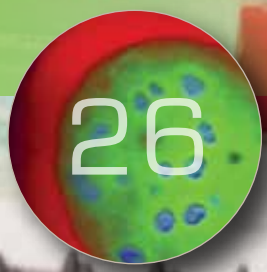
STOWERS REPORT

NEWS AND INSIGHT FROM THE STOWERS INSTITUTE FOR MEDICAL RESEARCH

SUMMER 2018



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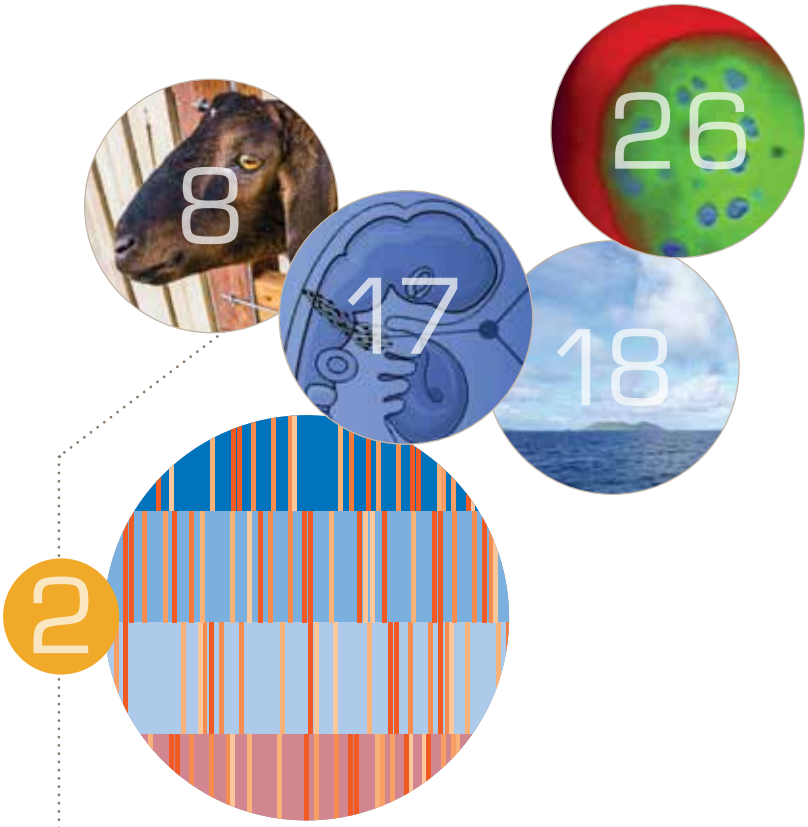

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In perspective

BY DAVID CHAO, PHD
PRESIDENT AND CEO

The Institute's mission to understand the secrets of life is timeless, but the approaches that Institute scientists use to pursue this mission are changing at a dizzying and ever-increasing pace.

Advances in areas such as automation, computing power, and communications have transformed the tools and methods scientists use to perform biological research. In this issue of the *Stowers Report*, our feature stories focus on how Stowers scientists are incorporating some of the latest approaches and technologies in their research efforts as well as creating new resources for Stowers labs and the larger scientific community.

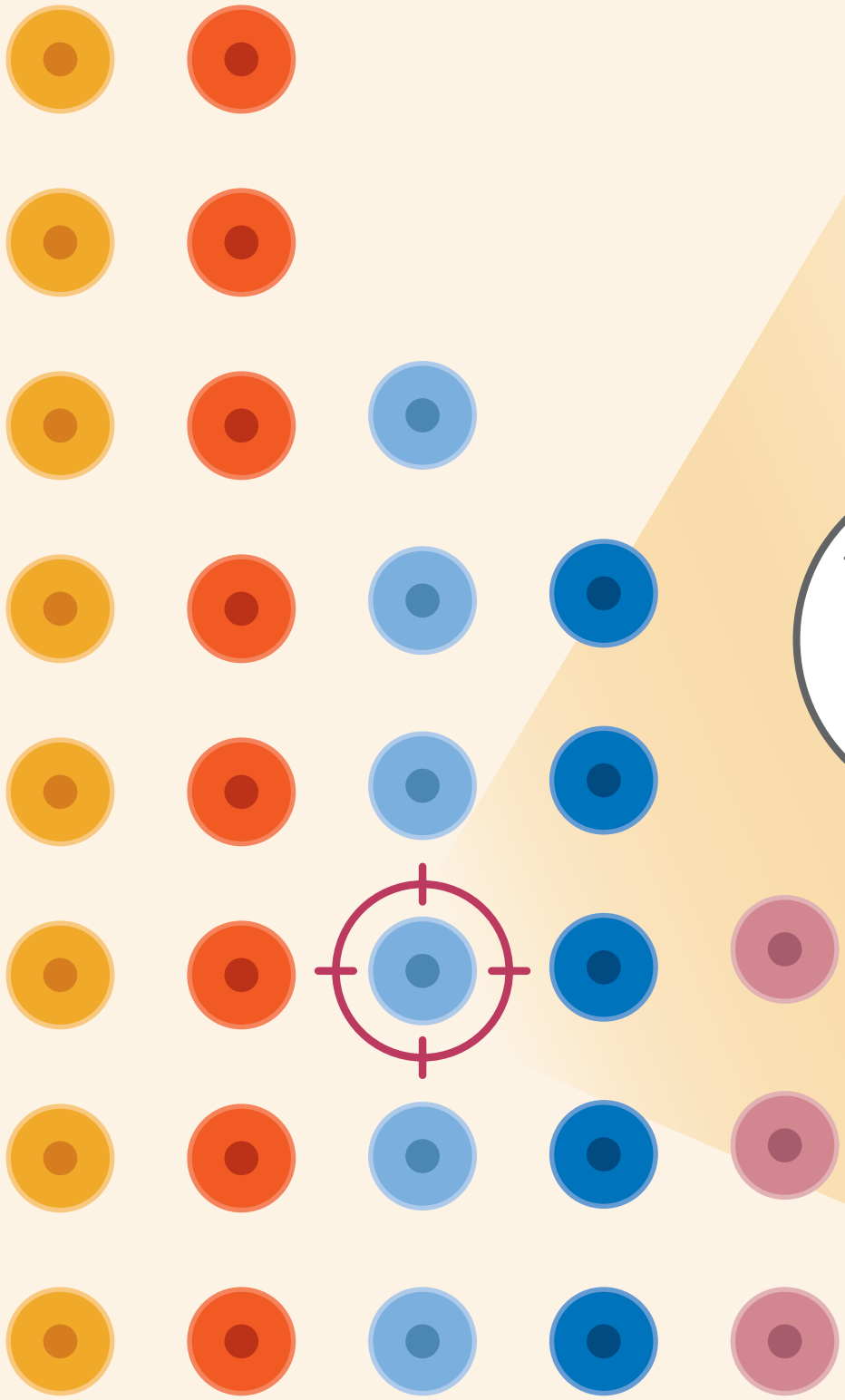
One leap forward that many Stowers labs have embraced is in the area of single-cell analysis, which allows scientists to take a deep dive into individual cells and examine what's going on with genes, proteins, and other molecules inside each one. By uncovering the molecular similarities and differences of cells, researchers not only learn more about the diversity of cells but also gain important clues about their distinctive roles and functions.

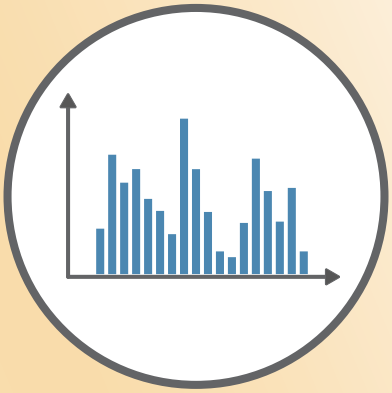
This issue's cover story describes how single-cell analysis is an important approach for Stowers researchers studying a wide range of topics—from understanding how certain cells lead others to migrate long distances to identifying specific genes involved in regeneration. With the latest techniques for analyzing single cells, researchers can examine a larger number of cells with unprecedented depth and speed.

It is perhaps not surprising that a common outcome of using more powerful research technologies is the generation of larger amounts of data. Another article in this issue describes the Institute's infrastructure for storing and sharing a rapidly growing amount of scientific data. One of these resources is a genomic data platform called "SIMRbase"—a portmanteau of the Institute's abbreviated name and "database." The customized database provides an online home for DNA sequencing data and other genomic information for emerging research organisms. SIMRbase also offers collaborative tools for ongoing updating and analysis of the data as research progresses in Stowers labs and elsewhere.

In other news, we mark the retirement of our colleague and friend Bill Neaves, who served as the Institute's CEO from 2000 to 2010 and president emeritus since then. Bill has also served as president of the Graduate School of the Stowers Institute since 2016. We thank Bill for his unwavering commitment to Jim and Virginia Stowers' vision for the Institute and for making expectations for collegiality and excellence such an integral part of the Institute's culture.

As we say goodbye to Bill, we welcome Betty Drees as the new president of the Graduate School. Betty is a physician, professor, and dean emerita at the University of Missouri-Kansas City (UMKC) School of Medicine. She brings more than 25 years of experience in research, clinical medicine, education, and administration to her new role here. We look forward to the continued success of the Graduate School under Betty's leadership.



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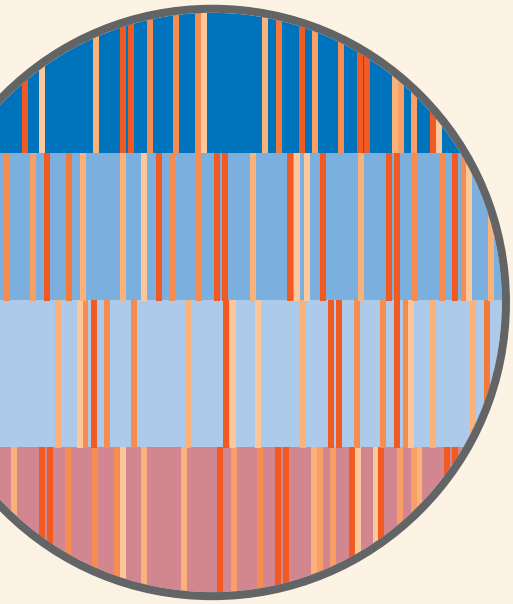
By Marla Vacek Broadfoot



ABOVE AVERAGE

Single-cell analysis takes research to the next level

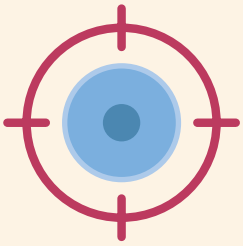
The average American adult has an IQ of 98, earns an annual income of $46,550, checks their phone 80 times a day, watches television 35 hours a week, eats 193 pounds of meat a year, and lives until the age of 78.

