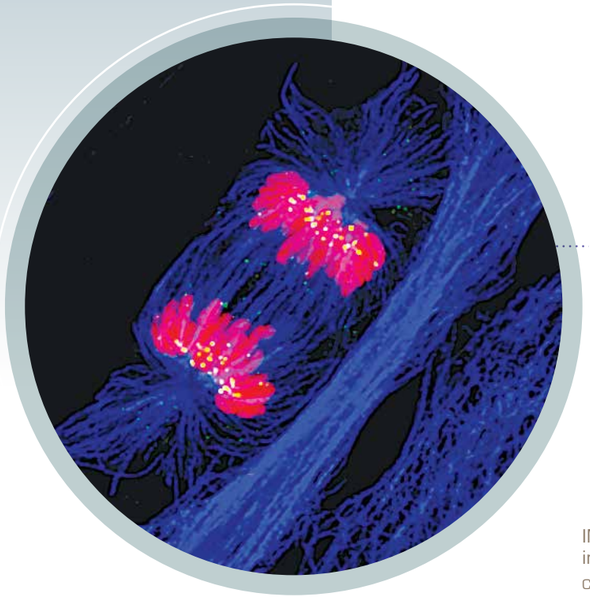
STOWERS INSTITUTE
FOR MEDICAL RESEARCH

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

Address Service Requested

OUR MISSION:

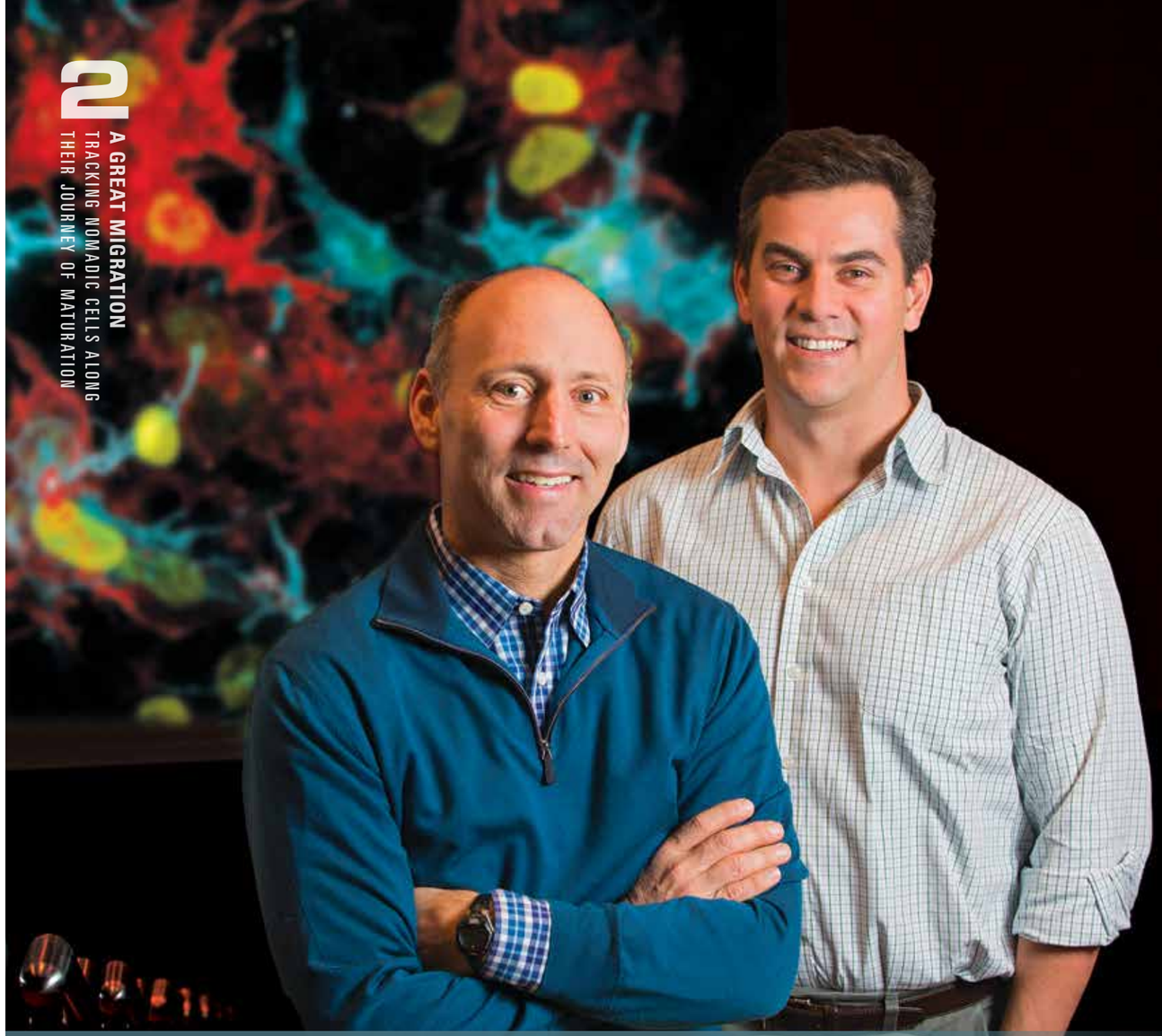
TO MAKE A SIGNIFICANT CONTRIBUTION TO HUMANITY THROUGH MEDICAL RESEARCH BY EXPANDING OUR UNDERSTANDING OF THE SECRETS OF LIFE AND BY IMPROVING LIFE'S QUALITY THROUGH INNOVATIVE APPROACHES TO THE CAUSES, TREATMENT, AND PREVENTION OF DISEASES.



ANEUPLOIDY AND POLYPLOIDY, WHICH LEAD TO ABNORMAL CHROMOSOME NUMBERS, ARE A HALLMARK OF CANCER CELLS. STOWERS INVESTIGATOR RONG LI STUDIES THE MOLECULAR MECHANISMS THAT ALLOW CELLS WITH EXTRA SETS OF CHROMOSOMES TO SLIP THROUGH A CELL'S "PLOIDY" CHECKPOINTS.

IMAGE: Microtubules separating chromosomes in a dividing human retina cell.

Courtesy of Tamara Potapova.



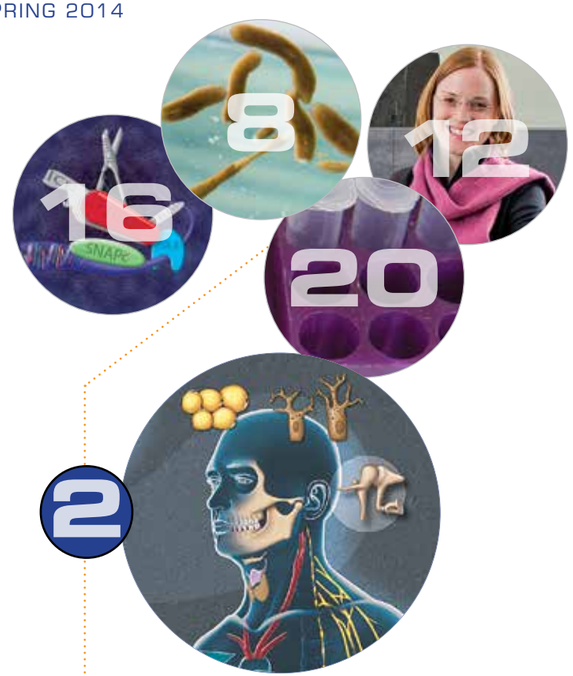
2 **A GREAT MIGRATION**
TRACKING NOMADIC CELLS ALONG THEIR JOURNEY OF MATURATION

STOWERS REPORT

NEWS AND INSIGHT FROM THE STOWERS INSTITUTE FOR MEDICAL RESEARCH SPRING 2014

STOWERS REPORT

PUBLISHED BY THE STOWERS INSTITUTE FOR MEDICAL RESEARCH
SPRING 2014



CONTRIBUTORS:

Editors
Kim Bland
Kristin Kessler
Gina Kirchweger

Copy editor
Linda Flynn

Web editor
Juan Carlos Grover

Scientific Illustration
Mark Miller

Photography
Mark McDonald

Design and production
Kuhn & Wittenborn

Visit the Stowers Institute at www.stowers.org or find us on Facebook at facebook.com/StowersInstitute

The Stowers Report is printed on recycled paper.

The Stowers Report is published by the Science Communications Department at the Stowers Institute for Medical Research. We welcome your input. Please send comments to communications@stowers.org or contact us at (816) 926-4015.

In perspective

BY DAVID CHAO, PHD
PRESIDENT AND CEO

Each year, approximately four million babies are born with birth defects severe enough to cause disability or death. Although birth defects can manifest themselves in a myriad of ways, they all arise from a flaw in the normal development process.

"Development" is the term used by biologists to describe the carefully balanced and highly choreographed process that generates trillions of cells and coordinates their interactions to form tissues, organs and, ultimately, the entire human body. Any disruption of normal development by genetic abnormalities, infectious pathogens, or environmental influences can result in a birth defect.

Much of the Institute's research focuses on answering fundamental questions about the development process. Our scientists use a variety of approaches in diverse settings in their quest for answers. Some of the stories in this issue of the Stowers Report describe the application of different approaches in yeast, birds, fish, and mice to understand the basic processes of development applicable to all organisms. By learning more about how different genes guide development and how the process can go awry, scientists are building an intellectual foundation for generating new strategies to prevent or treat specific birth defects.

This issue's cover story describes work on neural crest cells, an important group of cells involved in a startlingly diverse array of common birth defects. Neural crest cells are formed when early stage cells are pinched off during the formation of the neural cord. Soon afterwards in development, neural crest cells fan out along migratory pathways to numerous destinations throughout the body. There they contribute to a surprising diversity of specialized cells and tissues. Researcher Paul Kulesa and his lab develop and use sophisticated imaging technologies to track and study individual neural crest cells as they migrate. In a complementary approach, researcher Paul Trainor and his lab use mouse mutants to understand the mechanisms by which specific mutations lead to defects in neural crest cells.

In another area, researcher Jennifer Gerton and her team study the various functions of cohesins, ring-shaped protein complexes that help organize the DNA in cells. Mutations in cohesins and related proteins lead to a class of related birth defects called cohesinopathies. The Gerton laboratory's careful mechanistic studies of two cohesinopathies have laid the foundation for the long-term development of new therapies to treat these conditions.

I hope you enjoy reading these stories of fundamental discovery and scientific detective work. The breadth and depth of these research programs serve as concrete and inspiring examples of Jim and Virginia Stowers' vision of improving human health through basic research.

By Elise Lamar, PhD.

A GREAT MIGRATION

IN VERTEBRATES, BANDS OF MOBILE CELLS FAN OUT FROM THE EMBRYONIC BRAIN AND SPINAL CORD AND THEN RESETTLE IN FAR-FLUNG LOCALES TO FORM STRUCTURES AS DIVERSE AS BONE OR NERVES. PAUL TRAINOR AND PAUL KULESA TRACK THEIR JOURNEYS IN HOPES OF ILLUMINATING WHY BIRTH DEFECTS OCCUR WHEN CELLS GO OFF-TRACK.

Neither scientist set out to become an expert on neural crest cells, as these inveterate migrants are known. Paul Trainor, PhD, spent his youth on the beaches of his native Australia, more interested in sports than science. As a University of Sydney undergrad he got hooked on biology only after discovering that through genetic manipulation you could produce fruit flies with too many wings or misplaced antennae. Halfway around the world, Paul Kulesa, PhD, a midwesterner, was captivated by mathematics and space exploration. After earning a bachelor's degree in aerospace engineering at Notre Dame and a master's in applied mathematics at the University of Southern California, he became interested in mathematical equations that could help explain complex biological patterns.

Now, after two decades of graduate school and postdoctoral training between them, both are at the Stowers Institute for Medical Research studying neural crest cells, albeit from vantage points that couldn't be more different. Trainor, a Stowers investigator, is mainly interested in understanding the molecular intersections linking defects in the neural crest with craniofacial malformations. Kulesa, the director of Imaging, develops sophisticated imaging technology to understand how neural crest cells travel long distances and assemble various structures, such as the peripheral nervous system. Using mouse, chick or zebrafish models, both test what goes awry when mutations derail migrating neural crest cells in a developing embryo. In unique ways, each researcher's work directly impacts a broad class of human birth defects.

One name: multiple disorders

Neural crest cells spring from the crest or dorsal ridge of the embryonic brain and spinal cord and then migrate to faraway regions of the face, heart or gut. Although *neural* in origin, their name is slightly misleading: They mature just as readily into bone, muscle or connective tissue as they do into a neuron. Failure of neural crest cells to either complete their journey or mature on arrival causes widely varying birth defects known collectively as neurocristopathies.

One of Trainor's goals is to understand the molecular basis of these conditions. "Approximately one percent of all live births exhibit a minor or major congenital anomaly, and about a third of those display craniofacial abnormalities," he says. "To have any hope of preventing these disorders you must understand how they originate."

