers went fishing for comb jellyfish,

induced them to spawn in the lab and collected embryos at various stages of development. The goal: to carry out the first characterization of its "transcriptome," meaning the entire battery of genes that regulates its embryogenesis.

Sánchez Alvarado, who coincidentally launched his career by collecting flatworms out of a Barcelona fountain, plans to pioneer

an emerging model organism every summer. "Ours is not only a teaching exercise," he says. "Our goal is to practice discovery research as we teach what is known about developmental biology. The hope is that the data, knowledge and understanding obtained from these understudied organisms can

be brought together and published in a comprehensive, comparative paper authored by the students and faculty who participate on this multi-year project."

Like their CSHL counterparts, Woods
Hole students work 24/7. Days and nights
are filled with lab work and talks, many by
guest lecturers drawn from a Who's Who
of developmental biologists. At bench
sessions that go on past midnight, students
inject genes into embryos, learn microscopy
or hone homemade tools to manipulate
embryos. "We don't force students to do
work," says Sánchez Alvarado. "They do it
because they want to."

If his students are like Stowers scientist Paul Kulesa, PhD, he's right. Kulesa, who was a speaker and instructor this summer at a Light Microscopy course at McGill University in Montreal, recalls a six-week course where, as a student, he learned to use a confocal microscope to study wound healing using Xenopus tadpoles. "I would stay up all night refining the chamber, labeling cells, and making sure manipulation time was short, because cells moved very dynamically to close the wound," he says. "Over consecutive late nights I joined the ranks of 'confocal zombies.'" Kulesa now directs the Imaging Center at the Stowers Institute.

#### No need to raise your hand

Lectures at these courses are hardly didactic. Instead, intense interchanges among and between students and faculty are expected. Some are structured, like the one-hour discussion between students and faculty that follows immediately after each morning session and the short "Show and Tell" feedback sessions for the Embryology course students, or the all-day "Data Fest" that closes the yeast meeting. But important contacts are also made over a beer or during late nights in the lab.

Stowers Associate Investigator Paul Trainor, PhD, says these interactions flourish in part because, as on real summer vacations, people are far from the pressures of home and work. Apparently, even the superstars catch the sociability bug. "Visiting faculty often stay much longer than their teaching obligation requires because they like to discuss their science openly and get feedback," says Trainor, who in July hopscotched between CSHL and Woods Hole to instruct three classes, including the Embryology course mouse module. "The students are not yet encumbered by established dogma so they ask questions you wouldn't expect."

Dogma may also be scarce because students and faculty are diverse. "These courses gather groups of students from all over the world who are dedicated, motivated and love science," says Stowers Associate Investigator Tatjana Piotrowski, PhD, who co-led the Embryology course zebrafish module with Elke Ober, PhD, from the Medical Research Council in London. "Nothing is more stimulating than working together with people who share the same interest."

Piotrowski took the course in 1995 when she was a graduate student and said it profoundly influenced her career path. There, she also met another student, Sánchez Alvarado, whom she later married, proof that science fosters lifelong relationships.

### Exhausted but knowledgeable

Stowers Investigator Ali Shilatifard, PhD, has been jointly teaching the Eukaryotic Gene Expression course at CSHL with other leading experts in the field since 2003. This year, the Gene X course, as it is commonly known, marked its twenty-fifth anniversary, hosting sixteen students eager to learn the nuts and bolts of gene regulation in organisms (including mammals) whose chromosomes reside in a nucleus, known technically as eukaryotes.

Shilatifard and his colleagues create a new curriculum every year, convince colleagues with chromatin star power to fly out as guest speakers, and write the lab manual—no small feat in a field moving so fast that last year's manual is obsolete.

Over three weeks, the students familiarized themselves with eighteen different molecular approaches to manipulate DNA, RNA and proteins to understand how genes get switched on and off. "If they were back in my lab it could take them months to master just one of these techniques," says Shilatifard. "The students leave the course exhausted but knowledgeable."

Possibly adding to the exhaustion was the event that caps the course—a relay race run by students from concurrent courses while balancing stacks of agar plates stinking with old yeast and bacteria colonies. This year's event pitted Jaspersen's class against Shilatifard's. Although Yeast has a history of trouncing Gene X—the two courses are always held at the same time—fortunes were reversed when Shilatifard signed on as a coach. Since then, Gene X has won five out of the last six competitions. This year,

however, team Yeast rallied and reclaimed the title of plate race champion. "This teaches them the value of hard work," says Shilatifard proudly. "Plus, the spirited competition provides a welcome release from long hours in the lab."

But the real triumph, Shilatifard says, is when he sees students who came in with little knowledge of chromatin biology leave feeling like experts. "In the beginning of my career, somebody taught me," he says. "Now, it's my scientific duty to give back to the community."

The desire to give back is a sentiment echoed by all mentors, including Stowers Investigator and Dean of the Stowers graduate school Scott Hawley, PhD. For twenty years Hawley has taught various courses in the US, the UK, India and China. This summer he traveled to England to organize a Drosophila Genetics and Genomics course in Cambridge.

"It is an honor to pass knowledge to successive generations," says Hawley.
"When your student establishes their lab and becomes a terrific scientist, it feels good to think the course played some small role in the process."



### THE EXCHANGE

### A DISCUSSION WITH

# ROBB KRUMLAUF

Robb Krumlauf, PhD, took a career detour into chemical engineering before he finally found his calling as a biologist. During a postdoc at the Fox Chase Institute for Cancer Research in Philadelphia he did research on emerging techniques of inserting genes into the mouse germline to create "transgenic mice," which would help revolutionize mouse genetics and facilitate the use of mice as a model to understand human development and disease.

In his first faculty job, Krumlauf immersed himself in vertebrate developmental biology at the field's epicenter, England's National Institute for Medical Research in the Mill Hill region of London. His studies there were among the earliest to show that regulatory genes defining an organism's basic body plan were conserved structurally and functionally in the genomes of vertebrates and insects.

Initially, Krumlauf had planned only a short sojourn in the UK, but the mix of groundbreaking research and collegiality kept him at Mill Hill for sixteen years. During his last decade there he served as head of the Division of Developmental Neurobiology.

Lured by Jim and Virginia Stowers' vision for a new kind of research institute, located in Kansas City, Krumlauf returned to the US with a clear sense of the importance of interdisciplinary research and collegiality and a love of canal boating. He became the first senior faculty member of the Stowers Institute, when he took on the role of scientific director in 2000.

# WHAT DO YOU CONSIDER THE MOST IMPORTANT ASPECT OF YOUR RESEARCH?

Our discovery that Hox genes, which control formation of the basic body plan, are essentially the same in mice and flies had a big impact on thinking in the field: it helped people realize the value of studying model organisms and showed that we don't have to redo every experiment or restudy all basic processes in every species. We can study programmed cell death in worms and it immediately translates to other species. Now, everybody takes it for granted that there is a common genetic tool kit and that all organisms have surprisingly similar numbers of genes. The main difference may be in how they deploy those genes. This means we can effectively study human disease processes in model organisms when they are not tractable or can't be studied for ethical reasons in humans. It really drives home the power and value of basic research.