These statistics might give a snapshot of life in the United States, but in reality no one is average, at least not by all parameters. Reports that lump all 323 million Americans together and look at their average aptitudes, behaviors, and life trajectories inevitably obscure what makes each person unique. They lose sight of the many geniuses, billionaires, bibliophiles, technophobes, vegetarians, and octogenarians who call the United States home. Looking more closely at how individuals differ from statistical averages, as well as how they differ from other individuals, could reveal particular attributes that influence their diverse activities and roles in society.

It's amazing to think how far we have come. The single-cell field has grown so fast. Now, we can study the gene expression of thousands of individual cells, in just a few days, for a fraction of the cost.

– Anoja Perera

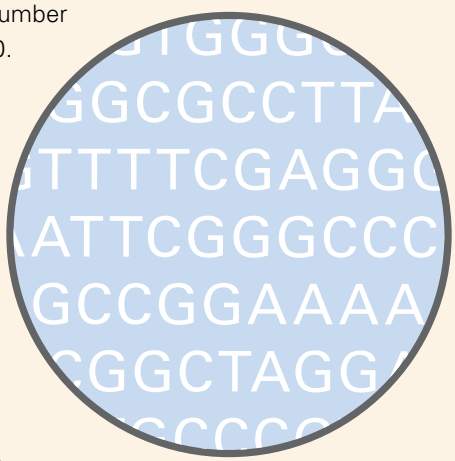
The same can be said for research on the inner workings of the human body. For decades, researchers have used traditional biology tools to study entire populations of cells—stem cells, hair cells, and cancer cells, just to name a few. These efforts have generated important insights into the mechanisms that underlie health and disease, but they are still predicated on the average life of the average cell. Many scientists at the Stowers Institute and other research institutions now believe if they want to know what makes each cell tick—and to pinpoint those with the extraordinary ability to fuel the spread of cancer or repair damaged tissues—they need to do it at the single-cell level.



"Looking at the single-cell level gives you a lot more power to understand in detail how processes occur in individual cells—which tells you something totally different, and I think much more valuable, than looking at an aggregated pooled sample," says Andrew Box, senior laboratory manager of the Stowers Cytometry Facility.

Scientists have long suspected that not all cells were created equal, but until recently they lacked the tools to fully explore the role single cells play in biological phenomena like cancer and regeneration. "The field of single-cell analysis has been propelled in recent years by technological advances in laser capture microscopy and microfluidics that enable researchers to isolate and analyze single cells from tissue sections or bulk cell populations, respectively," says Paul Kulesa, PhD, director of the Stowers Imaging Center and one of the first adopters of single-cell analysis at the Institute.

About five years ago, advances in -omics technology—designed to detect genes (genomics), transcripts (transcriptomics), proteins (proteomics), and metabolites (metabolomics)—made it possible for researchers to gain a glimpse into the complicated internal dialogue taking place in a single cell. They were surprised to find that cells that appeared to be of the same "type" were even more heterogeneous than they once thought. Previous estimates put the number of cell types in the human body at 200. Scientists now think we could house an order of magnitude more.

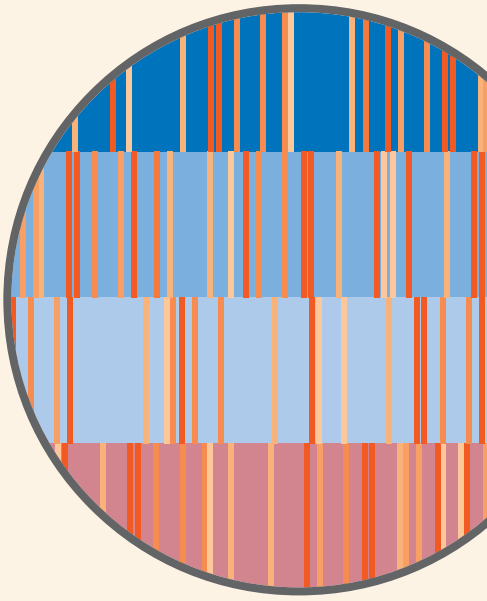


The introduction of automation, advances in chemical reagents, and miniaturization of reactions have made single-cell analysis techniques more mainstream, and as a result the pace of discovery has accelerated, says Anoja Perera, senior laboratory manager of the Molecular Biology Facility at Stowers. "It's amazing to think how far we have come," Perera says. "The single-cell field has grown so fast. Now, we can study the gene expression of thousands of individual cells, in just a few days, for a fraction of the cost."

HOW IT WORKS

So how do Stowers scientists study cells at the single-cell level? Their exact methods vary depending on what cell or model organism they are studying, and what question they are trying to answer. However, most scientists follow the same basic recipe, involving three to four steps. First, the scientists break up the collections of cells that make up their biological sample—perhaps a piece of tissue from a zebrafish or a colorectal tumor from a mouse—into single cells. This step sounds relatively simple, but it is often the most onerous. As soon as the cells are removed from an organism, their behavior starts to change. Their gene expression patterns shift as they go into a kind of cellular shock and begin to die off. At Stowers, specialists in the cytometry and molecular biology groups work with researchers to help them hone their methods of preparing samples—which could involve separating cells with chemicals or by mechanical means—to save as many cells as possible.

Jason Morrison, a research specialist in the Kulesa Lab, has been using single-cell analysis in chick embryos to look for a unique molecular signature shared by the most invasive neural crest cells that travel long distances from the brainstem to build tissues elsewhere in the body. Together with functional testing to confirm their results, this information would shed light on the genes critical to embryonic cell invasion and allow comparison to other molecular signatures being identified in metastatic cancer, wound healing, and the immune response. He says he has several collaborators at other institutions who covet his setup. "We want to capture the science before the cells realize they are no longer where they are supposed to be," Morrison says. "At Stowers, this is made seamless through the close coordination of people and different core facilities all in the same building."

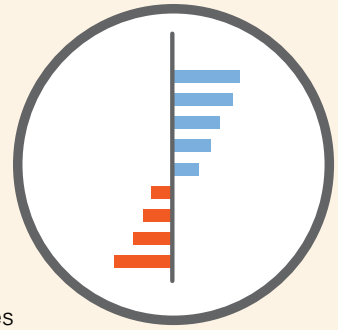


After dissociating their tissues into single cells, researchers might take their samples to the Cytometry Facility if they need to further sort out specific cells they want to study. If they were studying the regeneration of zebrafish sensory organs, for instance, they might use a marker — an antibody or a dye—to label a certain type of stem cell. Then a flow cytometer could detect the marker on those cells, collect them in a tube, and discard the rest. Box says their newest cell analyzer can look for 24 different colors, meaning they could, in theory, stain for different proteins on the surface of cells, different levels of DNA or RNA inside the cells, and different subcellular compartments like mitochondria or endoplasmic reticulum, all at the same time. He and Stowers Investigator Linheng Li, PhD, have discussed using this 20-plus color approach to isolate the many different cell types present in intestinal and colon tumors in his mouse models of cancer.

Once the scientists have isolated and separated their cells, they measure the expression of whatever interests them — perhaps RNA transcripts or protein — in each. This is where the advances in technology really shine. In January 2017, the Institute acquired a cutting-edge instrument called the 10x Chromium, a shoebox-sized machine that can partition cells into individual droplets, alongside all the reagents needed to conduct single-cell transcriptomics. Each individual cell is tagged with its own molecular barcode, and each of the tens of thousands of RNA transcripts receive a

unique barcode as well. After all the transcripts are sequenced, scientists can use these barcodes to figure out which genes are active in each cell. For example, Stowers Investigator Ting Xie, PhD, has used the technique to investigate how the niche that serves as a home base for stem cells orchestrates their differentiation into different cell types in ovarian tissues of the fruit fly. "The single-cell sequencing technology offers a unique opportunity for addressing this important question, which was almost impossible in the past," Xie says.

Finally, having gathered all the data, researchers set about analyzing their results. Whereas steps one through three could take days, this step could take months, even years. "The amount of data that comes out of each of these experiments is enormous—looking at the levels of thousands of different RNA or protein molecules in individual cells, a thousand cells at a time, and comparing changes in expression as the embryo grows," says Kulesa, who has used single-cell analysis to record the ups and downs of gene expression in single neural crest cells during different stages of migration. "The bioinformaticians have to develop new ways of coordinating, interrogating, and helping to interpret all of that information."



Stowers Investigator Tatjana Piotrowski, PhD, agrees the data analysis involved in single-cell studies can be cumbersome and requires a certain level of expertise. Her lab has been using single-cell analysis to look for genes that are turned on during the regeneration of hair cells in zebrafish, in the hopes of identifying molecular targets to treat the inner ear defects that cause hearing loss in humans. She has found that the data generated is often fraught with noise. "You need a bioinformatician to parse through the data," she says. "I couldn't do anything with it on my own." That's why Piotrowski decided about a year ago to add a bioinformatician, Daniel Diaz, to her team.

Bioinformaticians like Diaz collaborate with fellow lab members to develop testable models from these complex datasets. It is an iterative process, which eventually takes the researchers back to where they began—the bench. "The biology is the endpoint, and most importantly, it's the part you always need to keep in mind during an analysis," Diaz says. "So, in order to know whether or not a particular model is optimal, you as an analyst either have to have a tight collaboration with the research lab, or if you work in a lab, have a firm grasp of the system you are studying."

