FALL | 2022

WHERE CURES BEGIN.

InsideSalk

Find the right questions— you don't invent the answers, you reveal the answers.

— Jonas Salk

CONTENTS

ON THE COVER:

Jonas Salk, developer of the first safe and effective polio vaccine, founded the Salk Institute for Biological Studies in 1960.

PRESIDENT'S LETTER

Dear Friends,

When someone mentions the Salk Institute, many people likely think of the scientific breakthroughs that have consistently emerged from our labs over the past six decades.

While for others, it may be the majestic, iconic research towers high atop a bluff overlooking the Pacific Ocean, and the Institute being one of the world's most renowned architectural sites.

And for still others, it's the people of Salk who make the Institute as a whole a special place.

I'll admit, when we had this discussion internally this summer, the answers to what makes Salk special were numerous. That's why, for me, the correct answer is all of these things and much more make Salk the truly unique and special place it is. From our exceptional history and visionary architectural design to the trailblazing scientists who have collaborated on big ideas and pursued answers to the very foundations of life over the last 60-plus years, every ingredient has made the Salk Institute unique among elite research institutions.

Sadly, we lost two of our trailblazing scientists in recent months: Distinguished Professor Emerita Ursula Bellugi and Professor Emeritus Walter Eckhart. I hope you enjoy the tribute to Ursula in this issue of *Inside Salk*; the next issue will feature Walter. Both helped shape Salk into what it is today, and they will be missed.

In this issue we also take a deep dive into the elements that make the Institute so special and how these ingredients prime Salk for massive future success in the face of numerous formidable challenges facing people and the planet.

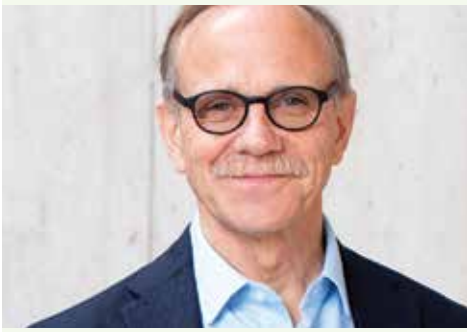
Additionally, Research Professor Margarita Behrens talks about her work toward understanding neural circuit formation and disruption. We also explore how Julie Auger, executive director of Research Operations, is shaping Salk's science through shared resources, and we detail how Postdoctoral Fellow Gaurav Mendiratta is using math to solve some of the hardest biological problems.

I would also be remiss if I didn't remind you that we are reaching the final deadline to take advantage of the tremendous generosity Joan and Irwin Jacobs have shown the Institute. As you'll remember, the Jacobs committed up to $100 million in matching funds to finance the Joan and Irwin Jacobs Science and Technology Center. We have until September 30, 2022, to raise $200 million in order to secure their $100 million gift. Please consider supporting Salk's Campaign and joining us for the next phase of our growth.

The future of Salk science is bright, as you will see in this issue. I want to take the opportunity to again thank you for your loyal and generous support as we blaze more trails of scientific discovery.

Sincerely,

Fred H. Gage
President



"From our exceptional history and visionary architectural design to the trailblazing scientists who have collaborated on big ideas and pursued answers to the very foundations of life over the last 60-plus years, every ingredient has made the Salk Institute unique among elite research institutions."

Salk welcomes four new leaders

Over the past few months, the Institute has welcomed four new leaders to the Salk community.

Professor Gerald Joyce was selected as Salk's new senior vice president and chief science officer, following the departure of Martin Hetzer; Marna Whittington was appointed Board chair, assuming the role from Daniel Lewis; Bryan Robinson was named vice president of External Relations to take over for the retiring Rebecca Newman; and Sue Bacino was appointed vice president of Human Resources.

GERALD JOYCE

Senior Vice President and Chief Science Officer

Joyce began his scientific career at Salk as a PhD student and postdoctoral scholar and returned as a faculty member in 2017. His research program focuses on the development of novel RNA and DNA enzymes and their potential application in clinical diagnostics and therapeutics. His work has led to the development of the first self-replicating RNA enzyme that is capable of exponential growth and evolution.

Joyce previously served as director of the Genomics Institute of the Novartis Research Foundation, dean of the faculty at Scripps Research, chair of the JASON scientific advisory group for US national security and member of the Technology Advisory Council of BP plc.

"I'm honored to serve Salk in this important role. I have a deep affection for the Institute, so this is truly special to me," Joyce says. "I'm not going to be focused on the 'chief' or 'officer' parts of 'chief science officer.' It is going to be all about the science. Our prime directive and the overarching goal of the Salk Institute is to produce high-impact science."

Joyce graduated with a BA from the University of Chicago in 1978 and both an MD and PhD from UC San Diego in 1984. He completed his postgraduate medical training at Mercy Hospital in San Diego and postdoctoral research training at the Salk Institute.

MARNA WHITTINGTON

Chair of the Board of Trustees

Whittington is the former CEO of Allianz Global Investors Capital and was elected as a Salk Trustee in 2005. She had served as vice-chair since 2016.

Whittington also served as chief operating officer of Allianz Global Investors, the parent company of Allianz Global Investors Capital. Prior to that, she was managing director and chief operating officer of Morgan Stanley Asset Management. Whittington also currently serves on the boards of Tower Hill School, Macy's Inc., the Philadelphia Contributionship (a company founded by Benjamin Franklin), Phillips 66 and Oaktree Capital Management.

"It is a privilege to be named chair of Salk's Board of Trustees," says Whittington. "I am honored to step into this role as we begin our five-year Campaign for the Future to expand our capabilities and advance science across the Institute. And I am proud to be a part of a Board that has a collective commitment to supporting Salk's esteemed faculty as they strive to find solutions to the most significant challenges impacting human health."

Whittington holds a master's degree and PhD from the University of Pittsburgh, both in quantitative methods, and a BA in mathematics from the University of Delaware.

BRYAN ROBINSON

Vice President of External Relations

Robinson joins Salk from The Jackson Laboratory, an independent, nonprofit biomedical research institution headquartered in Bar Harbor, Maine, where he served as the vice president for advancement and a senior member of the president's executive committee.

Prior to his role at The Jackson Laboratory, Robinson served as president of the UNCP Foundation and vice chancellor for advancement at The University of North Carolina at Pembroke. He served previously as the senior assistant vice president and interim vice president at the University of Louisville. Robinson was also a senior director of development and campaign planning at Indiana University and a state government appointee in Indiana.

"I feel honored and privileged to join this elite research institute," Robinson says. "I've seen myself how important education and science are, how transformative they can be to people's lives, and so I've spent my career working to support these efforts through philanthropy. There is so much opportunity here at Salk, with our strong leadership, Board of Trustees and External Relations team, as well as our new Campaign, to leverage all that's already been accomplished and build upon the Institute's outstanding history and reputation."

Robinson earned his undergraduate degree in pre-law studies and his master's degree in education administration at the University of Louisville. He earned a PhD in education and social change at Bellarmine University, during which time he completed field research at the University of Roehampton in London on the impact of poverty on child and youth development.

SUE BACINO

Vice President of Human Resources

Bacino joined Salk having most recently served as head of HR for a medical device company in Carlsbad. In that role—reporting to the CEO and serving as a key member of the leadership team—Bacino was responsible for the implementation of all HR-related processes and functions. Prior to that, she held the same position at the Genomics Institute of the Novartis Research Foundation, where she partnered with scientific leadership on recruiting, engaging and retaining talent.

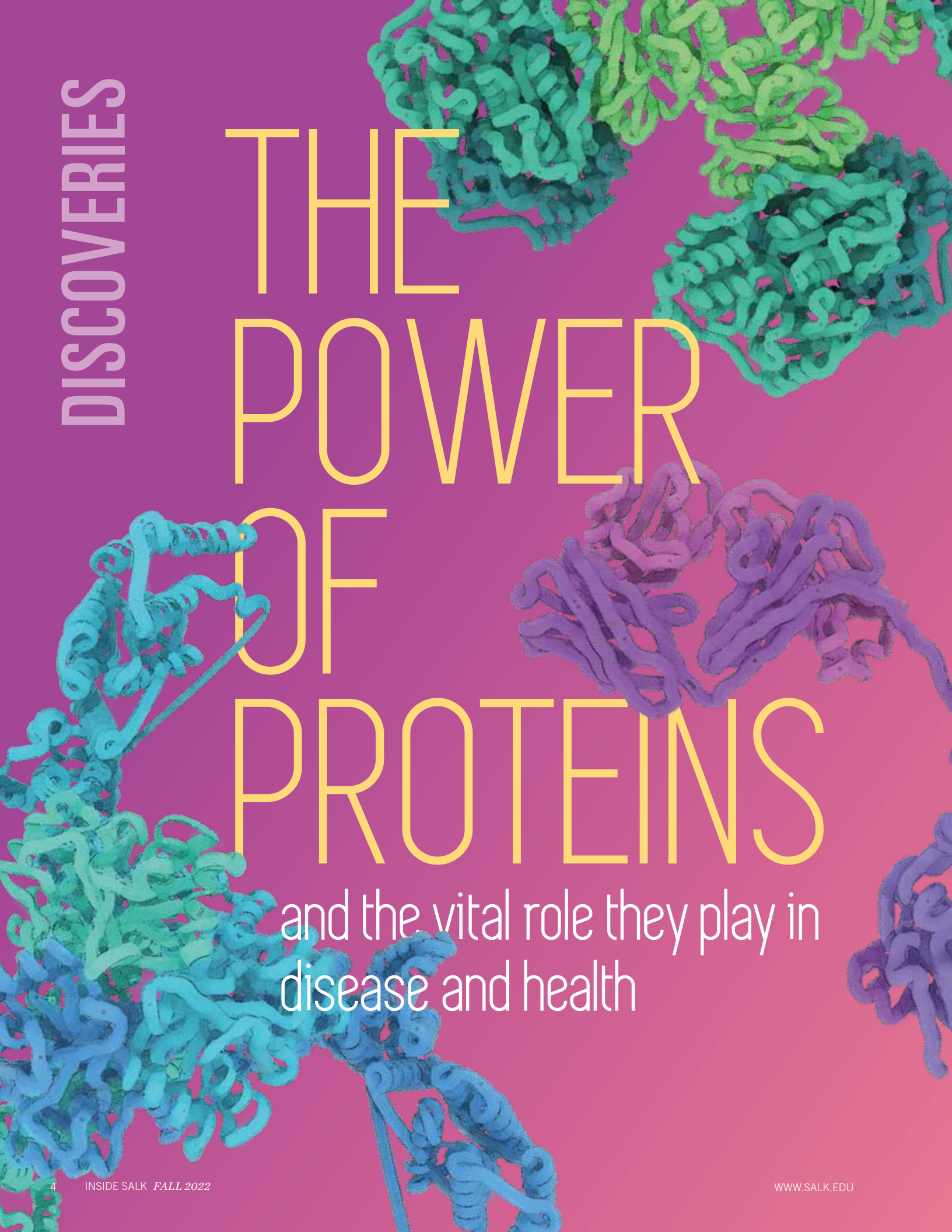
Bacino has also served as executive director of HR for Amylin Pharmaceuticals, and she held various leadership positions at Vical Incorporated before Amylin. Her experience beyond the med-tech field includes serving as vice president of HR for Father Joe's Villages and Breg, Inc.

"I'm honored to join the team at Salk," Bacino says. "While I am not a scientist, I am motivated to have a positive impact on this organization where the brightest human minds work to positively impact the human condition."

Bacino earned her BA degree from UC Davis and completed coursework in a Master of Administration program at San Diego State University.

THE POWER OF PROTEINS

and the vital role they play in disease and health



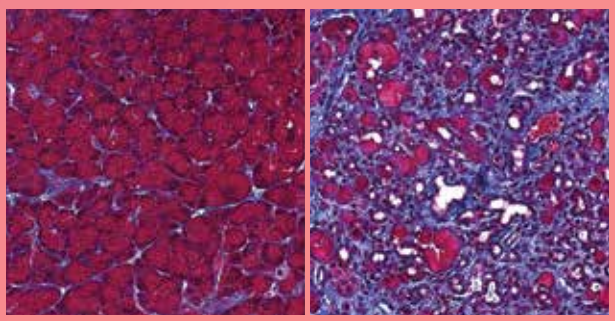
Proteins are complex molecules that bear the bulk of work within our cells. Made up of hundreds or thousands of smaller units known as amino acids, proteins form three-dimensional structures and perform a range of functions. For example, proteins support our immune response, speed up the rate of biochemical reactions, facilitate nutrient transport and synthesize hormones. They are also involved in many aspects of wound healing, tissue regeneration and nerve function. Scientists at Salk leverage the power of proteins to improve diagnostic and treatment options for a number of diseases, including cancer and Alzheimer's disease. We continue to build on this tradition as we explore new ways to examine how proteins behave.