### WHAT DID IT FEEL LIKE TO BE PART OF WHAT YOU ONCE DESCRIBED AS THE HEYDAY OF DEVELOPMENTAL BIOLOGY?

It felt wonderful and exciting. For one, we began to realize the importance of what technology could do for biology. I always thought science was progressing in modest increments and eventually they would all add up to a new insight. All of a sudden, new technologies allowed us to ask really big questions and we could ask them now. As a result, a small group of people, who interacted with each other and followed

creative and innovative ideas, made Mill Hill one of the leading if not the leading institute in mammalian developmental biology. I was proud to be associated with a group making so many cool discoveries. I had so much fun and so much joy that I never thought of leaving.

### WHAT CONVINCED YOU TO LEAVE FOR AN UNKNOWN FUTURE?

I was at one of the best places in the world to do science and it was, in part, my experience there that made me think that Stowers could succeed. Mill Hill had demonstrated that it was possible for

a small institute to become an outstanding place if you were focused and you had really good people. I was very attracted by Jim and Virginia's commitment to excellence and their vision of an institute that encouraged interdisciplinary science and was willing to fund the necessary expertise and cutting-edge technology that would help people do that.

be a great way to facilitate outstanding

science for other people. If I could help

make this work, that might be a better

YOU HAVE SHAPED THE STOWERS

INSTITUTE'S SCIENTIFIC DIRECTION

From day one, Bill Neaves [the founding

commitment to excellence. We wanted to

levels. Since we did not have a ready-made

culture like MIT or Harvard we had to carefully

craft our own. Hence, we also put a lot of

hire the best people we could find at all

SINCE ITS INCEPTION. WHAT ARE

president] and I were aligned in our

YOUR GUIDING PRINCIPLES?

I am proud of what we have done.

legacy than any science that I contributed.

WHAT WAS YOUR BIGGEST CONCERN? I hope that we will have had a positive impact on science not only through I wanted Jim and Virginia's vision to be successful and I mostly worried whether I could do what they wanted me to do. I had been focused primarily on my own research for a long time, but came to think this would be a way of giving back to honor people who had helped me so much during my career in science. I believed that this model for an institute could really work and would

### HOW DID YOU FIRST BECOME INTERESTED IN SCIENCE?

I came to biology late. When I was in high school the space race was in full swing and we were geared toward science and engineering, so I ended up in engineering school. I didn't take my first biology class until after I graduated from university and was working as an engineer. As I began to see the wonders of biology, I just fell in love with it and instantly knew I had to do this. I gave up my engineering career—which drove my parents crazy—and went back to school to get a PhD in developmental biology.

emphasis on collegiality, since interdisciplinary research requires people to work well together to create the necessary synergy to do pioneering work. Science and discovery should be fun, right? Our view was that if you had a collection of outstanding people who ask really interesting questions, like each other and push the envelope, you would have a powerful engine producing important discoveries.

### WHERE WOULD YOU LIKE TO SEE THE INSTITUTE DOWN THE ROAD?

I would like to see the institute as a key member of the elite group of institutions



While in England, Robb Krumlauf grew fond of canal-boating

that drive cutting-edge life science research significant contributions and discoveries made by researchers here but also through the people we train who will become future world leaders in science and go on to make major contributions by pursuing careers in science at other institutions. In that way, we will have capitalized on this amazing opportunity by giving not just to the city, the region and country but to the world.

#### WHAT'S THE BEST PART OF BEING A SCIENTIST?

Every day is different and you never know what you are going to learn. I love doing experiments to discover new things. It is so cool. My work as an engineer, however, was dreadfully predictable. Now I understand the frustration I felt at the time—I was not allowed to follow my natural curiosity and experience the joy of making new discoveries.

### WHAT WOULD YOU BE DOING IF YOU COULD NOT BE A SCIENTIST?

If I could not do science for a living, I would have loved to be an artist but

> I just have no artistic talent to speak of. My father tells me that he had to convince me not to major in art history. I also love to cook. I used to dream about owning a restaurant and a wine store, but I realize now that it is probably more fun to enjoy them than to actually run one.

### IF YOU HAD A MONTH OFF, WHERE **EVERYTHING STOPS—NO WORRYING** ABOUT DEADLINES OR ADMINISTRATIVE DUTIES-WHAT WOULD YOU DO WITH YOUR TIME?

I would head straight to the lab and do some experiments. The joy of having uninterrupted time to think while I am watching and doing experiments would be like a science holiday for me. It would also be fun to take a sabbatical in a different lab to learn new technologies. If the lab was off limits, I would either take a really long canal boat trip going through the English countryside or I would just go off and climb in the mountains for a month.

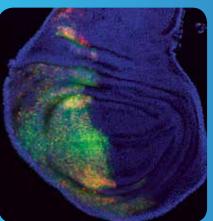
### WHAT'S YOUR CAREER ADVICE FOR YOUNG PEOPLE TRYING TO FIGURE **OUT WHETHER SCIENCE IS FOR THEM?**

Follow your passion. I could have stayed on as an engineer and probably would have been successful. I really derived no joy from that job and it was frustrating. I believe you need to explore and be bold enough to try different things. Success at whatever you do usually requires hard work, so finding something you are good at and enjoy makes the work more rewarding.

### IN A NUTSHELL

### **JARID2 MAY BREAK THE POLYCOMB SILENCE**

Historically, fly and human Polycomb proteins were considered textbook exemplars of transcriptional repressors, or proteins that silence the process by which DNA gives rise to new proteins. In a direct challenge to



that dogma, Stowers Investigator Ali Shilatifard, PhD, and his team report that in the fruit fly Drosophila melanogaster a component of the Polycomb repressive complex 2 (PRC2) occasionally activates gene expression.

Polycomb proteins, a group of chromatin-binding factors, were initially

found to control how developing fly embryos undergo segmentation. Subsequently, researchers discovered that humans also express a gaggle of proteins resembling fly Polycomb factors and that these proteins have crucially significant roles: under normal conditions PRC2 proteins are required for the differentiation of stem cells, but when overactive, they act as oncogenes in lymphoma and breast and prostate cancer.

"Our approach is to use *Drosophila* as a model to learn how Polycomb group proteins function in the context of cancer," says Shilatifard, who studies mechanisms underlying leukemia in yeast, fruit flies and mammalian cells. "In this study, we found that a new component of the PRC2 complex, Jarid2, maintains repression of some genes, but also potentially activates other target genes."

Recent reports implicate Jarid2 in diseases as diverse as multiple sclerosis and schizophrenia. But most significantly for the Shilatifard lab are studies linking both PRC2 and Jarid2 to myeloid cancers such as leukemia. "The theme of our lab is factors that regulate the vin and yang of transcription," says Shilatifard, citing his interest in both of the Polycomb proteins and their polar opposites, the Trithorax activator proteins, which have also been linked to leukemia. "Our overall goal is to gain insight into both." (S)

The study was published in the May 2012 issue of the journal *Molecular and Cellular Biology*.

## Smell is a symphony

Just as a road atlas faithfully maps real-world locations, our brain maps many aspects of our physical world: sensory inputs from our fingers are mapped next to each other in the somatosensory cortex, the auditory system is organized by sound frequency and the various tastes are signaled in different parts of the gustatory cortex.