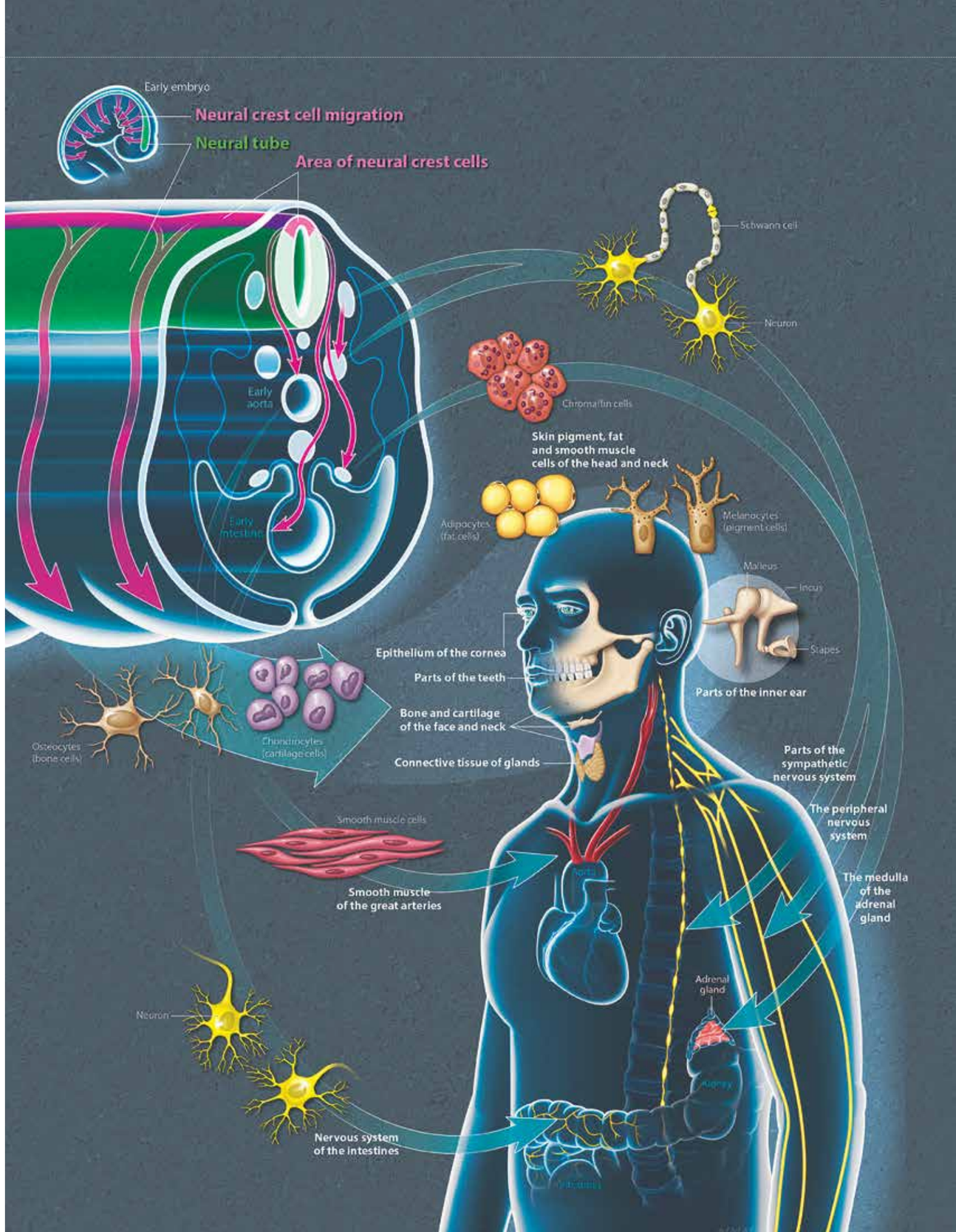
When Trainor arrived at Stowers, he initially focused on a birth defect called Treacher Collins syndrome (TCS). Babies born with TCS exhibit deformities of the cheek, eye or jaw, and some also suffer hearing loss or respiratory problems due to airway malformation. Scientists knew that the *Tcof1* gene is mutated in association with most TCS cases. In a 2006 paper published in *PNAS*, the Trainor lab reported that mice with mutations in the *Tcof1* gene also displayed severe facial deformities, mimicking the human condition. The group then analyzed mouse embryos using molecular markers and discovered that precursors of neural crest cells in the brain and spinal cord began dying even before crest cells destined to help build the face could start migrating.

In 2008, Trainor's group reported in *Nature Medicine* that blocking a gene that promotes cell death, called *p53*, allowed nascent neural crest cells in *Tcof1*-mutant mice to survive, preventing manifestation of the animals' craniofacial defects. This work is highly significant because, as a potential treatment option, erasing a mutation—in a whole embryo no less—will likely not be feasible. But this paper demonstrated that cells that harbor a disease-causing mutation can be rescued. "This outcome shows that we could potentially intervene and prevent defects, not just repair them," Trainor says.

In parallel, his lab conducted a labor-intensive mouse genetic screen to discover novel genes required for normal neural crest activity. That work culminated in a 2011 *Genesis* paper identifying ten mutations that underlie conditions as diverse as holoprosencephaly (in which the forebrain fails to partition into two hemispheres), neural tube defects, and cleft palate. More recently, in a 2013 *PLoS Genetics* study, they reported that mice lacking a gene called *Foxc1* model a human congenital defect called syngnathia, in which children are born with fused upper and lower jawbones.

These types of genetic analyses illustrate the challenge faced by researchers interested in preventing or treating neuroscristopathies. A single name may classify them in Wikipedia, but the field work of Trainor and colleagues demonstrates that multiple genes expressed either in a moving cell or somewhere along its path underlie neural crest-based defects. "In a condition like TCS we see a failure to make enough cells at the beginning of migration, while in syngnathia, crest cells migrate properly but make bone in the wrong place," says Trainor. "Collectively, these studies suggest that there isn't going to be any single way to prevent these disorders."

Which is precisely where basic research comes in. "One of our goals is to identify the genetic instruction sets needed to make a face," says Stowers Scientific Director Robb Krumlauf, PhD, whose ground-breaking research on Hox genes defined how neural crest cells, particularly those traveling toward the head, know where they're going. "It takes hundreds of genes and likely thousands of control steps to make structures of a face. Thus identifying pathways useful for therapeutic interventions will require putting together a complex jigsaw puzzle, piece by piece."



In the footsteps of trailblazers

By the mid-nineteenth century biologists had observed that a cell population migrated out of the vertebrate brain and spinal cord during embryogenesis, but an appreciation for where they went was possible only after scientists discovered how to track them. Building on the tissue transplantation techniques developed earlier in the twentieth century, renowned French embryologist Nicole Le Douarin grafted portions of the embryonic quail spinal cord into chick embryos prior to neural crest migration. After the neural crest cells had reached their final destination, she mapped where they ended up. Fifteen years later, Scott Fraser, a biophysicist at the California Institute of Technology and Kulesa's former mentor, developed techniques to microinject fluorescent vital dyes into single premigratory neural crest cells. This allowed him to analyze their lineage and dynamic behaviors in embryonic mice, chicks, or frogs using time-lapse video and confocal microscopy.

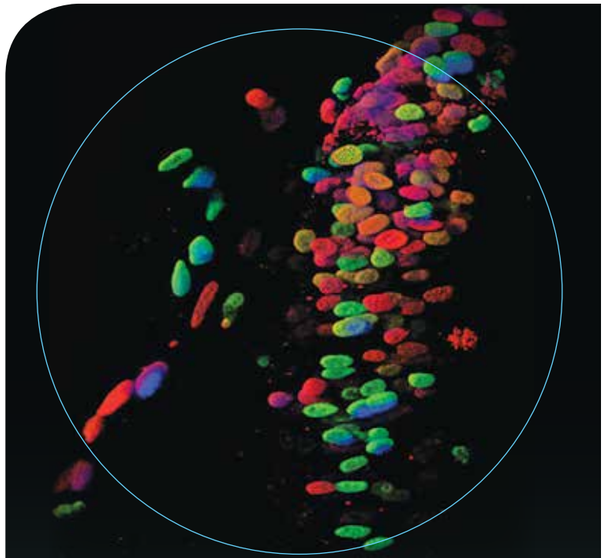
Kulesa walks in these pioneers' footsteps: Soon after arriving at Stowers, he began working on techniques to deliver a cocktail of rainbow-colored fluorescent proteins into neural crest cells and utilize a newly emerging microscopy tool called multispectral-imaging to distinguish each color. By labeling the cell nucleus, cell membrane and cytoplasm with different colors, single neural crest cells could be more efficiently identified and tracked within the complex cellular architecture of a living chick embryo. That initial work was reported in 2005 in *Biotechniques* and then refined in a 2010 *BMC Developmental Biology* paper.

"In the past scientists could only take snapshots of cells at an early stage and then at their final destination," says Krumlauf. "Now, at Stowers we are fortunate in having both cutting edge imaging and experts who can make movies of a cell's life in a living organism. It's revealing an amazing world with subtle complexities."

Remembering their roots

Given how rapidly the imaging field is evolving, Kulesa feels the next frontier will exploit multispectral-imaging to better visualize 3-D cell dynamics and link cell behaviors with molecular data. To do so, he now pairs spectral imaging with a method called laser capture microdissection (LCM) and quantitative polymerase chain reaction (qPCR). These approaches allow researchers to excise a small number of cells at specific points during migration and analyze their gene expression profile. Using this technique, Kulesa's team literally cut the leading cells from a pack of streaming neural crest cells in a chick embryo and found that they express unique genes associated with invasive behavior. These findings, which define factors expressed by neural crest trailblazers, were reported in *Development* in 2012.

Since then the Kulesa team has applied that strategy to explore a suspected link between neural crest migration and metastatic melanoma. Melanoma is an invasive cancer of pigment cells called melanocytes, and vertebrate melanocytes are yet another cell type born from neural crest cells. To determine if the embryonic neural crest microenvironment alters melanoma cell invasiveness, Kulesa transplanted human melanoma cells into chick embryos and then waited to see if they would invade along neural crest migratory pathways.



Single cell identification and tracking is more accurate using multicolor cell labeling and multispectral 3D confocal imaging. Here, individual cell nuclei within the early chick brainstem and migrating neural crest cells are distinctly visualized using a cocktail of fluorescent proteins.

As detailed in a series of papers culminating in a 2012 *Pigment Cell & Melanoma Research* report, not only did human metastatic melanoma cells start migrating but they followed host chick neural crest migratory pathways and reached peripheral targets. That study also revealed that melanoma cells transplanted into the chick microenvironment exploit neural crest genes to facilitate invasion. Overall, these discoveries show that when placed in a cellular neighborhood that reminds them of their birthplace, even cancer cells recognize what street they're on.

Kulesa now wonders whether other neural crest-related cancers hijack a neural crest cell gene expression program. One of those is neuroblastoma, the most common cancer in infants. Neuroblastomas are malignancies of sympathetic nervous system structures, such as adrenal glands.

"In neuroblastoma, neural crest cells fail to mature but instead remain like a multipotent progenitor cell," says Kulesa, referring to the fact that some cancer cells exhibit properties of normal, "good" stem cells. His lab is now testing whether human neuroblastoma cells respond to microenvironmental cues like the melanoma cells did, with a goal of thwarting them. "We are excited about creating in vivo systems in which we can transplant, visualize and profile human neuroblastoma cells and identify molecular signals that may reprogram them to become less destructive."

A move in a different direction

Trainor remains focused on the molecular dissection of cranial neural crest cells but has extended his analyses to a neural crest population headed the opposite way: cells that march toward the gut. At journey's end, those cells mature into neurons that innervate the colon, comprising the enteric nervous system. Mutations that slow or block their progress cause a congenital defect called Hirschsprung disease. Children born with Hirschsprung lack innervation of variable regions of the gastrointestinal tract and typically require surgery to repair bowel function.