GASTROENTEROLOGY
04/2022

The protein that keeps the pancreas from digesting itself

Every day, your pancreas produces about one cup of digestive juices, a mixture of molecules that can break down the food you eat. But if these powerful molecules become activated before they make their way to the gut, they can damage the pancreas itself—digesting the very cells that created them, leading to the painful inflammation known as pancreatitis and predisposing a person to pancreatic cancer. Now, Professor Ronald Evans, co-first author Tae Gyu Oh and colleagues have discovered that a protein called ERR gamma plays a crucial role in preventing pancreatic autodigestion in mice. What's more, they discovered that people with pancreatitis have lower levels of this protein in cells affected by inflammation.

From left: Annette Atkins, Weiwei Fan, Tae Gyu Oh, Ronald Evans, Ruth Yu and Michael Downes.



Left: Acinar cells (red) in a healthy pancreas. Right: Extensive pancreatic scarring (purple) when ERR gamma is lost from acinar cells.

The worm *Caenorhabditis elegans*.

"C. elegans are more sophisticated than we give them credit for. Their intestines sense a lack of food and report this to the brain. We believe these transcription factor movements are what guide the animal into making a risk-reward decision, like traversing an unpleasant barrier to get to food."

MOLLY MATTY

Why hungry worms take risks

Whether it's making rash decisions or feeling grumpy, hunger can make us think and act differently—"hangry," even. But little is known about how hunger signals in the gut communicate with the brain to change behavior. Associate Professor Sreekanth Chalasani, co-first author Molly Matty and colleagues are using worms as a model to examine the molecular underpinnings that help explain how hunger makes an organism sacrifice comfort and make risky decisions to get a meal. Their latest findings reveal that proteins in intestinal cells move dynamically to transmit signals about hunger, ultimately driving worms to cross toxic barriers to reach food. Similar mechanisms may also occur in humans and could explain how we prioritize basic needs over comfort.

From left: Sreekanth Chalasani and Molly Matty.

AN OCEAN IN YOUR BRAIN: INTERACTING BRAIN WAVES KEY TO HOW WE PROCESS INFORMATION

SCIENCE ADVANCES 04/2022

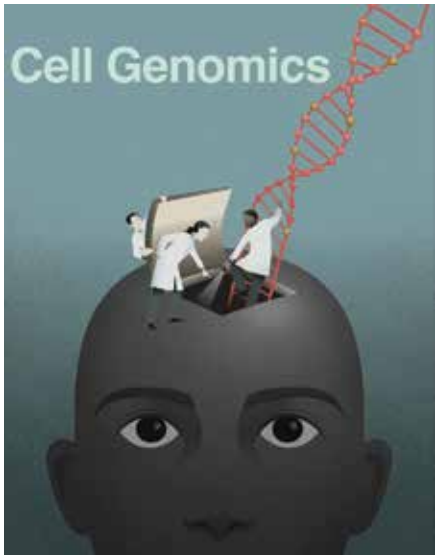
For years, the brain has been thought of as a biological computer that processes information through traditional circuits, whereby data zips straight from one cell to another. While that model is still accurate, a new study led by Professor Thomas Albright and Staff Scientist Sergei Gepshtein shows that there's also a second, very different way that the brain parses information: through the interactions of waves of neural activity. The findings will help researchers better understand how the brain processes information.

From left: Thomas Albright and Sergei Gepshtein.

"We've found that in some situations, brain activity is better described as an interaction of waves, which is similar to the description of light as a wave. Both views are needed for understanding the brain."

SERGEI GEPSHTEIN

NEUROSCIENCE



The journal's cover image depicts a new technology that can help researchers understand the inner workings of the human brain. Credit: *Cell Genomics*, Salk Institute and Scot Nicholls.

NEW TECHNOLOGY ENABLES AN UNPRECEDENTED GLIMPSE INSIDE SINGLE BRAIN CELLS

CELL GENOMICS 03/2022

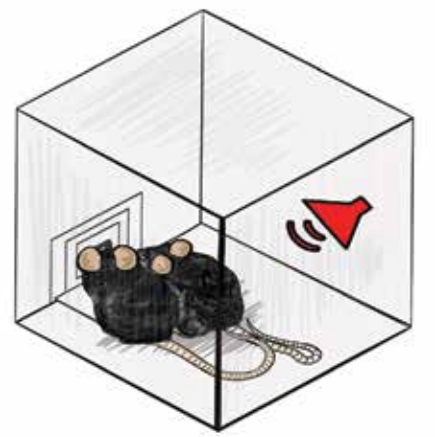
Professor Joseph Ecker and colleagues have developed a new genomic technology to simultaneously analyze the DNA, RNA and chromatin—a combination of DNA and protein—from a single cell. The method, which took five years to develop, is an important step forward for large collaborations where multiple teams are working simultaneously to classify thousands of new cell types. The new technology will help streamline analyses and provide an open-source cell catalog to better understand neurodegenerative diseases, such as Alzheimer's.

HOW THE BRAIN ENCODES SOCIAL RANK AND "WINNING MINDSET"

NATURE 03/2022

Most social animals, humans included, organize themselves into hierarchies that guide individual behavior. For instance, if you're reaching for the last piece of pizza at a party and you see another hand going for it at the same time, your next move probably depends both on how you feel and to whom the hand belongs. Your little sister—you might go ahead and grab the pizza. Your boss—you're likely to step back and give up the slice. But if you're hungry and feeling particularly confident, you might go for it. Professor Kay Tye, co-first authors Nancy Padilla-Coreano and Kanha Batra, and colleagues have made inroads in uncovering how mammalian brains encode social rank and use that information to shape our behaviors, such as whether to fight for that last pizza slice.

WATCH	www.salk.edu/tye202208



Mice that have formed a social hierarchy get placed in a box where they compete for a food reward. Salk scientists can use brain readouts to accurately predict which animal will win the reward and the social rank of the animal.

Kanha Batra and Kay Tye

Nancy Padilla-Coreano

CURRENT BIOLOGY 03/2022

C. elegans worm (right) escaping the predatory *P. pacificus* worm (left).

TINY WORMS MAKE COMPLEX DECISIONS, TOO

Whether it comes to foraging, defending a vital resource or seeking a mate, animals need to weigh options before picking a course of action. Scientists have spent decades trying to understand how animals make decisions by focusing on the brain cells and connections that might be involved. Associate Professor Sreekanth Chalasani and first author Kathleen Quach are taking a different approach—analyzing behavior, not neurons. They were surprised to find that worms can take multiple factors into account and choose between two different actions, despite having only 302 neurons compared to approximately 86 billion in humans. The findings provide a framework for understanding how decisions are made in more complex systems, such as humans.

Sreekanth Chalasani

Kathleen Quach

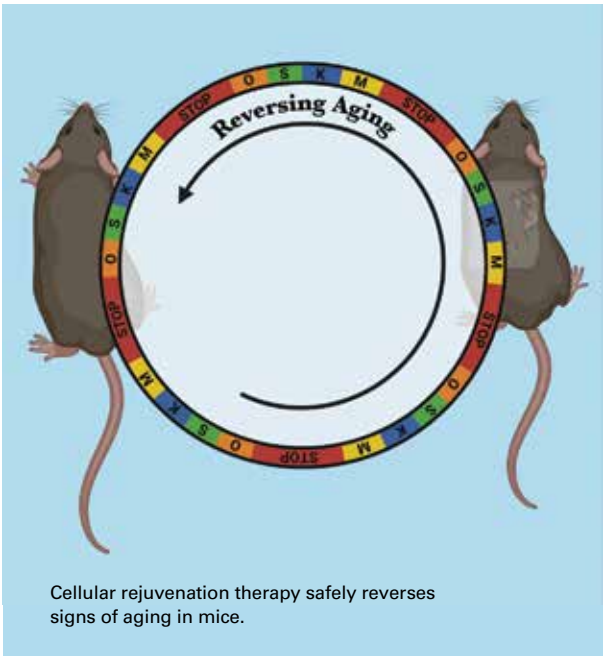
METABOLISM

HOW OBESITY CAN REWIRE THE IMMUNE SYSTEM AND THE RESPONSE TO IMMUNOTHERAPY—AND HOW TO CHANGE THAT

NATURE 03/2022

When mice with atopic dermatitis—a common type of allergic skin inflammation—are treated with drugs that target the immune system, their thickened, itchy skin generally heals quickly. Yet the same treatment in obese mice only worsens their skin, according to a study by Professor Ronald Evans, Associate Professor Ye Zheng and collaborators from Gladstone Institutes and UC San Francisco. Obesity changes the molecular underpinnings of allergic inflammation, both in mice and humans, the team found. Their study demonstrates how obesity can change the immune system and how available drugs might be able to improve health outcomes for people with obesity.

AGING



Cellular rejuvenation therapy safely reverses signs of aging in mice.

CELLULAR REJUVENATION THERAPY SAFELY REVERSES SIGNS OF AGING IN MICE

NATURE AGING 03/2022

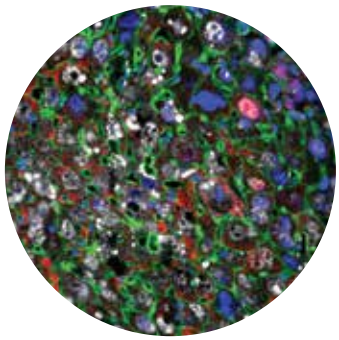
Age may be just a number, but it's a number that often carries unwanted side effects—from brittle bones and weaker muscles to increased risks of cardiovascular disease and cancer. In new research, Professor Juan Carlos Izpisua Belmonte and co-first author Pradeep Reddy, in collaboration with Genentech, a member of the Roche group, have shown that they can safely and effectively reverse the aging process in middle-aged and elderly mice by partially resetting their cells to more youthful states. This approach may provide the medical community with a new tool to restore tissue and overall health by improving cell function and resilience in conditions such as neurodegenerative diseases.

WATCH | www.salk.edu/belmonte202208

CELLULAR REGENERATION THERAPY RESTORES DAMAGED LIVER TISSUE FASTER THAN EVER

CELL REPORTS 04/2022

Mammals can't typically regenerate organs as efficiently as other vertebrates, such as fish and lizards. But now Professor Juan Carlos Izpisua Belmonte, co-first authors Tomoaki Hishida and Mako Yamamoto, and colleagues have found a way to partially reset liver cells to more youthful states—allowing them to heal damaged tissue at a faster rate than previously observed. The results reveal that the use of reprogramming molecules can improve cell growth, leading to better liver tissue regeneration in mice. The work has implications for treating infection, cancer and genetic liver diseases, as well as metabolic diseases such as nonalcoholic steatohepatitis (NASH).

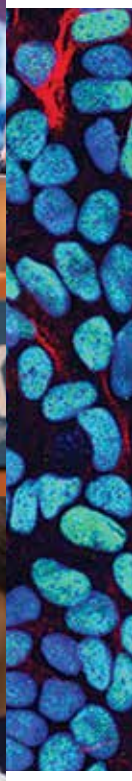


Liver cells were partially reprogrammed into younger cells (red) using Yamanaka factors (white). The cell nuclei (blue) and cytoskeletal proteins (green) are also shown.

From left: Concepción Rodriquez Esteban, Juan Carlos Izpisua Belmonte, Tomoaki Hishida and Mako Yamamoto.

Salk Education Outreach

Hands-On Science Education



teach
inspire
promote

Jonas Salk founded the Salk Institute with the philosophy that it should both drive scientific breakthroughs and inspire the next generation of elite scientists. Out of Jonas Salk's vision, the Institute's Education Outreach program was born. Its mission is threefold:

To teach
students, teachers and the community about scientific literacy in addition to the role of basic biological research in our world.

To inspire
enthusiasm and interest in advanced levels of science instruction, and particularly in science as a career.

To promote
public awareness of Salk and the value of basic research as it relates to career readiness, critical thinking skills and the development of an informed citizenry.

salk® | EDUCATION OUTREACH
Hands-On Science Education

Salk Education Outreach serves San Diego County students, teachers and other community members through its programs: Mobile Science Lab, Heithoff-Brody High School Summer Scholars, March of Dimes High School Science Day, SciChats@Salk and the Ellen Potter Research Connections for Teachers Symposium. These programs are offered at no cost to students, teachers and schools, thereby reducing economic barriers to high-quality STEM education. Over the past 40 years, Salk Education Outreach has delivered innovative, engaging STEM learning experiences to thousands of students—a majority of whom come from underrepresented and underserved communities.

To learn more about Education Outreach, please email **education@salk.edu**.

What's so special about Salk?

Every

An exceptional history, visionary design and trailblazing faculty make the Salk Institute unique among elite research institutions.