The olfactory system was believed to map similarly, where groups of chemically related odorants—amines, ketones or esters, for example—register with clusters of cells that are laid out next to each other. When Associate Investigator Ron Yu, PhD, and his team traced individual odor molecules' signal



deep into the brain, they found evidence that chemically related odorants mapped all over the olfactory bulb, which processes incoming olfactory information.

"From the animal's perspective, that makes perfect sense," says Yu. "The chemical structure of an odor molecule is not what's important to them. They really just

want to learn about their environment and associate olfactory information with food or other relevant information.

To explain their observations, Yu and his team developed a "tunotopic" hypothesis of the olfactory system. Individual olfactory receptors are "tuned" not to one particular kind of odorant but to a variety of molecules, allowing the animal to better distinguish among the nuances of odors.

Imagine a roomful of musicians. In chemotopy, the musicians play one instrument at a time and never play with other instruments. The team's tunotopic hypothesis is closer to an actual symphony: Different instruments overlap to create many more different sounds than the individual ones could.

The tunotopic hypothesis may help us understand visual, auditory and somatosensory processing as well. In the case of olfaction, tunotopy allows the animal to discriminate between tiny variations in odor. That precision, from an evolutionary perspective, would come in handy as the animal sorted through its environment.

The study was published in the March 19, 2012, issue of the Proceedings of the National Academy of Sciences



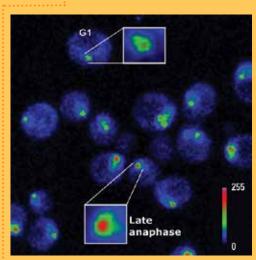
# DEBATE ENDS: EVERYONE WAS RIGHT

**CENTROMERES, SPECIALIZED** POINT OF THE "X" USED TO REPRESENT DUPLICATED **CHROMOSOMES. LINK THOSE DUPLICATED STRANDS WHEN CELLS ARE POISED TO DI-VIDE. AS DIVISION STARTS, A COMPLEX CELLULAR MACHINE** DRAGS EACH CHROMOSOME TO OPPOSITE POLES OF THE CELL BY GRABBING ONTO ING EACH ARM OF THE "X" INTO WHAT WILL BECOME A **DAUGHTER CELL. RESEARCH-ERS HAD KNOWN THAT A** OF DNA TWISTED AROUND A

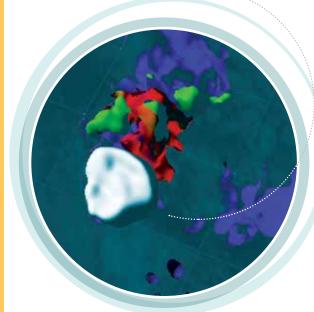
An interdisciplinary Stowers team led by Associate Investigator Jennifer Gerton, PhD, developed an innovative method to count the number of fluorescent molecules in a cluster and then applied the novel approach to settle a debate rampant among cell biologists—namely, how DNA twists into the centromere. "Understanding centromeres is critical because of the role they play in maintaining genomic integrity," says Gerton. "Losing a chromosome is catastrophic for any cell. And if it happens in sperm or egg cells, it is associated with conditions like Down syndrome."

Gerton, whose lab uses both the yeast Saccharomyces cerevisiae and mammalian cells to study the mechanics of cell division, explains that, previously, people had proposed at least six different centromere structures. "What we found is that centromeric nucleosomes change their structure during cell division," she says. "That explained why people had observed different structures. They had likely been looking at different phases of the cell cycle."

The study was published in the July 20, 2012,



### The Yin and Yang of stem cell quiescence and proliferation



Not all adult stem cells are created equal. Some are busy regenerating worn out or damaged tissues, while their guieter brethren serve as a strategic back-up crew that steps in only when demand shoots up. In a recent study, Stowers Investigator Linheng Li, PhD, and his team identified an important molecular cue that keeps quiescent mouse hematopoietic (or blood-forming) stem cells from proliferating when their services are not needed.

Ryohichi Sugimura, a graduate student in Li's lab, and his colleagues were able to show that Flamingo and Frizzled 8, a tag team best known for its role in establishing cell polarity, work together to maintain a quiescent reserve pool of hematopoietic stem cells in mouse bone marrow. Their finding adds new insight into the mechanism that controls the delicate balance between long-term maintenance of stem cells and the requirements of ongoing tissue maintenance

"Hematopoietic stem cells daily produce billions of blood cells via a strict hierarchy of lineage-specific progenitors," says Li. "Identifying the molecular signals that allow hematopoietic stem cell populations to sustain this level of output over a lifetime is fundamental to understanding the development of different cell types, the nature of tumor formation and the aging process. My hope is that these insights will help scientists make meaningful progress towards new therapies for diseases of the blood."

The study was published in the July 20, 2012, issue of Cell.

# ON THE MOVE

Many cell types migrate through surrounding tissue: nerve cells reaching for their final destination, immune cells on the prowl for intruding pathogens, fibroblasts called in to close wounds and stray cancer cells that have escaped the confines of the primary tumor.

Cells on the move reach forward with lamellipodia and filopodia, cytoplasmic sheets and rods supported by branched networks or tight bundles of actin filaments, which are constantly remodeled to push forward. The Arp2/3 complex, which localizes to lamellipodia, was thought to help build the web of actin filaments that shapes lamellipodia by initiating the branching process. But it had been unclear whether Arp2/3 is actually required for lamellipodia formation and how it would affect cell motility.

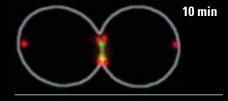
"Our work demonstrates that the Arp2/3 complex plays a critical role in the formation of the branched array of actin fibers that forms the structural backbone of lamellipodia," says Stowers Investigator Rong Li, PhD, who led the study. "Cells without functional lamellipodia are still highly motile but lose their ability to stay on track."

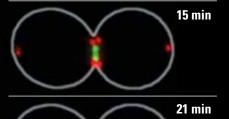
Their study provides new insight into cell motility, a complex and integrated process that, when gone awry, can lead to various disease conditions such as cancer metastasis, birth defects, cardiovascular disease and compromised immune function.

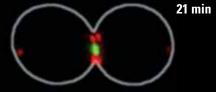
The study was published in the April 9, 2012, online issue of the Journal of Cell Biology.

# PINCHED OFF

# 2 min 10 min







DURING THE FINAL STAGE OF CELL DIVISION, A SHORT-LIVED CONTRACTILE RING CONSTRICTS THE CELLULAR MEMBRANE AND EVENTUALLY SEPARATES THE DIVIDING CELL IN TWO. ALTHOUGH THIS "MOLECULAR MUSCLE'S" COMPOSITION, MAINLY ACTIN AND MYOSIN, IS SIMILAR TO ITS SKELETAL COUNTERPART, THE FORCE-PRODUCING MECHANISM IS FUNDAMENTALLY DIFFERENT.

Combining traditional imaging and genetic approaches with a novel quantitative microscopy model, Stowers Investigator Rong Li, PhD, and her colleagues revealed that the depolymerization of actin filaments combined with actin cross-linkers—which act like pawls on a ratchet—and not the sliding myosin motors credited with contracting skeletal muscle is the main driving force behind the tightening of the actomyosin ring that completes cell division in budding yeast.