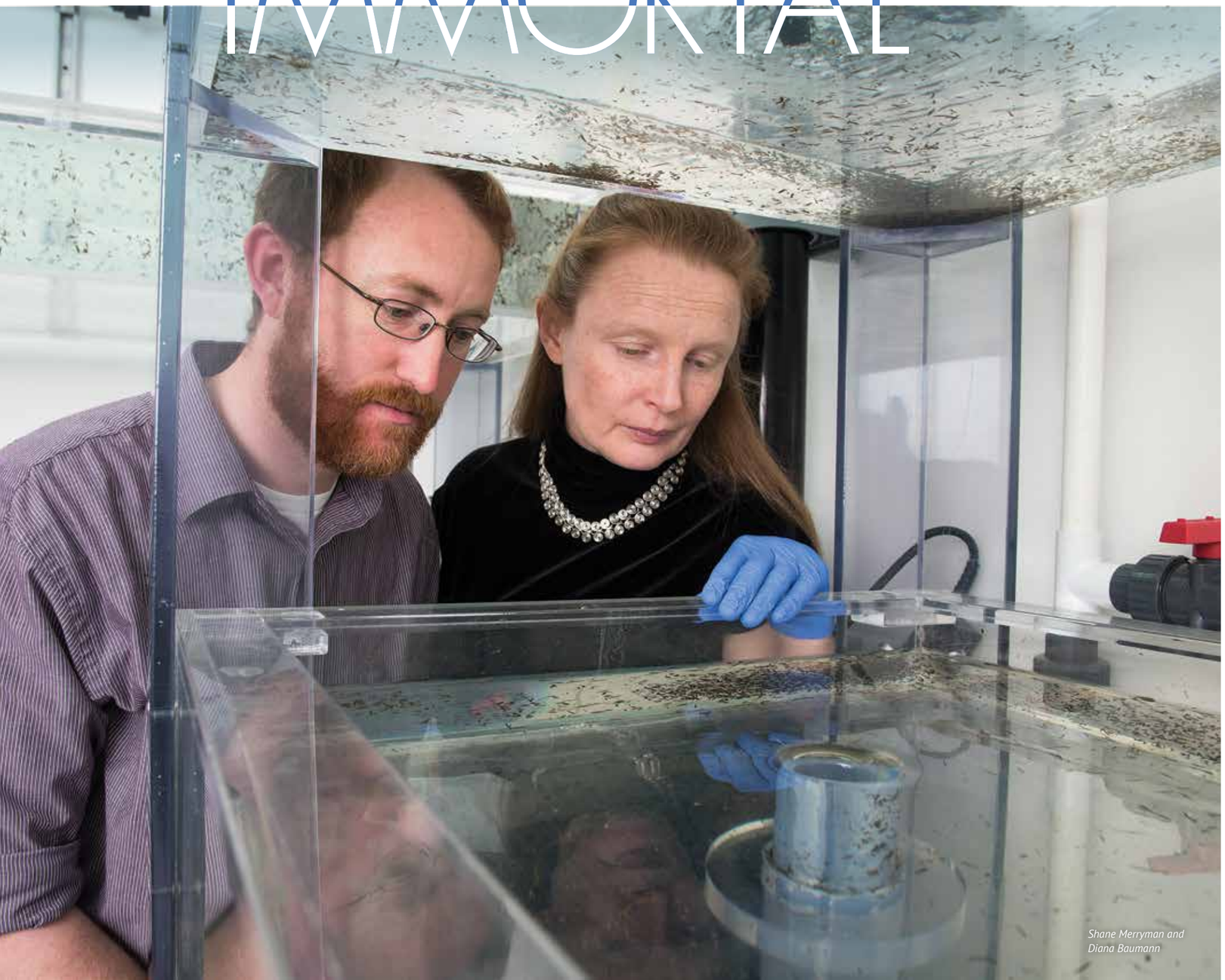
Last year, Trainor reported in *Human Molecular Genetics* that mice mutants in a specific pair of genes expressed in migrating crest cells mimicked human Hirschsprung disease. One of those genes was *Tcof1* (also a culprit in TCS) and the other was *Pax3*, a prime suspect in neurocristopathies affecting ear, face, and heart development. In mice expressing about half the normal allotment of both genes, fewer neural crest cells migrated out of the brain and spinal cord, and many died on the way to the gut. Significantly, mice expressing suboptimal levels of just one of those genes did not exhibit equivalent defects.

According to Trainor, these findings confirm the lesson that genome sequencing has taught us over the last decade: that many genetically based diseases emerge due to the malfunction of more than one gene. "Some neurocristopathies are multigenic," he says, noting this finding's biological and clinical significance. "As therapeutic interventions become available, proper diagnosis of these conditions will require genetic testing for combinations of mutations."

Trainor's interest in neurocristopathies is not confined to the lab. He helps write fact sheets for the National Organization for Rare Disorders to update TCS patient families and physicians on basic research and provide information about screening. And he draws inspiration from interacting personally with the TCS community. "It's the medical problems that keep us motivated," he says. "It makes us hopeful that somewhere down the track we will figure out how to prevent or at least ameliorate these conditions."

By Alissa Poh

Almost IMMORTAL



Shane Merryman and Diana Baumann

A LOOK AT STOWERS' FIRST-IN-KIND PLANARIA CORE FACILITY AND SOME OF THE SCIENCE INSPIRED BY THESE SIMPLE INVERTEBRATES

If humans had the regenerative capacity of planaria, executioners in centuries past—particularly those charged with quartering convicts already drawn and hanged —would have had a bad time. These minute aquatic flatworms are remarkably resilient: chop one in half and it becomes two. Or three, if sliced in thirds. Scottish nobleman Sir John Dalyell described it well in 1814: "No matter how I cut these animals, they could almost be called immortal under the edge of the knife."

Not that regeneration was a dark horse by then. Says Howard Hughes Medical Institute and Stowers Investigator Alejandro Sánchez Alvarado, PhD, "Everyone wanted to know if it was broadly distributed across animal species" during the mid-1700s, after Swiss naturalist Abraham Trembley observed this feat in Hydra (tiny freshwater animals). "Trembley influenced what's sometimes referred to as The Great Snail Controversy; many of his peers began decapitating garden snails and slicing salamanders just to see what might happen." Amazingly, the victims not only survived but fully regenerated. Religious intellectuals of the day were troubled—how, they wondered, could this be possible for organisms possessed of "indivisible souls?"

Since then, scientific understanding has grown by leaps and bounds, but Sánchez Alvarado still wants to know why the capacity for regeneration varies so widely across animal species. After discovering that a particular species of planaria, *Schmidtea mediterranea*, fulfilled his criteria for a choice model system—diploid organism, small genome size, high regenerative capacity, existence of sexual and asexual strains—he proceeded to make it genetically malleable for regeneration-centric investigations, and is widely regarded in the field as both pioneer and leading authority.

If you build it, they will go forth and multiply

Operation Planaria at Stowers started small: Besides caring for the likes of whiptail lizards, zebrafish, and other laboratory animals, the Reptile & Aquatics Facility staff housed a handful of flatworms in Rubbermaid containers, in a single incubator occupying an unused procedure room. Then Sánchez Alvarado joined the Institute in 2011, persuaded to move not just most of his human crew from the University of Utah's School of Medicine, but also his entire planaria colony.

"We ratcheted up almost to breaking point in terms of manpower needs," says Diana Baumann, head of the Reptile & Aquatics facility. "So an expansion plan became necessary, because we didn't want to be the factor limiting planaria-related scientific productivity."

Rapid evolution followed, culminating in the creation of the first core facility anywhere dedicated to planaria. These days, a total of 185 sexual and asexual flatworm strains occupy not only plastic containers, but two whole rooms—separated by method of reproduction—with a third room set aside for research and development. A five-member team, supervised by Aquatics Specialist Shane Merryman, provides full-time planaria care.

Not only that, but the asexual planaria—which reproduce by sticking their tails downward and swimming in the opposite direction until, like overstretched rubber bands, they snap in two—have already made themselves at home in the most advanced aquatic animal housing around, courtesy of Merryman and his group. It's called a recirculating system, where the water is continuously recycled after being filtered free of all possible contaminants. Baumann considers it "a fantastic time-saver that greatly improves the quality of care," given the current scale of this core facility. Housing planaria in individual containers such as the aforementioned Rubbermaid containers, each with static water that requires manual changing, is feasible only when grooming particular strains for specific research purposes.

No off-the-shelf planaria recirculating system exists, Baumann adds, so what the asexual planaria are currently enjoying is the result of much careful research on Merryman's part. For instance, water courses downward from the topmost of three stacked tanks before getting recirculated, mimicking a river's flow—and the worms' natural habitat. Like all animals, these creatures move around, albeit slowly, so the system's pipes are oriented to minimize the number of runaway worms that reach the water-collecting sieves below the bottom tank.

Prior to joining Stowers, Sánchez Alvarado and his research group had identified conditions to rear sexually reproducing animals in captivity, but had yet to optimize procedures to overcome one key obstacle: why, of multiple egg capsules from their sexual strains, few were actually gravid, that is containing developing embryos. Baumann recalls adjusting salt concentrations in the worms' watery home and adding crushed coral for calcium-enhancing purposes, among other troubleshooting efforts, before she went out on a limb and introduced them to a fresh water supply from the pond by her house. "Its surface runoff was completely free of insecticides and pesticides, and I thought the water might contain basic minerals these worms required," she says. "They finally began reproducing in this source, which we called 'BP water' for the longest time before revealing that it stood for 'Baumann Pond.'"

"We keep track of fertile eggs collected, and a recent monthly total came to almost 11,000," says Merryman, whom Baumann credits for building a meticulous database that records all things planaria. Every species and strain is barcoded, complete with scanners. Volumes, numbers, and other specifics are mere mouse clicks away; just about any question regarding this core facility is answerable—except, perhaps, the exact worm count on a given day.

Meanwhile, the critters themselves live like royalty. Their loyal servants prepare planaria chow three times weekly, mashing calves' livers shipped fresh from Chicago into a fine paste—"think making *pâté* en masse," Baumann quips—which is then loaded into syringes and hand-dispensed throughout the tanks. Every egg produced by the sexual planaria is laboriously collected, and while they await their own recirculating system (currently being designed by Merryman), their water has to be manually prepared in sixty-gallon rounds.

"These are itsy-bitsy worms with outsized care requirements," Baumann says. "But consistent, top-quality animal husbandry is what we're here to provide."

Happy, healthy worms = better science

Sánchez Alvarado is delighted that his sexual planaria have flourished at Stowers and even produced progeny equally capable of churning out fertile eggs—not necessarily a heritable trait from one generation to the next.

"Although we have not yet fully optimized sexual reproduction and production of large numbers of embryos in captivity, we are nonetheless at a point where it is possible to break ground in the interrogation of planarian embryogenesis." As Sánchez Alvarado points out: "The embryogenesis of *S. mediterranea* has yet to be described in detail, because until now, it's been difficult getting them to reproduce. Rather than trying to fit this process into any preconceived notions of developmental stages, we want to see if the transcription profiles of individual embryos, at different ages, can tell us more about the steps involved."

Asexual planaria reproduction: The flatworm stretches itself to the breaking point. Each new segment will regenerate into a fully viable individual worm.

WEB SPECIAL:
To view a video, please visit our online gallery at www.stowers.org/stowers-report/spring-2014/planaria

As for regeneration, it continues to fascinate even those largely unenamored of science and has long made popular culture's hit list of cool concepts: Take the Lizard, for instance, Spider-Man's nemesis and product of genetic tinkering gone badly wrong; or the injury-defying Wolverine of X-Men fame. But while research like Sánchez Alvarado's is key to increasing our understanding of many biological processes, including aging and tissue homeostasis, "it's fanciful to imagine we're within reach of restoring body parts," he says. "We're not even close. Should we get there, though, planaria will likely fit somewhere on the totem pole of creatures deserving credit."

By Alissa Poh

A DISCUSSION WITH

JULIA ZEITLINGER, PHD

Growing up in Germany, Associate Investigator Julia Zeitlinger, PhD, excelled in math and science in school with many seeing traits that would fit naturally with a scientific career: curiosity, a liking for theory construction and an analytical mind. But her decision to become a scientist was not without hesitation. She also loved the arts and has fond memories of stepping out onto a stage.

"Everything finally comes together on opening night; there's a deep quiet in the audience as lines are spoken and listened to, and you're really living in the moment," says Zeitlinger. "Sometimes I miss that electric atmosphere."

Ultimately, she fell in love with biology in college and her first stint at laboratory research at King's College London kindled a long-lasting spark that went far beyond the allure of opening night. On the heels of a PhD in developmental genetics from the European Molecular Biology Laboratory in Heidelberg, Zeitlinger pursued a postdoctoral fellowship at the Massachusetts Institute of Technology.

"The first microarray publications were just out and genomics was coming into its own; I wanted to be where cutting-edge discoveries were being made," she recalls. "I was intrigued by the prospects of probing the black box of transcription programs, and spending a few years in a different country."

Zeitlinger never intended to stay past those few years, but she fell in love again—only this time she got married and decided to make the US her permanent home. "Life takes unexpected twists and turns and it's important to recognize and seize the wonderful opportunities that present themselves when you least expect it," and adds with a laugh, "not unlike research."

Since Zeitlinger joined the Stowers Institute in 2007, she is ferreting out, in *Drosophila*, fresh threads linking DNA sequence with cellular function. In particular, she and her team have taken a closer look at promoters and learned that there's more to these DNA regions, responsible for initiating transcription of genes into messenger RNAs, than meets the scientific eye. They dictate, for instance, whether RNA polymerases, or the primary workhorses of transcription, face nonstop action or have the flexibility of pausing on the job. Varying developmental needs drive these and other behavioral cues, and promoters have all the necessary details.

"Promoters have often been dismissed as boring from a research standpoint," Zeitlinger says. "But we're finding otherwise. Basically, transcription isn't just this behemoth of proteins doing one job the same way."

WHAT ADVICE WOULD YOU OFFER SOMEONE CONTEMPLATING A CAREER IN SCIENCE WHILE ALSO TOYING WITH THE ARTS, GIVEN THAT NE'ER THE TWAIN SHALL MEET, PROFESSIONALLY SPEAKING?

