Stowers Report

FOUNDATIONAL SCIENCE. PROFOUND IMPLICATIONS.

2023

Stowers Institute

Stowers Report

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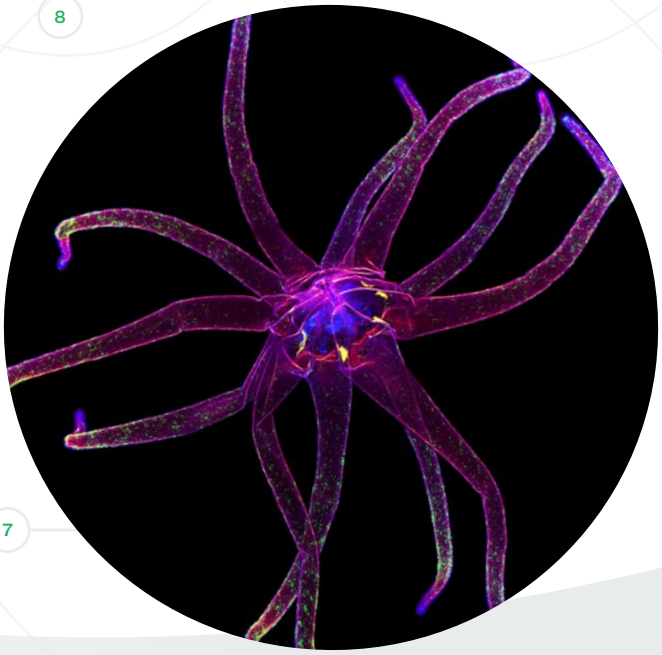
IN THIS ISSUE

FEATURED STORIES



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Visit the Stowers Institute at www.stowers.org.

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In Perspective

Billions of years ago, life began in primeval oceans and continues to flourish, inhabiting every corner of our planet. Throughout this time, life has confronted many challenges, including multiple bouts with extinction. And yet, life has managed to overcome these challenges, adapt and ultimately not only survive but also thrive. Understanding the molecular and cellular processes that life has evolved to perpetuate itself stands as one of the most important problems faced by life scientists today.

Twenty-three years ago, the Stowers Institute for Medical Research opened its doors. Its mission, like the 23 pairs of chromosomes we as humans harbor, is ingrained within us all: to audaciously push boundaries, to defy limitations, to dare to ask the most challenging questions that will enable us to reveal and understand the mysteries of life.

This year, we welcomed three driven, curious, and innovative new Investigators to our community, a testament to the rigorous yet exciting research environment the Institute offers. Siva Sankari, Ph.D., Neşet Özel, Ph.D., and Ameya Mashruwala, Ph.D., joined us as Assistant Investigators, increasing the total number of independent research labs from 17 to 20. Our new Investigators were recruited from top-tier institutions and aim to solve vexing problems in brain circuitry, cellular symbiosis, and the population dynamics of bacterial communities. These scientists are bringing their intellect, expertise and creativity to our Institute and we fully expect their efforts will significantly add and meaningfully impact the progress of foundational science at home and around the globe.

Extraordinary scientific discovery, innovation, and our enduring focus on convening and collaboration can be found throughout this report, highlighting 2023's many endeavors and achievements. True to Jim and Virginia Stowers' vision – "Hope for Life" – your continued support encourages our curiosity and strengthens our efforts to understand how life works for the benefit of humankind. •

Alejandro Sánchez Alvarado, Ph.D.
PRESIDENT AND CHIEF SCIENTIFIC OFFICER

Discovery

EXPANDING OUR RESEARCH SCOPE

Stowers Institute welcomes three new Investigators

Many biological mysteries remain unsolved, even those that have been studied for centuries or more. Cholera, for instance, is one of the oldest known scourges to society that has impacted civilization since its infancy and continues to wreak havoc today. Symbiosis, the communal and often beneficial living arrangement between two separate species, remains poorly understood even though it is known to play a key role in the health of plants and animals, including humans. And presently, we are still in the infancy of our understanding of how billions of neurons in the brain find one another and communicate essential information.

The Stowers Institute tirelessly pushes the boundaries of biological research such that life's most enduring secrets may be revealed. Expanding the scope of foundational biological science and research, this year, the Institute welcomed three new Assistant Investigators: Siva Sankari, Ph.D., Neşet Özel, Ph.D., and Ameya Mashruwala, Ph.D. These scientists have unique insights and approaches for tackling these unsolved mysteries, are fearless, creative, and daring in their pursuit of boundary-defying questions, and embody the Stowers' mission and motivation to understand life at its most fundamental level such that solutions can be found to the many, still untreatable diseases afflicting us today.

Siva Sankari, Ph.D.

Sankari, a plant biologist and biochemist, joined the Institute from the Massachusetts Institute of Technology as an Assistant Investigator in May 2023. Her lab investigates symbiosis, a mutually beneficial arrangement between bacteria and their host organisms. More specifically, Sankari studies the biochemical mechanisms for how plants harness microbes to perform essential functions. Plants produce peptides, small molecules built from amino acids, that in turn influence host-microbe interactions. Understanding the mechanisms governing the relatively simple symbiotic system between plants and microbes may provide key insights into host-bacteria relationships in more complex systems like humans.

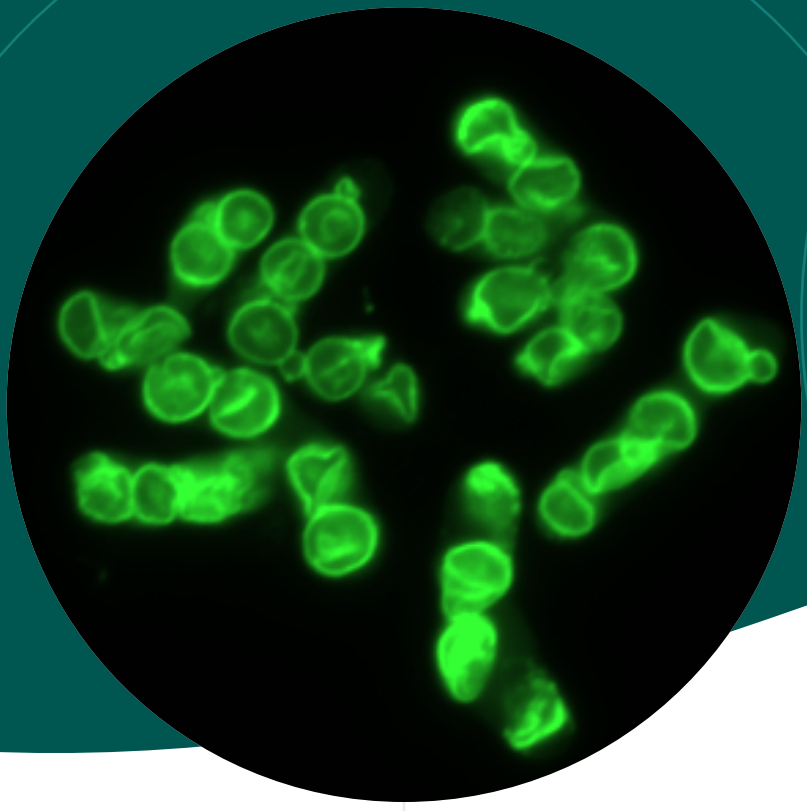
Neşet Özel, Ph.D.

From New York University, Özel, a neuroscientist, will join the Stowers Institute as an Assistant Investigator in January 2024. His research focuses on uncovering brain development by integrating developmental neurobiology, systems biology, and gene regulation studies. This multidisciplinary approach investigates the formation of complex neuronal circuitry in the brains of the fruit fly, *Drosophila melanogaster*, expanding the current understanding of brain cell identity and yielding insights into our ability to predictively alter neuronal identity and connectivity, ultimately leading to improved neuronal cell replacement therapy applications.

Ameya Mashruwala, Ph.D.

Also in January 2024, Mashruwala will join the Stowers Institute as an Assistant Investigator. Arriving from Princeton University, the Mashruwala Lab will study the properties of bacterial communities, including those that are responsible for cholera. Bacteria engage in fascinating social behaviors that enable them to establish communities and to participate in intentionally regulated cell death for collective community maintenance. While regulated cell death in multicellular organisms is a well understood process for development and regeneration, this feature in bacteria remains a mystery. Understanding the fundamental principles through which bacteria work together may reveal answers as well as shape the design of new classes of antibiotics to potentially combat cholera and other infectious diseases.

Neşet Özel, Ph.D., Siva Sankari, Ph.D., and Ameya Mashruwala, Ph.D.