MORE CELLS, MORE PARAMETERS

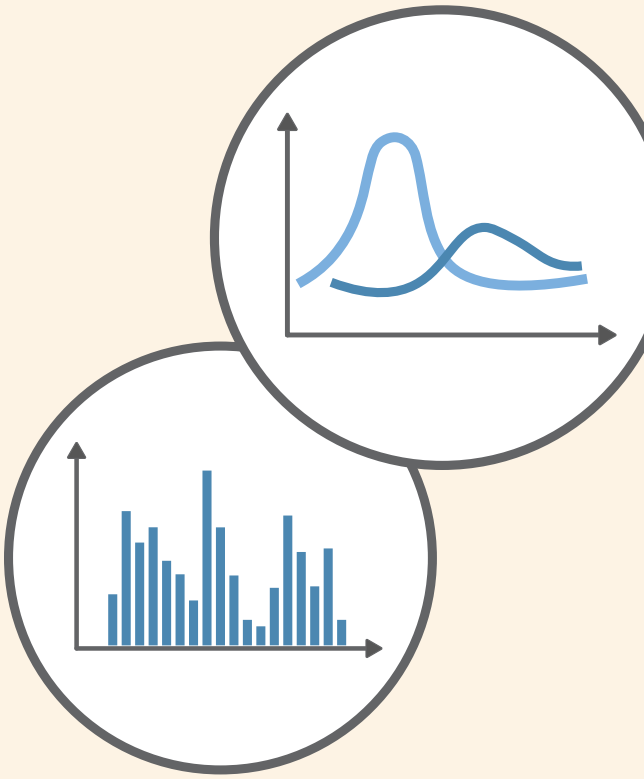
With a new model in hand, Piotrowski and other Stowers scientists can begin to manipulate genes in single cells to test whether the patterns uncovered by their sophisticated data analyses hold true in real life. In the end, each single-cell experiment drives the next experiment, and the next. "The process took over a year, where we sat down around a table with members of the cytometry, molecular biology, and bioinformatics teams, and tried to figure out how to do this project," Piotrowski says. "We had meetings after we did experiments to discuss results and what could be improved. I could not have done these experiments at any other place, because the scientific support groups here were so fantastic in working together and pulling us in the same direction."

The collaborative environment at the Institute means no one researcher needs to be an expert on everything, an asset in a rapidly evolving field like single-cell analysis. As little as five years ago, scientists would design an entire experiment around a handful of single cells. Today, the 10x Chromium can analyze 80,000 at a time. Some scientists are eager to design experiments that analyze even more cells—hundreds of thousands, even millions—to generate even cleaner, less noisy data. Looking at more cells not only gives their experiments more statistical power, but it also increases the chances that scientists will capture cells in as many states as possible, so they don't miss important biological states that could drive health and disease.

Stowers researchers are also adopting novel technologies that will enable them to glean more information from each and every cell passing through their hands. Jennifer Kasemeier, PhD, a senior research specialist in the Kulesa Lab, has been working with a powerful new instrument called Milo that can measure the expression of multiple proteins in each of thousands of single cells in a single run. She sees the future of single-cell research as one in which scientists can look at RNA transcripts, proteins, and a number of other markers simultaneously, to generate a more comprehensive picture of cellular activity so they can spot the handful of cells predicted to become metastatic.

"In cancer cell invasion, the whole tumor is not moving to a new site in the body—it is being led by a single cell, or a few cells. We want to figure out what differentiates those cells from the others," Kasemeier says. She recently demonstrated that a signal called nerve growth factor, or NGF, could reprogram metastatic melanoma cells into a more benign cell type. "If we could identify and target bad cells before they invade other tissues, it could have tremendous power therapeutically."

Ultimately, the goal of all single-cell analyses—whether they are on colon tumors in mice, stem cells in fruit flies, regeneration in zebrafish, or cancer metastasis in chicks—is to see what couldn't be seen before. To look beyond the average behavior of an average cell to gain a greater understanding of what makes each cell unique, recognizing that with every new insight comes an opportunity to dig deeper, ask bigger questions, and fundamentally change our view of the world.



Tools *of the* Trade

By Anissa Anderson Orr

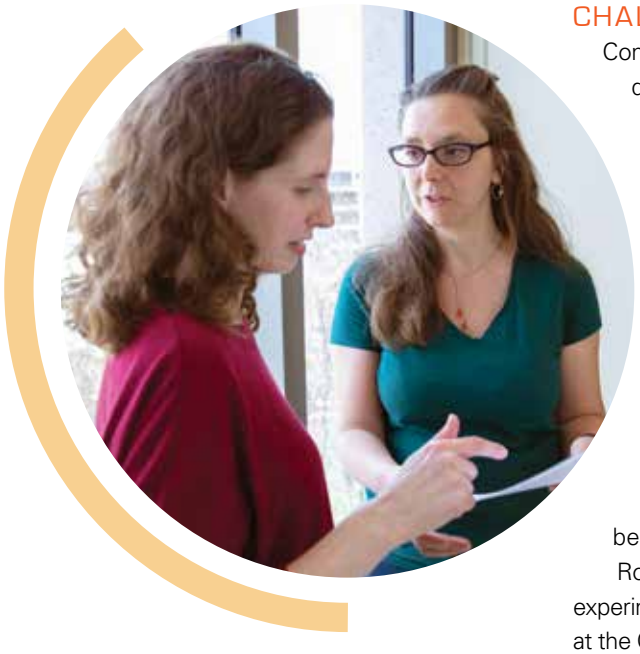
New approaches help analyze emerging model organisms

On a typical morning, Sofia Robb, PhD, and her three-year-old son Cedar tend to the sheep, goats, alpacas, and chickens behind her two-and-a-half-acre home in the stunning Utah mountains. When morning chores are finished, she drops Cedar off at preschool, then heads back to her home office, where she works remotely as a genomics scientist for the Stowers Institute.

After a cup of tea, Robb fires up her computer and launches SIMRbase, a website she constructed for the Institute to host genome sequences and related data, as well as computing tools to study them.

Up pop images of the menagerie whose genomic data she collects and cares for online—apple snail, mouse, planarian flatworm, cavefish, zebrafish, sea anemone, sea lamprey, and killifish.

They're not quite as cute and cuddly as the animals in her backyard petting zoo, but these emerging model organisms are vitally important to her colleagues more than 1,000 miles away in Kansas City, Missouri. Stowers scientists study a wide variety of organisms, rich in biological diversity, to explore questions that expand our understanding of life's biological processes and behavior. Robb gives their photos a glance and gets to work.



CHALLENGING TO STUDY

Compared to model organisms that have been part of scientific research for decades, emerging model organisms can be challenging to study. There are online repositories for the human genome (Ensembl), plant genomes (JGI Phytozome), and common model organisms like the fruit fly *Drosophila* melanogaster (FlyBase) and the roundworm *Caenorhabditis elegans* (WormBase), but few for the cavefish or apple snail, for example.

And while advances in DNA sequencing technology have made it easier than ever to sequence genes and genomes, making sense of the resulting data isn't simple.

"Right now, it's fairly common to say, 'Let's sequence an organism.' But If you don't have a bioinformaticist in your lab to help you organize and evaluate all of the data you generate, then what the heck do you do with it?" Robb says.

Fortunately, she has some ideas. Robb draws on her experience as a bench scientist to find solutions for Stowers scientists.

Robb began integrating computer scripting and databases with her lab experiments as a technician in the laboratory of Alejandro Sánchez Alvarado, PhD, at the Carnegie Institution for Science in Baltimore, Maryland. She stayed with the Sánchez Alvarado Lab after its move to the University of Utah for her doctoral work, where she studied histone modifying enzymes and their role in stem cell biology and regeneration in planaria. In the course of her thesis research, she constructed genomic tools for planaria. As a postdoctoral associate at the University of California, Riverside, she further honed her bioinformatics skills while working with the genome of rice. Now, she works on several genomics initiatives for the Stowers Institute, including SIMRbase, and customizes tools for Stowers scientists, including Sánchez Alvarado, who moved his lab to the Stowers Institute in 2011.

A HOME FOR GENOMES

Launched in 2015, SIMRbase is built on open source code and provides a common framework of genomics tools that can be tailored to specific organisms. Researchers can upload sequenced genes to the site, curate genes, and browse other genes to make comparisons. It uses a customizable plug-and-play approach to accommodate emerging research models, and to encourage collaboration and data sharing between scientists.

"The guiding idea was to help labs with their genomics research by saving them time and effort, and to help the ones that couldn't make the tools themselves," says Robb. As SIMRbase grows to include more research model genomes, the general approach is to provide initial access to Stowers scientists to support ongoing research at the Institute, and then, after further development and refinement, open access to the rest of the scientific community.

The site features many tools that assist researchers, but Robb mentions three in particular—**JBrowse** allows researchers to browse genomes and line up genomic data, such as genes that are switched on under certain conditions; **Tripal**, a web tool that interfaces with a database of genes and associated information, is used to create descriptive pages about genes; and **Apollo** helps researchers describe and edit gene features.

LIKE A SUDOKU PUZZLE

It's this last tool that Hugo Parker, PhD, uses the most, both in the lab and out.

Nights and weekends, you might find him using Apollo to curate sea lamprey genes. He inspects and aligns them. He changes the size of their exons, the portions of genes that encode proteins. He merges two genes that were initially predicted to be separate. The overall goal is to describe and validate sea lamprey genomic information based on experimental results.

"It's a little kind of mind puzzle, like doing a Sudoku puzzle. It's fun, and a nice distraction," he says.

Parker, a postdoctoral research associate in the lab of Stowers Scientific Director and Investigator Robb Krumlauf, PhD, and Jeramiah Smith, PhD, an associate professor in the Department of Biology at the University of Kentucky, used SIMRbase tools in their groundbreaking work, published in the January 2018 issue of *Nature Genetics*, to report the germline genome sequence of the sea lamprey.

These parasitic fish evolved from a lineage of jawless vertebrates that diverged early from the rest of vertebrates, about 550 million years ago, and are an important model organism for studying early vertebrate evolution.

Parker and Smith are investigating Hox genes, which control the layout of a developing embryo, marking where structures should appear along the body from head to tail.