I'd start by emphasizing that one is not somehow less creative than the other. Yes, creativity in science is often more hidden, especially at the beginning when you're establishing your own research niche and are swamped with experiments that seem tedious and endless. But it's a lot like artists with their first sketches—they're trying out a concept to see if it works visually, and if it doesn't, they come up with modifications. The final painting is not immediately evident. In science, the beauty is when things go in unexpected directions; if you're open to change, you'll find that's where not only surprises but the really important discoveries often lurk.

In the end, I would say follow your heart and do what you're most passionate about. Science can be a tough business of coping with failed experiments, confusing results and criticism from peers. Having a place within yourself to which you can always return, when the going gets rough, is key. I never felt that I had that confidence with acting, as much as I loved the stage.

REGARDING YOUR RESEARCH, WHAT'S THE MOST EXCITING QUESTION YOU'RE PLANNING TO TACKLE THIS YEAR?

I hope we come closer to solving what's known as the combinatorial code for transcription: basically, all the factors and signals that come together to turn on a gene. There's much we don't yet understand about this switchboard's manual. Which are the toggles to press, and in what order? To gain new insights, we've recently developed a technology called ChIP-nexus that allows us to zoom in at much higher resolution on not only DNA regions where transcription factors are found but on their precise binding sites in the genome. We can already see interesting results but the big challenge will be to find out how these pieces fit into the big puzzle.

We're also exploring the timing, or speed, of embryonic development in flies. It's thought of as a program with set steps, but it occurs at surprisingly different rates across the animal kingdom. Even among flies it is remarkably different – a mere 14 hours in *Drosophila yakuba*, for instance; and 32 hours in *Drosophila mojavensis*. Our measurements also show that the mean embryonic development times for different lines from a single *Drosophila melanogaster* population range from 18 to 23 hours. So genetic variation among individuals has its own impact here, yet we have no idea what mechanisms are at play. We've established a nice system that will allow us to hunt for and examine factors influencing these differences.

WHAT ARE YOUR THOUGHTS ON THE ENCODE (ENCYCLOPEDIA OF DNA ELEMENTS) PROJECT'S OVERALL APPLICABILITY AND IMPORTANCE?

I believe it's an important step toward understanding how genome information encodes cellular function and I hope it will make genome-centric research more mainstream. Genome-wide experiments are still viewed as a starting point for more detailed single-gene analyses. But I believe genomics should be a discipline in its own right, for it has its own methods of extracting information and testing hypotheses. The power lies in statistics on a genome-wide scale – with careful interpretation of correlations and P values, of course. For instance, if I'd first observed RNA polymerase II's pausing behavior through a single-gene analysis rather than genome-wide, I might have regarded the gene itself as weird or incorrectly mapped, rather than believe what I saw was real.

That said, at least some of what the public first heard about ENCODE in 2013 was oversimplified. This project contains huge, complex data sets, yet scientists had to come up with a simple punch line, which resulted in statements like "Junk DNA is not really junk." I prefer Eric Lander's seven-word summary in 2003: "Genome: bought the book; hard to read." Despite all the progress, it's still true.

HOW DO YOU FEEL ABOUT SCIENTISTS CHERRY-PICKING DATA TO REPORT – OR OMIT, AS THE CASE MAY BE – WHICH OCCURS EVEN MORE OFTEN THAN OUTRIGHT FRAUD?

I'm not sure trying to present the best or "nicest" data is necessarily cherry-picking, as long as you can show that your findings are real, reproducible and accompanied by robust statistics. Distinguishing between actual results and interpretation is key, however: the first needs to be solid, while the second can change.

There's also this tendency to start with just one hypothesis, for which confirmatory evidence is sought. As Karl Popper pointed out fifty years ago, that's not good science. It's critical to have and test multiple hypotheses; rejecting one doesn't mean any of the rest are correct, either. There could be other possibilities you might not have envisioned at the time.

WHERE DO YOU DO YOUR BEST THINKING?

For me, it's when more than where: in the morning, right after waking up. It's quiet and my eyes are still mostly closed; somehow, thoughts and ideas that were swirling around in my mind have crystallized overnight.

IN GENERAL, IS SAYING NO DIFFICULT OR EASY FOR YOU?

I used to be quite bad at it, until I read William Ury's *The Power of a Positive No*. It really woke me up to the importance of accounting for my own core values and priorities. If something isn't worthwhile to me, I can now say no and, as a pretty direct person at heart, I feel much better being frank. But it didn't come naturally.

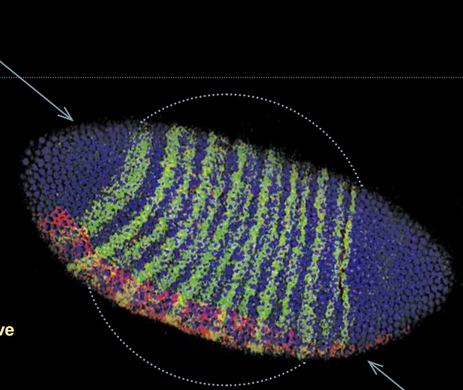
WHAT HISTORICAL PERIOD WOULD YOU MOST LIKE TO VISIT, IF IT WERE POSSIBLE?

I can think of two. For my son's sake, it would be great to scope out the Jurassic period and see actual dinosaur colors, as well as some of the earliest birds like *Archaeopteryx*. My own great interest is human evolution, so I'd choose a visit with the Neanderthals to get a better idea of just how similar to modern humans they were, how they communicated, and why they were eventually outcompeted.

WHAT DOES YOUR PERFECT DAY LOOK LIKE?

I had one last weekend, actually – half a day at work, where I was able to do some reading to catch up on topics of interest, before spending the rest of it with my family. Having a three- and five-year-old is definitely hectic, but we're making beautiful memories together and I wouldn't trade my life right now for anything else.

READ ME NOW!



When egg and sperm combine, the new embryo bustles with activity. Its cells multiply so rapidly they largely ignore their DNA, other than to copy it and to read just a few essential genes. The embryonic cells mainly rely on molecular instructions placed in the egg by its mother in the form of RNA. Then, during the so-called midblastula transition, cells start transcribing massive amounts of their own DNA.

Earlier in her career, Associate Investigator Julia Zeitlinger, PhD, discovered that sometimes the transcription machinery, or RNA polymerase II, pauses at the beginning of a gene as if taking a lunch break. More often than not, pausing occurred at genes important for development. When she and her team used fruit fly embryos to test whether pausing may help get these molecular construction workers on-site before a big work order becomes due during the midblastula transition, they were in for a surprise.

Before the midblastula transition, RNA polymerase II appeared to rarely pause as it transcribed roughly one hundred early genes. And no construction crews were sitting idle on inactive genes in preparation for the midblastula transition. Pausing only became widespread during the midblastula transition itself. "What we found was not what we expected at all," Zeitlinger says. "Instead of preparing for a huge workload, the construction crews were busy completing rush jobs."

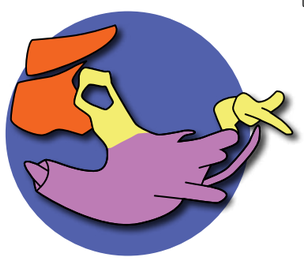
When the researchers computationally compared the regulatory elements at the beginning of each of the genes or promoters where pausing occurred with those where it didn't, a pattern emerged. They found that three different types of promoters correlated with the construction crew's pausing behavior.

"The most important result is that promoters are different," Zeitlinger says. "The general paradigm for a long time has been a promoter is a promoter. But really what we see is that they have different functions."

The study was published in the August 2013 issue of *eLife Sciences*.

First genetic model of a human jaw fusion defect known as SYNGNATHIA

Normal Jaw Structure



Syngnathia

Almost a third of all birth defects involve the head and face and most can be blamed on problems relevant to neural crest cells. These cells spring from neural tissue of the brain and embryonic spinal cord and travel throughout the body, where they morph into highly specialized bone structures, cartilage, connective tissue, and nerve cells. Occasionally, neural crest cell development goes awry, causing birth defects affecting regions as diverse as the head, heart or gut. *(See page 3 for more on neural crest cells.)*

In a recent study, Paul Trainor, PhD, and his team characterized a mutant mouse that mimics a congenital disorder known as syngnathia in which children are born with fused upper and lower jaws and related facial anomalies. They discovered that neural crest cells predestined to build the afflicted facial areas are formed normally and migrate properly, but mature incorrectly.

The Trainor lab also focuses on congenital malformations caused by impaired neural crest cell expansion or migration, such as the rare disorder Treacher Collins syndrome, in which children exhibit small cheekbones and jaws together with cleft palate, drooping eye slits and ear anomalies leading to hearing loss.

"In a condition like Treacher Collins we see a failure to make enough cells at the beginning of migration due to mutations in *Tcof 1*, while in syngnathia cells form properly but make bone in an inappropriate place due to loss of *Fpxc 1*," says Trainor. "This means there simply isn't going to be any one uniform way to address all of these disorders. If you want to prevent or treat them you must understand how each originates cellularly and genetically."

The study was published in the December 19, 2013, issue of *PLOS Genetics*.

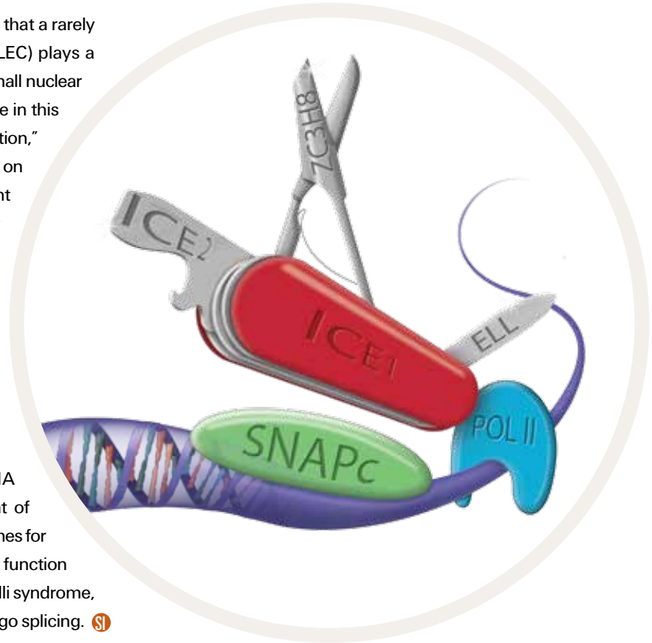
LEC: A multipurpose tool

The transcription process converts information encoded in DNA into various forms of RNA, including messenger RNA, which carries protein-making instructions, and snRNAs, which partner with proteins to form small nuclear ribonucleoproteins (snRNPs). In recent years, Investigator Ali Shilatifard, PhD, and his team have focused their work on a family of factors called ELL (Eleven-nineteen lysine-rich leukemia gene), which speed up the rate at which genes are expressed to help the transcription process along.

In their latest investigation, the Shilatifard Lab discovered that a rarely studied factor known as the Little Elongation Complex (LEC) plays a critical and previously unknown role in the transcription of small nuclear RNAs (snRNA). "We have found that LEC not only has a role in this process—it is like the 'Swiss Army knife' of snRNA transcription," says Shilatifard. "LEC does it all." The findings shed new light on the mystery of snRNA transcription, which is vitally important to gene expression and regulation, but has been poorly understood until now.

"As biologists we are very interested in defining the molecular machineries involved in life, and snRNA are very important in life," Shilatifard says. "The nucleus is a suitcase with all of the DNA information packaged in it. You need specific machinery to identify the right information to unpack to perform the exact process that's needed. Now we understand another piece of that machinery."

Understanding LEC and the machinery of snRNA transcription may also have implications for the treatment of disease. It could, for example, open the door to novel approaches for treating diseases that are associated with defective snRNA function and splicing, such as spinal muscular atrophy and Prader-Willi syndrome, or for attacking cancer cells, whose proteins may also undergo splicing.



The study was published in the August 22, 2013, issue of the journal *Molecular Cell*.

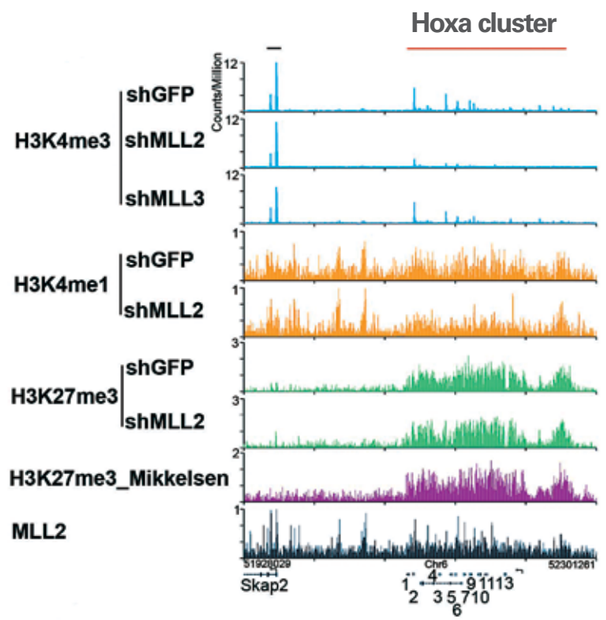
RETHINKING "THE CODE"

A decade ago, gene expression seemed so straightforward: Genes were either switched on or off. Not both. Then in 2006, a blockbuster finding reported that developmentally regulated genes in mouse embryonic stem cells can have marks associated with both active and repressed genes, and that such genes, which were referred to as "bivalently marked genes," can be committed either way during development and differentiation.