A culture of yeast spores

Research Highlights

Survival strategy of selfish genes

PUBLISHED ON DECEMBER 7, 2022, IN *PLOS GENETICS*

Killer meiotic drivers are selfish genes that not only bias their transmission to the next generation but destroy offspring that do not inherit them. Nicole Nuckolls, Ph.D., and Ananya Srinivasa, Ph.D., from the lab of SaraH Zanders, Ph.D., led research revealing the mechanism through which a selfish gene in yeast has persisted for over 100 million years.

The gene, *wtf4*, encodes a protein that poisons all spores—yeast's equivalent of eggs and sperm—in addition to a very similar protein, the antidote, that rescues only those offspring with the *wtf4* allele. Collective and collaborative advancement on understanding drive may one day lead to the eradication of pest populations that harm crops or even humans in the case of vector borne diseases.

Mexican tetra fish, *Astyanax mexicanus*: morphological differences between surface-dwelling river fish (back) compared with cavefish (front)

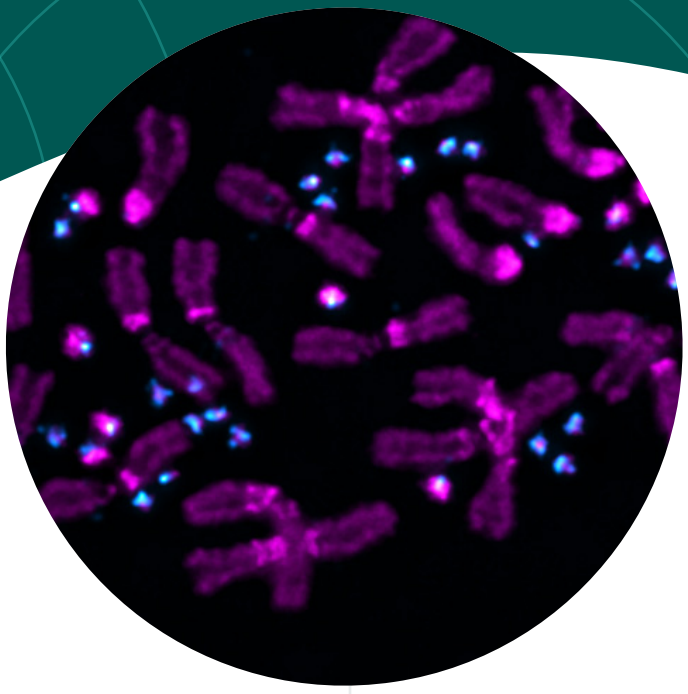
Surprising stamina of couch potato cavefish

PUBLISHED IN *PNAS* ON JANUARY 24, 2023

When Mexican tetra river fish flooded into underground caves 160,000 years ago, they independently and uniquely adapted unusual metabolic mechanisms to exploit their new feast or famine environments to survive and thrive.

In the absence of light and predators, cavefish display "couch potato" body types with high levels of fat and blood sugar. However, under stress, cavefish can swim just as fast as their river fish cousins, and for prolonged time periods.

Research led by Luke Olsen, Ph.D., in the lab of Nicolas Rohner, Ph.D., found that cavefish muscle metabolism had undergone genetic reprogramming. Their unexpected endurance is due to a switch in the way glycogen is stored and utilized, potentially shedding light on how humans may adapt to increasing inactivity on millennial timescales. These findings may lead to insights on conditions like diabetes, heart disease, and stroke. •



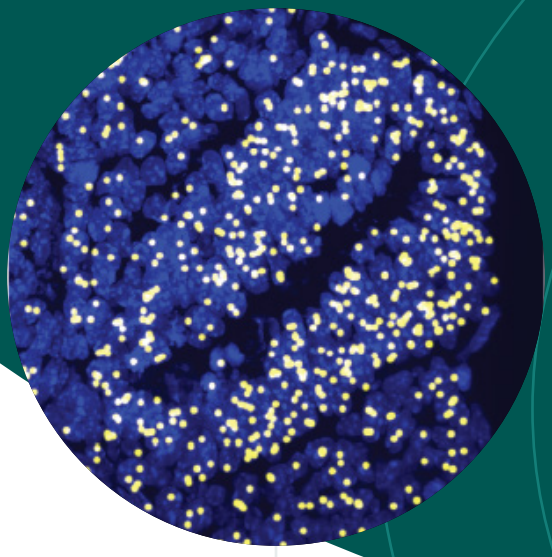
Chromosomes of the *Drosophila melanogaster* fruit fly

Origin and dynamics of contemporary chromosomes

PUBLISHED MAY 4, 2023, IN *CURRENT BIOLOGY*

The recent emergence of an extra chromosome in fruit flies can be correlated with similar kinds that arise in humans. These chromosomes are associated with certain therapy-resistant cancers and infertility. Stacey Hanlon, Ph.D., in the lab of Scott Hawley, Ph.D., led a study that uncovered the function and dynamics of the extra fruit fly chromosome, barely 20 years old, providing an ideal system for studying not only how the chromosomes arise but also how they may provide insight into more effective cancer and infertility treatments.

"Being able to understand how extra or supernumerary chromosomes arise and what their structures are can potentially illuminate their vulnerabilities," said Hawley. •



A mouse tissue neural tube cross-section showing Hoxb gene expression

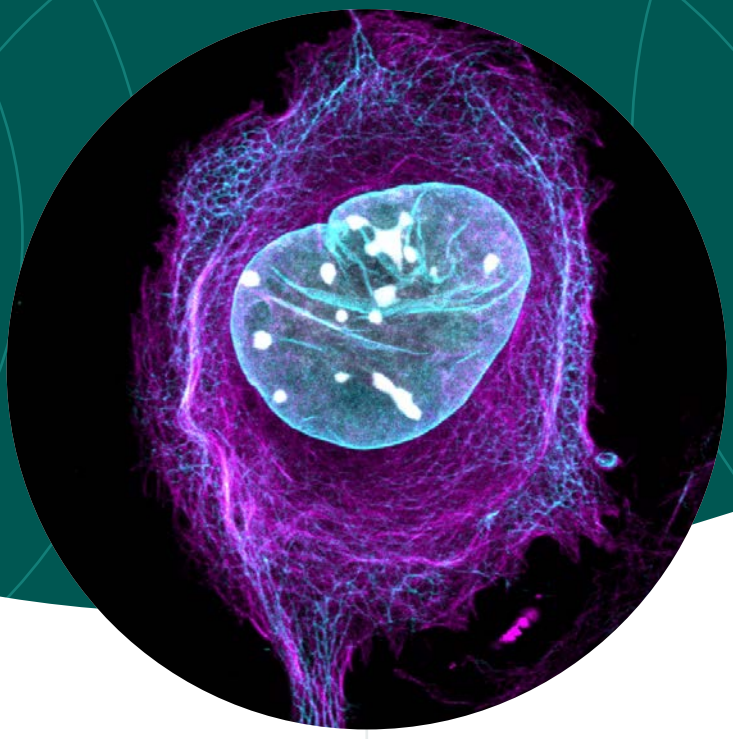
Gene regulation in time and space

PUBLISHED IN *DEVELOPMENT* ON MAY 24, 2023

Animal body parts are built in a specific order determined by the linear location of *hox* genes—evolutionarily conserved, master regulators of an organism's body plan—along a chromosome. However, regulatory sequences of DNA that precisely control expression of these genes are frequently far away.

In collaboration with multiple Technology Center members, Zainab Afzal, Ph.D., led research in the lab of Robb Krumlauf, Ph.D., illuminating the dynamics and cooperativity of regulatory elements that place them in proximity of and resolve the regulation of their target genes. Unraveling this is vital for understanding animal development, disease, and evolution.

"It may not matter exactly where a regulatory element is on a chromosome, but how it interacts with target genes in time and space to build a body is really important," said Krumlauf. •



Mouse trophoblast giant cell within placenta

Importance of the placenta

PUBLISHED IN *DEVELOPMENT* ON JUNE 6, 2023

The placenta is a vital organ during pregnancy that both protects the developing fetus and facilitates hormone and nutrient exchange. Research led by Vijay Singh, Ph.D., in the lab of Jennifer Gerton, Ph.D., discovered that many cell types comprising the placenta are polyploid, meaning they have multiple copies of genomes. These large cell sizes enable them to form a physical barrier between mom and baby.