In muscle cells, the so-called motor domain of myosin binds actin and generates tension through a "power-stroke" mechanism fueled by the energy released from ATP hydrolysis. However, budding yeast genetically engineered to lack the motor domain of

myosin suffers only minor ill effects. "It had long been known that the contractile ring is made up of actin and myosin, the same molecules that allow our muscles to contract," explains Li, who led the team. "As a result, it was logical to assume that these intracellular structures work the same way."

Their study breaks new ground in the field of cytokinesis and provides new insight into the contraction mechanisms of actomyosin structures in non-muscle cells, which play an important role in cell division but also in many other processes such as cell shape changes, cell adhesion and motility.

The study was published in the June 15, 2012, issue of

### A DOUBLE RING CEREMONY PREPARES TELOMERASE RNA TO WED ITS PROTEIN PARTNER

Few molecules are more interesting than DNA—except of course RNA. After two decades of research, that "other macromolecule" is no longer considered a mere messenger between glamorous DNA and protein-synthesizing machines. We now know that RNA has been leading a secret life, regulating gene expression and partnering with proteins to form catalytic ribonucleoprotein (RNP) complexes. One of those RNPs is telomerase, an enzyme that maintains chromosome integrity.

In a recent study, Stowers Investigator and Howard Hughes Medical Institute Early Career Scientist Peter Baumann, PhD, and his team discovered how the RNA TER 1, a component of telomerase, is sculpted to favor interaction with its protein partner: Two ring-like proteins sequentially slip onto unprocessed TER1 RNA and hold it while it is clipped to the optimum size, folded, and capped. That processing is

essential: without it TER1 could not engage its protein partner to form the active telomerase RNP.

The finding not only deepens our understanding of RNA biochemistry but also suggests novel pharmaceutical approaches to cancer and diseases of aging. "Cancer cells are exquisitely dependent on telomerase," says Baumann. "Drugs inhibiting telomerase could be a new class of cancer chemotherapeutics with far fewer side effects than drugs in use." Currently, biotechnology and pharmaceutical companies are actively seeking clinically useful telomerase inhibitors.

The study was published in the March 26, 2012, issue of Nature.



MOLECULAR GENETICISTS REFER TO BIG BOSS PROTEINS THAT SWITCH ON BROAD DEVELOPMENTAL OR METABOLIC PROGRAMS AS "MASTER REGULATORS." ONE SUCH FACTOR, THE ACTIVATING TRANSCRIPTION FACTOR 6 (ATF6) PROTEIN, TAKES CHARGE FOLLOWING A CELLULAR CRISIS KNOWN AS ENDOPLASMIC RETICULUM (ER) STRESS, WHICH IS TRIGGERED BY THE ACCUMULATION OF MISFOLDED AND AGGREGATED PROTEINS.

Molecularly, the ER stress emergency response is always poised for action. Inactive ATF6 is normally embedded in cellular membranes, but at the first hint of protein overload, its working end springs Supermanlike into the nucleus, binds DNA and kicks on a host of target genes whose job is to clear a protein logiam.

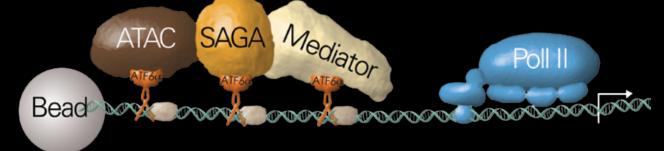
In their latest study, selected by the editors of the Journal of Biological Chemistry as "Paper of the Week," a team led by Stowers Investigators Ron and Joan Conaway reveal that, unlike the real Superman, ATF6 does not work solo. They found that it takes not a village but a metropolis to activate an ATF6 target.

Researchers know that all DNA-binding factors partner with other proteins to switch genes on or off. What is remarkable here is their sheer number. "It would be very interesting to find out whether this is the norm," says Ron Conaway, PhD, who with Joan Conaway, PhD, is co-corresponding author of the study. "This

work raises a ton of interesting questions about mechanism."

Solving these puzzles could reveal molecular targets for seemingly unrelated diseases. While a little ATF6 signaling is absolutely essential for cellular housekeeping, unrelieved ER stress is a hallmark of neurodegenerative conditions like Alzheimer's and Huntington's disease and is correlated with insulin insensitivity and type 2 diabetes.

The study was published in the June 29, 2012, issue of the Journal of Biological Chemistry





## RAUL DIAZ

## The reptile hunter

Although Raul Diaz hasn't even defended his thesis yet, his resume already reads like the resume of an accomplished faculty member. No wonder the enterprising rainforest ecologist-turnedmolecular biologist was offered an assistant professor position straight out of graduate school.

For Raul Diaz, defying expectations is second nature. He grew up in Baldwin Park, California in the eastern Los Angeles area where parents have many a reason to worry about their children's safety. "My mom didn't want me on the street and I spent a lot of time in the local library," remembers Diaz. Before long, he had read every reptile and amphibian book in the library and spent hours hunting for alligator lizards hurrying over sunbaked pavement near his house. By sixth grade he was breeding several species of tree frogs-much to his mother's dismayand working with local pet stores to start writing guides on how to breed frogs in captivity.

As soon as Diaz enrolled at La Sierra University in Riverside, California, he extended his reptile hunting forays from Southern California's urban concrete jungles to the rain forests of Southeast Asia and islands in the Caribbean. "On these trips I came across many animals that had developed similar adaptions to their environments although they were not related and lived in completely different corners of the world," recalls Diaz. "I became interested in how these organisms

> develop similar traits, a process that's known as convergent evolution '

studies. By the time he graduated with a bachelor's degree in integrative biology, he had half a dozen scientific publications to his name. He had also described several new species, made significant contributions to the Peterson Field Guides: Western Reptiles and Amphibians, traveled to Africa, founded a herpetology club at UC Berkeley and revived a peer-reviewed journal, Asiatic (now Asian) Herpetological Research, which he would continue to publish out of his apartment for almost a decade. The journal is now the main outlet for papers on reptile and amphibian biology from Asia to Australia.

Driven by a lifelong attraction to frogs—as his friends and tattoos on his right forearm can attest—Diaz started a PhD thesis on frog skeletal development and evolution at the University of Kansas Natural History Museum in Lawrence. He quickly became frustrated with the strict partitioning of departments into traditional disciplines such as ecology, development, morphology and molecular biology. "I realized that the field was headed towards combining molecular biology with morphological studies but, at the time, KU Lawrence didn't offer any interdisciplinary training in vertebrates." He finished up his frog project as part of a master's thesis and started working with former Stowers Investigator Olivier Pourquié, PhD, who studied snake segmentation





When Pourquié left to take a position in France, Diaz stayed on to take advantage of the Stowers Reptile and Aquatics facility. Undeterred by yet another change in plans, he joined the lab of Stowers Investigator Paul Trainor, PhD, an expert in craniofacial development, and dusted off an old interest he had developed during a summer internship at the Smithsonian Institution. "I had studied the crests of basilisk lizards," he explains. "On the outside they look similar to chameleons' crests but they are structurally different on the inside."