"Looking at the Hox genes, the big question was, 'How many Hox genes do lamprey have? How many Hox clusters do lamprey have?' These are important developmental clusters of genes that control anterior to posterior patterning. And to answer that, we needed a genome," says Parker.

While the lamprey genome had been sequenced before, it was taken from samples of the lamprey's blood and liver and didn't represent the full lamprey genome. The team extracted DNA from lamprey sperm, sequenced it, and sent the newly sequenced genome to Robb to upload to SIMRbase and make it public.

As SIMRbase grows to include more research model genomes, the general approach is to provide initial access to Stowers scientists to support ongoing research at the Institute, and then, after further development and refinement, open access to the rest of the scientific community.

Parker uses SIMRbase to identify important Hox gene clusters, look at the timing of expression of these genes in lamprey embryonic development, and design RNA probes to characterize where in the embryo these genes are activated. Ultimately, this enables comparisons between vertebrates as to how they are using these important genes during their embryonic development. Designing probes in lamprey has been difficult, because the organisms have many repetitive sequences within their genome. Now that the entire genome assembly is available in SIMRbase, with all the repeats mapped, Parker can better spot the genes he's seeking.

Both Parker and Smith say SIMRbase played a key role in their research. "For me, and for lamprey scientists in general, SIMRbase is critical because it serves as a place where anyone can go in and look at the same pocket of genome and the same annotations and use those for their work. It's a common framework," Smith says.

UNDERSTANDING CAVEFISH

Robert Peuss, PhD, a postdoctoral research associate working in the lab of Nick Rohner, PhD, on a fellowship funded by the German Research Society, uses SIMRbase tools to look at the immune cell composition of the blind cavefish *Astyanax mexicanus*. (See related story, page 21.)

The Mexican cavefish evolved from a species common in Mexican rivers. Between 100,000 and 200,000 years ago, flooding flushed some of the population into caves, trapping them in an environment that lacks most of their common parasites.

Over time, the fish underwent dramatic changes to survive in an environment devoid of light and food, losing their eyes and eating only when seasonal flooding pushed food into their caves. They also developed high body fat and insulin resistance, a discovery recently reported by Peuss, Rohner, and collaborators in a March 2018 paper in *Nature*.

"Our ultimate goal is to understand how these cavefish adapted to an environment with low parasite diversity without having these auto-inflammatory diseases that we see in human populations under similar environmental conditions," he says, citing the rise in allergies, diabetes, and other inflammatory illnesses in humans. The rise of these illnesses is thought to be due in part to living in much cleaner environments compared to past generations, with less exposure to parasites that help activate the immune system. Cavefish live in a similarly tidy environment.

"That makes them interesting in regard to how an immune system evolves," says Peuss. "How do you come to a point when your immune system attacks yourself? What are the environmental conditions that cause this? What are the genetic changes in the genome of cavefish that have enabled them to live under these parasite-free conditions?"

To find out, Peuss and his colleagues are using a process called QTL (quantitative trait locus) analysis to match sets of cavefish characteristics with specific genetic changes. SIMRbase is helpful for this type of analysis because of the sheer volume of cavefish that need to be sampled—up to

300 cavefish and their hybrid offspring—to complete a thorough analysis. With that data in hand, the scientists can target the genomic regions responsible for producing a fish with cavefish traits, Peuss says.

A PLANARIA BY ANY OTHER NAME

Over in the Sánchez Alvarado Lab, Erin Davies, PhD, a postdoctoral research associate, studies flatworm regeneration and embryogenesis, the process of growing from a single fertilized egg into a properly formed organism.

Planarian flatworms have an unparalleled ability to regenerate. If an adult worm is cut apart, almost any piece can form a new, fully functional animal within just two weeks. But this phenomenon is still poorly understood.

Wanting to know more, Davies and colleagues generated a staging series, or a set of unique molecular fingerprints, for planaria embryos, as well as a gene expression atlas describing embryonic tissues and the formation of major organ systems during embryogenesis. Robb created a user-friendly, accessible, community resource to house this data, called Planosphere (https://planosphere.stowers.org), a SIMRbase spinoff site, launched in January 2017 in conjunction with the researchers' report in *eLife*.

Their study was the first to discover that adult stem cells called neoblasts, key to planaria regeneration, arise during a specific stage of embryonic development, findings that could guide future therapeutic advances for patients suffering from degenerative diseases or traumatic injuries.

Now, Davies and Postdoctoral Research Associate Stephanie Nowotarski, PhD, have been busy adding terms to Planosphere's Planarian Anatomy Ontology, a standardized vocabulary for data annotation and cross-species comparisons. The ontology includes more than 300 terms and definitions for cellular organelles, cell types, tissues, organ systems, anatomical entities, life cycle stages, and developmental processes described in scientific literature.

"With planaria, there's a lot of cell biology that's really just being discovered and described for the first time," Davies says. "Our hope is that the Planarian Anatomy Ontology will be used by ourselves and other planarian researchers to curate genomic, imaging, and phenotypic data sets, and by researchers looking to make comparisons across different species."

Robb also uses SIMRbase to compare molecular functions during embryogenesis and adulthood, overlaying expression data to understand how genes are behaving during development, homeostasis, and regeneration. SIMRbase is packed with information and tools, making such comparisons easy, Davies says.

PLANS TO GROW

Going forward, Robb intends to add to the database of genomes available on SIMRbase and help provide scientists with whatever tools they need to succeed. In addition to the lamprey, she plans to make other emerging organisms public, and some of the tools as well.

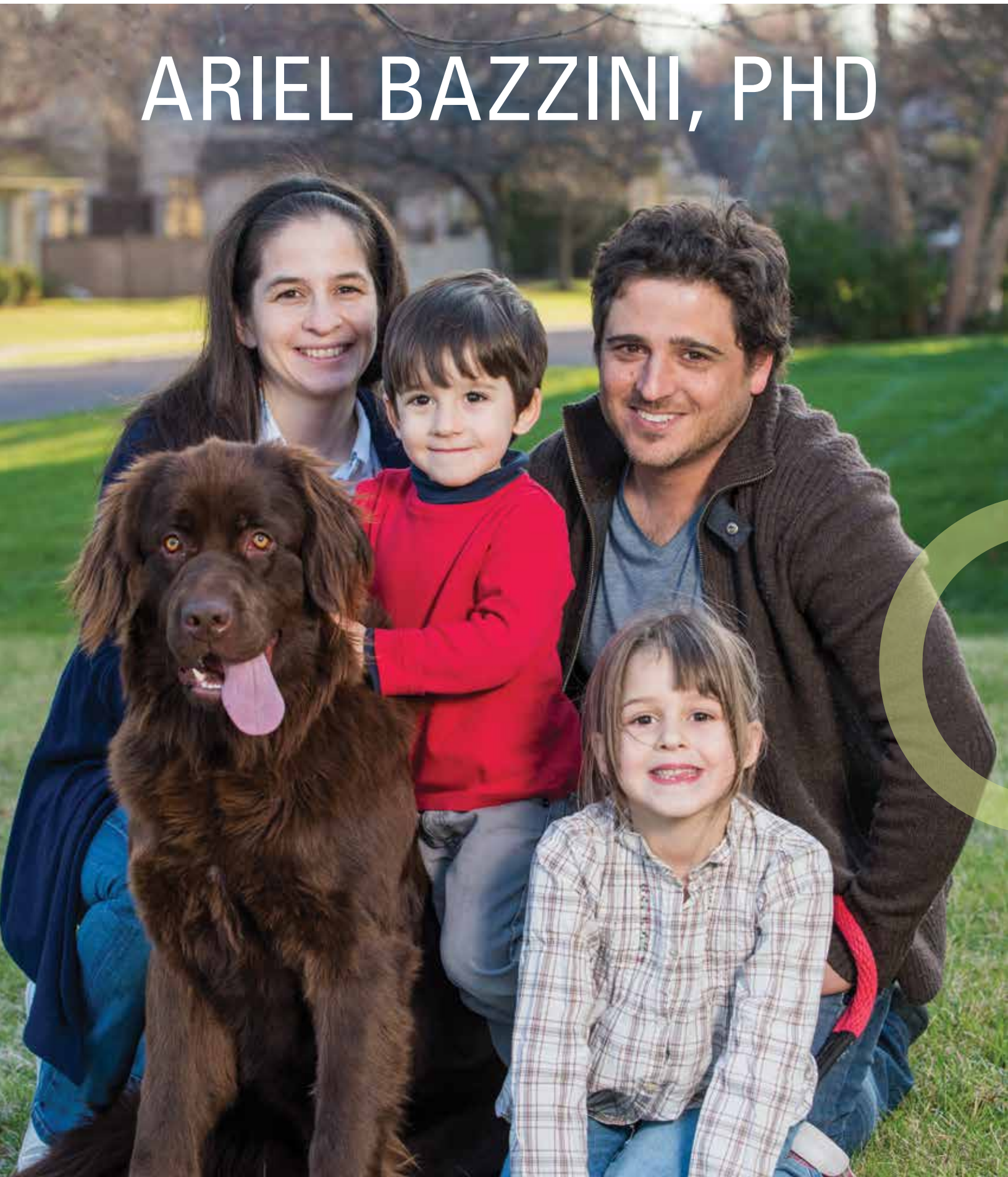
"The goal is to help the scientific community," she says, "and to promote sharing and collaboration, especially as a team."

The goal is to help the scientific community and to promote sharing and collaboration, especially as a team.

– Sofia Robb, PhD

A DISCUSSION WITH

ARIEL BAZZINI, PHD



By Jessica Johns Pool

Ariel Bazzini's life is dominated by three loves—family, science, and soccer. Some of his earliest childhood memories are built around playing soccer near his home in Buenos Aires, Argentina, or football, as it's known there. Then, when he was around 15, he heard about the Human Genome Project and was hooked for life on science.