Because the placenta can sometimes lead to disease in a baby, understanding its function is paramount. Insights from this study on mice may help inform scientists and clinicians how the placenta supports healthy human pregnancies. •

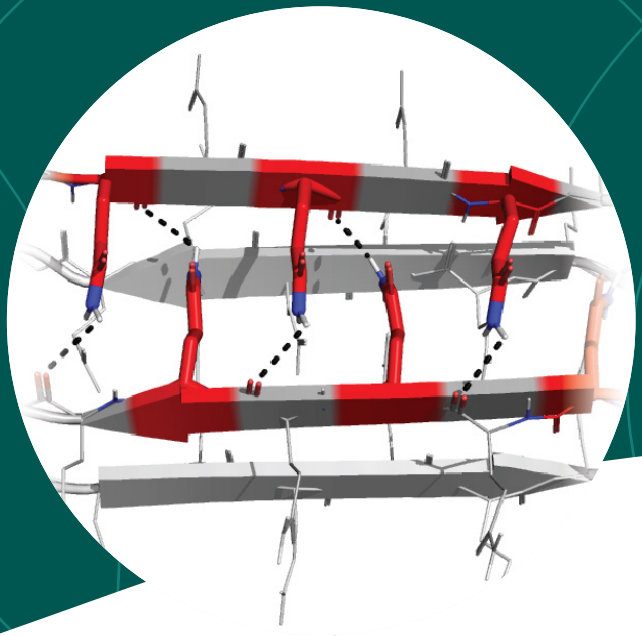


Illustration of the initiating structure of the amyloid implicated in Huntington's disease

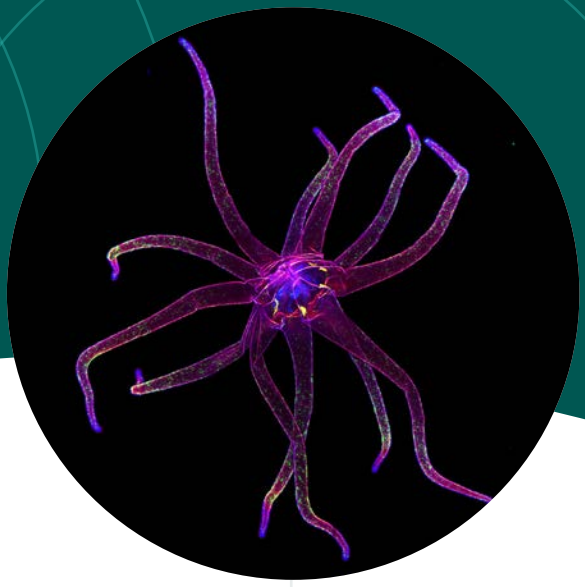
Uncovering the heart of Huntington's

PUBLISHED ON JUNE 13, 2023, IN *ELIFE*

The start of amyloid formation—protein aggregations that accumulate in the brain—implicated in neurodegenerative diseases like Huntington's and Alzheimer's has remained mysterious. So too have effective therapeutic treatments.

Tej Kandola, Ph.D., and Shriram Venkatesan, Ph.D., from the lab of Randal Halfmann, Ph.D., through a thorough systematic analysis of protein sequence variants, have deduced the initial Huntington's amyloid structure called the nucleus. Finding the first link in the chain for this 30-year-old problem reveals not just how Huntington's starts but also indicates a novel treatment: Prevent the nucleus from ever forming.

"The emerging paradigm is that everything follows from a single event, a spontaneous change in protein shape," said Halfmann. "That event ignites the chain reaction for amyloids that kill cells and may provide critical insight into how amyloids cause disease." •



Sea anemone, *Nematostella vectensis* displaying body segmentation and tentacle development

The time machine: From sea anemones to humans

PUBLISHED IN *CURRENT BIOLOGY* ON JUNE 13, 2023

Humans and sea anemones are drastically different in appearance. Research led by Shuonan He, Ph.D., from the lab of Matt Gibson, Ph.D., uncovered a common genetic toolkit driving development despite obvious disparities in body plan.

Cnidarians are pre-bilaterian—without a left and right side. During development, however, sea anemones not only have internal bilateral symmetry but were also found to use genes conserved throughout evolution that direct developing body segments along a gradient. These same programs operate in advanced bilateral organisms including humans.

"Comparing the logic of sea anemone and vertebrate development allows us to extrapolate hundreds of millions of years back in time to understand how animals likely developed," said Gibson. •

Training the next generation

Stowers Graduate School celebrates graduation

Discovery and innovation are only as powerful as our effort to train, prepare, and inspire the next generation to pursue science. The Stowers Institute is dedicated to fostering emerging scientists toward a future in biological research.

Eleven years after its founding, in May 2023, The Graduate School of the Stowers Institute for Medical Research held its first in-person graduation ceremony since 2019. The ceremony celebrated 23 predoctoral researchers' successful completion of their Ph.D. program requirements. Fourteen individuals who earned their degree over the past three years were in attendance, along with friends, families, and the faculty members who mentored them along the way.

Stowers Graduate School President Betty Drees, M.D., addressed the graduates and members of the Institute along with remarks from Dean Matt Gibson, Ph.D., Graduate Joaquín Navajas Acedo, Ph.D., and Board Member Nipam Patel, Ph.D. Many graduates are now continuing their scientific discovery at institutions including Harvard, the Mayo Clinic, University of Pennsylvania, Northwestern University, and Rockefeller University.

ENVISIONING A FUTURE

Welcoming the Newest Class of Predocs

THE 2023-2024 PREDOCTORAL RESEARCH CLASS

FRONT ROW (LEFT TO RIGHT)

Kelsey Scott
University of California, Santa Barbara

Erika Pinto
Pontifical Catholic University of Ecuador and Technical Particular University of Loja

Francisco Guerra Garcia
Pablo de Olavide University

MIDDLE ROW (LEFT TO RIGHT)

Fahad Kamulegeya
Makerere University

Graciela Monfort Anez
Pennsylvania State University

Yuri Iwamura
Nara Women's University and Kyoto University

Hannah Kimbrough
Truman State University

BACK ROW (LEFT TO RIGHT)

Wenhao Song
Tsinghua University

Siddharth Kurne
Indian Institute of Science Education and Research, Thiruvananthapuram

Samuel Campbell
University of Kansas

Logan Sabin
University of Missouri-Kansas City

Brandon Fagen
Harding University

In August 2023, the Stowers Graduate School welcomed 12 new predoctoral researchers into its Ph.D. program. This program is designed to provide early-career researchers with invaluable training and immersive experiences that will refine their skills, expand their intellectual horizons, and guide them into becoming accomplished scientists.

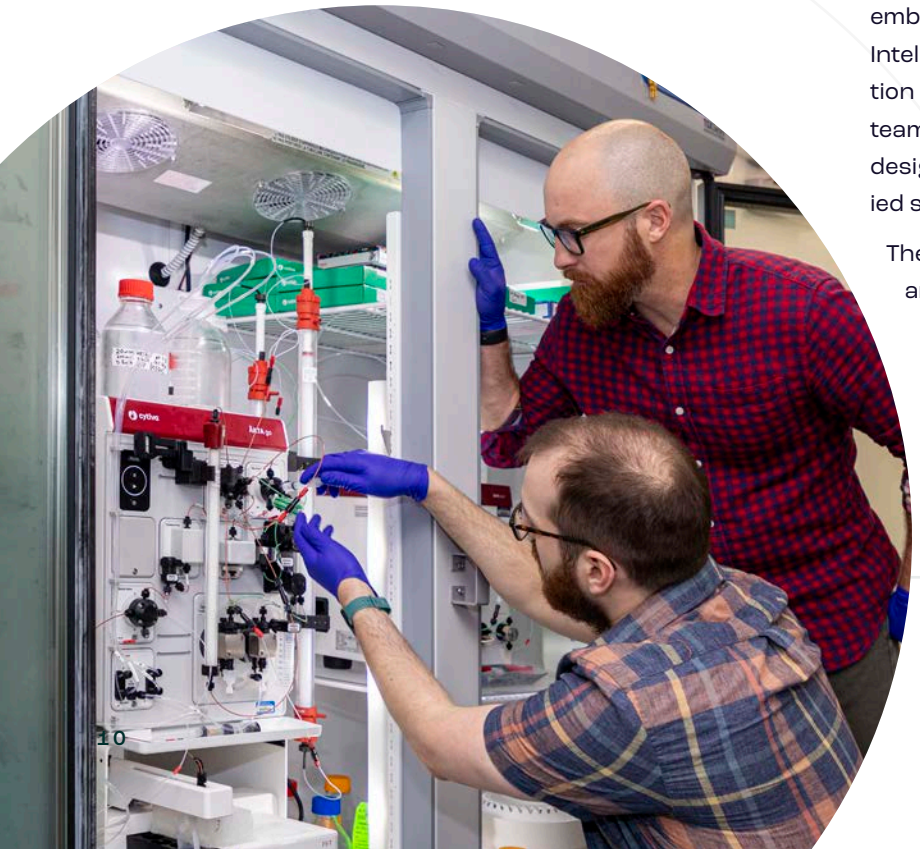
At the heart of the program lies a strong emphasis on cultivating critical thinking and fostering experimental expertise. These individuals will be challenged to identify a novel and significant biological question that will guide their intellectual explorations for the next several years.