VISION

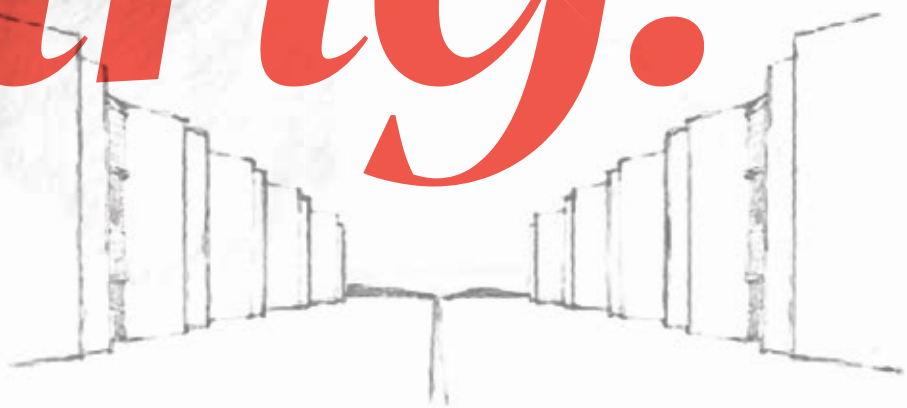
In August 1921, a dozen years before he became President of the United States, Franklin Delano Roosevelt was enjoying some much-needed family time with his wife, Eleanor, and their five children at the family's summer home on Campobello Island, off the coast of New Brunswick, Canada. After an active day spent sailing, swimming and running races with the children, Roosevelt began to feel achy and chilled. He went to bed early, awaking the next morning with a fever and diminishing control of his legs.

Two weeks later and still quite ill, Roosevelt was diagnosed with poliomyelitis (polio), a highly contagious virus that attacks motor neurons—cells that, among other things, enable us to swallow, breathe and move our limbs. Despite his hopes for a complete recovery, he would never walk unassisted again.

In the early 20th century, before Jonas Salk developed the first polio vaccine, Roosevelt was one of tens of thousands of Americans whose lives were upended by the infection. The experience was so life-changing that Roosevelt became dedicated to finding a cure for polio as well as helping other survivors—mostly children (polio was also known as infantile paralysis)—recover.

Although Salk and Roosevelt would never meet, their shared vision of a world without polio would lead not only to the lifesaving vaccine but also to a pioneering research institution like no other: the Salk Institute.

thing.



Above: Photo illustration of Jonas Salk.

01

Unique beginnings

From left: Francis Crick, Jonas Salk and Leo Szilard.

Credit: Special Collections & Archives, UC San Diego.

"Jonas was well aware that the development of his institute would be an evolutionary process, and he viewed it as an experiment."

SUZANNE BOURGEOIS

In 1938, during his second term, Roosevelt set up a nonpartisan organization called the Foundation for Infantile Paralysis (later called the March of Dimes), which was dedicated to finding a cure for polio as well as helping survivors. Over the next several decades, the foundation would fund the work of numerous researchers, including a young Jonas Salk, first at the University of Michigan, where he researched an influenza vaccine, and then at the University of Pittsburgh, where he would develop the polio vaccine.

When Salk's polio vaccine was declared safe and effective in 1955, he instantly became the most famous scientist in the world. With that success, the 40-year-old researcher began to envision an institute at which basic scientific research could be conducted for other human diseases.

One of Salk's early conversations on the topic was with Leo Szilard, a Hungarian-born physicist who had studied with Albert Einstein in Berlin and was a friend of the Nobel Prize winner. In 1933, Szilard had realized how an atomic chain

"The remarkable history and architecture of the Institute inspires our scientists daily to forge new scientific paths with the same bold spirit of discovery as the Institute's founders."

RUSTY GAGE

INSPIRING

reaction could be harnessed in a bomb. In 1939, he convinced Einstein, who was then at the Institute for Advanced Study in Princeton, to write a letter to President Roosevelt warning him that the Germans were attempting to make an atomic bomb. (A one-act play about Szilard's efforts to control the bomb, *Uranium + Peaches*, premiered at the Salk Institute on June 21, 2018.)

Szilard, who turned to biology after World War II, had long dreamed of an institution devoted to public health research. So when he met Salk at a biology conference in 1956, the two had a great deal to discuss. A few years later, Szilard would be among the first Nonresident Fellows at the Salk Institute—faculty members not permanently based at the Institute.

Jonas Salk also consulted another physicist, Robert Oppenheimer. Both Szilard and Oppenheimer were part of the Manhattan Project, which was a US government research project that ran from 1942 to 1945 to develop the first atomic bomb. The effort resulted in the bombs dropped on Hiroshima and Nagasaki, Japan, leading to the end of World War II. After the war, Oppenheimer became head of the Institute for Advanced Study. That institute appealed to Salk as a model for his own. Coincidentally, Oppenheimer was invited to be on a committee to assess whether to establish Salk's proposed institute at the University of Pittsburgh.

When those negotiations stalled, Oppenheimer, who respected what Salk was attempting, asked whether Salk had considered going to California.

Salk had, in fact, been considering a number of locations for his institute, among them Palo Alto and La Jolla, California. The location decision was a difficult one, so Salk reached out to a friend and confidant, famed journalist Edward R. Murrow, for advice. Murrow had become a household name through his coverage of World War II for CBS. His 1955 coverage of the polio vaccine made Jonas Salk a household name as well, and the two became close. In 1961, Murrow would become a member of the Salk Institute's first Board of Trustees.

Ultimately, the offer of land from the City of San Diego and proximity to the new UC San Diego campus made La Jolla the more attractive option, and the Salk Institute was founded there—at least on paper, to begin with—in 1960.

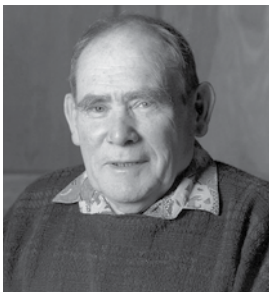
"Jonas was well aware that the development of his institute would be an evolutionary process, and he viewed it as an experiment," says Professor Emerita Suzanne Bourgeois in a book she wrote about the Institute (see sidebar, page 21). "The experiment continues today, and in these changing times the Salk Institute is evolving and adapting as well. It has the brains that made it a scientific success story, and the inspirational building that made it a historical landmark."

02

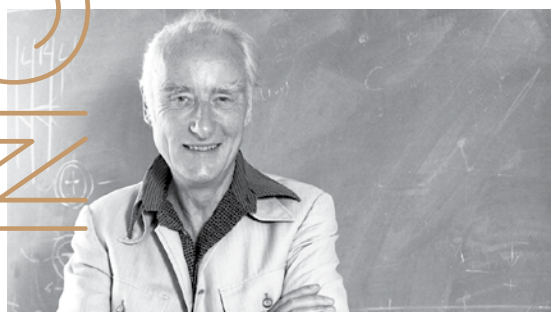
Exceptional people

NOBEL

Elizabeth Blackburn
— 2009 Nobel Laureate

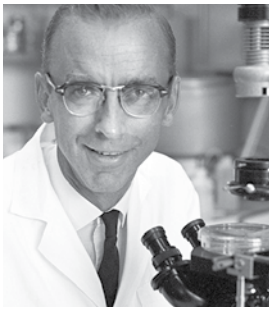


Sydney Brenner
— 2002 Nobel Laureate

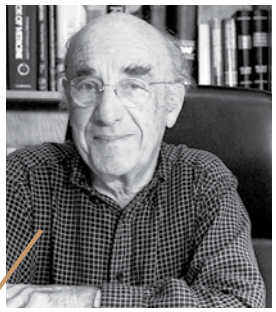


Francis Crick
— 1962 Nobel Laureate

Jacques Monod
— 1965 Nobel Laureate



Robert Holley
— 1968 Nobel Laureate



Roger Guillemin
— 1977 Nobel Laureate

As negotiations for an institute location were underway in 1959-60, Salk was busily recruiting faculty. Salk offered something few research institutions did—an extraordinary amount of freedom. No teaching, no clinical work, no intellectual constraints—faculty would not be pigeon-holed into research "silos" but could explore ideas across disciplines, learning with and from each other.

This appealed to biophysicist Francis Crick, who had discovered the double-helix structure of DNA with James Watson in 1953 and would win the Nobel Prize for that discovery in 1962, around the time he also became a Nonresident Fellow at the Salk Institute. That same year, Salk's vision also attracted biochemist Jacques Monod, who would win the Nobel Prize in 1965 for some of the earliest work showing how genes are regulated (turned on or off). Virologist Renato Dulbecco left Caltech for the Salk Institute in 1962, also. In 1975, he would win the Nobel Prize for the discovery that viruses can cause cancer by inserting genes into the chromosomes of infected cells. Chemist Robert Holley left Cornell University for Salk in 1968, the same year he won the Nobel Prize for his role in discovering how a molecule called tRNA transports the building blocks of proteins—amino acids—based on the DNA code. And neuroscientist Roger Guillemin left Baylor College for Salk in 1970. In 1973, he discovered a brain hormone, somatostatin, which is used to treat neuroendocrine tumors and other conditions. In 1977, he won the Nobel Prize for his discovery of peptide hormones in the brain.

These pioneering scientists—several already famous—were willing to leave the safety of established universities for an

Salk offered something few research institutions did—an extraordinary amount of freedom.

Renato Dulbecco
— 1975 Nobel Laureate

entirely new type of institution and exemplified the daring approach to scientific discovery that has come to characterize the Salk Institute.

Walter Eckhart joined Salk as a postdoctoral scholar in the lab of Renato Dulbecco in 1965 and became one of the first assistant professors at the Institute in 1969, remaining until retiring as professor emeritus. Eckhart, who died unexpectedly in June 2022, was a leader in understanding cell growth and the biology of cancer and served as director of the Salk Cancer Center and Molecular and Cell Biology Laboratory for more than 30 years.

"I was attracted by the world-class research being done at the Institute," said Eckhart shortly before his death. "The collaborative, interactive environment was exceptional."

Professor Emerita Catherine Rivier arrived as a graduate student in 1970, moving to the Institute with her mentor, Roger Guillemin. She became an assistant professor shortly thereafter. "What I liked best about the Institute was that we were left alone to do our research, and I cannot tell you how important and precious this was, particularly when compared to what my colleagues elsewhere had to deal with," says Rivier. "No teaching unless we wanted to, very limited committee participation and an administration that supported us but stayed out of our way. This allowed us to devote all our time and energy to research, which was a unique gift."

03

Inspiring and collaborative environment

As the number of notable scientists and supporters of the new institute grew, Jonas Salk looked for an architect who could design a building that embodied his pioneering idea of collaborative research without intellectual boundaries.

He found such a partner in Louis Kahn, a University of Pennsylvania architecture professor who was building a laboratory for the university. Their shared interest in the interplay between art and science led Salk to ask Kahn to "create a facility worthy of Picasso."

Kahn's resulting structure of concrete, steel, teak and travertine marble has been called "a cathedral to science" and is considered one of the finest examples of modern architecture in the world. Every year, thousands of domestic and international visitors marvel at the majestic building high atop a bluff overlooking the Pacific Ocean.

Salk wanted the scientists working within the concrete walls to be inspired by the location and the structure, whose marble courtyard forms what Mexican architect Luis Barragán termed "a façade to the sky." Salk wanted them to interact and collaborate, and Kahn's design encourages this with continuous expanses of laboratory spaces without permanent walls, where one lab runs into the next. Shared kitchens, lounges and meeting rooms further promote a sense of community.

Jonas Salk's strategy was effective: Scientists at the Institute are inspired to ask big questions and make groundbreaking discoveries.

04 CROSS

Above: Leslie Orgel
Right: Gerald Joyce

Conversations that drive change

From the beginning, the structure and culture of the Institute have spurred dynamic conversations among faculty, no matter their discipline. Often this cross talk—which happens more freely than at other institutions—leads their research in new and unexpected directions.

Biophysicist Francis Crick and chemist Leslie Orgel, who both arrived at the Institute in 1964, met regularly for lunch to discuss the origins of life and other topics. Orgel and Crick were early proponents of the idea that life on Earth was based on RNA (DNA's cousin) before it was based on DNA, a concept known as the "RNA World" hypothesis. Their conversations led to efforts to re-create replicating, evolving RNA molecules in a test tube through a combination of chemistry and directed evolution. Salk Professor and Chief Science Officer Gerald Joyce, who was a student with Orgel, continues to be a leader in this field. Re-creating plausible facsimiles in the lab may give insight into early evolutionary processes, as well as how to design synthetic RNA molecules for therapeutic uses in cancer, immune disorders and other diseases.

"Those were heady days at Salk," Joyce says. "Both when Crick and Orgel were leaders at the dawn of molecular biology, and when I was a student here in the 1980s and the opportunity to reconstruct RNA-based life first became an experimental possibility."