Drawing on Trainor's expertise in craniofacial development, Diaz was able to look at crest development with molecular tools. "Compared to other lizards, the chameleon has a substantially modified body plan," he says. "Molecular signals are 'recycled' across different body parts, which is the key to understanding these developmental modifications and ultimately how reptile body forms change during evolution."

In his own lab at La Sierra University, with an adjunct position at Loma Linda University Medical Center, Diaz will continue his research program on skull morphology and the biology of reptiles and amphibians of mainland and Southeast Asia. In addition, he plans to study reptile hands. All chameleons have a split in their hand that helps them climb the plants they inhabit. "Certain human birth defects look very similar to chameleons" split hand and foot," he explains. "Most of these cases can be explained by genetic mutations but lab studies have hinted at environmental causes as well. Perhaps the chameleon can provide some unique insight into these extreme structural defects."

But Diaz is most excited about the opportunity to teach the very same course at La Sierra University that allowed him to explore rain forests all over the globe, while also teaching development and genetics. He hopes that "expanding the lab to the jungles will hopefully produce students as excited about science as I am!" (§)



# **Annual Young** Investigator Research Days:

### An exhibition game

A throng of interested scientists gathers around like football players huddled on the field, waiting for the quarterback to call the play. They listen intently as the scientist describes in detail the experiments illustrated on the large glossy poster. This scene played out repeatedly at the Stowers Institute's Young Investigator Research Days 2012.

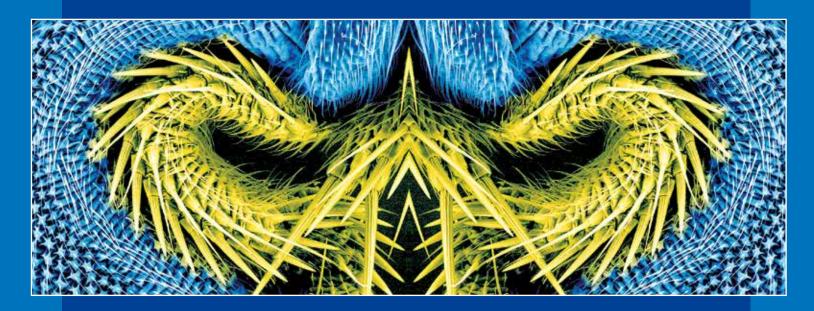
On May 14 and 15, eighty-one Stowers researchers presented their experimental work to fellow scientists, investigators and staff during the poster and oral sessions at the seventh annual Young Investigator Research Days (YIRD). Judging teams composed of senior researchers and principal investigators selected the winners of each session who each received a small cash prize.

The shifting crowd of interested scientists posed questions to the young researchers and provided an opportunity for spontaneous consultation and collaboration between members of different labs. "Discussions among colleagues always provide food for thought, and a few suggestions have changed the course of my work for the better," said Ryan Mohan, PhD, a postdoctoral research associate

Competition was ratcheted up a notch this year with an all-institute vote for most popular poster and oral presentation. A highly coveted trophy category was also introduced which resulted in a tie between the Gibson and Jaspersen labs, placing pressure on each to out-represent the other at next year's event.

This collective showcase of projects serves as more than just a friendly competition and tell-all of Stowers research. Its primary function is to provide an opportunity for the professional development of predoctoral and postdoctoral researchers. "YIRD gives young students and postdocs an opportunity to gain experience and build confidence in presenting and describing their work to others," shared Kenny Lee, PhD, co-organizer of the first YIRD, held in 2006.

Much like a football exhibition game that highlights new talent and tests out new plays as a way to build a better team, YIRD provides the same valuable opportunity for young scientists. Former Lab Assistant Jennifer Friederichs, who presented a poster featuring a systematic analysis of yeast genes involved with the SUN-like protein Slp 1, finds the entire experience a great opportunity to fine-tune her presentation skills. "It is great practice to prepare a poster and talk for a general scientific audience, just like we need to do at big international meetings." Mohan concurred, and added, "YIRD helps prepare you to make the most out of every meeting."



### Flying high on the wings of the wind

Winner of the Stunning Science – 2012 YIRD Imaging Competition

The winning image was submitted by Liang Liang, a graduate student in the Gibson Lab who uses fruit fly wings as a model to study tissue growth, cell division and morphogenesis. She visualized the delicate structures on the surface of an adult fruit fly's wing ready to emerge from the pupa in a scanning electron microscope and manipulated it for dramatic effect.

Almost all of the approximately 30,000 cells making up an adult wing form a single bristle (shown in yellow) or hair (shown in blue). The longer bristles sit on the edge of the wing and detect changes in taste and mechanical force, while the shorter hairs cover the whole wing blade and passively direct airflow. A single gene mutation can disrupt the well-defined pattern of the wing, causing an abnormal number of bristles or hair, disordered hair-hair spacing, or loss of wing hair polarity.

### **Congratulations to the following members!**

#### **Poster Session I:**

Winner - Lili Pan (Baumann) Runner-up – Hiroshi Kurosaka (Trainor) Honorable mention – Aissam Ikmi (Gibson)

#### Poster Session II:

Winner – Ryan Mohan (Workman) Runner-up – Kiki Kanakousaki (Gibson) Honorable mention – Arnob Dutta (Workman)

### Oral Session I:

Winner - Sarah Smith (R. Li) Runner-up – Marina Venero-Galanternik (Piotrowski)

### **Oral Session II:**

Winner – Swaminathan Venkatesh (Workman) Runner-up – Liang Liang (Gibson)

#### **Most Popular Poster Presentation, selected by members:**

Malini Natarajan (Zeitlinger)

**Most Popular Oral Presentation, selected by members:** Annita Achilleos (Trainor)

YIRD Award for Highest Scientific Representation by a Lab:

Gibson and Jaspersen (tie)

# A CATAPULT INTO SCIENTIFIC RESEARCH

Wearing a freshly starched lab coat and bright blue nitrile gloves, a young scientist used a pipette to transfer a concentrated salt solution into a small 1.5 ml tube in preparation for separating cellular proteins and debris from DNA. Next door, another listened as a scientist explained the conclusions drawn from a colorful neuronal precursor cell image splayed across a 10-foot tall screen. It was all in a day's work for this year's Stowers Scholars, who spent ten weeks immersed in a defined research project, which culminated in an institute-wide presentation of their research.

The program that started with eight participants in 2004 has grown to accommodate thirty-nine undergraduate researchers in the summer class of 2012. With nearly two hundred students applying to the program, Stowers investigators are able to select the most promising candidates for projects in their labs. For undergraduates with an interest in science, but unsure of the rigors and demands of scientific bench work, experiences like these may be the trigger that catapults young scientific hopefuls into a lifelong career in research.

Stowers Scholars Program Coordinator Ana Pedraza, PhD, explained that while the experience does provide participants with the opportunity to learn some of the technical skills necessary for a bench-based job in research, it aspires to achieve much more than that. "It is our goal to provide a context for aspiring scientists to participate in the collaborative nature of researchbased science," she said. "We want them to gain an overall impression of a career in science, not just the rote tasks of an experiment."