Throughout this journey, these researchers will be mentored by some of the most distinguished scientists in the world and will have unrestricted access to technologies and state-of-the-art instrumentation to help propel them to the forefront of groundbreaking science. •

Innovation

New Technology Center enhances protein research

The Custom Protein Resources Technology Center was first established in 2022 and expanded in 2023 to help Stowers scientists accelerate their research involving proteins, the molecules critical for cellular function and life. Proteins play crucial roles within every cell: They facilitate chemical reactions like metabolism, provide structural support, and help transmit signals that coordinate vital biological processes such as gene expression.

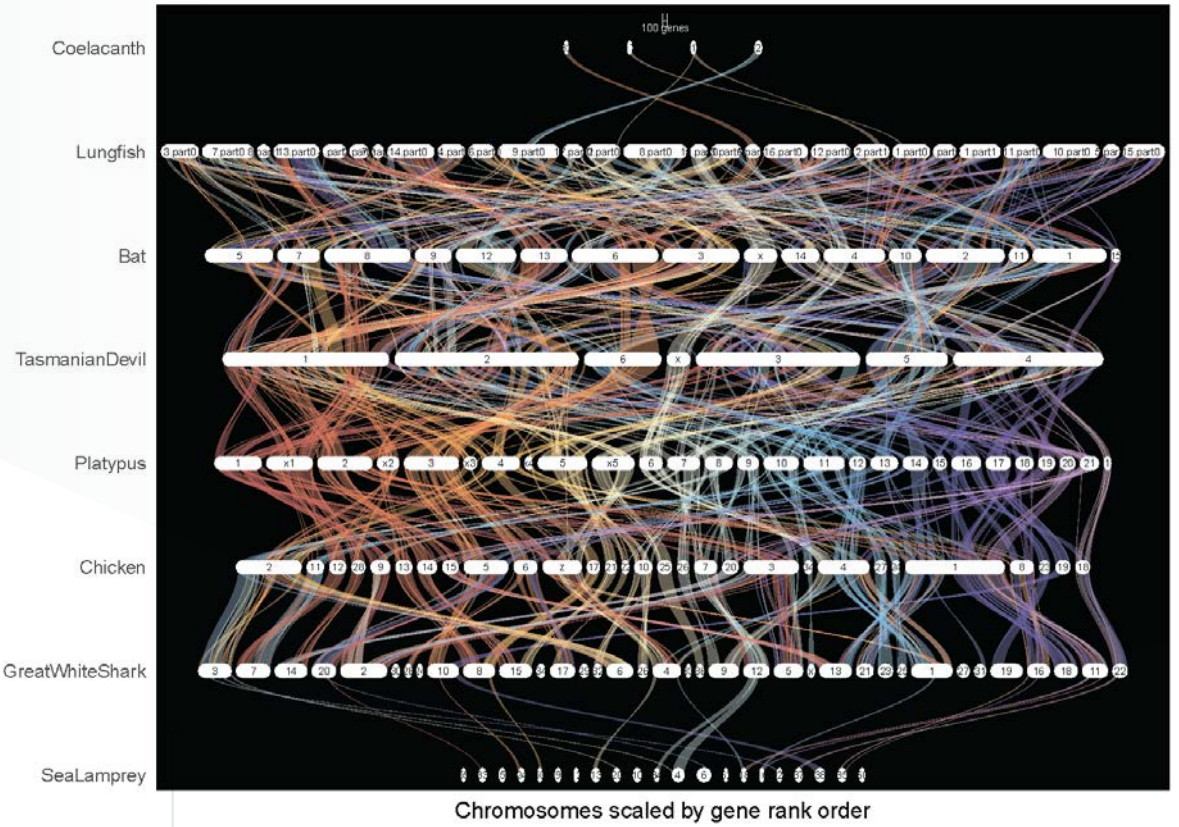


The newer team is comprised of biochemists and structural biologists who specialize in producing, isolating, and characterizing proteins from the complex mixture of cellular components. They can engineer proteins tailored for specific research inquiries and offer diverse courses, consultations, and training opportunities centered on protein isolation and characterization.

Through close collaboration with the Big Data and AI Technology Center, Custom Protein Resources has embraced AlphaFold and RFDiffusion, new Artificial Intelligence-based methods to interrogate the connection between structure and function of proteins. The team uses these tools to help researchers rationally design proteins, investigate proteins from understudied species, and even develop entirely new proteins.

The Stowers Institute has invested in personnel and instrumentation to build the center's capacity to facilitate research needs. Custom Protein Resources now houses a range of protein isolation and characterization instruments and has expanded its staff; the team is committed to translating advancements in protein-based research for Stowers scientists.

Members of Custom Protein Resources preparing protein chromatography equipment



An example of data output from the high performance computing cluster showing chromosome comparisons for various species

Computational biology receives boost

Scaling computational processes in biology like protein structure prediction and image analysis from running one at a time to running thousands at a time is key to analyzing and developing predictive models to better understand biological diversity.

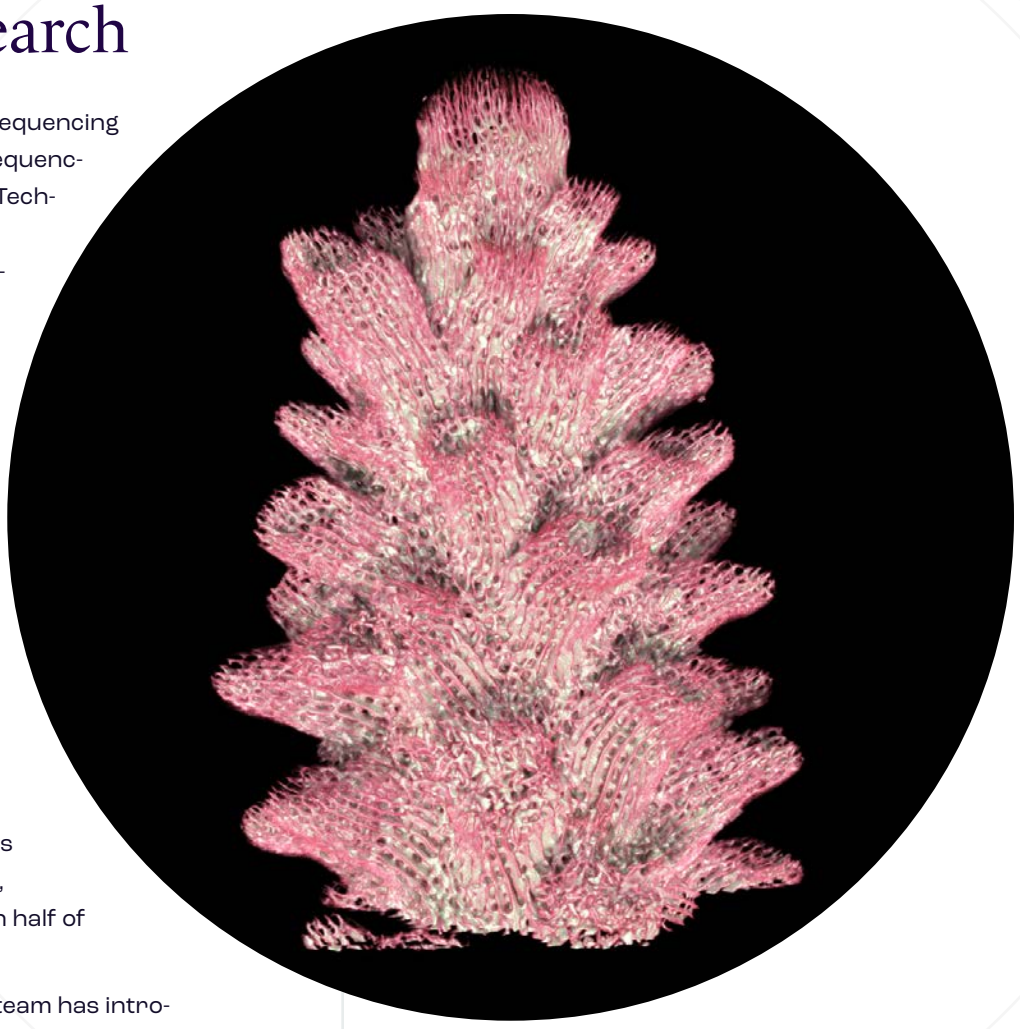
The Stowers Institute made a significant investment toward high performance computing by establishing a flexible, centralized computational cluster—many connected computers performing the same task in tandem—to enable efficient AI, interactive analysis, and traditional scaled computing tasks.