In 2007, neuroscientists Professor Edward Callaway and his graduate student Ian Wickersham came up with a technique that revolutionized brain research. A key piece of this method came from a collaboration with then-Salk Professor John Young, a virologist now at Roche. Callaway was describing to Young the problems with using viruses that naturally infect neurons, such as rabies, to trace connections between the mammalian cells used in the lab. Because rabies spreads nonstop between cells, it's very hard to devise an accurate map of how individual neurons are connected to one another, which is essential if we want to understand how neuronal communication is disrupted in diseases such as schizophrenia, autism and Alzheimer's.

From a lab in Germany, Callaway's team had already received a genetically modified rabies virus that didn't spread nonstop, but they were having difficulties targeting it to the specific neurons of interest. Young immediately had a solution: use a protein combination found in a bird virus that his lab studied. The EnvA protein on the outside of the bird virus gets into bird cells by attaching to a receptor protein on the cells called TVA. EnvA is like a key and TVA is like a lock; together they enable entry into a cell.

Wickersham worked with Young's postdoctoral researcher to customize the German virus to carry the EnvA "key" on the outside. Then, by genetically modifying the mammalian neurons of interest with the TVA "lock," they were able to selectively infect those cells. Fluorescent proteins expressed from the virus allowed the researchers, using microscopes, to see the path traced between connected cells. The method, now known as monosynaptic neural circuit tracing, has become one of the most useful tools in neuroscience research.

TALK

From left: Edward Callaway, Ian Wickersham and John Young.

"Cross-disciplinary collaboration is one of the best ways to approach the types of complex scientific and health-related questions we ask at Salk."

SUSAN KAECH

More recently, conversations between faculty on the topic of aging have led to several exciting collaborations. Professors Jan Karlseder, an expert on telomeres (the protective DNA caps at the end of chromosomes), and Gerald Shadel, an expert in mitochondria (structures that generate energy for cells), have teamed up to explore cross talk between the two. So far, they have discovered that shortening telomeres kick off a cascade of molecular signals that ultimately trigger the destruction of aging, unstable cells with critically short telomeres, preventing them from becoming cancerous. Stabilizing this pathway could offer a new approach for preventing age-related cancers.

Associate Professor Diana Hargreaves, who studies how mutations can make cells forget their identity and turn cancerous, and Professor Susan Kaech, director of the NOMIS Center for Immunobiology and Microbial Pathogenesis, are working together to study cancer immunotherapy—using the body's immune system to recognize and destroy cancer.

"Cross-disciplinary collaboration is one of the best ways to approach the types of complex scientific and health-related questions we ask at Salk," says Kaech. "Other places may talk about the importance of collaborating, but Salk actually encourages and supports it with institutional resources."

Some of Salk's more unusual collaborations involve plants. Professor Wolfgang Busch, co-director of the Harnessing Plants Initiative, has teamed up with Professor Reuben Shaw, director of the Salk Cancer Center, to study starvation signals in plants. Shaw's cancer research lab has been studying genes altered in lung cancer whose normal function is to sense when cells are starving for nutrients. It turns out the cancer genes go so far back in evolutionary time that a common ancestor of plants and animals passed them on to both groups. Thus, these genes also control the response to starvation in plants.

Busch and Shaw wondered whether one of the genes, AMPK, might also be active in plants. Recently, Shaw's team had some new potential activators of the AMPK pathway in human cells and were curious to see whether any of them might also trigger responses in plants and what effect that might have on roots and carbon storage, which is Busch's area of expertise. Their preliminary work suggests some AMPK activators are active in plants and might prove helpful to the Initiative's effort to increase the amount of carbon plants can store in their roots as a means to mitigate climate change.

"Faculty are attracted to Salk because of its intimate size and the opportunity to think really big about their field," says Shaw. "There aren't many other places where a cancer biologist and a plant biologist would team up, but at Salk, collaborations like Wolfgang's and mine happen naturally. It's early days, but it's the kind of cross-pollination that could only happen at Salk."

Plants use sensory proteins to detect and respond to touch signals from animals and neighboring plants. With a 2022 Salk Innovation Grant, Professor Joanne Chory, Associate Professor Sreekanth Chalasani and Staff Scientist Carl Procko will investigate these proteins to see if they are sensitive to high-frequency sound waves. The work could help scientists modify how plants behave in the presence of other plants and contribute to the growing body of research on "sonogenetics," a method Chalasani developed for noninvasively controlling cells with sound waves. Their findings could also lead to new ways for treating conditions like chronic pain, epilepsy and PTSD.

05

A history of pioneering discoveries

Thanks to the way the Institute was founded and designed—and the conversations and collaborations it has spurred—Salk Institute researchers have been making revolutionary discoveries for more than 60 years.

In 1979, Professor Tony Hunter discovered a molecular switch called tyrosine phosphorylation, which turns cells cancerous. The discovery enabled the development of an entire class of lifesaving cancer drugs called tyrosine kinase inhibitors, which includes Gleevec, Iressa and Tarceva.

In 1985, Professor Ronald Evans discovered a large family of molecules called nuclear hormone receptors, which respond to various steroid and thyroid hormones as well as to vitamins. Because these hormones help control sugar, salt, calcium and fat metabolism, they affect our daily health as well as treatment of disease. The receptors Evans discovered are primary targets

ICONIC

Salk's first female faculty

Although women were not well represented in science for much of the 20th century, four of Salk's early faculty were highly accomplished female scientists. Ursula Bellugi and Suzanne Bourgeois were recruited to the Institute in 1968 and 1969, respectively; Catherine Rivier joined in 1970. Marguerite Vogt arrived in 1963 as a research fellow in Renato Dulbecco's group and was appointed research professor in 1973.

Professor Emerita Ursula Bellugi pioneered the study of the biological foundation of language. She is regarded as the founder of the neurobiology of American Sign Language (ASL) because her work was the first to show it as a true language as processed by the brain, revealing more about how the brain learns, interprets and forgets language. Her expertise in neurobiological, genetic and behavioral studies allowed humanity to better understand Williams syndrome and autism, two conditions that affect social behaviors in opposite ways. Together, her studies on Williams syndrome, autism and sign language helped paint a picture of the biology humans use to interact with the world around us. In 2019, the Salk Women & Science program renamed its Trailblazer Award in honor of Bellugi, who established an endowed fund to support those who have pioneered changes within the STEAM (science, technology, engineering, art and math) fields. Bellugi died on April 17, 2022, at the age of 91. (Read more about Bellugi's life and legacy on page 28.)

in the treatment of breast cancer, prostate cancer, pancreatic cancer and leukemia, as well as osteoporosis and asthma.

One of the receptors, PPAR delta, has led to a new class of PPAR delta drugs called exercise mimetics, which promote the benefits of fitness without the need to train. Clinical trials are underway on these drugs, which represent an important advance in addressing problems arising from excess weight and obesity, such as frailty, muscular dystrophy and type 2 diabetes.

Also in 1985, Professor Ursula Bellugi, a pioneer in the neurobiology of American Sign Language, led the way to the watershed discovery that the left hemisphere of the brain becomes specialized for languages, both spoken and signed. (See In Memoriam, page 28.)

In 2002, Professor Rusty Gage, now Salk's president, discovered that—contrary to the thinking at the time—the adult brain continues producing new neurons throughout the life span in a process called neurogenesis.

"The story of the Salk Institute's origins is the story of a number of 20th century icons, including Jonas Salk himself," says Gage. "The remarkable history and architecture of the Institute inspire our scientists daily to forge new scientific paths with the same bold spirit of discovery as the Institute's founders."

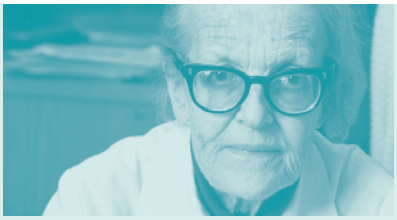
—and we're just getting started

Today, Salk faculty are making discoveries that may one day turn the tide on Alzheimer's, aging, cancers, climate change and more. The Institute that Jonas Salk established in 1960 is unique among elite research institutions for its exceptional history, visionary collaboration-promoting design and trailblazing faculty, past and present.

"Salk truly is different than any other research organization," says Gage. "Our brilliant faculty, inspired by Louis Kahn's magnificent building, are committed to Jonas Salk's vision of helping humanity through basic scientific research.

Professor Emerita Suzanne Bourgeois conducted pioneering work on the regulation of gene expression—the process cells use to turn genes on or off—using the bacterial lactose (lac) operon as a model system. In the 1960s, when little was known about the circuit, Bourgeois demonstrated that the lac repressor was a protein. She used the system for the first characterization of the interaction of a regulatory protein with DNA. She later studied the regulation of genes in animal cells and eventually identified compounds that could be useful to reverse multidrug resistance in cancer. After Bourgeois retired from Salk, she wrote the authoritative book on the founding of the Salk Institute, *Genesis of the Salk Institute: The Epic of Its Founders*. Bourgeois was married to one of the Institute's founders, Melvin Cohn, from 1963 until his death in 2018. She established the Suzanne Bourgeois Women & Science Fund to advance the work of female Salk faculty.

Professor Emerita Catherine Rivier was instrumental in explaining how specialized areas of the brain respond to stressors and communicate with the rest of the body via hormones. She studied how a variety of stressors such as fear, avoidance of unfavorable environments, infection, inflammation and drugs of abuse are conveyed to the brain, and how the hypothalamus mounts adequate responses. Rivier also investigated the role of the hypothalamic peptide GnRH on testicular function. In collaboration with her husband and colleague, Salk Professor Jean Rivier, she designed antagonists to this peptide, which are currently used clinically to treat steroid-dependent conditions such as prostate cancer, endometriosis and precocious puberty. Finally, her team identified a new pathway through which the brain controls the activity of the testes, a discovery that offered insights into puzzling cases of low testosterone secretion connected to stressors or diseases. In 2018, Catherine Rivier was honored with the inaugural Trailblazer Award from Salk Women & Science.



Research Professor Marguerite Vogt was a Salk icon until she retired in 1993. Born in 1914 to German neuroscientists, Vogt grew up studying the genetics of fruit flies. She obtained her medical degree from the University of Berlin in 1937, but her work and life were disrupted by World War II. In 1950, she immigrated to the US to take a research position at Caltech, where she met Renato Dulbecco (see more on page 16). The two collaborated on polio studies and were the first to successfully grow the polio virus in the lab. In 1963, she followed Dulbecco to the Salk Institute, where they worked on cancer. Vogt contributed to the work for which Dulbecco won the Nobel Prize in 1975. Not one to care about accolades for herself, Vogt worked 10-hour days into her 90s and educated or helped train scores of scientists, young postdoctoral fellows and graduate students. Those under her tutelage include four Nobel Prize laureates. Vogt died in 2007 at age 94.

NATIONAL CANCER INSTITUTE-DESIGNATED CANCER CENTER

Exploiting cancer's vulnerabilities. By tackling cancer from many angles and with input from many disciplines, Salk's scientists are finding universal ways to put a stop to the elements that allow tumors to thrive—no matter the cancer type.

CRICK-JACOBS CENTER FOR THEORETICAL AND COMPUTATIONAL BIOLOGY

Using computation and engineering to solve biology's biggest challenges. At Salk, basic lab researchers and applied scientists work together in an iterative process that sends ideas, discoveries and new technologies back and forth, enabling the most profound innovations in every field.

BUILDING A MORE RESILIENT WORLD AND A

NEW SCIENCE AND TECHNOLOGY CENTER

In 2021, the Salk Institute launched the Campaign for the Future: Building a More Resilient World—a bold, five-year, $500 million effort to attract the people and acquire the technology and space necessary to expand and accelerate Salk's life-changing discoveries for decades to come. At the center of this audacious goal is the plan to build the 100,000-square-foot Joan and Irwin Jacobs Science and Technology Center on the east side of the Institute's iconic campus, in keeping with Jonas Salk's vision to inspire scientists to ask the big questions, collaborate without barriers and leverage the latest technologies to find answers.

CENTER FOR HEALTHY AGING

Leveraging diversity to improve health span. Salk scientists are exploring diverse influences on aging at every level—from molecular drivers to lifestyles and the environment—so new interventions help people of all backgrounds live longer and healthier lives.

CENTER FOR PLANT BIOLOGY

Optimizing plants to help save the planet. In the face of a crisis, we can't simply maintain the status quo—Salk scientists are leveraging the Institute's pioneering discoveries in plant genetics and epigenetics to build crop resiliency, improve soil health and mitigate climate change now.