This paradoxical state—akin to figuring out how to navigate a red and green traffic signal—has since undergone scrutiny by labs worldwide. When a team led by Investigator Ali Shilatifard, PhD, revisited that notion, the researchers not only identified the protein complex that implements the activating histone mark specifically at "poised" genes in mouse embryonic stem (ES) cells, but also found that its loss has little effect on developmental gene activation during differentiation. This suggests there is more to learn about interpreting histone modification patterns in embryonic and even cancer cells.

"There has been a lot of excitement over the idea that promoters of developmentally regulated genes exhibit both the stop and go signals," explains Shilatifard. "That work supports the idea that histone modifications could constitute a code that regulates gene expression. However, we have argued that the code is not absolute and is context dependent."

The study's findings also potentially impact oncogenesis, as tumor-initiating cancer stem cells exhibit bivalent histone marks at some genes. "Cancer stem cells are resistant to chemotherapy, making them difficult to eradicate," says postdoctoral fellow and the study's first author Deqing Hu, PhD. "Our work could shed light on how cancer stem cells form a tumor or suggest a way to shut these genes down."



The study was published in the August 2013 issue of *Nature Structural and Molecular Biology*.

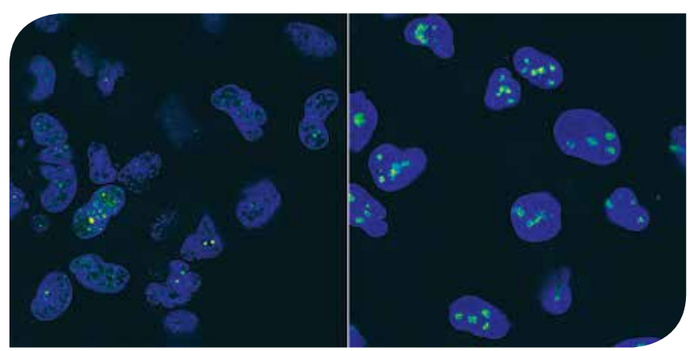
THE BASIC BIOLOGY OF ROBERTS SYNDROME

CHILDREN BORN WITH DEVELOPMENTAL DISORDERS CALLED COHESINOPATHIES CAN SUFFER SEVERE CONSEQUENCES, INCLUDING INTELLECTUAL DISABILITIES, LIMB SHORTENING, CRANIOFACIAL ANOMALIES, AND SLOWED GROWTH. COHESINOPATHIES RESULT FROM MUTATIONS IN GENES ENCODING COHESINS AND THE FACTORS THAT REGULATE THEIR FUNCTION. COHESINS FORM RING-SHAPED PROTEIN COMPLEXES THAT HELP ORGANIZE THE GENOME. ALTHOUGH RESEARCHERS KNOW WHICH MUTATIONS UNDERLIE SOME COHESINOPATHIES, LITTLE IS KNOWN ABOUT THE RESULTING DISRUPTION OF DOWNSTREAM SIGNALS.

Recently, Investigator Jennifer Gerton, PhD, reported that mTOR signaling, a prominent signaling pathway that drives cell growth, is inhibited in the cohesinopathy known as Roberts syndrome (RBS). That work, which analyzes patient cells and zebrafish models of RBS, shows that jump-starting the sluggish signaling pathway with the amino acid L-leucine partially rescues defects associated with the disease at both the cellular and organismal level.

Gerton is encouraged but cautious about these findings. "Use of a nontoxic, inexpensive amino acid to treat human disease could be of benefit," she says, noting that L-leucine dietary supplementation is being tested in clinical trials for Diamond-Blackfan anemia, a genetic disorder. "Many aspects of RBS are unlikely to respond to postnatal leucine treatment, but leucine supplementation might improve some disease manifestations in RBS."

RBS is a rare cohesinopathy, but a related condition called Cornelia de Lange syndrome (CdLS) occurs more frequently—about one in 10,000 live births. Researchers have defined mutations causing CdLS, and CdLS zebrafish models are also available. In fact, Gerton recently received a grant from the Cornelia de Lange Syndrome Foundation to assess the effect of L-leucine supplementation in those fish (see page 25).



The study was published in the October 2013 issue of *PLoS Genetics*.

First study of Ataxin-7 in fruit flies

Disruptive clumps of mutated protein are often blamed for clogging cells and interfering with brain function in patients with the neurodegenerative diseases known as spinocerebellar ataxias.

The protein clumps result from genes that develop a genetic "stutter" in which a three-letter segment of the DNA code is repeated over and over, leading to proteins containing long, redundant strings of a single amino acid called glutamine. These abnormal proteins are prone to aggregating with one another inside cells.

But a new study in fruit flies suggests that for at least one of these neurodegenerative diseases, the defective proteins may not need to form clumps to do harm. Researchers led by Investigators Jerry Workman, PhD, and Susan Abmayr, PhD, found a fruit fly version of Ataxin-7 which is mutated in patients with spinocerebellar ataxia type 7 (SCA7) disease. In humans, Ataxin-7 was known to aggregate in the cells of patients with SCA7 disease, but there was no direct evidence linking the aggregates to neurodegeneration.

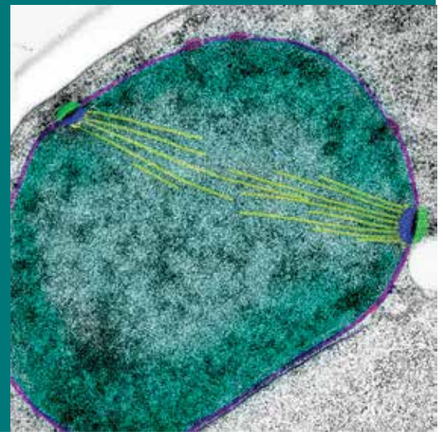
The team found that fruit flies that lack Ataxin-7 experience neurodegeneration in the brain and the eye—paralleling the effects of the human disease. "The assumption has been that the disease is caused by the aggregated proteins," Workman says. "But in the mutated fly, there's no aggregated protein. There's no soluble protein. It's not there at all. The lack of Ataxin-7 causes neurodegeneration in the fruit fly."

"This sheds new light on what we think could be the cause of the SCA7 disease phenotype," Abmayr says. The fruit fly has the potential to reveal more about Ataxin-7's role in disease, say the scientists, who are now planning additional studies.

The study was published February 1, 2014, in the journal *Genes & Development.*

PROTEIN SHUTTLE SERVICE

Researchers have glimpsed two proteins working together inside living cells to facilitate communication between the cell's nucleus and its exterior compartment, the cytoplasm. The research provides new clues into how a crucial protein that is found in organisms from yeast to humans does its work.



The study, led by Investigator Sue Jaspersen, PhD, focused on a protein called Ndc1, which controls when and where a cell inserts holes into the double-walled membrane that surrounds its nucleus. In yeast, these holes become the sites for two essential structures: passageways called nuclear pore complexes, and spindle pole bodies, which anchor the cytoskeletal filaments that pull chromosomes to opposite sides of a dividing cell. "Too many or too few insertion sites will have disastrous consequences," Jaspersen says.

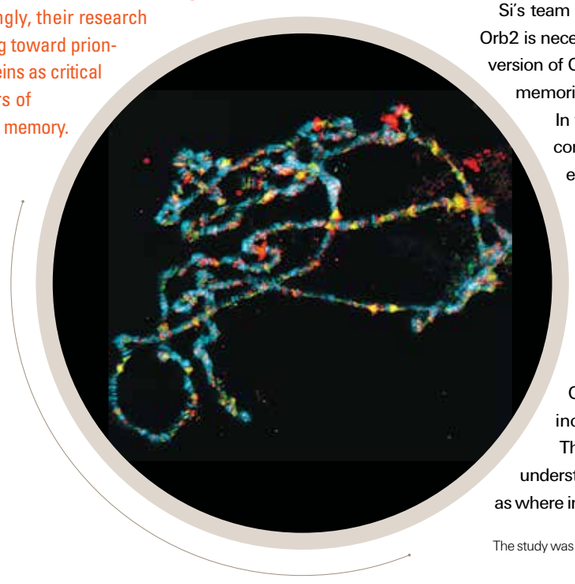
The Jaspersen team created yeast with mutations in the Ndc1 gene. As expected, changes that disrupted Ndc1's interaction with its known partners in the nuclear core complex or the spindle pole body were lethal. One mutation puzzled the scientists, however. The altered Ndc1 protein bound to the expected components of both the nuclear pore complex and the spindle pole body, just like the normal protein. But when yeast cells produced this altered version of Ndc1, they died, suggesting another critical interaction partner.

Using a method to detect interactions at the nuclear envelope, the Jaspersen team found that Ndc1 bound to a protein called Mps3. Mps3 and Ndc1 came together in the nuclear envelope, but away from the two structures the team had set out to study. This led them to speculate that Mps3 might help shuttle Ndc1 to the sites where it is needed, controlling the distribution of nuclear pore complexes and spindle pole bodies. The Jaspersen team is now planning further experiments to test how Ndc1 and Mps3 maintain the appropriate balance of these critical structures.

The findings were published in the February 10, 2014, issue of the *Journal of Cell Biology.*

What makes memories last?

Finding the molecular alterations that encode a memory in specific neurons as it endures for days, months, or years—even as the cells' proteins are degraded and renewed—is a focus of research in the lab of Investigator Kausik Si, PhD. Increasingly, their research is pointing toward prion-like proteins as critical regulators of long-term memory.



Prions can be notoriously destructive, spurring proteins to misfold and interfere with cellular function as they spread without control. Certain prion-like proteins, however, can be precisely controlled so that they are generated only in a specific time and place. These prion-like proteins are not involved in disease processes; rather, they are essential for creating and maintaining long-term memories. "This protein is not toxic; it's important for memory to persist," says Si who led the study in collaboration with researchers at the University of Kansas Medical Center.

Si's team had previously found that in fruit flies, the prionforming protein Orb2 is necessary for memories to persist. Fruit flies that produce a mutated version of Orb2 that is unable to form prions learn new behaviors, but their memories are short-lived.

In the new study, Si wanted to find out how this process could be controlled so that memories form at the right time. "We know that all experiences do not form long-term memory—somehow the nervous system has a way to discriminate. So if prion-formation is the biochemical basis of memory, it must be regulated." Si says

Si and his colleagues knew that Orb2 existed in two forms—Orb2A and Orb2B. Orb2B is widespread throughout the fruit fly's nervous system, but Orb2A appears only briefly in a few neurons, at extremely low concentrations. Their experiments revealed that when a protein called TOB associates with Orb2A, Orb2A becomes much more stable and longer lived which increases the prevalence of the prion-like state.