Bazzini received a PhD in molecular biology in 2007 from the University of Buenos Aires. For his doctoral dissertation, he studied plant genetics in the laboratory of Sebastian Asurmendi, PhD, at the Institute of Biotechnology in Argentina's National Institute of Agricultural Technology (INTA). He started off studying ways to protect plants from viral infections, which led to an interest in investigating molecular gene interactions between hosts and pathogens. Around the same time, other scientists were uncovering important roles for small RNAs called microRNAs as master gene regulators. Since then, Bazzini has immersed himself in that RNA world to understand how genes are regulated.

His passion for microRNAs took him to Yale University next, where he was a postdoctoral fellow and subsequently an associate research scientist in the laboratory of Antonio J. Giraldez, PhD, in the Department of Genetics. Bazzini's current focus on the regulation of gene expression in vertebrates originated during his time at Yale. Moving from plants to zebrafish was challenging; however, Bazzini enjoys the faster pace of the research.

And while Bazzini's research programs now involve fish, his family finds it somewhat surprising because when fishing with his brother and cousin, Bazzini never wanted to touch a fish and, in fact, has a mild allergy to them.

Bazzini joined the Stowers Institute as an assistant investigator in 2016. Bazzini's wife, Florencia del Viso, PhD, also works at the Institute in the Gibson Lab.

WHAT DREW YOU TO SCIENCE AS A CAREER? WHAT ARE YOUR EARLIEST MEMORIES RELATED TO SCIENCE?

My mother is a hematologist and would take me to the hospital where she worked. It was then that I learned that single mutation or translocation in one gene could cause terrible blood diseases. When I was in high school, I heard for the first time that the human genome had been sequenced. I found that extremely interesting because by identifying many more genes, scientists could start understanding their various functions. We knew the sequence—now we needed to understand it! I was stunned to learn that most human diseases were related to abnormal gene function.

I also remember my mom traveling around the world going to hematology conferences and coming back with information about the advances that biologists were making in this area of research. From one of her trips, she brought home a micropipetter for her hospital. In the late 1990s, it was very hard to get one of these instruments for transferring liquids in Argentina, and I was amazed at how much easier it was to use compared to squeezing a rubber bulb pipetter or using your mouth!

WHAT BROUGHT YOU TO THE UNITED STATES FROM ARGENTINA? WHAT ARE SOME OF THE DIFFERENCES BETWEEN CONDUCTING SCIENCE IN THE TWO COUNTRIES?

Science, science and science!!! I love how dynamic science is in the US. The speed at which you can develop an idea and then actually conduct an experiment is just amazing.

I love Argentina. My country has incredibly good scientists, but the economy is not strong and that has an impact on the scientific community. Despite this situation, there are many groups doing amazing research with very low budgets, and our public universities are still generating outstanding students even on reduced budgets.

Ordering scientific supplies in Argentina was sometimes a multiple-week ordeal. Here in the US, you can usually get a similar shipment in only 24 hours. However, the situation in Argentina was a tremendous learning opportunity because it made us think very deeply and in advance about the entire experiment. And when the mail carrier arrived with the delivery of supplies months later, it was like getting a Christmas present!!!

I hope the economic situation will change for scientists in Argentina and the rest of Latin America, but in the meantime, I try to support the scientists there as much as I can.

HOW IS SOCCER DIFFERENT HERE THAN WHEN YOU PLAYED IN ARGENTINA?

In Argentina, I founded a team with my brother and we played for more than ten years. We think that during those ten years more than 200 friends and friends-of-friends played. I really enjoyed having a team with my cousins and friends from my elementary school, high school, and university, all of them on the same team. All the Argentinean leagues or tournaments are very competitive, sometimes rough, but we had so much fun.

Playing in the US is completely different for me. The styles are very different. Here, people get excited when you make a long pass. In Argentina, it's all about dribbling. However, I have been impressed by how much recreational soccer has improved in the US, especially in Kansas City.

DO YOU HAVE OTHER HOBBIES BESIDES SOCCER?

I love playing with my two kids. They are very demanding, but my wife and I love to do things with them, to be outside with them, to travel. We also take them to the swimming pool and we climb trees. We both think that Kansas City is a great place to live and grow a family.

Growing up in Argentina, we lived in a huge city (Buenos Aires) in an apartment, so my parents only allowed me to have small dogs, Yorkshire terriers, which weigh maybe 15 pounds. Now, living in Kansas, where the space is not a big limitation, we have a Newfoundland dog. She is only nine months old, but she already weighs over 95 pounds. She looks like a small brown bear yet she is extremely sweet with the kids.

I also love cooking and building things with my hands. Right now, I am trying to make an Argentine concrete grill and stone oven for pizza, but so far it is only 30 percent done. Having a lab and two kids doesn't leave much time!

WHEN TALKING TO NONSCIENTISTS, WHAT DO YOU TELL THEM ABOUT YOUR LAB AND ITS PROJECTS? WHAT DO YOU SAY TO HELP THEM UNDERSTAND THE SCIENCE?

It is always a challenge to talk about my research work with lay people, but we HAVE to do it. The scientific community needs to open up and talk.

I usually tell people that we are made up of a bunch of cells. On your first day, in your mother's belly, you were a single cell, then your cell started dividing and you went from two to four to eight cells, then developed as a baby. All your cells have the same information, the same genes, but somehow those cells differentiated, and you became who you are. You are a well-developed organism that talks, walks, thinks, and maybe even plays soccer. My research team works to understand how one cell becomes a complex organism, and how and which genes turn on, turn off, or modulate cell division and cell differentiation to give rise to a very complex and unique creature.

WHAT DO YOU LIKE BEST ABOUT THE INSTITUTE?

The thing I enjoy most about being at Stowers is that we have the freedom to research whatever we want. Plus, the collaboration that occurs between the labs here makes it an interesting and supportive environment. The incredible support from the core facilities allows us to explore techniques and fields that we might not be experts in. With their dedication and contagious motivation, our group gets to use a large variety of molecular tools. For me, the most invaluable resources of the Institute are the people. "Good people make the difference," I've heard. The Stowers Institute is full of great people and outstanding scientists who are always willing to help and talk through a scientific problem.

IN A NUTSHELL

Molecular signature of "trailblazer" neural crest cells gives insight into development and cancer

Collective cell migration describes the movement of a group of cells in a directed and cohesive manner, and it plays a critical role in embryonic development, wound healing, cancer spreading, and the immune response. In the scientific journal *eLife*, Stowers Institute researchers recently reported the first comprehensive analysis of the molecular transitions and gene expression signatures of single migrating cells from the neural crest, a cell population crucial to organ development and the ancestral cell type of two deadly forms of human cancer. Stowers Director of Imaging Paul Kulesa, PhD, explains that they discovered a signature of 1,300 differentially expressed genes indicative of an invasive subset of migrating cells known as "trailblazers." These genes appear to drive migration and may be part of a broader molecular signature in other biological phenomena involving cell invasion. Kulesa and his colleagues plan further studies to explore the actions of these trailblazer cells.

This study was published December 4, 2017, in the journal eLife.

Chris Smoyer

A SEASONED STOWERS RESEARCHER

By Jessica Johns Pool

Christine "Chris" Smoyer began her scientific research career at the Stowers Institute in 2005 when she was an undergraduate at the University of Kansas. She was taking a genetics class from Stowers Investigator Scott Hawley, PhD, when Hawley mentioned that he was hiring for summer research positions.

Smoyer immediately applied for a position in Hawley's lab and soon decided a career in science was in her future. She had already worked as a waitress, on a road paving crew, as a retail store manager, and in the banking business for a few years. When she started getting bored with crunching numbers, she began taking science classes at her local community college in Overland Park, Kansas. Wise investments allowed her to take classes as she explored what she would do next.

Smoyer quickly found that science captured her imagination in a way that banking had not, and she enrolled in the Molecular Biosciences program at the University of Kansas. Working on fruit fly genetics in the Hawley Lab made it easy to say goodbye to her previous career.

"I was attracted to science because there is so much to figure out, so much to discover," Smoyer says. "Textbooks make it seem like all the important questions have been answered. That first experience working in a lab made me realize how much of life's complexity is still unexplored, and I wanted to do that exploring."

Within days of taking her last undergraduate final in 2007, she was hired as a research technician by Sue Jaspersen, PhD, Stowers associate investigator. In the Jaspersen lab, she started studying yeast models to better understand mechanisms of cell division.

A few years later, the Stowers Institute announced that it was accepting applications for the newly established Graduate School of the Stowers Institute. With Jaspersen's encouragement, Smoyer applied and was admitted to the inaugural class in 2012.

"There was a high level of excitement for everybody in that class because we were part of the first group," Smoyer recalls. "It was fun to get into the labs so quickly, and we felt like we contributed to the development of the program because everyone really listened to our feedback about how to improve things even more. It's pretty neat to feel like you have input like that."

As evidence of her early scientific success, Smoyer published her first paper as lead author in the *Journal of Cell Biology*. Smoyer and coauthors used split green fluorescent protein to localize known and predicted integral membrane proteins to the inner nuclear membrane of the budding yeast *Saccharomyces cerevisiae*. She has continued to expand upon this research and is now working on her second paper.

When asked about her time at the Institute and what makes it special, Smoyer says, "Stowers is a great environment to talk about your science with others and I especially enjoy all the guest speakers who visit us during the academic season of fall through spring. There are amazing scientific support groups that help you with your research. It makes all the difference. I've learned so much from the Microscopy Center team especially."

Never one to let moss gather, Smoyer plans to pursue her postdoctoral studies in cellular genetics, and possibly its applications to neuroscience. "I can see myself looking further into different areas related to understanding behavior and memory."

When she isn't exploring biological mysteries in the lab, Smoyer loves to travel. She celebrated the publication of her first paper as lead author with a sailing trip around the British Virgin Islands. When her research life slows down, Smoyer plans to return to her passions of paddleboarding, gardening, and training for 5K runs and triathlons.

PREDOCS SNAG NIH GRANTS

Karla Terrazas, a predoctoral researcher in the Graduate School of the Stowers Institute, has been awarded a three-year fellowship from the National Institute of Dental and Craniofacial Research at the National Institutes of Health (NIH).