The new cluster effort is more of a shifting paradigm in how biologists use high performance computing for their work. Users can test novel computational ideas while using shared resources compatible with the rapid pace of software development, adapt to challenging traditional small-scale problems, and respond to the new and ever-changing landscape of computational biology. •

New Technology Center instruments advance research

The field of next-generation sequencing is rapidly evolving, and the Sequencing and Discovery Genomics Technology Center acquired two new state-of-the-art sequencing platforms in 2023: AVITI from Element Biosciences and the G4 from Singular Genomics.

The G4 sequencer enables multiple projects to process independently at the same time, providing quick and cost-effective results for projects with smaller data requirements. The AVITI sequencer utilizes a unique chemistry that lowers the amount of expensive reagents needed for a sequencing run, reducing the cost to less than half of previous technology.



MicroCT image of coral skeleton

Additionally, the Sequencing team has introduced the Biomek i7 liquid handling robot to automate workflows, reducing reaction setup time and improving reproducibility. These additions enhance capabilities and increase efficiency for researchers at the Institute.

The Electron and Light Microscopy Technology Center added a new microCT instrument to its imaging arsenal. The SKYSCAN 1272 allows researchers to image and reconstruct in three dimensions the bones and soft tissues of animals like fish and mice.

Convening Power

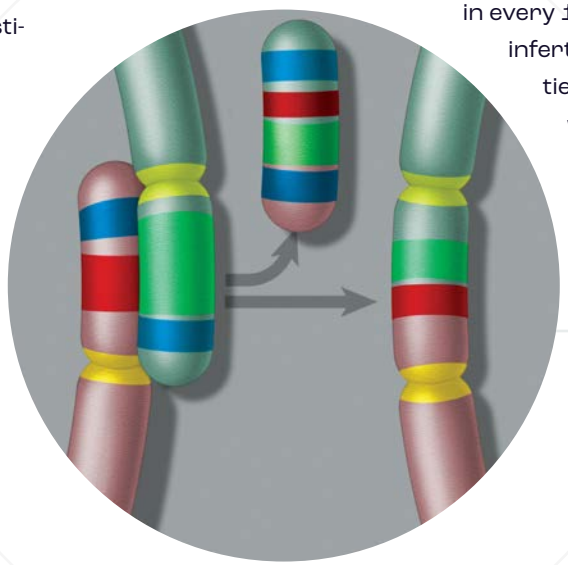
Curiosity and collaboration propel research

The Human Genome Project—the complete sequencing of an individual genome—was a momentous achievement in modern biology. Yet, to uncover what underlies our individuality, along with our similarities, a comprehensive understanding of human genetics requires a comparative approach from diverse datasets.

This is where the Human Pangenome Reference Consortium enters the picture. Stowers Investigator Jennifer Gerton, Ph.D., and her team, in collaboration with researchers from the National Human Genome Institute, the Institute of Genetics and Biophysics at the Italian National Research Council, and the University of Tennessee Health Science Center, investigated natural genetic variation between 94 human genomes.

Gerton said, "By analyzing nearly 100 complete human genomes representing diverse geographic backgrounds, our team aims to unravel the intricacies of human-to-human genetic variations."

During analysis of the assembled genomes, researchers uncovered the mechanism behind the formation of a specific type of chromosomal abnormality called Robertsonian translocations. In this anomaly, a fragment of one chromosome breaks off and becomes fused to another chromosome. Robertsonian translocations, which occur in approximately one in every 1,000 individuals, contribute to infertility and genomic abnormalities, including those associated with Down syndrome. Despite its prevalence, the molecular basis underlying this type of translocation has remained elusive until now.



Graphical illustration of a chromosomal abnormality called Robertsonian translocation

Alejandro Sánchez Alvarado, Ph.D., gives Kate the Chemist a tour of the Stowers planaria facility.

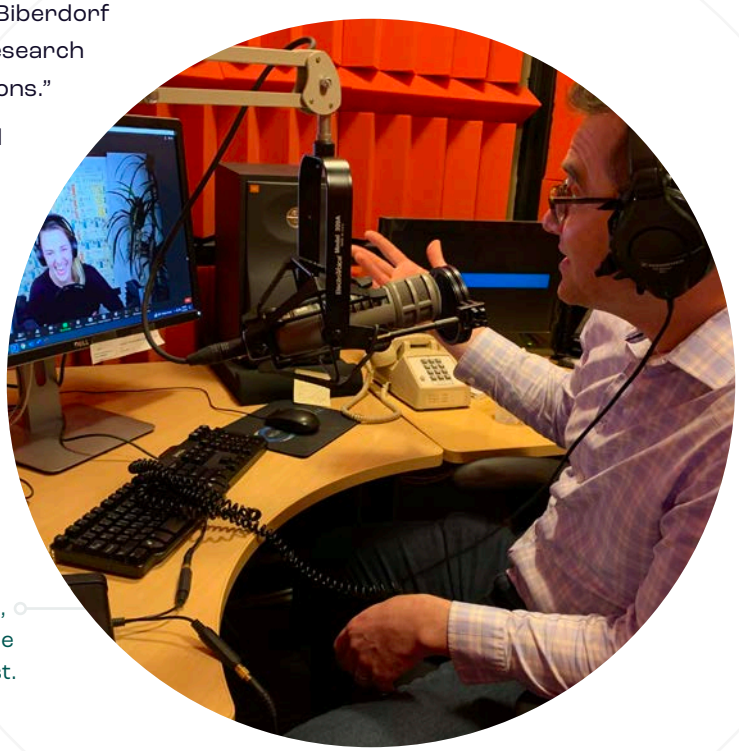
Stowers Institute and KCUR launch new podcast

The Stowers Institute, in collaboration with KCUR-FM, Kansas City's NPR affiliate, launched Seeking a Scientist, a podcast that celebrates the wonders of science. Hosted by Kate Biberdorf, Ph.D., also known as Kate the Chemist, this podcast taps leading scientists, including some from the Institute, who delve into pressing topics such as aging, disease, and climate change.

Seeking a Scientist aims to demystify science and provide educational content to listeners in the Kansas City region and beyond. Biberdorf said, "We call on rockstar experts to expand on their research and share real insights that explain life's biggest questions."

The inaugural episode, titled "Halting Aging," premiered in April and featured Alejandro Sánchez Alvarado, Ph.D., President and Chief Scientific Officer of the Stowers Institute; Nir Barzilai, Ph.D., Director of the Institute for Aging Research at the Albert Einstein College of Medicine; and David Sinclair, Ph.D., a genetics professor at Harvard and author of the book Lifespan: Why We Age and Why We Don't Have To.

All six episodes of the podcast are available on podcast platforms and SeekingAScientist.org.



Associate Investigator Randal Halfmann, Ph.D., is interviewed by Kate the Chemist for the podcast Seeking a Scientist.

Workshop teaches new methods

Scientists from around the world gathered at the Stowers Institute last winter for the Planarian Transgenesis Workshop. Funded by the National Science Foundation's Enabling Discovery through Genomics program, the workshop taught researchers how to insert a reporter gene—a nucleic acid sequence that can "report" or indicate that a transplantation method is working—into a live worm and observed cells generating the reporter protein in real-time.

From a scientific perspective, investigating and perfecting this research technique within the whole-body regenerating planarian flatworm, *Schmidtea mediterranea*, could provide scientists with powerful tools to understand regenerative processes at unprecedented resolution. Uncovering primary principles at the molecular and cellular level may allow the development of approaches to induce regeneration in other organisms, including humans.

"This workshop is an example of best practices in a scientific community—sharing key methods, reagents, and technologies," said Alejandro Sánchez Alvarado, Ph.D., whose lab hosted the workshop. Conceived in part by a former postdoctoral researcher in the Sánchez Alvarado Lab, the workshop brought together scientists from 20 institutions spanning three continents.