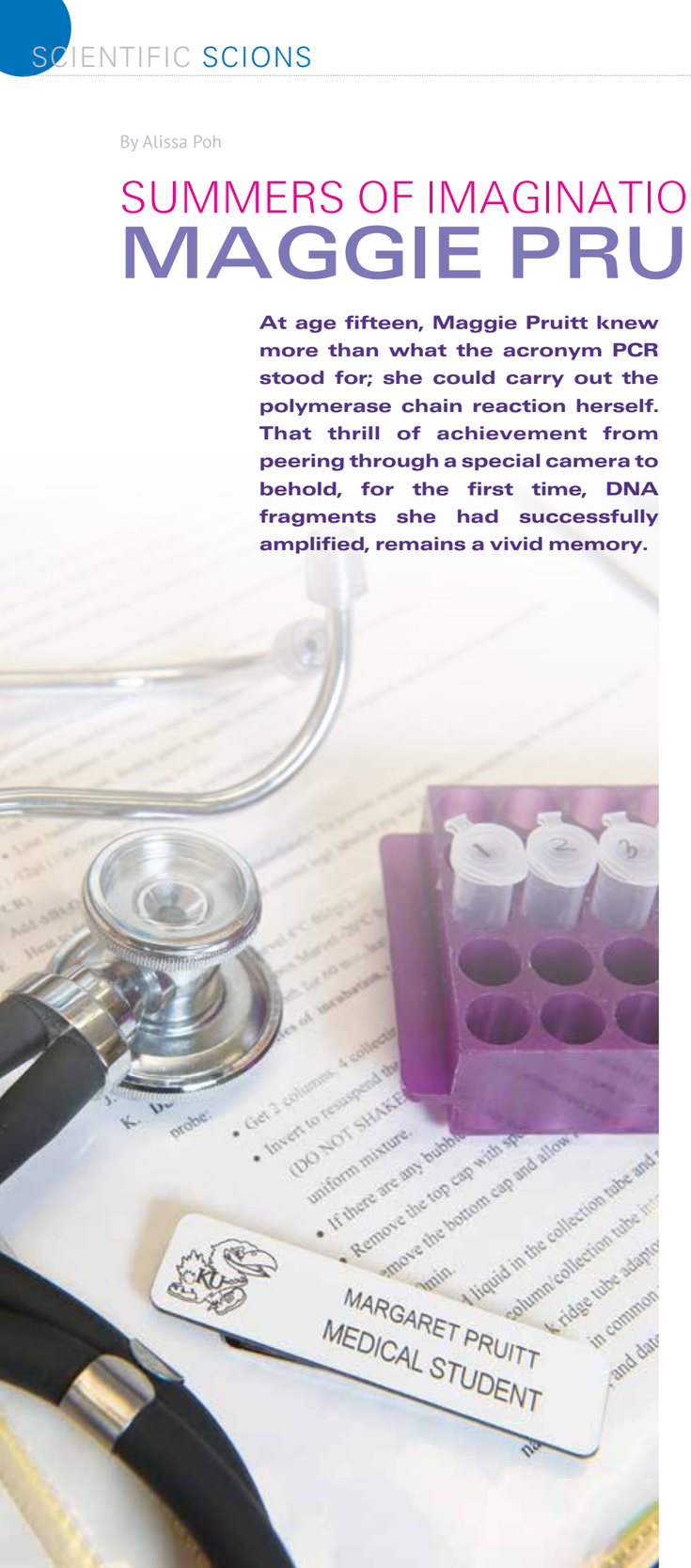
The findings raise a host of new questions for Si, who now wants to understand what happens when Orb2 enters its prion-like state, as well as where in the brain the process occurs.

The study was published in the February 11, 2014, issue of *PLOS Biology.*

By Alissa Poh

SUMMERS OF IMAGINATION: MAGGIE PRUITT

At age fifteen, Maggie Pruitt knew more than what the acronym PCR stood for; she could carry out the polymerase chain reaction herself. That thrill of achievement from peering through a special camera to behold, for the first time, DNA fragments she had successfully amplified, remains a vivid memory.



Best of all, this hands-on tinkering with fundamental scientific concepts occurred in an environment that also allowed students to explore autonomous living. From high school through college, as part of Temple University's, NIH-funded, longitudinal Physician Scientist Training Program (developed to encourage minority students to explore biomedical research), Pruitt reveled in the heady independence of summer-long dorm life with peers. Young as they were, the participants quickly grasped that clinical medicine and basic science, far from mutually exclusive, could be fused into one extraordinarily interesting career.

"One thing the program exploited in full was a child's imagination—this idea that something we couldn't otherwise see, like DNA, could be amplified in a tube and visualized," Pruitt says. "More importantly to almost any kid, our mentors gave us the basic tools yet left us to figure things out for ourselves. They believed in our potential and that really facilitated our growing passion for science.

Pruitt credits her mother for the decade of amazing scientific summers following that first introduction to PCR. "Before, I was forever peppering my mom with questions," she says, recalling the tragedy which prompted these queries: at just six, Pruitt lost her father to brain cancer. "So she decided I should be exposed to biomedical research as early as possible. We'd settled in Maryland after moving around a lot while my dad was in the Army, and I attended Stone Ridge School of the Sacred Heart in Bethesda, right across the street from the National Institutes of Health. I like to think my mom had this notion that one day I'd cross the street, literally and figuratively, into science."

As it turns out, Pruitt did just that. With Alan Hinnebusch, PhD, at the National Institute of Child Health and Human Development, she studied translation initiation in yeast cells. She also explored cancer genetics and biology with Beverly Mock, PhD, at the National Cancer Institute; Mock was impressed enough to offer her a job, which Pruitt accepted after graduating from Duke University in 2009. "Until then, my laboratory stints were only for the duration of a summer," she explains, "and I wanted to see if I could handle research full-time."

But Pruitt also wanted her career to include clinical medicine, so she began exploring MD-PhD programs around the country. Coming to the University of Kansas Medical Center in 2011 made perfect sense in more ways than one: Pruitt was born in Leavenworth, KS, where most of her maternal relatives still reside—including her ninety-three-year-old grandmother, who routinely defeats her at bridge. The partnership between Stowers Institute and KU Medical Center (students in the MD-PhD program can complete their research training at either place) also proved irresistible. After breezing through her first two years of medical school, Pruitt readily picked the laboratory of Stowers Investigator Peter Baumann, PhD, as her new scientific stomping ground.

"Our first conversation lasted a couple of hours and I left really energized—my mind was reeling with all the research possibilities," she recalls. "When it comes to science, Peter's enthusiasm and spontaneous curiosity are pretty contagious. If something intrigues him, he'll find a way to pursue it, and that's how I picture running my future lab."

Pruitt's predoctoral research revolves around telomeres: repetitive regions that are added to chromosome ends. "Why they have a G-rich composition is still unclear," she says. "I'm trying to see if alternative sequences exist by which telomeres could be produced and still maintain the gamut of telomeric functions and, if so, what else we might learn about the relationship between telomere sequence and mechanisms of telomere maintenance. Telomeres are much more than the solution to the, 'end-replication problem,' and I'd love to study a mechanism that would not only inform but perhaps even challenge our basic assumptions about their biology and pathology."

Science may have grabbed her early on, but if she were to pick something else, professional dancing would be right up there for Pruitt, who enjoys salsa and swing, among other forms of creative expression. Her appreciation for creativity is also evident as she describes the artwork lining her living space: a black birch Madonna and Child from Santa Maria de Montserrat near Barcelona; Masai tribal paintings on banana leaves; pink sand from Bermuda; a blown-up canvas of the sunset in Aruba, which Pruitt captured with her new camera.

"Working in a health policy think tank might have been another option," she muses, "because my family background is one of community activism." Pruitt's father became the first president of the high school his class integrated in Bryan, TX, where her paternal grandparents also established the Brazos Valley African American Museum in 2006.

Not that Pruitt isn't a community activist in her own right. Soon after arriving at KU, she and three classmates established a mentoring program—now financially bolstered by the Medical Society of Johnson and Wyandotte Counties—that pairs medical students with J.C. Harmon high-schoolers. "The goal is to give underprivileged students access to resources we take for granted," she says. "Our first class of mentees came to us as sophomores, and I'm thrilled that we'll help them with college applications this year."

As if she weren't busy enough, Pruitt is also a KUMC teaching assistant for first- and second-year medical students, while volunteering at least once a month at the JayDoc Free Clinic. "Staying active helps me deal with stress," she smiles. "And it's nice to have more than a scientific perspective on clinical problems. Interacting with patients motivates me more than ever to return to the bench."

Graduate of the last decade

Dan Bradford, a research technician in the Stowers molecular biology core, received the Graduate of the Last Decade (GOLD) Award, an early career award that recognizes outstanding achievements and accomplishments by graduates of Missouri Western State University. The GOLD award is one of the highest honors the MWSU Alumni Association bestows on recent alumni.

As a kid growing up in Independence, Missouri, Dan Bradford never imagined he would find himself working at a world-class research institute alongside colleagues from all over the globe. Although encouraged by his parents to attend college, Bradford never gave it much consideration and eventually ended up in a less-than-satisfying production job. It was only after his wife finally had enough of his continuous job complaints and encouraged him to think about what he would really like to do with his life that Bradford decided on a career in science. Starting with an associate of arts degree from a local community college, Bradford went on to attend Missouri Western State University where he completed his BS in biology.

It was at MWSU that Bradford caught the eye of one of his teachers. Todd Eckdahl, PhD, professor and chair of the biology department, had just graded his genetics course's midterm exams when he approached Bradford. "When he confronted me about my midterm I thought he was going to have bad news," Bradford remembers. "Instead, he told me I had aced it and invited me to work in his research lab." Eckdahl explained to Bradford that only once before had a student received a perfect score on this genetics exam and that she had gone on to get her PhD from Duke University.

In Eckdahl's lab Bradford developed a genotyping assay for paddlefish, one of the largest freshwater fish in North America and a protected species in most of its habitats. The test allows scientists to distinguish farmed from wild-caught paddlefish and to even identify individual populations. On another project, working with little funding, Bradford came up with a creative low-cost alternative to real time polymerase chain reaction (PCR), a powerful gene analysis technique, which resulted in his first published paper in *Cell Biology Education*.

Bradford credits the experience and training he received in Eckdahl's lab for perfectly preparing him for his initial position as a research technician at Stowers. "I was able to tick off all the requirements listed in the job description the Institute posted," he says. And although Eckdahl had encouraged Bradford to pursue a graduate degree, he knew Bradford had found a perfect fit in the molecular biology core at Stowers.

In 2013, ten years after Bradford left his lab for a position at Stowers, Eckdahl nominated his former student for the MWSU Graduate of the Last Decade Award. Eckdahl specifically noted Bradford's participation in a project from the lab of Stowers Investigator Rong Li that involved developing a means to karyotype yeast by quantitative PCR, which resulted in a publication in *Nature*. Eckdahl says, "Dan is a focused and smart research scientist with an impressive co-authorship list. Not many scientists with a four-year degree can accomplish what he has accomplished."

Stowers Institute Library recognized for excellence

Sherry Lockwood and Rose Owens

The Stowers Institute Library, led by librarians Sherry Lockwood and Rose Owens, received the 2013 award for "Excellent Return on Investment in a Health Science Library" from the Health Sciences Library Network of Kansas City (HSLNKC). In addition to being recognized for the outstanding return on the budgetary investment made in its operation, the library was acknowledged for its professional excellence and unflagging dedication to providing superior resources to the Institute's scientists and researchers during the HSLNKC Annual Awards and Recognition Ceremony held at Stowers on January 22, 2014.

While Stowers Scientific Director Robb Krumlauf, PhD, notes the significance of the library's selection as an outstanding service provider, he is particularly proud of librarians Lockwood and Owens. "Good libraries have extensive collections, but great libraries always have great librarians who engage their users and help fulfill their aspirations, and the Stowers library is no exception," he says.

Both Lockwood and Owens derive great satisfaction assisting researchers with the process of scientific discovery, including performing reference and literature searches, obtaining interlibrary journal and book loans, maintaining scientific journal subscriptions, and managing internal scientific publication and data deposits in the Institute's online data repository.

Lockwood shares that it is especially gratifying that those outside Stowers are noticing their work. "This award means so much to us because it illustrates that we are recognized in the library community as well as by our researchers at Stowers."

AAA postdoctoral fellowship awarded to Caleb Bailey

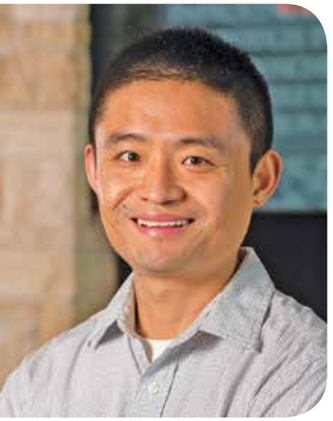
Caleb Bailey, PhD, a postdoctoral research associate in Paul Kulesa's lab, has been selected as an American Association of Anatomists Scholar. He will receive a $20,000 fellowship to explore new approaches at the forefront of melanoma metastasis and a travel allowance to present his findings at the association's annual meeting.

Melanoma, a very aggressive tumor that spreads readily, derives from a highly invasive embryonic cell population known as the neural crest.

The award will allow Bailey to build on his earlier findings that melanoma is intrinsically predisposed to aggressive, metastatic behavior resulting from its ancestral relationship to the neural crest. Specifically, he seeks to understand the cellular sensors that enable migrating melanoma cells to respond to the molecular waymarkers that guide neural crest cells along their migratory routes and to follow in their tracks.

Identifying the mechanisms associated with guidance receptor function may point to specific processes during metastasis that could be successfully interrupted with new therapeutics.

Meng Zhao collects scientific poster award at annual ISSCR meeting

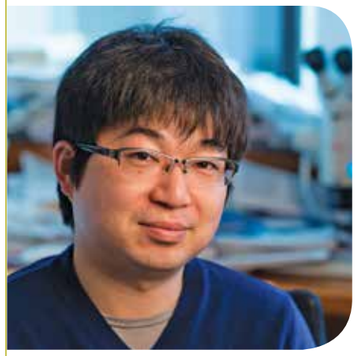


Postdoctoral fellow Meng Zhao's poster presentation was among a half dozen winners selected from nearly 1,000 eligible abstracts on display during last year's annual meeting of the International Society for Stem Cell Research in Boston. Zhao received a $250 stipend, one-year subscriptions to *Cell Stem Cell* and *Current Protocols in Stem Cell Research*, and a complimentary registration to next year's ISSCR's annual meeting in Vancouver.