Craniofacial malformations account for approximately one-third of congenital anomalies and are a significant cause of infant mortality. Terrazas' research project focuses on understanding the etiology and pathogenesis of ribosomopathy disorders and their associated craniofacial birth defects. A ribosomopathy results from errors in ribosome biogenesis, which is a mechanism required for cell growth, proliferation, and survival. Understanding the biological mechanisms that govern this process is essential for developing strategies for the prevention and treatment of ribosomopathy disorders.

Blake Ebner, a predoctoral researcher in the MD-PhD Physician Scientist Training Program at the University of Kansas Medical Center who is completing his research project in the Si Lab, received a four-year NIH fellowship from the National Institute on Aging.

Ebner studies prion-like proteins called CPEB and Orb2 that may play a role in the formation and maintenance of long-term memory. Unlike prions that cause neurodegenerative disease when aggregated, these prion-like proteins seem to perform normal cellular functions. Ebner believes that a greater understanding of the cellular mechanisms that regulate these prion-like proteins may provide insight for controlling aggregation of other disease-causing prions and prion-like proteins.

GENETICS SOCIETY OF AMERICA FUNDS TRAVEL FOR STOWERS RESEARCHERS

Not one but two researchers from Stowers attended scientific conferences, thanks in part to the Genetics Society of America (GSA). Each was awarded travel funds to attend meetings that advance the professional development of young scientists in the field of genetics.

Stowers predoctoral researcher and Zanders Lab member María Angélica Bravo Núñez attended the Meiosis Gordon Research Seminar and Meiosis Gordon Research Conference from June 9-15, 2018. Bravo Núñez received the competitive DeLill Nasser Award, which is named for a long-time GSA member and National Science Foundation Program Director in Eukaryotic Genetics.

University of Missouri-Kansas City student Elizabeth Hemenway received The Victoria Finnerty Undergraduate Travel Award. This award funded Hemenway's travel to the GSA's Annual Drosophila Research Conference in April of this year. The award's namesake was also a longtime GSA member and served the *Drosophila* and genetics communities by being a gifted teacher and research scientist. Hemenway conducted undergraduate research in the Hawley Lab at the Stowers Institute.

BOLD INNOVATION DRIVES STOWERS ALUM MARY-LEE DEQUÉANT

By Jessica Johns Pool

We were encouraged to be cutting-edge, creative, and bold and didn't have to worry about funding limitations.

– Mary-Lee Dequéant, PhD

Nothing in her professional life has gone according to plan, laughs Mary-Lee Dequéant, PhD. She thought she'd get her PhD in France but ended up earning her degree from the University of Kansas Medical Center in Kansas City. Then, she thought she would return to France after her graduate work but instead detoured to Harvard Medical School for postdoctoral training.

As she finished at Harvard, a chance invitation to give a seminar from a former Stowers colleague, Chad Cowan, PhD, brought her to the new start-up company of Emmanuelle Charpentier (co-inventer of the CRISPR/Cas9 technology) set up in Boston. That seminar led to a job offer, which put a twist in her plans to remain in academia.

Today, Dequéant works as program lead scientist at CRISPR Therapeutics, where she leads programs to develop and launch allogeneic CAR-T cell therapies. CAR-T therapy is an extremely promising cancer treatment in which human immune T cells are genetically engineered to recognize, attack, and kill cancer cells.

"It's a game changer because the precision and efficiency of our multiplexed editing approach with CRISPR/Cas9 enable the rapid creation of allogeneic CAR-T cells," explains Dequéant. "I really enjoy this work because you can see all the steps from early-stage research to identifying a treatment that can be advanced to the clinic, with the ultimate goal of developing a transformative medicine."

Dequéant feels her time at the Stowers Institute prepared her well for her current position, which requires her to lead cross-functional teams and to interact with colleagues from different disciplines, including bench research, manufacturing, toxicology, and regulatory.

"I have to say that the Stowers environment was exceptional," says Dequéant. "We were encouraged to be cutting-edge, creative, and bold and didn't have to worry about funding limitations. This approach, combined with the collaborative mindset of the Institute, was a big enabler to making our project happen and successful."

Findings from her groundbreaking thesis, "Analysis of the transcriptional landscapes of the segmentation clock in mouse and chick embryos: identification of novel cyclic genes," were published in a 2006 *Science* paper**.** This research led to another project that eventually revealed the evolutionary plasticity of the gene regulatory networks across different vertebrate species.

While at the Institute, Dequéant also led a collaborative project supported by DARPA FunBio (an ambitious program aimed at discovering the Fundamental Laws of Biology), involving an international team of bioinformaticians, physicists, and mathematicians to develop new methods for global analysis of gene expression pattern detection in large datasets.

Upon leaving Stowers, Dequéant was attracted to Norbert Perrimon's lab at Harvard for its reputation for innovation. While there, supported by HHMI and a Starr Cancer Consortium grant award, Dequéant characterized the first immortalization system for embryonic progenitor *Drosophila* cell lines that can be differentiated *in vitro*, and used this model to find new regulators of fly muscle stem cells.

Now at CRISPR Therapeutics, her gene editing expertise may assist in the quest to find a last-chance cancer treatment for people without other alternatives.

Dequéant earned an engineering degree from the Institut National Agronomique Paris-Grignon and a master of science from AgroParisTech. A first lab experience at Stanford School of Medicine gave her a taste for developmental biology. She then came to the Stowers Institute when her mentor and former Stowers Investigator Olivier Pourquié, PhD, moved his lab to the Institute.

She thoroughly enjoys living in Boston for its robust biotech community and lively museum and arts scene, but when speaking of Kansas City, it's clear she misses the Nelson-Atkins Museum of Art, the live jazz and blues shows, and friendly Midwesterners. Finally, she thanks Robb Krumlauf and all of her previous colleagues at the Stowers for their conviviality; the entire experience left her with many excellent memories.

GERMAN FELLOWSHIP GOES TO STOWERS POSTDOC FOR RESEARCH OF HOST-PARASITE INTERACTIONS

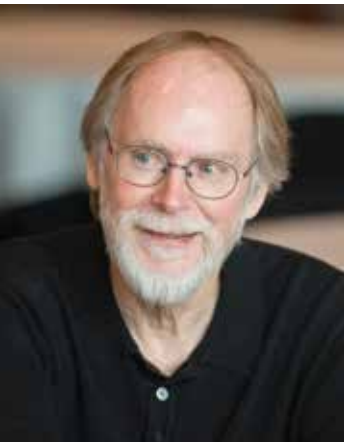
Postdoctoral Research Associate Robert Peuss, PhD, was awarded a highly competitive and well-regarded German fellowship for his research on the Mexican cavefish *Astyanax mexicanus*. Peuss' research proposal to the Deutsche Forschungsgemeinschaft (DFG) landed him a two-year grant that totals about $135,000.

Host-parasites are a major driving force in evolution. The loss of parasite diversity in modern society correlates with an increase in autoimmune diseases. This correlation suggests that this co-evolutionary dynamic created a necessity for a vertebrate host to develop a functional immune system. Peuss has identified *Astyanax* as a suitable model organism to investigate this emerging topic in the field of evolutionary medicine and is addressing the question of how natural changes in parasite diversity alter the evolutionary trajectory of the host immune system. Peuss' work in the Rohner Lab will provide foundational knowledge of the immune system of this fascinating model organism.

Robb Krumlauf awarded society medal

Scientific Director Robb Krumlauf, PhD, was awarded the 2018 Edwin G. Conklin Medal for his contributions to the field of developmental biology and mentorship of the next generation of scientists.

Krumlauf received the prestigious award from the Society for Developmental Biology (SDB) for his extensive body of work on the role of Hox genes in regulating the vertebrate body plan.



Krumlauf was the first to publish a description of spatiotemporal expression of Hox genes in a mammal. His detailed analysis of Hox clusters and how they are regulated to control segment identity provided foundational studies in his field. His comparative studies in mouse, chick, and zebrafish continue to provide critical information on how different species deploy their conserved gene regulatory networks to form diverse structures.

Throughout Krumlauf's career, first as head of the Division of Developmental Neurobiology at the National Institute for Medical Research in London and then as investigator and scientific director of the Stowers Institute, he has provided mentorship to countless students and postdocs.

Krumlauf will receive his award and present a feature lecture at the SDB 77th Annual Meeting in July 2018.

Up close with science and art

Scientific images generated by microscopy are gaining mainstream popularity as objects of art. Perhaps it's the intricate imagery, or the vivid coloration of fluorescent dyes and proteins used as biological markers, or simply the wonder of seeing features of organisms that are normally hidden from the naked eye.

Stowers Investigator Jennifer Gerton, PhD, appreciates the art and beauty that result from scientific imaging. Last fall, Gerton invited some members of the InterUrban ArtHouse in Overland Park, Kansas, to the Institute. Their tour passed by some stunning images on display outside the Stowers Microscopy Center. The Microscopy Center's display stimulated discussions of science and art, and eventually sparked the idea of a public display of Stowers research images. "I am motivated to share these beautiful images with the public and was glad to find many others shared this enthusiasm," Gerton says.

With help from the InterUrban ArtHouse, the idea grew into a collaboration between the Institute and the Johnson County Library to sponsor an image exhibit that would provide the public a glimpse into the dazzling images produced by Stowers scientists as well as an opportunity to meet and talk with the researchers themselves.

The exhibit, titled "Scientific Micro Imaging," went on display at the Cedar Roe location in Roeland Park, Kansas, in early February. The exhibit featured ten scientific images that represented three general scales—whole organisms and biological systems, tissues and cells, and subcellular biology.

A public reception for the exhibit, titled "Up Close with Science and Art," was hosted in early April. The reception provided an opportunity for library patrons and members of the community to learn more about the images in the exhibit and mingle with Stowers scientists and InterUrban ArtHouse artists.

Johnson County Library Information Specialist and co-organizer of the event, Michelle Holden, says, "This is exactly the kind of event we seek to provide our community. It's an opportunity to connect with experts in their fields and expand our understanding of science and art."

The exhibit traveled to the Gardner Library in Gardner, Kansas, for the summer and will be on display at the Lackman Library in Lenexa, Kansas, in the fall.