> "This workshop is an example of best practices in a scientific community—sharing key methods, reagents, and technologies."
>
> **Alejandro Sánchez Alvarado, Ph.D.**

On Campus

"Bringing music into our lives and our community at Stowers is a joyous occasion."

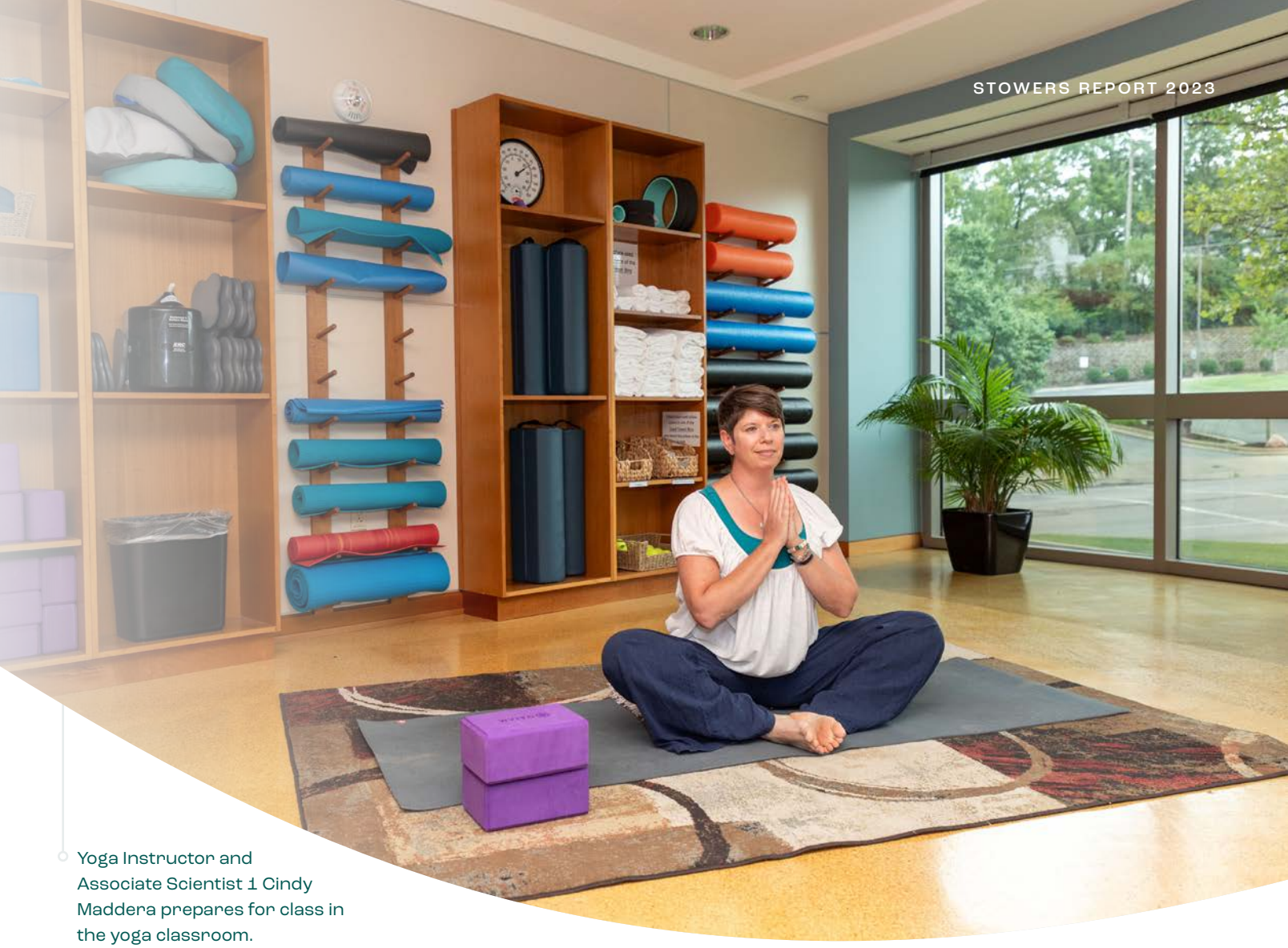
Alejandro Sánchez Alvarado, Ph.D.

The joy of music

"Music hath charms to soothe a savage breast." A famous line from the 1697 play The Mourning Bride, encapsulates the profound impact of music in relieving stress, uplifting moods, and cultivating happiness and joy.

This year, the Stowers Office of Scientific Leadership sponsored a special concert series called "Experiments in Sound." The series showcased three spring performances by the newEar Contemporary Chamber Ensemble, featuring innovative musical compositions by contemporary living composers. Stowers members and their guests were invited to attend the hour-long performances.

"Bringing music into our lives and our community at Stowers is a joyous occasion," said President and Chief Scientific Officer Alejandro Sánchez Alvarado.



Yoga Instructor and Associate Scientist 1 Cindy Maddera prepares for class in the yoga classroom.

Wellness programs expanded

Multiple studies have shown that healthy employees have a better quality of life, increased work productivity, and lower risk of disease and illness. The Stowers Institute's expanded Wellness department aims to support and enrich the well-being of Stowers members with a wide spectrum of programs focused on movement, nutrition, preventative care, mental health, and education.

In addition to traditional offerings like annual vaccine clinics, on-site mammography, fitness classes, and chair massage, the Wellness team has broadened offerings to include more mental health and mindfulness initiatives, including meditation classes and designated rest and reflection spaces, mental health first aid training, and life and well-being coaching. Additionally, cooking classes and dietician services focus on educating members about the impact of food on overall well-being.

With this expansion of services and programs, the ultimate goal is to foster a healthy, balanced environment for Stowers members.

Stronger together

The Stowers Diversity, Equity, and Inclusion (DEI) Council is dedicated to cultivating an atmosphere of inclusivity and openness. Its primary objective is to eliminate barriers that hinder the sense of belonging among Stowers members while providing an environment that allows everyone to excel irrespective of their background, education, or life experiences.

Throughout the year, the DEI Council hosted or supported a variety of cultural celebrations including Holi, Asian, Asian American, and Pacific Islander Heritage Month, Hispanic Heritage Month, Juneteenth, and Pride Month. These events provide our members with opportunities to learn more about their colleagues and foster a deeper understanding and appreciation of different cultures.

The Council also organized educational events like a workshop designed to “turn well-meaning people into culturally competent champions equipped to create a more equitable, inclusive, and just world.” By actively fostering diversity, equity, and inclusion, the Stowers DEI Council is paving the way for a more cohesive and supportive community that values and respects the contributions of every individual.

Organizational Highlights

Investigator Emeritus program launched

Stowers Office of Scientific Leadership recently announced the launch of the Emeritus Investigator Program at the Institute. This program recognizes long-standing contributions and dedication of Stowers Investigators to the Institute.

Robb Krumlauf, Ph.D., and Scott Hawley, Ph.D., have accepted appointments as inaugural members of the program.

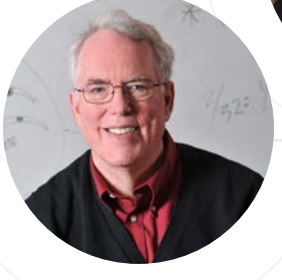
"We recognize Robb and Scott for their scientific and institutional leadership over their long, distinguished and productive scientific careers," said Stowers President and Chief Scientific Officer Alejandro Sánchez Alvarado.

Krumlauf joined the Stowers Institute in 2000 as an Investigator and the founding Scientific Director. He is a renowned developmental biologist known for his pioneering work on Hox genes, those responsible for the development of the animal body plan. Krumlauf joined the faculty of the Stowers Graduate School when it was established in 2012. In 2019, Krumlauf stepped away from his role as Scientific Director to devote his time to research.

Hawley joined the Institute as an Investigator in 2001. Hawley is an acclaimed researcher, particularly noted for his groundbreaking work on meiosis, the cell division process giving rise to eggs and sperm. In 2012, he became the founding Dean of the Stowers Graduate School, building a program that emphasizes hands-on scientific experience and critical thinking skills. In 2019, he became Dean Emeritus.

Among many honors and awards, Krumlauf and Hawley are members of the National Academy of Sciences and the American Academy of Arts and Sciences.

Robb Krumlauf, Ph.D.



Scott Hawley, Ph.D.

A sustainability approach like no other

Sustainability is often described as the ability to exist and develop today without compromising the future. It can encompass fair and transparent business conduct, diverse, equitable and inclusive workplace policies, sustainable investing, sustainable environmental practices, robust business ethics and more. To American Century Investments, the global asset management company founded by Jim Stowers, Jr., sustainability is doing good for the world while doing well for its clients.