Over the years, Associate Investigator Ron Yu, PhD, has been lab host and mentor to a large number of Stowers Scholars. "The curiosity and enthusiasm these young researchers bring to the lab is inspiring," he says. At first, Yu thought the scholars could be extra sets of hands for already established research projects, but he soon learned that by allowing them intellectual

When 2007 Scholar Stephen Gradwohl returned to Yu's lab the following summer, he was presented with a large data set of responses to odor stimuli but no way to easily process or analyze it. Driven by a desire to "figure

space for development, combined with the right amount of support, amazing things can happen.

Nimish Mittal and Matthew Bruce

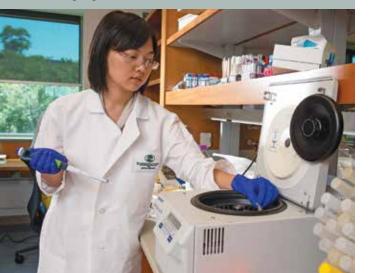
things out," Gradwohl developed a custom script that condensed the analysis to just a week rather than the months previously required. "His contribution was an essential catalyst for the lab to move into systems-level neurobiology and his effort triggered two other similar projects to streamline data processing," said Yu.

While most scholars might not have that kind of scientific epiphany during their short tenure, they do come away with a much greater understanding and appreciation of the amount of work and dedication that it takes to work in research. "I learned an ethos while a Stowers Scholar that has benefited me throughout my work experience," said Lauren Shelton, a former scholar who now works as a research technician in the Abmayr lab. "The immersion into a real-life work experience gave me the opportunity to learn a sense of ownership and responsibility for my work."

Jerry Yin, 2012 Scholar and biomedical engineering student at the University of Wisconsin-Madison, experienced the power of collaboration during his time in the Yu lab firsthand. He spent his summer improving the design of an olfactometer, a machine that delivers highly controlled odors for behavioral studies of mice. Yin took a basic design from Yu's lab and set about improving the machine's capability. He successfully built a machine that simultaneously controls two independent behavior boxes, allowing researchers to run two experiments in parallel.

Yin credits his success to the freedom he was given to try out new ideas and to the generous help he received from various departments at the institute. "Everyone was so friendly and eager to help," said Yin. He specifically acknowledged the information management team for help with software and Senior Biomedical Equipment Technician Tony Torello, who assisted with the fabrication of the machine. "This experience has given me an opportunity to see what can happen when everyone works together," Yin reflected. "It is something that I am going to try do to more of when I return to the University of Wisconsin-Madison."

Zheng Xing





### STOWERS SCIENTIST JULIA ZEITLINGER AVVARDED 2012 HUDSON PRIZE

Dr. Julia Zeitlinger, a Stowers Institute assistant investigator, has been named the recipient of the 2012 Hudson Prize by the M.R. and Evelyn Hudson Foundation.

Through the Hudson Prize, the Texas-based M.R. and Evelyn Hudson Foundation encourages early career scientists to pursue research that leads to important medical breakthroughs and treatments.

"Julia is an extremely accomplished young scientist who is not afraid to take risks and venture into uncharted territory," said Robb Krumlauf, PhD, scientific director of

creative period in her career."



Zeitlinger received a one-time grant of \$50,000 to take her search for the general principles that govern global gene expression in new directions. A deeper understanding of these mechanisms will help illustrate how higher organisms such as humans develop and how flaws in the regulation of genes may lead to diseases such as cancer.

Each one of our body's trillions of cells contains the same genetic information that makes us who we are, but the details of our appearance, behavior and metabolism are determined by gene regulation. In a tightly orchestrated process, a complex network of regulatory factors governs which genes are turned on where, when and for how long.

For a long time researchers studied genes and their genetic switches one by one, but Zeitlinger decided to take it a step further. Instead of scrutinizing individual genes, she scours whole genomes to identify globally applicable rules that, one day, may allow her to predict the fate of individual cells.

Currently, Zeitlinger's lab is exploring two main modes of gene regulation: regulation dictated by DNA sequence and regulation based on the state of chromatin—the combination of DNA with the protein molecules that provide the packaging inside the cell's nucleus.







THE SPOTLIGHT

Graduate students and postdoctoral researchers play a pivotal role in the day-to-day business of conducting world-class research. These young scientists benefit from immersion within one of the world's premier basic research institutions, but equally important, their mentors benefit from the opportunity to work with bright young minds who bring unbridled enthusiasm and an unending stream of fresh ideas to the lab. In recognition of their achievement, three successful young Stowers scientists have been named the recipients of highly competitive awards.

Tamara Potapova, PhD, submitted a winning fellowship proposal to the American Cancer Society to study aneuploidy or abnormal chromosome number, a prominent hallmark of cancer cells. The prestigious \$150,000 fellowship is intended to encourage the nation's most promising young investigators to pursue innovative research projects that have the potential to transform the way we prevent, diagnose and treat cancer.

Potapova, a postdoctoral researcher in the lab of Stowers Investigator Rong Li, PhD, will be using the funds to uncover the molecular mechanisms that allow cells with extra sets of chromosomes to slip through a "ploidy"-checkpoint and produce aneuploid progeny. She hopes that her work may lead to a better understanding of carcinogenesis and potentially translate into new targets for anti-cancer drug development.

**Inês Mendes Pinto's** doctoral thesis was recognized for its outstanding level of scholarship by the Portuguese Foundation for Science and Technology. In a wide-reaching interdisciplinary approach, Mendes Pinto, PhD, combined traditional imaging and genetic tools with physics and mathematics to study the biomechanics of the molecular machinery that physically separates cells during cell division and the signals that initiate the process.

The work, which Mendes Pinto performed under the mentorship of Stowers Investigator Rong Li, broke new ground in the field of cytokinesis, the final stage of the process that separates dividing cells. It also provided new insight into the mechanisms that generate contractile forces in non-muscle cells, which play an important role in cell division and also in many other processes such as cell shape changes, cell adhesion and motility.

**Guangbo Chen**, a graduate student at the University of Kansas Medical School, who conducts his dissertation research in the lab of Stowers Investigator Rong Li, has been selected by the Genetics Society of America as one of only six students to receive a DeLill Nasser Award for Professional Development in Genetics. The award is named in honor of DeLill Nasser (1929-2000), who was instrumental in promoting genetics research during her tenure as National Science Foundation

Program Director in Eukaryotic Genetics. Nasser was particularly supportive of young scientists, those at the beginning of their careers, and those trying to open new areas of genetic inquiry.

As part of his graduate thesis, Chen was able to show that under stressful conditions yeast cells' genomes become unstable, readily acquiring or

losing whole chromosomes to enable rapid adaption to changing environments. He will apply the funds toward attending the course "Gene Regulatory Networks for Development" held at the Marine Biological Laboratory at Woods Hole, Massachusetts.

From left to right: Tamara Potapova, Guangbo Chen, Inês Mendes Pinto.



### PROMOTIONS



## PAUL TRAINOR Promoted to Investigator

Paul Trainor studies craniofacial pathologies that emerge from defects in the neural crest, a population of embryonic cells that migrate extensively during development and give rise to many different tissues, including most of the bone and cartilage of the head skeleton.