Stowers Scientist Sarah Zanders receives 2018 Basil O'Connor Award

The March of Dimes Foundation has presented Assistant Investigator Sarah Zanders, PhD, with the Basil O'Connor Starter Scholar Research Award. This highly competitive award is designed for scientists embarking on their independent research career. It provides Zanders with $150,000 over two years.

Zanders' research centers on understanding how selfish genetic elements exploit cell division and lead to an abnormal number of chromosomes, a common cause of genetic disorders including some human birth defects. Some cancer cells also have abnormal numbers of chromosomes.

While most genes expressed in meiosis—the cell division process that gives rise to gametes such as eggs and sperm—contribute positively to fertility, the selfish DNA sequences persist without providing any known benefit. These selfish genetic elements are commonly referred to as gamete-killing meiotic drivers and exist in a variety of organisms, including some mammals. However, they have not yet been identified in humans.

Zanders will continue to study gamete-killing meiotic drivers in yeast to gain a better understanding of how meiotic drivers exploit cell division. Eventually she hopes to be able to expand the studies to human sperm samples to search for evidence of meiotic drivers in humans. This research has the potential to provide insight into human chromosomal defects and disorders, and ultimately improve human fertility.

Paul Trainor named fellow of American Association of Anatomists

Investigator Paul Trainor, PhD, was recently recognized for his expertise in and contributions to the anatomical sciences by being named a Fellow of the American Association of Anatomists.

Trainor focuses his research program on neural crest cells, a migratory population of cells born early during embryonic development. Neural crest cells ultimately generate much of the bone, cartilage, and connective tissue of the head and face as well as neurons and glia in the peripheral nervous system. In fact, neural crest cells contribute to nearly every organ in the body. Abnormalities during the formation, proliferation, migration, or differentiation of neural crest cells can lead to congenital birth defects.

Trainor has been a longtime member of the American Association of Anatomists and currently serves as the editor in chief of the association's developmental biology journal, *Developmental Dynamics*.

Creating a legacy

A Labor of Love

By Bob Inderman

Some 18 years ago, Stowers Scientific Director Robb Krumlauf, PhD, placed a call to friends in Dallas seeking personal insight on a scientist about to take the reins of the fledgling Stowers Institute.

There was much to love about this Texan, they told Krumlauf. William (Bill) Neaves, PhD, was instrumental in building biomedical sciences at the University of Texas Southwestern Medical School, recruited stellar leaders of research programs, and held everyone to rigorous scientific and ethical standards. Krumlauf was particularly pleased to hear about Neaves' total commitment to recruiting and hiring the best scientists.

However, there was a quirk worth knowing.

"They said, 'the good news is we no longer will have to listen to Bill's little anecdotal stories. The bad news is that we no longer will be able to listen to those little anecdotal stories," Krumlauf says. "We have come to know what they meant. And we, too, will truly miss them," he adds.

From the very beginning, he ensured that the Institute was centered on a commitment to excellence and collegiality. This attitude still permeates the Institute today, and I hope it never changes.

– Robb Krumlauf, PhD

Neaves, president emeritus of the Institute, and his wife, Priscilla, decided earlier this year that it was time to retire and return to Texas. During his nearly two decades at the Institute, Neaves oversaw the opening and expansion of its facilities, employee growth from about 50 to about 500 members, and the recruitment of almost two dozen principal investigators.

Stowers President and CEO David Chao, PhD, believes Neaves' storytelling talent is a singularly effective strategy at persuasion. Each story is personal and always embedded with an important, subtle truth. That proves particularly potent in recruiting talent or to heighten a team's or individual's performance.

"His biographical memory is astounding. He can immediately recount an event in his history perfectly pertinent to the discussion at hand," Chao says. "Bill will lean forward in his Bill Neaves sort of way and draw you in with his congeniality. I love that the stories put people at ease and exude a warmth that encourages you to buy in."

Neaves' association with the Institute first began in the late 1990s when he provided formative strategy, organization, and operations guidance to Jim and Virginia Stowers and their advisors. Neaves spent many hours in planning meetings with Dick Brown, who would become the chairman of the board of directors of the Institute; David Welte, who would become the Institute's executive vice president and general counsel; and advisor Robert Gust from the University of Washington School of Medicine.

As the meetings and discussions progressed, Neaves felt a growing aspiration to serve a larger, more direct role in what was taking shape. He joined the Institute as president in June 2000, and took the title president emeritus in 2010.

"Any startup faces legions of doubters, and the Institute was no exception," Chao recalls. "Bill was able to present Jim and Virginia's compelling vision and persuade others to join a grand experiment in American science. That unwavering conviction that the Stowers were serious about science persuaded a rapidly growing number of pioneers to join the Institute."

Krumlauf believes Neaves' legacy will be that visionary leadership during those formative months of the startup.

"From the very beginning, he ensured that the Institute was centered on a commitment to excellence and collegiality. This attitude still permeates the Institute today, and I hope it never changes," he says. "Bill gave us a united focus. In those early years, a frequent refrain you heard when solving problems or setting up infrastructure was, 'Is this good for science?'"

Virginia Stowers agrees, "Without Bill Neaves, the Institute would not be as successful as it is."

Neaves remembers "the incredibly dedicated colleagues who worked so diligently to lift the Institute to an unprecedented level of performance in such a short time."

"Jim and Virginia left us a tremendous gift that must be cherished and energized. We are indebted to them for having the hope and the daring to commit to building the world-class research institute that we are all a part of today," Neaves says.

Chao adds that "the difference between the Institute at the start and end of Bill's tenure is remarkable and almost unimaginable. It is no longer considered a grand experiment. It is an exemplary model of smooth operation. We all say, 'thank you, Bill.'"

BETTY DREES, MD, NAMED GRADUATE SCHOOL PRESIDENT

Esteemed physician and educator Betty M. Drees, MD, was appointed president of the Graduate School of the Stowers Institute for Medical Research following the retirement of President William B. Neaves, PhD.

"We are fortunate to have recruited a physician-educator of Betty Drees' caliber to lead the Stowers graduate program," says Robb Krumlauf, PhD, a member of the Board of Directors of the Graduate School and scientific director of the Stowers Institute. "Her experience training medical students in the biological sciences will prove invaluable in shaping our young scientists into tomorrow's leaders."

With more than twenty-five years in clinical practice, research, education, and administration, Drees is dean emerita and the immediate past dean of the University of Missouri-Kansas City (UMKC) School of Medicine. She served thirteen years in that role, from 2001 to 2014.

Drees serves as an endocrinologist and a professor in the Department of Internal Medicine and the Department of Biomedical and Health Informatics at UMKC, roles she will continue to serve concurrently with her role in the Graduate School. She currently serves as president of the Community Leadership Board of the Kansas City American Diabetes Association.

"It was an honor to be elected to lead the graduate program at the Graduate School of the Stowers Institute," says Drees. "The Graduate School has a very committed faculty and talented predoctoral researchers, so I hope the administrative experience I bring can help them continue to grow. I want to help the researchers who join the program meet their career goals and get experience that prepares them for the future."

2008-2018

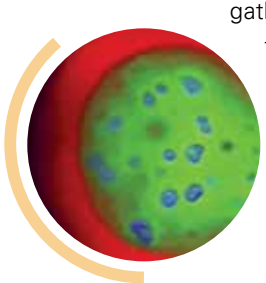
TEN YEARS: BEATING THE TREND

According to the Bureau of Labor Statistics, the average length of time an employee stays with a company is only 4.2 years. In 2017, there were twenty-seven members who celebrated a ten-year anniversary at the Institute. Their long-term dedication and commitment reflect the vision of our founders, who viewed establishing the Stowers Institute as a long-term investment in advancing our knowledge of fundamental biology for the benefit of all. This year's awardees can be proud of contributing ten years of work that builds upon itself toward that vision. Congratulations to all!

Front row (seated, left to right): Jungeun Park, Maria Katt, Dorothy Stanley, Carolyn Randolph, Steve Hoffman, Dan Burkholder. Second row: Tara Gillett, Mary Penne Mays, Ariel Paulson, Jenny McGee, Ana Pedraza, Lisa Lassise, Lauren Horsewood, Karen Tannen, Boris Rubinstein, Jim Mathis. Third row: Gabriel Keele, Stacey Billinger, Milissa Doolin, Dan Stranathan, David Latzman, Julia Zeitlinger, Heidi Monnin, Fengli Guo, Melissa Childers, Kim Dziedzic, Ying Zhang.

STOWERS WELCOMES ASBMB SCIENTISTS

Hosting a scientific conference requires months of planning and execution, yet the days of scientific discourse that result can be an invaluable tool for moving science forward. Last fall, Stowers Investigator Jennifer Gerton, PhD, her colleague Thoru Pederson of the University of Massachusetts Medical School, and the American Society for Biochemistry and Molecular Biology gathered scientists focused on the emerging roles for the nucleolus at the Stowers Institute.



For three days, scientists presented their most recent research findings to one another, engaged in lengthy conversations, and asked probing questions of each other. "Scientists come to these meetings not just to highlight their latest findings, but to establish collaborations and gain feedback that can push their research even further forward," says Gerton. "In hosting this kind of scientific meeting, the Stowers Institute is serving all of science, not just that being conducted here."

The fall symposium featured research on the nucleolus, a subnuclear organelle that was first recognized under the microscope in the 1830s. This organelle has long been known for its function as a ribosome factory. Ribosomes are the protein machines that make all the proteins in the cell. However, the nucleolus is also a hub for many other nuclear activities. Fundamental functions of the nucleolus and its role in human health and disease were discussed at the meeting. ASBMB will sponsor another nucleolus meeting in 2019, to be held again at the Stowers Institute.

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

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

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

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

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

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

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

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CHRISTMAS LETTERS PRESERVE CONNECTION

For almost 30 years, David Karr, Stowers head of technical services and support, has kept in touch with Judith Vogt, PhD, his former professor at Fort Hays State University (FHSU) in Hays, Kansas.

"I particularly enjoy David's annual Christmas letters, which are often hilarious descriptions of his family's adventures during the past year," says Vogt, former professor of biology and head of FHSU's medical technology program.