When the new Jacobs Center opens, it will be home to four Centers of Excellence (above). Meanwhile, space in the Institute's current facilities will be reimagined to expand research capabilities for two additional centers:

NOMIS CENTER FOR IMMUNOBIOLOGY AND MICROBIAL PATHOGENESIS

Balancing inflammation. The immune system keeps us safe from infection, yet chronic inflammation is a core part of everything from lower back pain to cancer to Alzheimer's disease. Salk scientists are determining what tips immune function from helpful to harmful, and how to tip the scale back to preserve health.

CENTER OF EXCELLENCE FOR NEUROSCIENCE

Adapting our brains to fit today's world. Because our society and environment are changing faster than ever before, making it harder for our brains to adapt, Salk scientists are uncovering how our natural neural protections work so we can build resilience in the face of stress, aging and disease.

Help us build a more resilient world. Between now and September 30, 2022, Joan and Irwin Jacobs, longtime supporters of the Salk Institute, will contribute $1 for every $2 donated—up to $100 million, which would translate to a total of $300 million with matching funds—for gifts or pledges made toward the campaign. Science is a collaborative pursuit, and we invite you to join us in building a more resilient world:

www.salk.edu/resilient

salk®

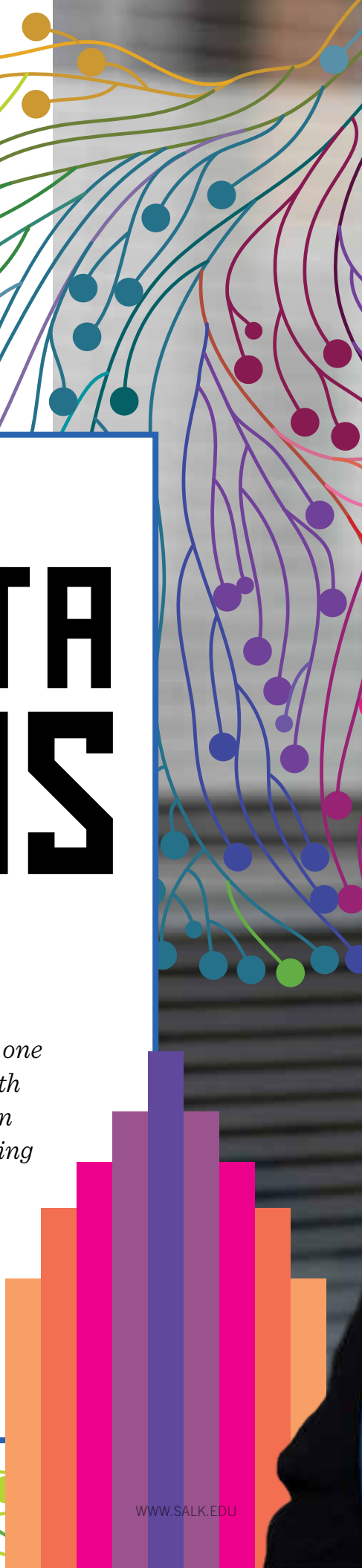
CAMPAIGN FOR THE FUTURE

BUILDING A MORE RESILIENT WORLD

MARGARITA BEHRENS

Master of brain circuits

Research Professor Margarita Behrens was born in Uruguay but moved to Chile at a young age. She was one of six girls born to two chemists. Behrens grew up with a passion for understanding the relationship between structure and function and was torn between becoming an architect and a scientist. She ultimately decided to pursue biochemistry in college and graduate school. At Salk, Behrens applies her biochemistry training to better understand how neurons develop in the brain. Her findings have implications for neurodevelopmental disorders, such as schizophrenia and autism.



Inside Salk *sat down with Behrens to learn about her work to understand neural circuit formation and disruption, as well as her love of architecture.*

When did you know you wanted to be a neuroscientist?

MB: I was always fascinated by the brain. When I was in school, the brain was still considered a black box. Psychiatrists would talk about it as this black box on the outside, and neurologists would talk about when it breaks down on the inside. But to me, mental disorders spanned this boundary between the two, where the brain looked physically normal but was not acting normal. This disparity captured my fascination and drove me to pursue neuroscience. Although I must admit that another love of mine was architecture.

What interested you about architecture?

MB: I studied architecture for a year and a half prior to pursuing science. I had thought I wanted to be an architect since I was 10 years old. I just loved it. But during school, I suddenly realized that I would get bored pursuing it for the rest of my life. I love a challenge and, although there is a lot of challenge in architecture, the daily routine mostly involves drawing, and I wanted to do more. I do still like architecture. In fact, several members of my family are architects, and I love talking to them and imagining spaces, but it's more of a hobby for me. So I switched to science.

Did you study the brain right away once you made the switch to science?

MB: Not exactly. I followed a wiggly road to becoming a neuroscientist. I did my master's in biochemistry at the University of Chile, where I studied cell signaling during development in an aquatic fungus. I was trying to understand the mechanisms and genetic networks involved during the transition from a cyst—a dormant state—to a live individual fungus. During my PhD in biochemistry, I worked in yeast. I looked at signaling mechanisms when a cell transitions from one state to another.

For my first postdoctoral fellowship at the Universidad Autònoma in Madrid, Spain, I examined the brine shrimp *Artemia salina*, which are similar to the popular Sea-Monkeys pets. I studied the transition from when the inactive powder becomes a live organism. It turns out that everything exists in this dormant cyst and then when water is added, these genetic cascades occur that translate the proteins to create a little swimming animal. Pretty incredible!

How did you transition from Sea-Monkeys to brains?

MB: I transitioned to neuroscience during my second postdoctoral fellowship. I felt I now had enough of a scientific background to approach a complex organ like the brain. So I joined a lab at Washington University in St. Louis, where I looked at the mechanisms involved in neuronal degeneration, which can happen during stroke. During a stroke, blood flow is lost to a certain region of the brain, which triggers a series of events in the neurons. When the blood comes back to the region, a whole new series of reactions takes place. For example, during the week after a stroke, the damaged brain area expands. I was interested in what is happening to the brain during this period of time. I found that because the neurons are dying in this location, they start to dump their excitatory neurotransmitters, which can alter the way certain neurons are communicating.

But what this fellowship really taught me was how to grow neurons in the lab to answer a specific question I'm interested in. One of the big problems in science is having too many variables, so it's important to be able to culture the neurons the same way each time.

You've studied science all over the world. Do you think you've gleaned a global perspective of the field?

MB: I have worked in so many places with different cultures. The umbrella of science is similar, but the culture is specific to each place. Science is like its own country, and you can easily transition within the country. The rules of the game might change, but it's the same game. For example, if you're playing bridge with a new group of people, they might do their signs to each other in a new way, but the game is still bridge. Working in these different countries provides perspective that science is not black and white. What you learn today might be wrong tomorrow, but it's these sorts of challenges that keep my interest piqued.

How did you end up at Salk?

MB: I was working in the geriatrics department at UC San Diego as a project scientist. I was looking at how inhibitory neurons—those that reduce brain activity to help the brain function smoothly—are related to schizophrenia. I made an important discovery showing how certain pro-psychotic drugs like ketamine target a subset of neurons called PV interneurons. My findings support the idea that PV interneurons could be a new target for future schizophrenia therapies.

It was serendipitous that I met Salk Professor Terrence Sejnowski at a dinner party I was hosting for a friend. We started chatting, and we realized that

> *"Salk is a wonderful environment for collaborations, and because it is small, I can interact with people regularly."*
>
> MARGARITA BEHRENS

our work overlapped, as he was looking at inhibitory neurons from a modeling point of view. We decided to write a grant together, which I don't think we were awarded, but we had a lot of fun writing. When I was looking to move on from UC San Diego, he convinced me to come to Salk.

Do you think your love of architecture was also a part of the draw to join Salk?

MB: No. It was the science. But I do enjoy the space, and I find it inspiring. I have a lot of pictures of the sunset outside of my window and the colors it gives to the north building. When I'm showing the building to friends and family, I get to switch back to thinking like an architect.

And what are you working on now at Salk?

MB: Most neuronal circuits are established during the perinatal period (the third trimester of pregnancy and the first few weeks after birth), so my lab focuses on this time in our research. We're interested in how chemical tags on DNA—called methylation—affect the electrical activity of neurons, circuit formation and maturation. I want to know why some people experience neurodevelopmental disorders, while others do not.

I spend a lot of my time dissecting the prefrontal cortex of rodent brains because I have the hands-on experience and knowledge to take a brain apart and put it back together again. Dissecting a brain takes a lot of pattern recognition to be able to see small landmarks and changes in cellular density to know where to slice.

Why have you chosen to focus on the prefrontal cortex of the brain?

MB: This brain region develops slower than other regions. In humans, it doesn't reach maturity until 25 years of age. These neurons are defined by the perinatal period, but they haven't made the connections they need with other neurons. There is a growth spurt of connectivity until two years of age, so the cortex grows like crazy during this time. Then it starts a very sharp pruning of cells and connections that are not useful.

The prefrontal cortex is interesting to me because it acts like the central command. It receives inputs from almost every other region of the brain, and it sends out a ton of connections. It also allows us to make decisions. That means that anytime there is an alteration in this brain region, usually decision-making is affected. Mental disorders often affect the prefrontal cortex, so I focus my research here to figure out what goes wrong.

Can you tell me about your involvement with the NIH's BRAIN Initiative Cell Census Network?

MB: I've partnered with Salk Professor Joseph Ecker and a few other colleagues as part of the BRAIN Initiative to analyze brain regions containing millions of cells to see how methylation is turning genes on and off to affect health and disease.

Specifically, we are identifying new subtypes of neurons based on their chemical patterns called epigenomic signatures. These signatures can then tell us which part of the brain the neurons are from. For example, neurons in the front and back of the mouse brain are very similar, but they are not interchangeable. As animals grow and develop, neurons crystalize into different states and become functionally different. We're interested in looking at how stable these differences are and what it means if these neurons are altered.

Through this research, we now have a much better idea about the composition of neurons in the mouse brain. In order to treat brain diseases, we need to be able to tell which exact cells are misfunctioning. Then we can target these cells, instead of broader regions, to develop more tailored and effective therapies.

What keeps you at Salk?

MB: Salk is a wonderful environment for collaborations, and because it is small, I can interact with people regularly. I've been able to work with multiple other faculty members, including Professors Sejnowski and Ecker, as I mentioned. Salk is also unique in that the Institute really facilitates science, and there is less red tape than at other institutions. That means we can move new, exciting projects along faster than expected.

IN MEMORIAM

A TRAILBLAZER'S LASTING LEGACY:

URSULA BELLUGI

BRIDGED HUMANITY AND SCIENCE

Despite being a world-renowned, award-winning scientific pioneer, Ursula Bellugi didn't like to say she was smart. Instead, she credited her tremendous success to her insatiable curiosity and her willingness to ask the right questions.

Last spring, the world lost a true trailblazer.

Bellugi, Distinguished Professor Emerita and Founder's Chair at the Salk Institute, 2008 inductee to the National Academy of Sciences and winner of the Jacob Javits Neuroscience Investigator Award, passed away peacefully on April 17, 2022, in La Jolla, at the age of 91.

She was predeceased by her husband Edward S. Klima and her son David Bellugi. She is survived by her son Rob Klima, her sister Ruth Rosenberg, her brother Hans Herzberger, and by four grandchildren and five great-grandchildren.

"The entire Salk community is grieved by the loss of Ursula Bellugi," says Salk President Rusty Gage. "She leaves an indelible legacy of shedding light on how humans communicate and socialize. The humanity and compassion she brought to her work were truly special, and we all will miss her dearly."

> *"People forget that most professors at that time were males. Here was a woman who was really interested in children but was also a top-flight researcher. I had never seen anything like her before."*
>
> RACHEL MAYBERRY

Above: Ursula Bellugi (third from right) stands among her peers in the Courtyard of the Salk Institute, 1984.

A WORLD-CLASS SCIENTIST

Bellugi's contributions to our understanding of the role biology plays in communication are virtually unparalleled; she is widely regarded as the founder of the neurobiology of American Sign Language (ASL). She was the first to demonstrate that ASL is a true language. She studied its neurological facets extensively, leading to the discovery that the same areas of the human brain that specialize in spoken language are activated by sign language—a striking demonstration of neuronal plasticity. This work also provided significant insights into how the brain learns and interprets (and even forgets) language.

"She and my father were able to prove American Sign Language was a real language, with all of the syntax and grammar as spoken language," her son Rob Klima says. "My mother's contributions opened a lot of doors for Deaf people and allowed them a chance to flourish like they never had before. Before her work, Deaf people were discouraged from signing. They were pushed to assimilate, as it was thought that signing was pantomime or a cheap substitute for spoken language."