In pioneering work, he and his team discovered that Treacher Collins syndrome, which is marked by severe jaw, palate and ear defects, is caused by the premature death of neural stem cells, the precursors of neural crest cells. Without them, the embryo cannot produce enough neural crest cells to properly build the head and face. In a follow-up study they showed that blocking the p53 gene, which promotes cell death, restores neural crest cells and rescues craniofacial abnormalities in a mouse model of Treacher Collins syndrome.

In a systematic search for novel genes regulating cranial crest development, Trainor's team identified and characterized several novel mouse mutants showing differing craniofacial anomalies. Interestingly, one of the implicated genes encodes an enzyme involved in vitamin A metabolism, which needs to be tightly controlled since both deficiencies in vitamin A as well as an excess of vitamin A can cause severe birth defects.



# PETER BAUMANN Promoted to Investigator

Peter Baumann's primary research interest focuses on learning how the natural ends of chromosomes, known as telomeres, are maintained. Specifically, he wants to know how telomeres, which look just like broken strands of DNA that a cell's repair machinery is designed to fix, are protected from being mistakenly joined together. He discovered that a complex of two proteins keeps telomeres from being mended, which would set the stage for the development of cancer in successive generations of cells.

In related work, he isolated the long-sought RNA subunit of fission yeast telomerase, the enzyme that maintains telomeres. In studying the precursors to that subunit, he discovered an entirely new and unanticipated pathway for processing RNA, allowing him to examine how telomerase is assembled and controlled.

In completely unrelated work, Baumann discovered how all-female lizard species successfully reproduce without any males while avoiding the genetic monotony and disease vulnerability that often results from asexual reproduction. Celibate lizards maintain their genetic diversity by starting with twice the number of chromosomes and swapping information between identical sister chromosomes rather than lining up one set from each parent as sexual species do.



## SUE JASPERSEN Promoted to Associate Investigator

Sue Jaspersen is interested in the nuclear structures required for yeast cell division. Nuclear architecture has dramatic effects on gene expression and genomic instability, and disruptions in normal nuclear organization have been linked to cancer and other diseases, making her work on yeast nuclear structure a valuable model for human conditions. Most of her work focuses on a cellular component known as the spindle pole body, which forms the mitotic spindle apparatus that helps pull the chromosomes apart. Each time a cell dividesand it takes millions of cell divisions to create a fully grown human body from a single fertilized cell—its chromosomes have to be accurately divvied up between both daughter cells.

Most recently, Jaspersen and her team discovered that a protein known as Mps3 ensures not only that cells have two functional spindle pole bodies but also that both spindle pole bodies are properly anchored in the nuclear membrane via Mps3. In earlier work, she reported that Mps3 pokes into the nuclear interior and tethers chromosome ends, known as telomeres, indicating that it governs chromosome position within the nucleus and potentially functions in silencing genomic regions adjacent to telomeres.

# CELEBRATING 25 YEARS OF SCIENTIFIC PHILANTHROPY

More than two hundred guests gathered at the Stowers Institute on April 19 to celebrate Jim and Virginia Stowers' extraordinary generosity and unwavering belief in the power of basic biomedical research to generate new therapies, prevent suffering and save lives.

A quarter century ago, when Jim Stowers was diagnosed with prostate cancer, he applied the same determination and tenacity that had helped him launch the world's most successful mutual fund company to conquering his cancer. He pursued an aggressive treatment that left him cancer-free but also with concerns about those who might not find the right treatment or have the same access to early detection of the disease. Determined to find a way to help, Jim and Virginia established the Stowers Foundation to fund free prostate exams for early detection of cancer.

Only a few years later, Virginia's own battle with breast cancer reinforced the couple's decision to pursue an audacious vision: to build the world's most innovative basic biomedical research institute, filled with brilliant minds from all over the globe and the most advanced scientific equipment, working to discover the secrets held by genes, and set the stage for the development of new treatments for a wide range of diseases.

"Barely two decades later, Jim and Virginia's vision has become a remarkable reality," said Scientific Director Robb Krumlauf, PhD, who helped shape the institute's scientific direction from day one. "The success of the Institute is a direct result of their generous philanthropy."

The magnitude of the Stowers' giving was perhaps most obvious to the celebrants who were treated to a behind-the-scenes tour of the institute led by the scientists engaged in the cutting-edge science that has made the Stowers Institute a worldwide powerhouse for biomedical research. The visitors looked in amazement through a microscope at a cellular protein that may provide answers to why cancer migrates and spreads, marveled at the fly-flipping robot that transfers thousands of flies from vial to fresh vial each week and listened in fascination as they learned that the latest generation of sequencing machines can read the entire human genome in one week's time.

Throughout the evening's festivities, guests offered their congratulations to Jim and Virginia on their milestone of achievement. All agreed, as one well-wisher shared, "There really is no more fitting tribute to this philanthropic couple than this amazing facility and the research that is being conducted here at Stowers."



From left to right: Fred Hartwig, Jim Stowers Jr., Bill Dunn Sr.



om left to right: Shawsie Branton, Virginia Stowers, Jeannette Nichols



From left to right: Anoja Perera, Dan Blegen, Jim Maliszewski, Samuel Goller



Left to right: Susan Creidenberg, Jan Creidenberg, Tyler Benson Stacy Benson, Ashley Fritz

# A TEN-YEAR MILESTONE

Last spring, twenty-six members were honored for ten years of dedicated service to the Stowers Institute at an afternoon tea.

In 2001, when this group of members joined, Stowers was only a fledgling institute with a decade of extraordinary growth and change ahead of it. As noted by CEO and President Dave Chao,

PhD, at the beginning of 2001 the institute counted eighty-one employees and ended 2011 with 524. While the Institute boasted seven published papers in 2001, by 2011, Stowers scientists had published a cumulative 700 scientific papers. And although fifty phone lines and one hundred desktop computers were sufficient for the needs of the Institute back in 2001, ten years later they required 500 phone lines and 1,200 computers.

Highlighting the role of each dedicated honoree, from

scientists making groundbreaking discoveries to support staff keeping the furnaces fired and the computers humming, to administrative staff posting purchases, balancing the books and cutting the checks, Scientific Director Robb Krumlauf, PhD, and President Chao emphasized that each and everyone's contribution was vital to the mission of the Institute.

Yet, collectively these members accomplished something much bigger. Together they laid a foundation of values based on a uniquely collaborative spirit that now permeates the institute. "The Stowers Institute is the antidote for cynicism," remarked Mike Levine, PhD, chair of the Stowers External Scientific Advisory Board, during his last visit to the institute.

As guests mingled, refreshments in hand, one question kept popping up: "What's your number?" An employee number is assigned to each individual upon being hired—the lower the number the longer one's tenure. Proud replies included numbers as low as 84, 92 and 174. Indicative of the institute's growth over



the last ten years, currently, new employees are assigned numbers in the range of 1,500.

Vice President of Administration and event organizer Abby Freeman offered each member congratulations on reaching this special milestone and perhaps summed up the event best. She said, "Stowers was built, in part, by each of these individuals, and this is our opportunity to show our appreciation of their time, energy and effort in making Stowers the exceptional place that it is today." Upon departure, each guest of honor was presented with a framed certificate of appreciation and a replica statue of the "Hope for Life" helix.