"Sustainability isn't just something we practice; it is part of who we are as a company and how we view our role as global citizens," said Jonathan Thomas, President and CEO of American Century.

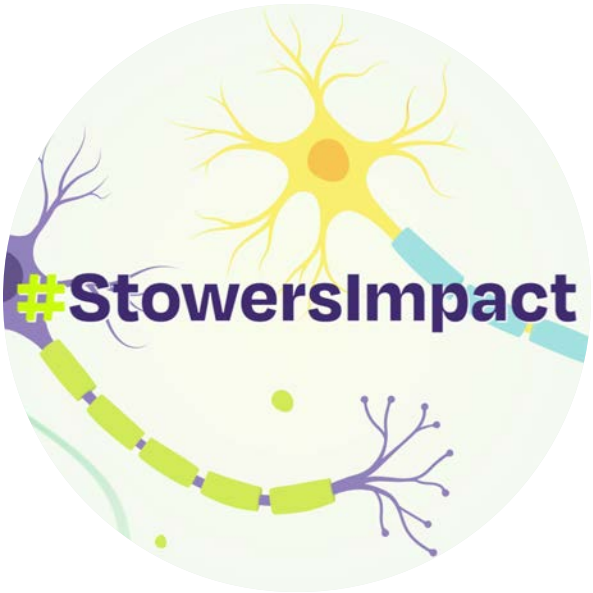
The firm's embodiment of sustainability is multifaceted. This goes beyond sustainable investing to encompass the highest standards for ethical business conduct, equitable workplace policies, programs promoting employee health and well-being, community involvement opportunities, and green office initiatives.

Arising from the ingenuity and generosity of Jim and Virginia Stowers, American Century also has a direct and long-term impact on improving human health. Jim and Virginia granted an equity stake in American Century to the Stowers Institute with more than 40 percent of its profits distributed annually to support the Institute's foundational biology research.

American Century's ownership structure is the only one like it in the industry, giving the firm its unique standing as an asset manager with an impact on well-being.

"Sustainability is truly in our genes," said Thomas.

Scientific Director Kausik Si, Ph.D. shows Jonathan Thomas a robot used to help maintain colonies of fruit flies.



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Making an impact and providing hope

From diabetes to neurodegeneration, infertility to regeneration, and aging to cancer, the profound impact of the Institute's foundational research is paving the way for future breakthroughs in how to alleviate and treat disease.

The Stowers Impact series explores the transformative potential of the Institute's research. An immersive collection of stories and videos is available on **stowers.org/impact**. By harnessing technologies that were unimaginable just a few years ago, researchers can now delve deeper into the intricate complexities of life. Gifts from the Institute's supporters help accelerate these life-changing discoveries and improve the future of human health, providing hope for better, healthier, and happier lives.

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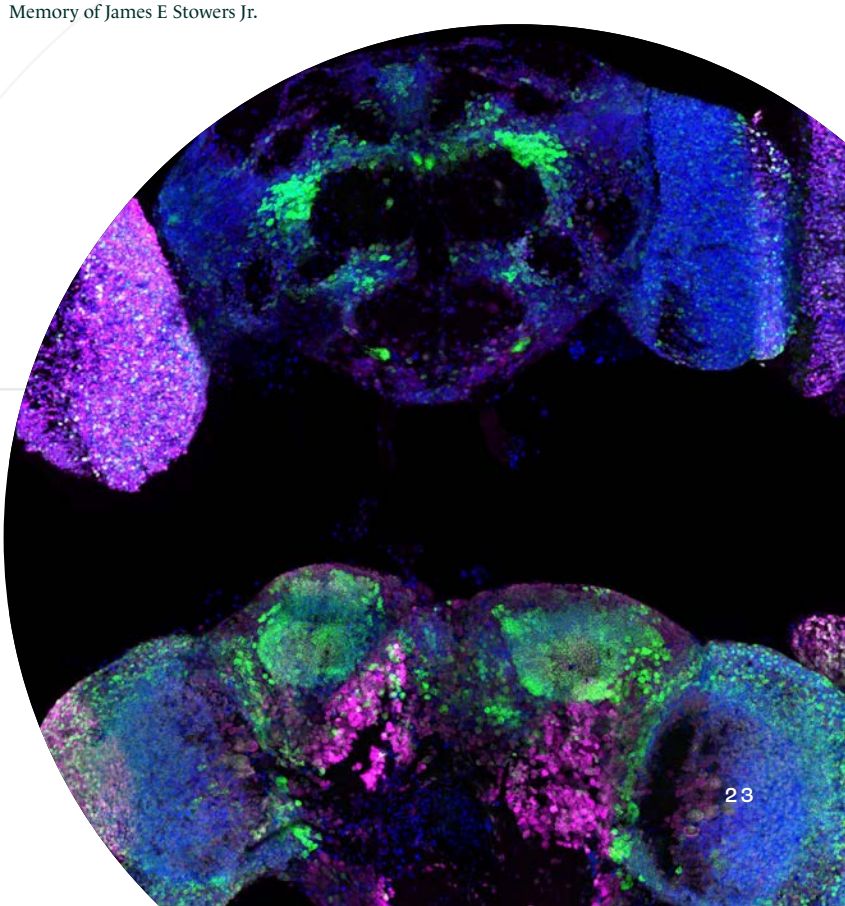
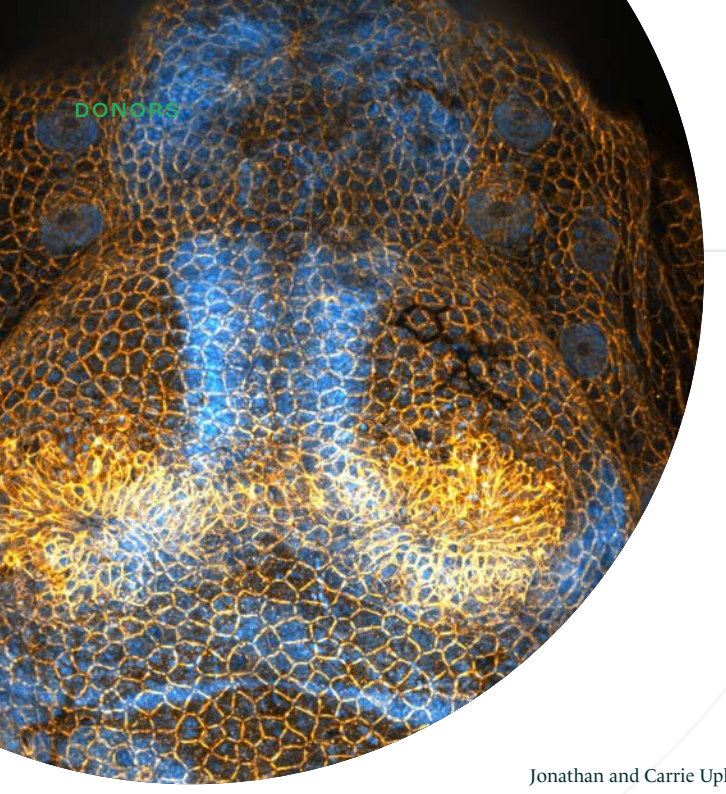


Anterior (top) and posterior (bottom) view of a fruit fly brain fluorescently labeled for two different RNA binding proteins shown in magenta and green. DNA is blue.

Image author: Stowers Graduate School Predoctoral Researcher Roberta Fiorino, Si Lab



A view of the head region of a 5-day old Mexican tetra river fish, *Astyanax mexicanus*. This fish larvae shows intercellular junctions (orange) and nuclei (blue) labeled with fluorescent markers.

Image author: Stowers Graduate School Predoctoral Researcher Fanning Xia, Rohner Lab

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Stowers members honored for 20 years of service

In October, the Stowers Institute recognized 49 members who had reached 20 years of service.

Congratulations to these members of the Stowers Institute on reaching this milestone of dedication and service.