Zhao's winning poster described an unexpected role for megakaryocytes—large precursor cells that give rise to blood platelets—in the maintenance and regeneration of hematopoietic, or blood-forming, stem cells. Megakaryocytes reside in the bone marrow in close proximity to hematopoietic stem cells where they help form a specialized microenvironment for hematopoietic stem cells. There, megakaryocytes provide molecular cues to keep quiescent mouse hematopoietic stem cells from proliferating when their services are not needed and to help jump-start their numbers in times of increased need, such as after chemotherapeutic treatment.

"This finding suggests that megakaryocytes might be used clinically for hematopoietic stem cell regeneration and to expand cultured hematopoietic stem cells for transplants," explains Zhao. The transplantation of human hematopoietic stem cells isolated from bone marrow is used in the treatment of anemia, immune deficiencies and other diseases, including cancer.

Postdoctoral researcher lands Japan Society for the Promotion of Science fellowship



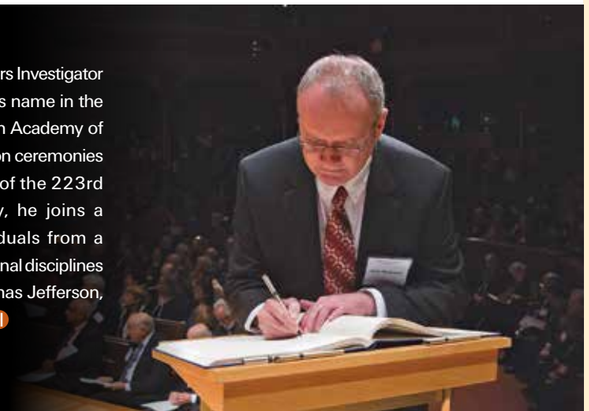
Yuichiro Nakajima, PhD, has been awarded a two-year, postdoctoral fellowship from the Japan Society for the Promotion of Science (JSPS) to study the cellular and molecular mechanisms that maintain the highly organized architecture of epithelial sheets, single layers of cells that line every body cavity from the gut to mammary glands. The fellowship is Japan's most prestigious academic award for PhD graduates. It provides the recipient with a generous stipend, as well as travel funds.

Using simple animal fruit flies, Nakajima, a postdoctoral researcher in Associate Investigator Matt Gibson's lab, investigates how epithelial cells maintain order while being jostled by cell division. As long as epithelial cells pack tightly and adhere to their neighbors, the cellular business of building tissue barriers and constructing ducts goes smoothly. But if epithelial cells fail to hold together, they die, or worse, produce jumbled masses resembling tumors known ollectively as carcinomas.

In a 2013 *Nature* study, Nakajima and his collaborators demonstrated that the way the mitotic spindle—the machinery that separates chromosomes into daughter cells during cell division—aligns relative to the cell layer surface is essential for the maintenance of epithelial integrity. The finding also hints at a surprising way that cells initiate a gene expression program seen in invasive cancers when that process goes awry.

WORKMAN INDUCTED INTO THE AMERICAN ACADEMY OF ARTS AND SCIENCES

In a time-honored tradition, Stowers Investigator Jerry L. Workman, PhD, signs his name in the registration book of the American Academy of Arts and Sciences during induction ceremonies on October 12, 2013. As part of the 223rd class of the honorary society, he joins a distinguished group of individuals from a variety of academic and professional disciplines including notables such as Thomas Jefferson, Charles Darwin, and T. S. Eliot.



Innovative research earns Gerton a research grant from national nonprofit

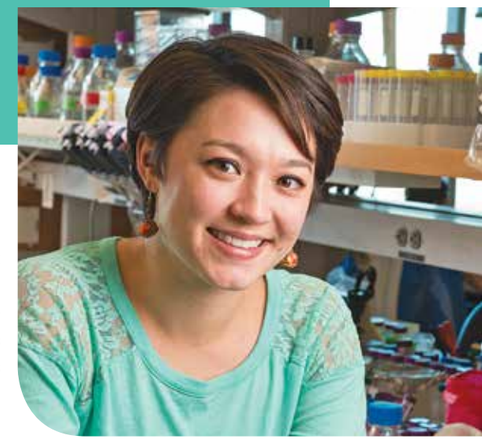
The Cornelia de Lange Syndrome (CdLS) Foundation has selected Stowers Investigator Jennifer Gerton, PhD, as the recipient of a CdLS research grant. Gerton will use the funding to study Cornelia de Lange syndrome in a zebrafish model of the disease and to determine whether some developmental defects can be ameliorated though treatment with the amino acid L-leucine.

Cornelia de Lange syndrome is a developmental disorder that affects males and females equally across all human populations. Although the symptoms can range from mild to very severe, most affected individuals have similar physical characteristics: stunted growth; small hands and feet; thin eyebrows that meet in the middle; long eyelashes; upturned nose; and thin, downturned lips. Common medical problems include gastroesophageal reflux, bowel malrotation, hearing loss and congenital heart defects.

Gerton and her team recently linked a dampened growth signal to Roberts syndrome (RBS), a related condition that responded well to treatment with L-leucine in RBS zebrafish. "Both RBS and CdLS are caused by mutations that affect cohesin, although the molecular basis of CdLS is less well understood," she says. "A logical next step was to determine whether our work on RBS has any relationship to CdLS."

Founded in 1981, the Cornelia de Lange Syndrome Foundation is a national family support organization that exists to ensure early and accurate diagnosis of CdLS, to promote research into the causes and manifestations of the syndrome, and to help people with a CdLS diagnosis and their families to make informed decisions throughout their lifetimes.

Naomi Tjaden wins Ruth L. Kirschstein National Research Service Award



Naomi Tjaden, an MD-PhD student enrolled in the MD-PhD program at the University of Kansas Medical Center, has been selected for a Ruth L. Kirschstein National Research Service Award. The National Institutes of Health-funded award supports the training of physician-scientists who can apply both their medical and research training to investigate problems of disease in humans.

The high-profile, competitive four-year fellowship will support Tjaden, who plans on pursuing pediatric gastroenterology and maintaining an active research program in the future, during the remaining research portion of her dual degree and the last two years of medical school.

Under the mentorship of Stowers Investigator Paul Trainor, PhD, Tjaden studies the role of vitamin A metabolism in the development of the embryonic gastrointestinal tract nervous system. Using mouse models deficient in enzymes necessary for converting vitamin A to retinoic acid, she will test the effects of retinoids on the proliferation, migration, and differentiation of a cell population called neural crest cells. These cells travel long distances to form structures in the heart and face, as well as the neurons of the peripheral nervous system, including those that innervate the gut.

Disruptions in neural crest cells have been linked to a variety of other birth defects, collectively known as neurocristopathies. A failure of neural crest cell development in the gut results in Hirschsprung's disease, a congenital absence of neurons in a portion of the gastrointestinal tract. This congenital disorder occurs in one out of five thousand live births, and typically requires surgical correction. *(This issue's cover story discusses neural crest cells in more detail.)*

Ruth L. Kirschstein NRSA grants honor the late doctor for her service to the National Institutes of Health and her pioneering research toward the development of improved, safer polio vaccines.

SCIENTIFIC MEETINGS: THOUGHT INCUBATORS

Invited speaker David Arnosti, PhD.

All scientific knowledge builds upon that which came before; therefore, sharing information is vital to advancing science. Scientific meetings gather researchers from all over the world to do just that—as well as create intellectual collisions that spark new ideas. In 2013, the Stowers Institute hosted two international scientific meetings.

In October, Julia Zeitlinger, PhD, and Ali Shilatifard, PhD, co-organized a three-day meeting focused on current biochemical and genetic findings on enhancer function and how perturbation of enhancer activity could result in disease pathogenesis including cancer. Enhancers are elements that regulate the precise expression patterns of genes throughout development. Recent genome-wide studies in the cataloging of somatic mutations in cancer have identified mutations in enhancer elements and in factors that can regulate enhancer-promoter communications.

Then, in November, Investigators Jennifer Gerton, PhD, and Paul Trainor, PhD, hosted visiting scientists for discussions of ribosome function and ribosomopathies to better understand the cause and outcome of ribosome defects, from basic biology to human disease. Ribosomopathies compose a collection of genetic disorders that cause impaired ribosome biogenesis and function. In the last ten years, it has become apparent that changes in the ribosome's translational control can contribute to developmental defects and cancer.

Paul Trainor, PhD, invited speakers David Sabatini, PhD, and Joost Zomerdijk, PhD, and Jennifer Gerton, PhD.

2003-2013: TEN-YEAR MEMBERS HONORED

In January, Vice President of Administration Abby Freeman and COO Brent Kreider recognized twenty-three members for ten years of dedicated service to the Institute.

Front row left to right: Selene Swanson, Abby Freeman, Amy Ubben, (seated) Nina Kolich, Rachel Nielsen, Cathy Lake, Mimi Krasovec, Joanne Chatfield, Shannon Scott, Debra Dukes, and Tamaki Suganuma.

Back row left to right: Mike Washburn, Tony Torrello, Laurence Florens, Susan Abmayr, Jerry Workman, Judy Zimmerman, Diana Bauman, Erica Frazier, Brent Kreider, Kym Delventhal, Carol Robinson, and Chris Seidel.

Not pictured: Jessica Teddy

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

Cancer. Alzheimer's disease. Diabetes. Cardiovascular disease. Birth defects.

Chances are, you or someone you know has been affected by at least one of these conditions, which are all too common in our society.

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

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

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

Any individual or cumulative contribution of $1,000 or more establishes a Hope Shares account, which can be opened in the donor's name or in memory or honor of someone they love. All Hope Shares account holders receive an annual Hope Shares statement and regular updates on the progress our researchers have made.

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

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

LIFETIME CONTRIBUTIONS

The information listed below represents contributions from, in memory of, or in honor of the following as of December 31, 2013.

$10 Million+

Pamela Stowers

$1 Million+

American Century Investments Foundation

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

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

Pamela Stowers in Memory of Laura S Stowers

$500,000+

Dunn Family Foundation

Barnett and Shirley Helzberg

Margaret Lichtenauer Estate

Frederick and Mary McCoy

$100,000+

American Century Investments Employees

Richard and Jeanette Brown

Cerner Corporation (in kind)

Country Club Bank

The Richard H. Driehaus Charitable Lead Trust

Frederick and Louis Hartwig Family Fund

Felix and Helen Juda Foundation

Tom and Nancy Juda Foundation

James Kemper Jr.

David and Wendy Welte

Hank Young (*Gameface* book proceeds)

$50,000+

Fowler Family Fund II

William and Priscilla Neaves, *including*
In Memory of Betty Mae Patterson
In Memory of Pam Stowers
In Memory of Arveta Washington

Polsinelli Shughart PC

Marilyn N. Prewitt Trust *including in Memory of Marilyn Prewitt*

Jim and Michele Stowers

Roderick and Linda Sturgeon, *including In Memory of Steve Sturgeon*

Jonathan and Cyndi Thomas

JAY AND CATHRYN LINNEY

GIFTING THE FUTURE

The decision to support a particular cause is usually driven by either a personal experience or a professional interest. For Cathryn and Jay Linney, it is both.

The couple's initial donation to the Institute in 2003 was a gift from Jay to Cathryn in memory of her father William Cordes, who passed away after a valiant fight with an advanced stage of multiple myeloma. Cathryn explains that her father was a warrior in his battle, never letting cancer define him. In fact, he traveled and worked up until days before he passed away. "He set such a fine example of someone living life to the fullest," she says. "I try to set that same example every day for my own three children."

With the next generation in mind, the Linneys continue to give to the Institute. Cathryn explains, "For us, contributing to an organization that grows basic scientific knowledge and has a lasting impact on how we prevent and treat disease is very gratifying."

Both Cathryn's and Jay's professional backgrounds provide them with a profound appreciation for the kind of fundamental questions pursued by Stowers researchers. During her stint as a Howard Hughes Medical Institute summer fellow at Washington University in St. Louis, Cathryn worked on research projects that were part of the Human Genome Project. And as a senior vice president at Cerner Corporation, Jay fully appreciates the practical and clinical applications of the knowledge gleaned from basic research.

The Linneys hope for exciting discoveries that lead to targeted treatments for cancer as well as chronic diseases. Meanwhile, they find great joy in the discoveries that Stowers scientists have made to date as well as immense satisfaction in knowing they are helping to fund world-class research.

$25,000+

Enrique Chang and Catherine Farley

David Chao and Julia Zeitlinger

Mildred E. Coats Trust

JE Dunn Construction Company (in kind)

Irving Kuraner

Labconco Corporation

Bill and Peggy Lyons

Menorah Medical Center Inc. (in kind)

Mistler Family Foundation

Jim Potter and Kathleen Stowers-Potter, *including*
In Memory of Julie Carlson
In Memory of Gunnar Hughes
In Memory of Mauri Olsen

Rubin Postaer and Associates

In Memory of Robert Ruisch Jr.