#### **2001-2011: List of Honorees**

Back row, left to right: Shigeo Sato, David Karr, Charles Clark, Arcady Mushegian, Terry Hartness, Scott Hawley, David Stiens, Chris Locke, Dirk Hacker, Bob Reece, Max Lyle, Tim Geary Front row, left to right: Paul Trainor, Toni Ford, Val Perry, Chieri Sato, Carrie Sims, Janice Ridgley, Not Pictured: Pam Babcock and Karin Zueckert-Gaudenz



### **STOWERS INSTITUTE AMONG** "BEST PLACES TO WORK"

The Stowers Institute received not one but two feathers in its cap this year, when it was ranked among the top three institutes listed as "Best Places to Work, Academia: 2012" and among the top ten "Best Places to Work." Postdocs: 2012" by The Scientist magazine.

"Since we did not have a ready-made culture like MIT or Harvard, we had to carefully craft our own. To complement our commitment to supporting outstanding science, we put a lot of emphasis on collegiality, since interdisciplinary research requires people to work well together to create the necessary synergy to do pioneering work," said Scientific Director Robb Krumlauf, PhD, who has helped shape the scientific vision of the institute since it opened in 2000. "The results of The Scientist's surveys are a welcome endorsement of the goals we hoped to achieve."

In addition to its founding principles of collaboration and collegiality, the Stowers Institute prides itself on providing its research labs with a first-rate scientific infrastructure and easy access to experts in cutting-edge technologies, both of which were cited as key factors in why scientists working at the institute not only love their work, but also their workplace.

"The core facilities and technology centers at the Stowers Institute are among the most technically advanced available for biomedical research in the world," said Jeffrey Haug, BS, who manages the Cytometry Center at the institute, "but they are not just high-tech laundromats. They function as transient extensions of the labs giving core scientists a stake in the outcome of experiments and the intellectual satisfaction that comes with contributing to world-class science."

The high-level engagement particularly benefits the research and training of postdoctoral researchers, who carry out the bulk of everyday research activities and come to the Stowers Institute to broaden their skills and prepare for an independent research career.

"I am delighted that the Stowers Institute has been recognized by *The Scientist* as one of the best places for postdocs to work. It is even more gratifying to know that this ranking is determined directly from the responses of the people who know this institute best—our own postdocs," said Stowers Investigator Jerry Workman, PhD, who heads the postdoctoral program at the Stowers Institute.

### THE SOUNDS OF SCIENCE AND MUSIC

A visitor to the Stowers Institute would normally hear the sounds of science emanating from its corridors—the gentle whir of a centrifuge, the clanking of a glassware cart rolling down the hall or the subtle pop of plastic Eppendorf tube lids snapping into place.

and visitors instead were greeted by the sweet singing voices of violin and viola, the warm and tender hum of cello and the resonating harmony of piano, when members of Park University's International School of Music were joined by scientist and guest performer Mark Ptashne, PhD, in an Extravaganza Showcase Concert.

Ptashne, a scientist well known for his pioneering research on gene regulation, holds the Ludwig Chair of Molecular Biology at Memorial Sloan-Kettering Cancer Center in New York. His work has garnered numerous national and international awards including the Lasker Prize for Basic Research. An accomplished violinist who only began seriously pursuing violin as an adult, Ptashne has studied under the tutelage of master teachers Roman Totenberg, Eric Rosenblith, Patty Kopec and, most recently, Mela Tennenbaum.

Conversations with scientific colleague and Stowers Investigator Jerry Workman, PhD, and musical colleague and local Park University professor of violin Ben Sayevich was all it took to kindle the idea of a music concert in the Stowers Institute auditorium, more commonly home to scientific lectures. The result was a stunning evening of Ravel, Tchaikovsky and Paganini, to name a few, performed by students in the Park University's music program. Ptashne thrilled his fellow scientists by joining the students in Bach's Double Violin Concerto in D Minor.

This was not your average student recital though. In fact, these students are internationally recognized musicians. Violin student Christian Fatu is regarded as one of classical music's most exciting young artists. He has won multiple international awards and prizes and has already released two CD recordings. After his performance of Carmen Fantasy, Op. 25, However, on one spring evening in April, Stowers members bravos could be heard throughout the makeshift music hall.

> At a reception following the night's performance, guests agreed that mingling the sounds of science with music was a wonderful experience. All are looking forward to an encore performance. §



### STOWERS INSTITUTE LAUNCHES



The ODR team from left to right: Sean McKinney, Eric Ross, Tim Geary, Winfried Wiegraebe, Darren Wright, Jessica Witt, Laurence Florens, Mike Newhouse, Judy Zimmermann, Chris Wood, Jeff Haug, Brian Slaughter, Michael Gaffney, Dirk Hacker.

IN JULY, THE STOWERS INSTITUTE FOR MEDICAL RESEARCH PUBLICLY LAUNCHED THE STOWERS ORIGINAL DATA REPOSITORY (ODR). AS A STRONG SUPPORTER OF THE SCIENTIFIC IDEALS OF TRANSPARENCY AND OPENNESS, THE STOWERS INSTITUTE BELIEVES THAT THE DATA UNDERLYING ITS PUBLISHED WORK SHOULD BE FREELY ACCESSIBLE TO THE **SCIENTIFIC COMMUNITY** 

### ORIGINAL DATA REPOSITORY

"The open sharing of data is an important component of the scientific process because scientists build on the work of others to create new knowledge," said Scientific Director Robb Krumlauf, PhD. "We believe that data sharing enhances scientific inquiry by facilitating independent follow-up analyses to confirm, extend or re-interpret findings from the Institute."

A few scientific journals encourage or require authors to submit all data on which their conclusions are based. The Stowers Institute now requires its members to deposit all original data files underlying published work into the Stowers Original Data Repository or into repositories maintained by third parties. To the best of its knowledge, the Stowers Institute is the first basic biomedical research organization to implement an institution-wide original data repository.

"Modern technologies in areas like imaging and genomics generate huge data sets, which may go through a series of processing steps to extract meaningful information," said Winfried Wiegraebe, PhD, who heads the Stowers Microscopy Center and spearheaded the implementation of the Stowers ODR.

"Because only the final, processed data is typically published, members of the scientific community may find it challenging to make an independent, fully informed assessment of the published results. The ODR supports independent validation and analysis by providing the scientific community with open access to the original data underlying work published by scientists at the Stowers Institute," he said.



The Stowers Institute's scientific effort is made possible by the proceeds we receive from our Hope Shares Endowment. The Institute welcomes contributions to the Endowment in any amount. Individual or cumulative contributions of \$1,000 or more establish a Hope Shares account, which can be opened in your name or in memory or honor of someone you love.



### LIFETIME CONTRIBUTIONS

The information listed below represents contributions from, in memory of, or in honor of the following as of June 30, 2012.

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#### \$1 Million+

American Century Investments Foundation Pamela Stowers In Memory of Laura Stowers

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For more information on how to establish a Hope Shares account, please visit www.stowers.org/support or call (816) 926-4065.