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Charlene McCracken

1999
Berry Alexander

2000
Chad Harvey
Jeff Haug
Xi He
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Linheng Li
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Leanne Wiedemann

2001
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Jennifer Gerton
Christof Nolte
Rose Owens
Tari Parmely
Jamie Peterson
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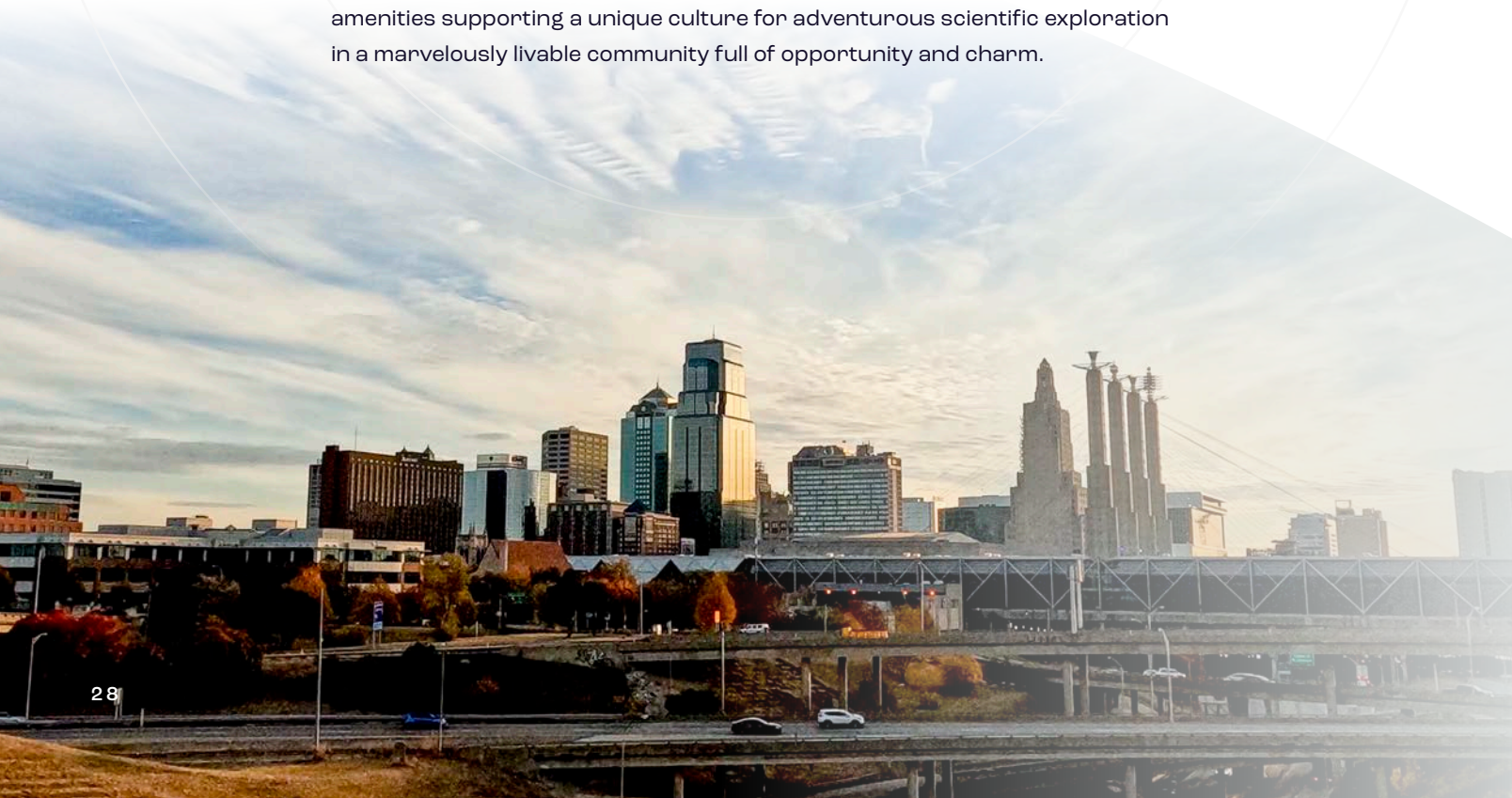
Erica Frazier
Cathy Lake
Carol Robinson
Shannon Scott
Chris Seidel
Tamaki Suganuma
Selene Swanson
Tony Torello
Jerry Workman
Judy Zimmerman

Behind the Science

The Stowers Institute is proudly located in America's heartland in Kansas City. It is the city where co-founder James E. "Jim" Stowers, Jr., was born, raised, and launched American Century Investments, which would enable him and his wife, Virginia, to make their audacious vision of a world-class biomedical research institute a tangible reality.

The greater Kansas City metropolitan area is where some of the brightest minds in science have planted roots and where many talented scientists have launched their careers.

The region has experienced explosive growth in the past decade and offers amenities supporting a unique culture for adventurous scientific exploration in a marvelously livable community full of opportunity and charm.



THE GREATER KANSAS CITY AREA BY THE NUMBERS

1 Rank in least congested major metros in the U.S.

4 Cities in the region named "Top 100 Best Places To Live in the U.S. Today" by Livability.com.

11 Professional sports teams in the area including football, baseball, soccer, hockey, and roller derby.

18 Counties spanning two states make up the Kansas City metropolitan area.

24 Minutes is the average commute time for the area.

25 Colleges and universities in the region produce approximately 31,000 students into the workforce each year.

38.2 Median age of the regional population.

71 Wineries, 74 breweries, and 25 distilleries in the area.

100+ Languages spoken in the region.

142.2 Decibels recorded on Sep. 29, 2014, at a Kansas City Chiefs game at Arrowhead Stadium, setting the Guinness World Record for the loudest crowd roar at a sports stadium.

276 Million dollars in economic impact from arts and culture organizations in the metropolitan region.

300 Life sciences companies operating in the region.

1,506 Parks in the metro area.

2,125 Miles of bikeways and trails in the region.

2,600,000 Population of the Greater Kansas City metropolitan area.

Stowers Institute™
for Medical Research

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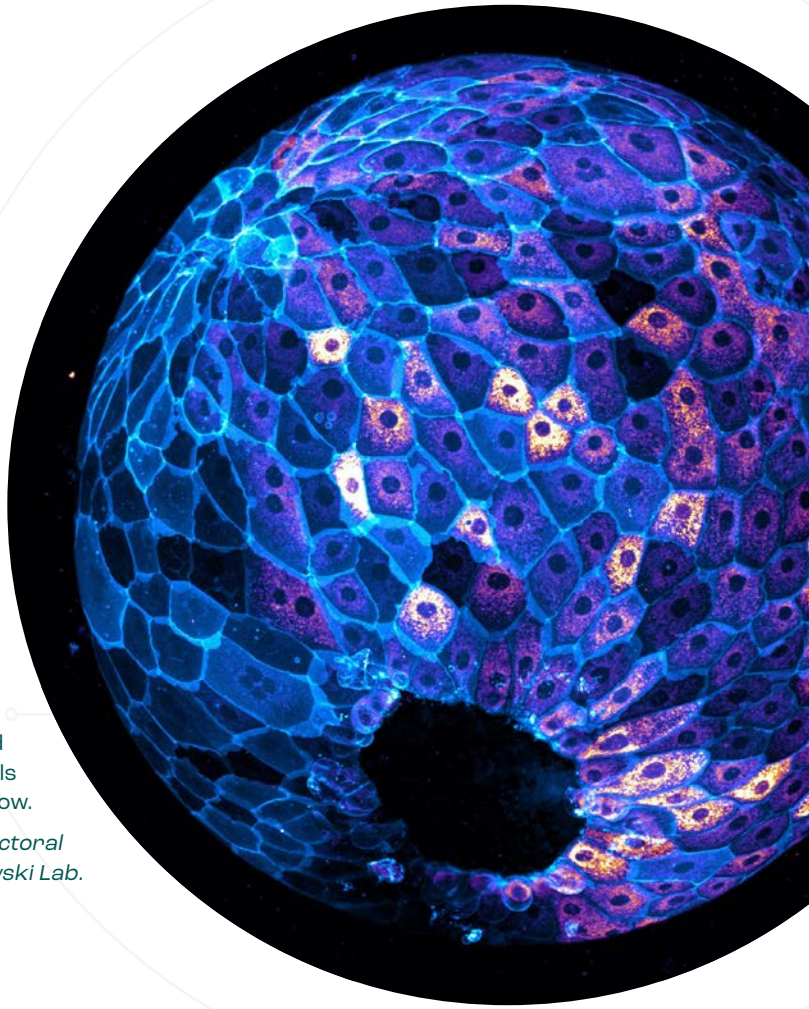

A zebrafish embryo 9 hours after fertilization. Cell membranes are visible in blue, and mitochondria – the organelles that give cells energy – are visible in purple and yellow.

Image author: Stowers Graduate School Predoctoral Researcher Julia Peloggia de Castro, Piotrowski Lab.

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.

FSC