"Her work with her husband was absolutely foundational. What she did with sign language turned the science upside down and sideways," says Rachel Mayberry, a professor in the Department of Linguistics at UC San Diego. Mayberry worked in Bellugi's lab during the summer of 1973 and considers Bellugi a role model. "People forget that most professors at that time were males. Here was a woman who was really interested in children but was also a top-flight researcher. I had never seen anything like her before."

Not content to remain a pioneer of one foundational area of research, Bellugi pivoted her focus in 1981 to an untapped field of research: Williams syndrome. Meeting a young San Diego girl with Williams syndrome piqued her curiosity about the condition.

Williams syndrome is a genetic condition present at birth that affects an estimated 20,000 to 30,000 people in the US. It is characterized by a number of health issues, including cardiovascular disease, developmental delays and learning challenges. Children with Williams syndrome tend to be particularly social and friendly, according to the Williams Syndrome Association.

Bellugi leveraged her expertise to better understand Williams syndrome and autism, two conditions that affect social behaviors in opposite ways. Through her use of advanced imaging technologies, Bellugi was able to visualize how related gene deletions alter brain activity, map the affected

neural circuits and develop stem cell reprogramming techniques to reveal the biological basis of these drastically different disorders.

Today, Bellugi is widely regarded as pioneering the study of Williams syndrome.

"We didn't limit ourselves to anything," Bellugi said in a 2018 video recorded by the Williams Syndrome Association. "We wanted to know everything about Williams syndrome… The most important thing we found is that Williams syndrome holds keys to some of the most basic questions about what it means to be human."

EARLY LIFE AND JOURNEY TO SALK

Bellugi was born in Jena, Germany (about 45 miles southwest of Leipzig) on February 21, 1931, to Max and Edith Herzberger. Her family immigrated to the United States when Bellugi was young, fleeing Germany in 1934 on the encouragement of Albert Einstein, Max's friend and former teacher in Berlin, as Hitler was rising in power. Bellugi's father took a job at Eastman Kodak's optical research laboratories, a job arranged for him by Einstein.

Bellugi attended Antioch College in Yellow Springs, Ohio, majoring in psychology and graduating in 1952.

In 1953, she married Italian composer and conductor Piero Bellugi. The couple had two boys, Rob and David, but divorced in 1959. Bellugi then moved with her sons to Rochester, New York, to live with her parents.

Rob Klima describes the period of his mother's life that followed as "hard times." The small family bounced around the country, living with various relatives for several years. Then, Bellugi moved them to Cambridge, Massachusetts, to attend Harvard University, where she would go on to earn her Doctorate of Education in 1967, all the while raising her sons as a single mother. Shortly after completing her PhD, she became an associate professor at Harvard.

It was during this time Bellugi met and married linguist Edward S. Klima, who would adopt her sons. The new family moved to La Jolla, California, where Klima took a teaching position at UC San Diego and Bellugi began working at the Salk Institute in 1968. Two years later she was named director of Salk's Laboratory for Cognitive Neuroscience.

"That was a really wonderful time," Rob Klima says. "My brother and I hated the bitter cold of the Northeast; and then we went to living above Black's Beach. It was really the best place to grow up."

"Jonas Salk actually asked me to set up a little lab [at the Salk Institute]," Bellugi said in the Williams Syndrome Association video. "I was the only one working with people directly. I've always been fascinated with language. At the time, nobody thought there was anything like language among Deaf people. We discovered and uncovered the particular languages that Deaf people invented on their own, and they were languages of the hand and in the eyes."

Top: Ursula and husband Edward Klima (provided by Rob Klima); Bottom from left: Ursula Bellugi's mother, Edith Herzberger, Ursula and Francis Crick (provided by Rob Klima).

A PEOPLE PERSON

Affectionately referred to as "Ursie" by many closest to her, including colleagues, lab workers and students, Bellugi loved people, a quality that shone through in every facet of her life.

"Ursula had a real passion for people," says Professor Joanne Chory, who joined Salk in 1988 and got to know Bellugi well over the years. "She was such a sweetie."

While most Salk labs focus on preclinical work in test tubes, Petri dishes and animal models, Bellugi was one of the first researchers to include people in her studies. In addition, she hired many Deaf researchers to work in her lab over the years.

Beyond the lab, she was always sure to embrace the human side of her work. She held annual gatherings for children with Williams syndrome who participated in her studies. The events were eagerly anticipated by researchers and participants alike.

On one such occasion in 2001, actor Alan Alda visited the Salk campus and filmed an episode of a television program called *Scientific American Frontiers*, highlighting Bellugi and her work with children with Williams syndrome, who gathered for a picnic on the Institute's north lawn. In the video, children can be seen playing lawn games, receiving prizes, carrying balloon animals and simply enjoying everyone's company.

From left: MaryAnn Klima, Ursula Bellugi and Rob Klima.

Ursula Bellugi with actor Alan Alda.

Simple efforts such as these were Bellugi's way to ensure that any work conducted at Salk was grounded in the people who made it possible.

"She loved being around people and took every opportunity to get to know them on both a personal and professional level," Klima says. "Whether they were colleagues at the Salk Institute or people she encountered at her weekly hairdresser appointment, she loved interacting with people and becoming a part of their lives."

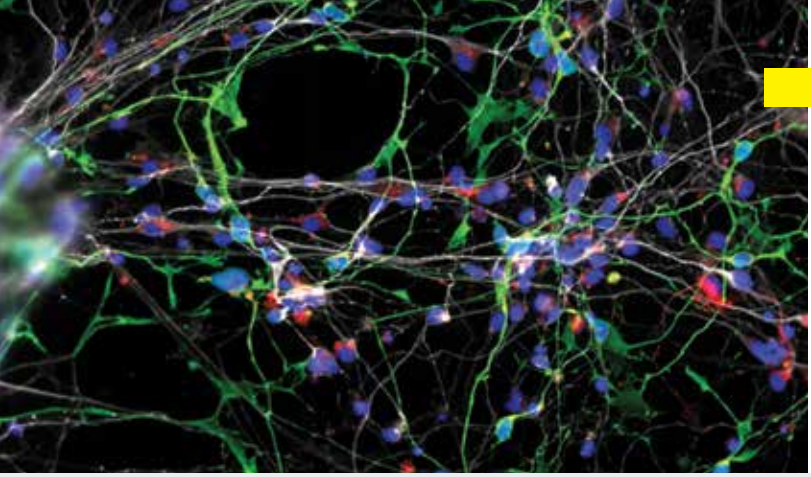
AN INSPIRATIONAL MENTOR

Her love of people also informed her role as a mentor. Bellugi's contributions to science can't be fully told without acknowledging the profound impact she made on her students and lab workers.

"As an academic mentor and research leader, Ursula contributed to evolutionary thinking in linguistics, neuropsychology and biology. She inspired all of us to stretch to our limits," says Robbin M. Battison, who was a graduate student in Bellugi's lab from 1970 to 1973.

"I learned from watching Ursie work that you can't be afraid of what you don't know. You have to embrace it," Rachel Mayberry says.

Bellugi's supportive nature extended beyond students and her lab workers. Her colleagues recount how inspiring she was to them as well.



Williams syndrome-derived neurons in culture.
Credit: UC San Diego.

WILLIAMS SYNDROME IS A GENETIC CONDITION PRESENT AT BIRTH THAT AFFECTS AN ESTIMATED 20,000 TO 30,000 PEOPLE IN THE US. IT IS CHARACTERIZED BY A NUMBER OF HEALTH ISSUES, INCLUDING CARDIOVASCULAR DISEASE, DEVELOPMENTAL DELAYS AND LEARNING CHALLENGES. **BELLUGI IS WIDELY REGARDED AS PIONEERING THE STUDY OF WILLIAMS SYNDROME.**

"Ursula was really sweet to me," says Chory, adding that she appreciated Bellugi. "She was like me. She lived under the radar, and when you work that way, you can do whatever you want. We bonded over that."

Virologist and Salk alum Matthew Weitzman considered Bellugi a treasured friend and mentor.

"Our science was very different, but she always wanted to grasp what I was working on or find out what the driving question of the research was," says Weitzman, who was a member of Salk's faculty with Bellugi from 1997 to 2011. "After everyone else had left faculty lunch on Fridays, we would linger behind and chat about science, careers, family and philosophy. She would ask probing and insightful questions. She was always interested in the larger implications of our work."

AWARD-WINNER

Bellugi authored numerous books and was a much sought-after speaker on the subjects of neurobiology, language and other topics. *The Signs of Language*, published in 1979 and written with her late husband Edward Klima and several colleagues, is considered a seminal publication on the grammar and psychology of signed language. It is still taught in university linguistics programs today.

In addition to the Javits Neuroscience Investigator Award, Bellugi was the recipient of numerous awards recognizing her contributions to linguistics and neurobiology. These included being elected to the National Academy of Sciences and the American Association for the Advancement of Science. She was honored with two MERIT awards from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, a Woman of the Decade Award from the City of Los Angeles and a Distinguished Scientific Contribution Award from the American Psychological Association.

In 2019, the Salk Women & Science Trailblazer Award was renamed in honor of Bellugi, who established an endowed fund to support those who have pioneered changes within STEAM (science, technology, engineering, art and mathematics) fields. The Ursula Bellugi Trailblazer Award recognizes outstanding achievements made by women in their fields. (See page 48 to learn about the latest award recipient.)

> *"The love of her life, other than her family, was the Salk Institute. Salk gave her an opportunity and she ran with it."*
>
> ROB KLIMA

Ursula Bellugi with her lab team, 2014.

My work is a joy. I have a passion for this. I don't know how to explain it any other way."

URSULA BELLUGI

A PASSION FOR WORK AND SALK

Even as she aged, Bellugi never lost her ability to derive happiness from her work. When, in the course of a 2015 interview by the *San Diego Union-Tribune*, she was asked why she had continued to work well into her eighties, she "cocked her head, as if to say, 'are you really asking me why I still have a lab at 84?'" Her answer to the question summed up her attitude toward research: "My work is a joy," she said, "I have a passion for this. I don't know how to explain it any other way."

Bellugi retired and closed her Salk lab in 2018, at the age of 87, but her curiosity and love for research never waned. Rob Klima says she enjoyed being at the computer, where she loved to email friends and colleagues. Even when her health declined to the point of needing to remain in bed, Klima set her up with an iPad so she could remain plugged in.

"She had an incredibly curious mind. Always wanting to learn, always wanting to research," Klima says.

Another thing she loved to do was stay informed about Salk happenings. She read issues of *Inside Salk* and anything else Salk-related she could find.

Joanne Chory shares that one of her fondest Bellugi memories is how Bellugi would proudly show off a photo she kept on her phone of herself, her mother, and Nobel laureate and Salk faculty member Francis Crick, co-discoverer of the structure of DNA (page 31).

"The love of her life, other than her family, was the Salk Institute," Klima says. "Salk gave her an opportunity and she ran with it."

In June 2022, the Institute lost another pioneer: Professor Emeritus **Walter Eckhart**, who led the Salk Cancer Center for more than 30 years. A tribute to Eckhart, a treasured colleague and mentor, will appear in the Winter 2022 issue of *Inside Salk*.

Support a legacy where cures begin.

The power of charitable gift annuities

Did you know a gift to the Salk Institute of $20,000 or more can provide fixed payments for you and your loved ones? Charitable gift annuities provide tax savings and an income for you, while benefitting research and discovery at the Salk Institute. By creating a charitable gift annuity, you can be confident that you've made a smart decision about your financial and philanthropic priorities.

Learn more about the many benefits of a charitable gift annuity by contacting Cheryl Dean, Planned Giving Counsel, at (858) 500-4884 or cdean@salk.edu

Your age(s) and current interest rates determine the rate Salk can offer.

Sample Rates

YOUR AGE(S)	RATE
70	5.3%
80	7.0%
90	9.1%

salk®
Where cures begin.

Shaping Salk's science through shared resources

Julie Auger's mother, a nurse, was at a conference in Illinois in the mid-1980s when she met medical researcher Jonas Salk—someone she had long admired for his development of the first safe and effective polio vaccine. She got his autograph and mailed it to Auger with a note saying, "Don't ever stop trying to achieve your dreams."

Auger took her mom's advice, and today she is the executive director of Research Operations at the Salk Institute, which was founded by Jonas Salk in 1960. At the Institute, Auger manages the shared research core facilities. Cores are laboratories filled with technology and instrumentation that are typically too expensive for a single researcher to purchase. Instead, specialized equipment, such as high-powered microscopes, is purchased and located in dedicated, centralized laboratories. The cores enable scientists to perform cutting-edge experiments with the guidance of expert core personnel. This approach ensures innovative technologies are available to all and leads to more team-centered science, increasing collaboration and scientific discovery.

INSIGHTS

Julie Auger

INSPIRATION

"My mother was extremely influential in my life. She always told me to not expect anyone else to take care of you. Women can achieve anything they want," says Auger. "My mom taught me to be brave, and, importantly, that being a mother does not mean you have to give up on professional dreams."