There is a lesson to this story—sometimes it pays to keep up your holiday correspondence.

– Judith Vogt, PhD

In late 2017, when Vogt wanted to donate $25,000 to cancer research, she telephoned Karr. "I was very surprised to see her name on my caller ID," Karr recalls. "We had not spoken to each other since my wedding in 1992." Their only communication since then had been via letters, not telephone or even email.

"After catching up with one another, Dr. Vogt asked me whether the Stowers Institute would be a good place to contribute some money that she had inherited," says Karr. Vogt had received the funds from a friend, Charles Frank Guinzio, who died from cancer in October 2017.

Vogt knew about the Institute because Karr had mailed issues of the Stowers Report to her. "I wanted to show her where I was working and wanted her to learn all about the interesting research going on here," he says. But that alone wasn't enough for Vogt, who took the responsibility of her role as trustee of this money seriously. "She wanted to know whether I felt that the Institute would put the money to good use," he says.

With Karr's descriptions of the research programs and assurances of strong financial stewardship, Vogt was convinced and mailed a $25,000 check to support the Institute's research.

"There is a lesson to this story—sometimes it pays to keep up your holiday correspondence," Vogt jokes.

Vogt met Karr soon after he received a BS degree in agriculture at FHSU in 1984 and was a research assistant at the Kansas State Agricultural Experiment Station (KSAES)'s plant pathology lab. "My boss felt I needed more training in microbiology so he arranged for me to enroll in Dr. Vogt's microbiology class," recalls Karr.

"I think Dr. Vogt took an interest in me because I was a nontraditional student," Karr says. "She recognized that I was able to apply real-world application to her class material. Dr. Vogt learned that I worked at KSAES and visited the lab. A big portion of our work was screening experimental wheat and sorghum varieties for virus resistance. She was quite interested in our technique."

In 1988, Karr returned to FHSU to obtain a BS degree in biology and a teaching certificate. He worked as Vogt's lab assistant "making media and helping prepare for her labs. We developed a mutual respect for each other. She even came to my wedding," he says.

While studying for her PhD, Vogt studied radiation biology at the Manhattan Project's plutonium production site in Washington during World War II. She subsequently was a Peace Corps volunteer in Togo, West Africa, a Colorado State Hospital medical technician, and a Pfizer Diagnostics sales representative in Los Angeles. She joined FHSU as an assistant professor of biology in 1975. After retirement, Vogt created a computer-assisted instruction course in immunology that she taught through FHSU's Virtual College.

Retired since 2001 and now living in Michigan, Vogt stays busy with various activities at her retirement community. She looks forward to receiving her Christmas card from Karr this year.

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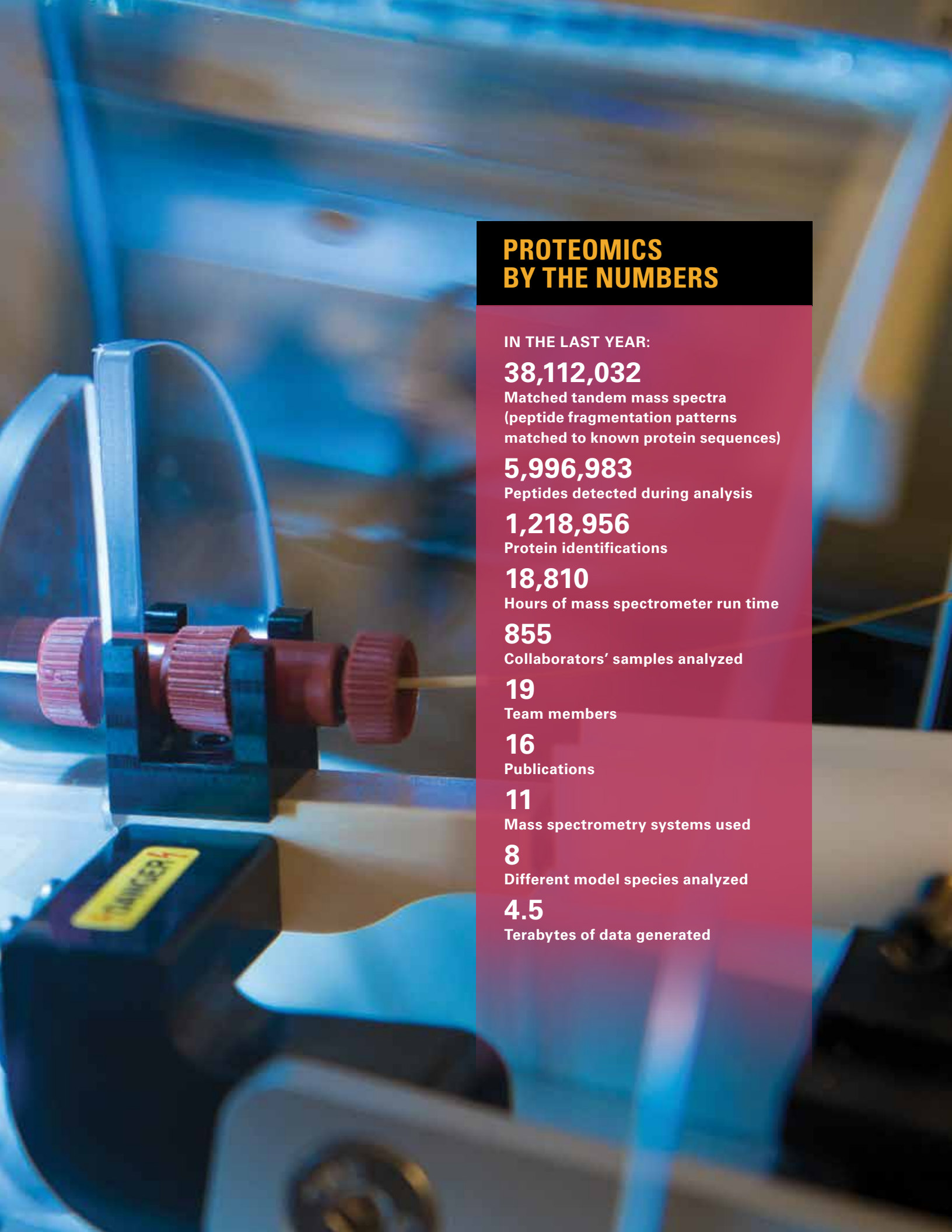
BACKSTAGE PASS

Proteomics is the study of proteomes—very large collections of proteins such as all the proteins contained in a cell, tissue, or organism at a particular time.

Proteomics researchers are interested in determining not only the individual members in a particular protein collection but also their interactions with each other and the overall dynamics and principles of the networks they form. A common analysis method is mass spectrometry, which detects and quantifies small protein segments called peptides.

The Proteomics Center at the Stowers Institute is a highly collaborative, interdisciplinary team that applies proteomics approaches to many different biological research projects. They collaborate within their group as well as with other labs inside and outside of the Stowers Institute with the overall goal of achieving a better understanding of the mechanisms that drive health and disease.



PROTEOMICS BY THE NUMBERS

IN THE LAST YEAR:

38,112,032
Matched tandem mass spectra (peptide fragmentation patterns matched to known protein sequences)

5,996,983
Peptides detected during analysis

1,218,956
Protein identifications

18,810
Hours of mass spectrometer run time

855
Collaborators' samples analyzed

19
Team members

16
Publications

11
Mass spectrometry systems used

8
Different model species analyzed

4.5
Terabytes of data generated

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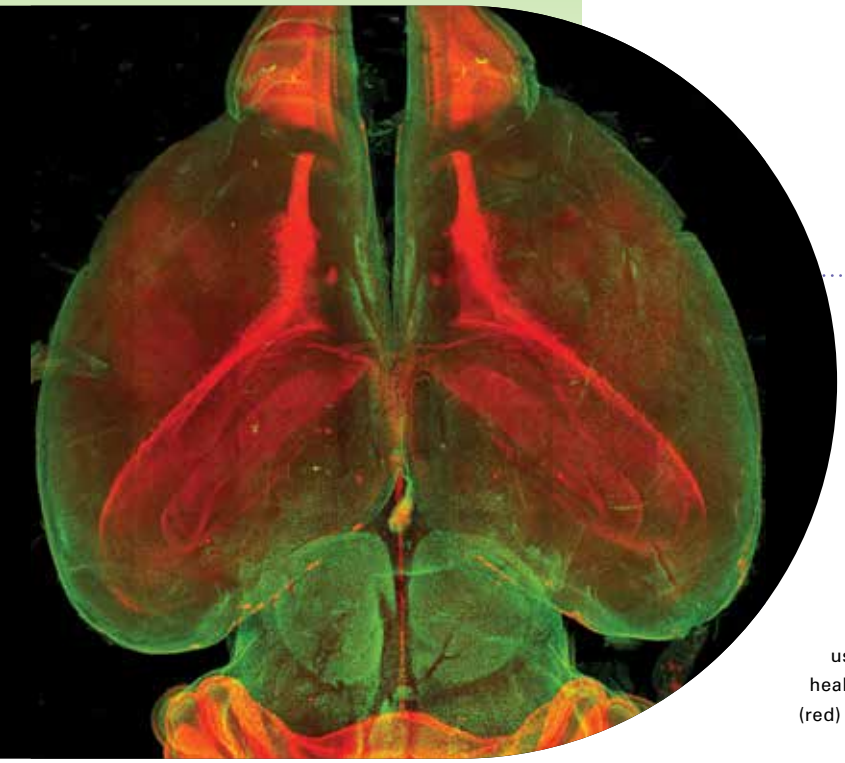

A "WHOLESOME" VIEW OF THE BRAIN

Historically, visualization of structures and features within the brain has been a tedious task, often requiring researchers to dissect a brain sample and cut it into thin slices to allow access of stains and dyes to the tissue. New techniques that use chemical treatments to render the entire brain transparent have revolutionized the field of brain imaging. In a cleared brain, molecules, individual cells, and their connections can be visualized throughout the whole specimen. The Yu Lab uses this technology to study brain organization and function in both normal health and pathological conditions. This image shows where a gene product (red) and cell nuclei (green) are located in a transparent mouse brain.