John and Shirley Wagner

Bruce and Laurie Wimberly in Memory of Virginia Wimberly

$10,000+

Patrick and Dawn Bannigan

Cisco Systems Inc. (in kind)

Michael and Jenny Cormack

Charles W. and Nona J. Fowler Family Fund

Gilmore and Bell PC

Webb Gilmore

Richard and Andrea Hall

Ruth C. Hill Trust

Allan and Margot Huber

IBM (in kind)

Brian Jeter

In Memory of Carlo Jonathan

Jack and Rena Jonathan

David and Susan Keefer

Mark and Ann Killen Charitable Fund

In Memory of Helen Kirby

Bo Kreiling in memory of Helen Jayne Kreiling

In Memory of Helen Lebens

Barbara Marshall

Mark and Martha Miller

Amy Noelker

Tom and Jeanne Olofson

The J. B. Reynolds Foundation

Landon Rowland, Kansas City Impact Fund

Sanders Morris Harris

Gino and Paetra Serra

In Memory of Richard Smith, Wendell Smith, and Laura Stowers

Rick and Betsey Solberg

Jim and Virginia Stowers in Memory of Felix Juda

David and Jeannine Strandjord

Byron Thompson

In Memory of Vernon Voorhees II

Michael and Louise Zolezzi

$5,000+

Janice Beatty

Clay Blair Family Foundation

Mary Breed Brink

Cancer Golf Association

Frederick and Carolyn Coulson in Memory of Frederick Jr. and Mary Coulson

Phillip Davidson

David and Nancy Dilley

Barry and Deborah Fink

Stephen and Patricia Gound

James E Griffin III and Margo Denke in Memory of James E Griffin Jr.

Irv and Ellen Hockaday

Thomas Kmak Family

Dawn Lind

Linney Family Foundation, *including Jay and Cathryn Linney in Memory of William Cordes*

Lucent Technologies (in kind)

John and Susan McMeel in Memory of John O'Day

Catherine Netherland

Robert and Jan Peterson

Don and George-Ann Pratt

David and Eden Thorne in Memory of Mark Dover and Elwood Thomas

John Whitten

Austin and Laura Wilson

$1,000+

Herbert and Estelle Adler

Alexander Family Foundation

Don and Christine Alexander

Rob Aneweer in Memory of Dave and Jim Aneweer

Elmer and Verna Armbruster

Malcolm and Kathy Aslin

Donald and Margaret Austin

In Memory of Alex Bartlett

Paul Jr. and Joan Bartlett

Jonathan Bauman

Janice Beatty

Joan and Bert Berkley

Gregory Broome

In Memory of Carol Ann Brown

Mary Jo Browne

In Memory of Evelyn "Lovey" Byrer

Michael and Gretchen Carter

Shirley Christian

In Memory of Alice "Penny" Cohn

Gilbert and Lois Cole

Ron and Joan Conaway

Lauren and Ryan Contillo and Kathleen Stowers-Potter in Memory of Lawrence Joseph Contillo

Lauren and Ryan Contillo, Alex Potter, Jim Potter and Kathleen Stowers-Potter in Memory of James William Cordes

Jody Craven

Alan Critchell

Marshall and Jill Dean

In Memory of Carol Denicole

Parris Dobbs Spirit of the Heart Fund

Terrence and Peggy Dunn

William Dunn Sr. in Honor of Jim and Virginia Stowers

In Memory of Dana Eckles

In Memory of William Edwards

Ron and June Estabrook

Joseph Fairfax

Jill Farrell

Banning Flynn

David Ford, *including In Memory of Theresa Ford*

Jody Anne Frederickson

Abby Freeman

Stephen Garcia

The William George Family Charitable Trust

Mark and Rhonda Gilstrap

Marsha and Jules Goldman

Samuel Goller

Samuel Goller and Melody Goller

Michael Green, *including In Memory of Mary Lee Prico*

Laura Greenbaum

Mary Louise Greene
In Memory of Bud Greenwald
Jeanne Greenwald
Edward Jr. and Jody Griffin
Benard Hamblin
Brett Hart, *including*
In Memory of Delmar and Alberta Brumley In Memory of Theresa Ford
Andrea Lynn Hazle
Henson Trust Fund
Betty Henson in Memory of Paul Henson
John and Connie Hoye
In Memory of Estelline Huey
Husch Blackwell LLP
Barbara Irick
Robert and Lynette Jackson
Harrison Jedel
Jeffries LLC
Jeff Johnson
Leroy Larsh Johnson
Wes and Nancy Kabance
Sandra Kasahara
Otto and Margarete Katke Charitable Foundation
Kelly Kerr
In Memory of Gary Kostuke
Bob and Myrna Krohn
Kuhn and Wittenborn Advertising
Linheng Li
In Memory of Jane Lundgaard
Linsley and Jane Lundgaard
Patricia Mansker
Scott Marolf
John and Marilyn McConnell in Memory of Priscilla Wood Neaves to the "Priscilla Wood Neaves Endowed Chair in Biomedical Sciences"
Susan McCune
Mary Kay McPhee
In Memory of Hazel Meany
Kirk and Frances Meany
Robert and Shirley Meneilly
Merriman Foundation in Memory of Pam Stowers
Brendan Murray
Kathie Nelkin in Memory of Edward Lane
Kathleen Nelson
Jeannette Nichols
Jennifer Noland
Stephen Novak
Frank Leo O'Gara
James and Josephine Olson
Robert Pearson
Michael and Terese Raddie
Michael J. Rainen Family Foundation
Isabelle Berry Reed Revocable Living Trust
Katherine Richardson
Craig and Maryanne Roepke
Felix and Carmen Sabates
Alejandro Sánchez Alvarado
Gale Sayers
Michael and Dana Schaadt
Norma Schank
Larry and Janine Schmidt
Jack Searcy in Memory of Barbara Searcy
Daniel Shiffman
Sierra Aviation in Honor of Jim and Virginia Stowers
In Memory of Eleanor Smith
Darrell and Marjorie Spaedy
In Memory of Paul Stoffel and Aimee Stoffel
Robert and Kathleen Stout
Jim and Virginia Stowers In Memory of Arthur Brand
Jim and Virginia Stowers in Memory of Walter Day
Jim and Virginia Stowers In Memory of Paul Henson
Mark A. Susz Revocable Trust
Ten Ten Foundation
Stephen Thune, *including*
In Memory of Theresa Ford
Harold and Ruthie Tivol
Robert and Roselle Tomsovic
Charles and Carol Diane Tritschler
David Tucker
John and Ollie Urie
Howard and Frances Vaughan Charitable Foundation
Dennis and Sally Von Waaden
In Memory of Arthur Weitzmann
William and Teresa Wong
Jon Zindel

Every attempt has been made to ensure the accuracy of the lists of contributors. In case of error or omission, the Stowers Institute wishes to be advised.
For more information on how to establish a Hope Shares account, please visit www.stowers.org/support or call (816) 926-4065.

A LEGACY of HELPING OTHERS

FREDERICK AND MARY McCOY

As a distinguished physician and professor of surgery, Frederick J. McCoy and his wife Mary, a skilled surgical nurse, devoted their lives to helping others. But the couple wanted to continue making an impact on people's lives beyond their own lifetimes.

Their professional careers had left the McCoys with a great appreciation for the role of basic research in understanding the cause of cancer and other cruel diseases they encountered in their clinical practices. When the McCoys formulated their estate plan, they decided to leave an especially meaningful legacy to an organization that embodies their belief that new life-saving treatments have their origins in the lab.

In 2000, Frederick and Mary McCoy dedicated $500,000 of their estate to the Stowers Institute. In a letter to his friend Jim Stowers Jr., McCoy wrote that their gift "confirms our personal dedication to the vision and integrity of our longtime friends Jim and Virginia Stowers whose vision and generosity have created a significant and far-reaching impetus to medicine in Kansas City, and indeed the world."

The Institute accepted Dr. and Mrs. McCoy's gift with the passing of Dr. McCoy in 2006 and Mrs. McCoy in late 2012. Their forward-looking planning will allow Stowers researchers to continue to seek understanding for some of life's basic mechanisms and to translate that into effective clinical diagnostics and disease treatments.

2013 CONTRIBUTIONS

In 2013, contributions were received from, in memory of, or in honor of the following:

$100,000+

American Century Investments Foundation
Helen Nelson Medical Research Fund for the "Helen Nelson Distinguished Chair"
Frederick and Mary McCoy

$25,000+

Enrique Chang and Catherine Farley
Fowler Family Fund II

$10,000+

Richard and Jeanette Brown
David Chao and Julia Zeitlinger
Charles W. and Nona J. Fowler Family Fund
Mark and Ann Killen Charitable Fund
Roderick and Linda Sturgeon
David and Wendy Welte

$5,000+

Patrick and Dawn Bannigan
Gilmore and Bell PC
Mistler Family Foundation
Gino and Paetra Serra
Jonathan and Cyndi Thomas

$1,000+

In Memory of Alex Bartlett
John and Corrine Beakley
Michael and Sandra Becker
Jean Carnahan
Lori Levine and Jim Clardy
Commercial Bank of West Port
Kirby and Melanie Crane
Coleman and Rose Faherty
Dale and Caroline Hermeling
Steven and Judy Howard
Husch Blackwell LLP
Jefferson Bank of Missouri
Paul and Sarah Maguffee
John Pletz
Harvey and Ann Tettlebaum
James and Barbara Vossen
R Lawrence and C Joan Ward
Leslye Winslow
Kenneth and Alice Wolters
Barbara Wood
Jonathan Bauman
Janice Beatty
Ron and Joan Conaway
Phillip Davidson
William Dunn Sr. in Honor of Jim and Virginia Stowers
Stephen and Patricia Gound
Richard and Andrea Hall
Brett Hart in Memory of Delmar and Alberta Brumley
Allan and Margot Huber
Bo Kreiling in Memory of Helen J Kreiling
Wes and Nancy Kabance
David and Susan Keefer
Robb Krumlauf and Leanne Wiedemann In Memory of Arveta Washington
Labconco Corporation
Linney Family Foundation
Barbara Marshall
John and Marilyn McConnell in Honor of Priscilla Wood Neaves to the "Priscilla Wood Neaves Endowed Chair in Biomedical Sciences"
William and Priscilla Neaves in Memory of Betty Mae Patterson
William and Priscilla Neaves in Memory of Pamela Stowers
William and Priscilla Neaves in Memory of Arveta Washington
Kathie Nelkin in Memory of Edward J Lane
Amy Noelker
Jennifer Noland
James and Josephine Olson
Robert and Jan Peterson
Jim Potter and Kathleen Stowers-Potter in Memory of Julie Carlson
Jim Potter and Kathleen Stowers-Potter in Memory of Mauri Olsen
Don and George-Ann Pratt
Michael and Terese Raddie
David and Eden Thorne in Memory of Honorable Elwood Thomas
Jean Weitzmann in Memory of Arthur Weitzmann
John Whitten
William and Teresa Wong

Up to $999

George Ballew
Peter Baumann
Judith Beard
Cloverdyke Family in Memory of Bud Greenwald
Fred and Carolyn Coulson
Alan Critchell
Nadine Dean in Memory of Shirley Dean Modrcin
Hans Drigalla
Mary Lea Easton
Abby Freeman in Memory of Thomas Chesher
Cynthia Gassman
Owen Geisz
Teresa George
Michael Green
Jeanne Greenwald in Memory of Bud Greenwald
James E Griffin III & Margo Denke in Memory of James E Griffin Jr
Tracey and Stacey Hoffman
John and Connie Hoye
Barbara Irick
JP Morgan Chase Foundation
Kelly Kerr
Paul Kulesa
Linheng Li
Bill and Peggy Lyons
Patricia Mansker
Scott Marolf
Susan McCune
John and Susan McMeel in Memory of John O'Day
Kirk and Frances Meany
Jana Meyers
William and Priscilla Neaves
Terri Norris
Frank Leo O'Gara
Tanya Ratliff
Alejandro Sánchez Alvarado
Daniel Shiffman
William Shilling
Alexander Stark
Mike and Lisa Suess
Dan Summerford
Mark and Heather Terranova in Memory of Janice Haefele
Stephen Thune
Robert and Merrill Walz
Carl Westring
Lorna Wright
Ting Xie
YourCause LLC

BACKSTAGE PASS

From the moment scientists trained the first light microscopes on biological tissues, no laboratory has been complete without them. The development of electron microscopes with their highly increased resolving power—up to two million times the magnification of a standard light microscope—opened new windows into cells' architecture enabling scientists to view objects in greater magnification than ever before.

Instead of light, electron microscopes use a focused beam of high voltage electrons to generate extraordinarily detailed and striking images. In addition to being highly trained microscopists, members of the Stowers electron microscopy core provide skilled assistance in preparing specimens for analysis including chemical fixation, staining, dehydration, sectioning, freezing and coating.

ELECTRON MICROSCOPY BY THE NUMBERS

500,000x
magnification factor compared to the human eye

100,000x
factor by which visible light's wavelength exceeds that of electrons

1,000x
magnification factor compared to a compound light microscope

600
images visualized per month

100
number of sections a typical cell nucleus will render for visualization

40-70
width of a transmission electron microscopy section in nanometers

0.2-0.5
size in nanometers of objects that an electron microscope can visualize