EARLY LIFE

Auger grew up in Strum, a small Wisconsin farming community of about 750 people. There were no scientists in Strum. "Winters in Wisconsin were freezing cold. I survived those winters reading anything I could get my hands on," she says. But summers on the prairies were wonderful, and Auger enjoyed roaming the countryside in search of wild raspberries, frogs and birds.

When Auger was in eighth grade her mother's best friend died of breast cancer. That experience solidified her commitment to scientific discovery, and she promised her mother that she would try to find a cure for cancer. Auger has played a strong role in many influential cancer research centers that have made great strides toward more effective cancer therapies.

PATH TO SALK

Auger's interest in science was nurtured by her high school biology teacher and many mentors along her journey. She attended Saint Mary's University of Minnesota and shortly after graduating got a job working at the Mayo Clinic Rochester in a flow cytometry lab, a technology that rapidly analyzes particles and cells to detect and quantify their chemical and physical properties.

Flow cytometry was a novel technique at the time, and the University of Illinois at Urbana-Champaign was creating a new flow cytometry core facility. Despite not having an advanced degree and being a young working mom, Auger readily accepted the challenge to develop the new technology center.

"For a long time, I felt like I was not worthy of the position. I was in a leadership role, guiding the science, but I didn't have a PhD," says Auger. "Then one day I was told by one of the scientists, 'Julie, as long as you know more than anyone else here about flow cytometry, you are the expert.' That was a pivotal moment as it gave me the confidence to better direct the conversation, accept even greater responsibility and continue to remain the expert."

Auger directed that flow cytometry core for eight years before she was recruited to the University of Chicago to develop its cytometry core facility, as well as a few other shared research laboratories. At the request of renowned cancer researcher Janet Rowley, Auger also created an administrative structure to support all biomedical cores at the university. Seventeen years later, she was recruited by UC San Francisco, to do the same thing there—create central, coordinated administrative core facilities. She then built a similar structure at UC Davis.

She later consulted about the management structure of Salk's core facilities. "I could see a few strategic changes that could benefit the Institute, and I thought it would be rewarding to lead those changes myself," she says. She joined Salk in November 2021 as the executive director of Research Operations.

DAY-TO-DAY

Nearly every investigator at Salk uses one or more of the 11 cores that are managed by Auger. She must understand the science being conducted in the cores to properly support the scientists and essentially acts as the broker between the scientists and the Institute's administration. For example, the Viral Vector Core might be developing a new cell delivery system using the rabies virus, while the Mass Spectrometry Core is focused on profiling protein complexes. She then communicates the scientists' needs to Human Resources, Finance and other groups to acquire the necessary tools to make improvements and advance the facilities.

"My day-to-day includes a lot of learning about the needs of our scientists," says Auger. "I also serve the needs of the core facilities staff and provide Salk's executive leadership team with information about research infrastructure."

LEISURE TIME

Most of Auger's leisure time is spent in her garden in Davis, California, where she lives on the weekends with her husband. She is an avid native plant gardener and affectionately refers to her home as the "Six B Ranch," which stands for birds, butterflies, bats, bees and other bugs on the bank. A keen birder, Auger is also an amateur photographer who enjoys taking pictures of all the "Bs" that reside in her garden. Global travel is also high on her list of leisure priorities.

LONG VIEW/FUTURE PROJECTS

Shared research facilities are centers of expertise and technologies, and they are extremely important pillars of discovery science. Because core scientists focus on more broad research topics, they have the inherent ability to make a big impact on the scientific literature. "We need to continue to invest in, support and respect core scientists to make innovative discoveries," says Auger. "Salk is a leader in investing in core scientists, and we can be a symbol in showing others how to continue to move from individual science to team science, which is the future."

Gaurav MENDIRATTA

Using math to solve cancer

Jumping from theoretical physics to cancer research with no prior training in biological sciences wasn't an easy transition for Gaurav Mendiratta. Couple this with a move across the world and the birth of his first child shortly after starting his postdoctoral training in a newly opened laboratory—Mendiratta had his work cut out for him.

"A month in, I picked up a pipette for the first time and had to learn how to culture stem cells," Mendiratta recalls. "Naturally, the project was a complete mess, but I was learning. In science, we need to persevere to get anywhere."

Born and raised in a small town near New Delhi, India, Mendiratta avoided the intense heat by spending the summers indoors playing with his favorite toy: a screwdriver. "My parents did buy me real toys," he jokes. "But they wouldn't last long because I would take them apart with my screwdriver to see how they worked." No toy, radio or household appliance was safe from Mendiratta's curiosity.

He carried this inquisitiveness into his high school years, where he'd spend countless hours studying for his favorite classes—math and physics. Although Mendiratta loved learning how logic and critical thinking could demystify real-world phenomena, his peers would tease him for being passionate about science.

"As a teen, I didn't feel accepted by my classmates," Mendiratta says. "But when I started hanging around academic circles, I realized there were others just like me. I wasn't so strange after all!"

"Being able to use my mathematical skills to explore equally complex systems in biology lit a fire in me. The idea of helping people got me hooked!"

GAURAV MENDIRATTA

After high school, Mendiratta completed his bachelor's degree at the University of Delhi, where his passion for quantitative reasoning blossomed. Upon graduation, he pursued his master's in theoretical and mathematical physics and his doctoral degree in elementary particle physics at the Indian Institute of Science in Bengaluru (formerly called Bangalore), where he developed models to address long-standing questions in astrophysical dark matter.

Although Mendiratta found the work enthralling, toward the end of his doctoral program he began to see how abstract his research was. "I realized that the theories I studied in particle physics were hard to test. They needed decades of planning and expensive equipment to even start exploring experimentally."

In the final year of his studies, Mendiratta began consulting at a hospital in Bengaluru. He built a computational framework that used the body's radioactive potassium concentration to noninvasively monitor a baby's metabolism during pregnancy as well as metabolic states in cancer patients. "Being able to use my mathematical skills to explore equally complex systems in biology lit a fire in me," says Mendiratta. "The idea of helping people got me hooked!"

In 2017, he started developing a mathematical model of tumor growth and immune system interactions, which he presented at several seminars. At the Southern California Systems Biology Conference at UC Irvine, he met his now mentor, Salk Assistant Professor Edward Stites.

"Meeting Ed at that conference was a stroke of good luck," says Mendiratta. "He's an MD/PhD, so he keeps our work clinically centered, but he was also a math major, so he speaks my language!"

At this fortuitous encounter, Mendiratta learned that Stites had just started a lab at Salk, where Stites and his team use computational and mathematical modeling to better understand complex protein interactions in cancer with the goal of offering patients more effective treatments. Mendiratta joined Stites' lab as his first postdoctoral researcher, where he began applying his background in quantitative analysis to study the ways genetic mutations influence the development of cancer.

Mendiratta investigated how some cancer-associated genes and their mutations can be over- or underrepresented in some populations because of variability in sampling each type of cancer. Historically, only a handful of well-funded cancer centers have had the ability to sequence cancer patients' tumor genomes. He found that this led to an inaccuracy in cancer data—the few patients who had access to these centers were not representative of cancer patients throughout the rest of the US.

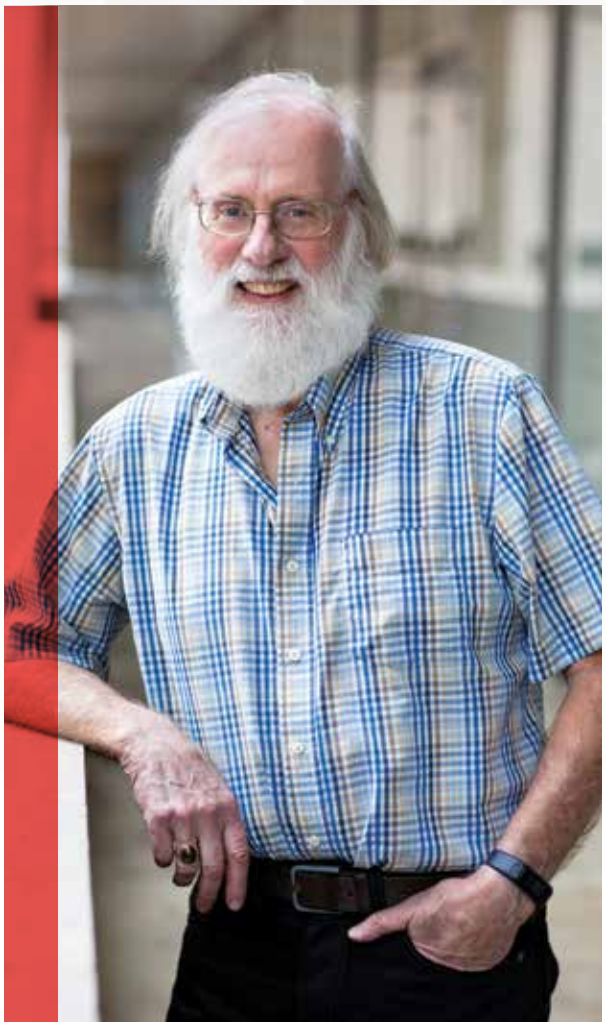
"This oversight prompted us to better account for the population of patients seen across the country when calculating gene mutation rates in cancer," says Mendiratta.

To address this issue, he helped develop a new classification tool called ROSETTA, along with a method to pool cancer data and statistics from several databases. This work provides researchers, clinicians and policymakers with a better understanding of the incidence of cancer-related gene mutations within US populations, a key step for evaluating resource allocation and research priorities to achieve the best outcomes for cancer patients.

Mendiratta and Stites are also applying their mathematical expertise to piece together a major puzzle in treating melanomas—certain treatments that reduce tumor size inadvertently lead to the formation of a second tumor. They created a computer-based simulation to model the interactions between the cancers and the drugs, and discovered complex molecular reactions that were previously unaccounted for, findings that could aid efforts in diagnosing and treating melanomas.

"Computational modeling can help us solve some of the hardest biological problems," Mendiratta says. "Because when we think quantitatively, we're throwing the darts with a clearer view of the board, which gives us a better chance of hitting the bullseye."

SPOTLIGHT



TONY HUNTER

"I am deeply honored to have been recognized by the AACR in this way. This award reflects not only my own contributions but those of everyone who has worked in my group over the past 45 years, as well as my many talented colleagues at the Institute that I have been privileged to collaborate with during my career."

TONY HUNTER

Professor Tony Hunter receives 2022 AACR Lifetime Achievement Award

AACR American Association for Cancer Research

Hunter received the 2022 American Association for Cancer Research (AACR) Award for Lifetime Achievement in Cancer Research at the group's annual meeting in April. AACR is the largest cancer research organization in the world dedicated to preventing and curing all cancers. This major award is a significant recognition of Hunter's contributions to cancer research, which have led to the development of the highly effective leukemia drug Gleevec.

Hunter, who is an American Cancer Society Professor and holds the Renato Dulbecco Chair at Salk, studies the molecular basis of normal cell growth control and cell cycle regulation, and what happens when these processes are disrupted—such as occurs in tumors. He is widely known for his 1979 discovery of a molecular switch called tyrosine phosphorylation that, when flipped on permanently, can trigger cancer cell proliferation. This discovery launched an entirely new field of research and has led to a new class of anti-cancer drugs known as tyrosine kinase inhibitors.

MARTYN GOULDING

Credit: Yolanda Leenders-Goulding

Professor Martyn Goulding wins Brain Prize

Goulding received the Lundbeck Foundation's 2022 Brain Prize for pioneering research on the neuronal circuits that control movement.

Goulding shares the prize—the world's top recognition in neuroscience, totaling 10 million DKK (approximately $1.5 million)—with Professor Ole Kiehn at the University of Copenhagen in Denmark and Professor Silvia Arber at the University of Basel and Friedrich Miescher Institute in Switzerland. His Royal Highness The Crown Prince of Denmark bestowed the prize to the trio at an event in Copenhagen on May 24.

PROFESSOR TERRENCE SEJNOWSKI AWARDED GRUBER PRIZE

Sejnowski was awarded the 2022 Gruber Neuroscience Prize by the Gruber Foundation for his "pioneering contributions to computational and theoretical neuroscience." He shares the $500,000 award with three other scientists from three different institutions.

Sejnowski, who is head of Salk's Computational Neurobiology Laboratory and a distinguished professor at UC San Diego, has helped shape the fields of neuroeconomics, neuroanatomy, neurophysiology, psychology and artificial intelligence.

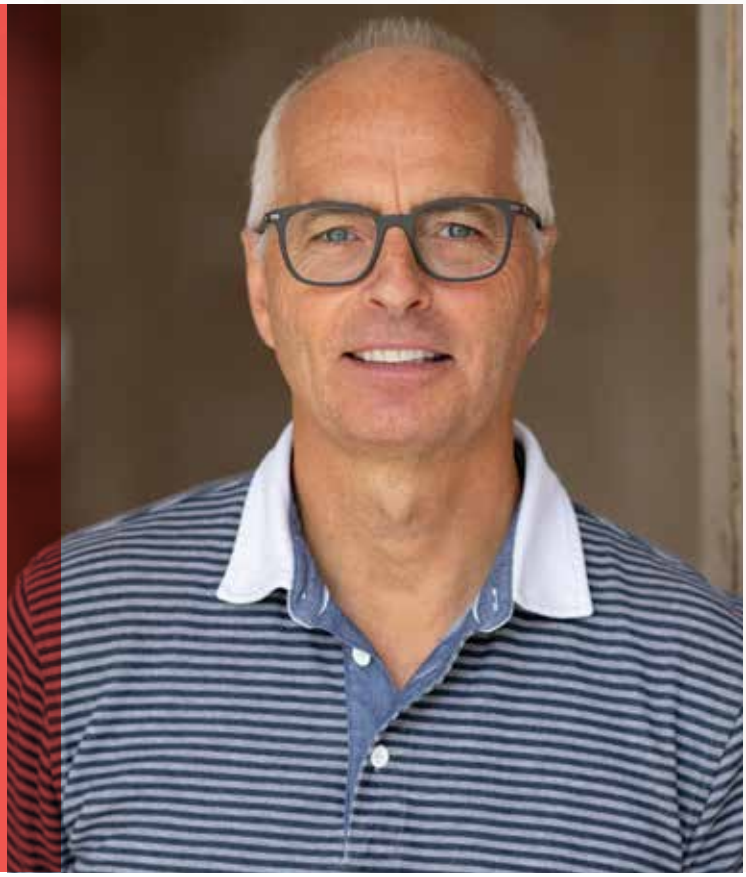
TERRENCE SEJNOWSKI

PROFESSOR SUSAN KAECH ELECTED AS AMERICAN ASSOCIATION OF IMMUNOLOGISTS COUNCILOR

Kaech, director of Salk's NOMIS Center for Immunobiology and Microbial Pathogenesis, was elected to the American Association of Immunologists (AAI) to serve as councilor from 2022 to 2026. The AAI Council comprises eight scientists who are collectively responsible for advancing knowledge of immunology and its related disciplines.

In her lab, Kaech studies a class of immune cells, known as memory T cells, that are responsible for developing long-term immunity to infection. Memory T cells could be used to treat cancer by leveraging the body's own immune system—a budding field called cancer immunotherapy. She also studies how immune cells are metabolically regulated by the types of nutrients they consume in cancer. Kaech will bring her expertise to the AAI Council to promote advances in immunology education, public awareness, advocacy and research.

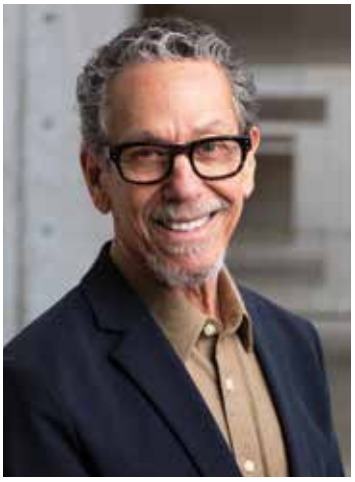
SUSAN KAECH



SAMUEL PFAFF

Professor Samuel Pfaff awarded $1 million by the W.M. Keck Foundation

Pfaff was awarded $1 million by the W.M. Keck Foundation. The funding will allow Pfaff, who is a professor in Salk's Gene Expression Laboratory and the Benjamin H. Lewis Chair, and his team to develop a new technology to better characterize neural circuits in the brain. The method will provide information about gene expression and function using a novel RNA detection system.



RONALD EVANS

PROFESSOR RONALD EVANS RECEIVES AACR-G.H.A. CLOWES AWARD

At the April annual meeting of the American Association for Cancer Research (AACR), Evans was awarded the 2022 AACR-G.H.A. Clowes Award for Outstanding Basic Cancer Research.

Evans was recognized for his work on a large family of molecules called nuclear hormone receptors. The receptors Evans discovered are primary targets in the treatment of breast cancer, prostate cancer, pancreatic cancer and leukemia, as well as osteoporosis and asthma.

SALK SCIENTISTS AND SAN DIEGO BOTANIC GARDEN COLLABORATE TO CREATE NATIONAL MEDICINAL PLANTS COLLECTION

The San Diego Botanic Garden, in collaboration with Salk scientists, launched a national medicinal plants collection and research consortium made possible by a $384,000 grant from the Conrad Prebys Foundation. The consortium's goal is to acquire and grow at least 500 new medicinal plants, develop comprehensive living plant collection protocols to optimize drug discovery and establish a garden to teach botanic garden visitors about medicinal plants.

Salk scientists receive 2022 Mark Foundation Endeavor Award to study lung cancer

Professors Reuben Shaw, Susan Kaech, Christian Metallo and Alan Saghatelian have received a 2022 Mark Foundation for Cancer Research Endeavor Award to support their research exploring the metabolic changes that help lung cancers develop. The $3 million Endeavor Award promotes collaborative science to tackle some of the toughest challenges in cancer research. The Salk team—one of four teams chosen out of nearly 200 applications submitted by institutions around the world—hopes their work will lead to the development of more effective lung cancer treatments.

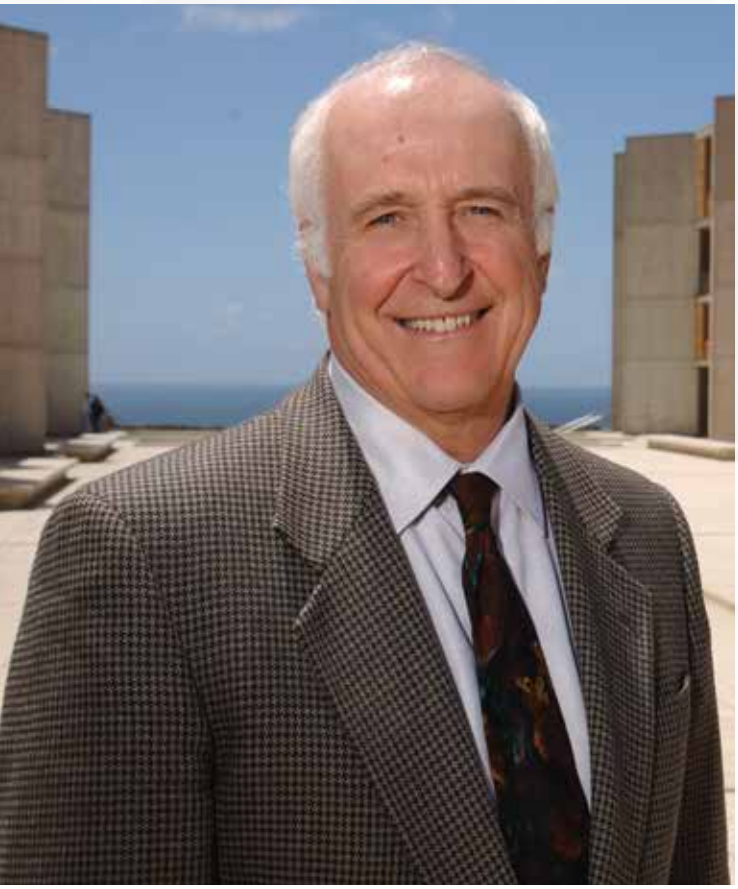
From left: Alan Saghatelian, Susan Kaech, Christian Metallo and Reuben Shaw.

BIOPHARMACEUTICAL EXECUTIVE CAROL GALLAGHER JOINS SALK BOARD OF TRUSTEES

In May, the Salk Board of Trustees welcomed Carol Gallagher as a new trustee. Gallagher brings a wealth of experience in the business and investment side of the life sciences industry to Salk's board. She is a venture partner at New Enterprise Associates, a US-based, worldwide venture capital firm focused on a variety of investment stages ranging from seed through growth stage, and across a broad array of industry sectors. She has 30 years of experience in commercial, drug development and business development roles. Gallagher's current work focuses on the biopharmaceutical industry.

At Salk, Gallagher also serves as chair of the Salk Women & Science Advisory Committee. Recently, she and her husband, John Gallagher, helped establish the Swati Tyagi Memorial Fund at Salk.

CAROL GALLAGHER Credit: Robert Schwieger



RICHARD MURPHY

Richard Murphy, former Salk Institute president and CEO, dies at 77

The Salk Institute mourns the loss of Richard "Rich" Murphy, who died March 24 in La Quinta, California, at the age of 77. Murphy served as the Institute's president and CEO from 2000 to 2007.

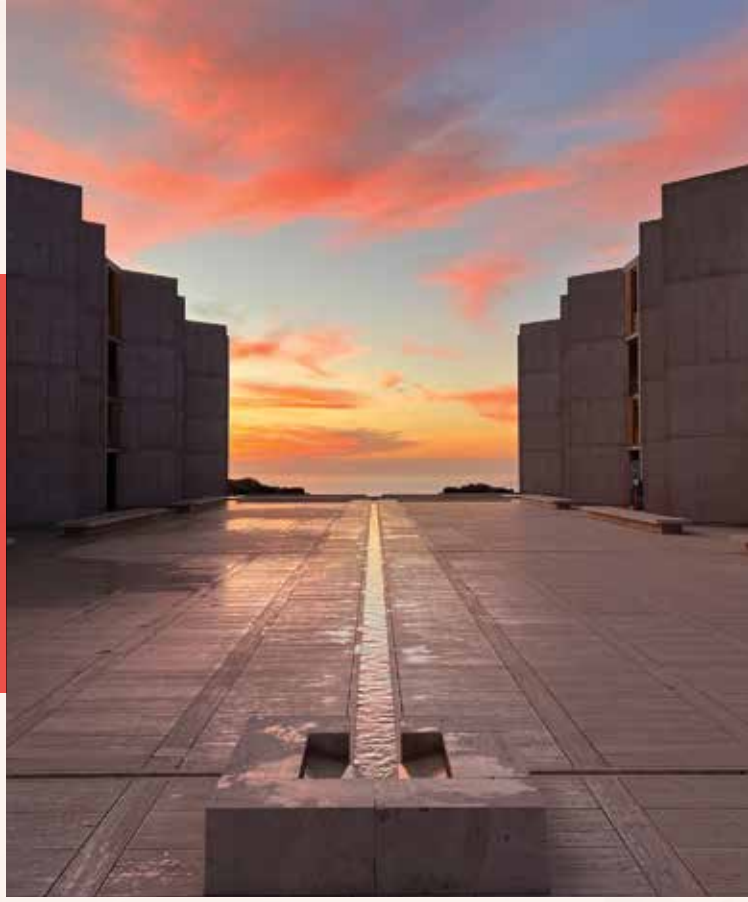
During his tenure, Murphy led the renovation of nearly a third of Salk's research space and the hiring of 16 new investigators to strengthen the Institute's cancer, plant biology and gene regulation research programs.

POSTDOCTORAL FELLOW KATIA TROHA NAMED 2022 LEADING EDGE FELLOW

Leading Edge is an initiative to improve the gender diversity of life sciences faculty in the United States by providing women and nonbinary postdocs with presentation, networking, mentorship and career development opportunities. As a 2022 Fellow, Troha joins an elite group of 45 superstar postdocs conducting cutting-edge research in biochemistry, cell and developmental biology, neuroscience, microbiology, bioinformatics, bioengineering and more. Troha studies mechanisms of asymptomatic infection in the lab of Professor Janelle Ayres.

KATIA TROHA

Salk Institute receives Charity Navigator's highest rating for 11th consecutive time



For the 11th consecutive time, the Salk Institute earned the highest ranking—four out of four stars—from Charity Navigator, America's largest independent charity and nonprofit evaluator. Only two percent of the approximately 10,000 nonprofits evaluated have achieved this recognition 10 consecutive times. The coveted ranking indicates the Salk Institute has demonstrated strong financial health and commitment to accountability and transparency, outperforming most other charities in the United States with respect to executing best fiscal practices and carrying out its mission in a financially efficient way.

"We are proud to once again receive Charity Navigator's highest level of fiscal accountability and transparency among our peers. Donations to Salk help drive life-changing research in aging, cancer, neuroscience, climate change and other critical areas."

RUSTY GAGE, SALK PRESIDENT

Charity Navigator's data-driven analysis of the 1.5 million American charities has been covered by *Forbes*, *Business Week* and others for providing donors with a way to recognize nonprofits that provide greater accountability, transparency and concrete results.

Since receiving its previous rating from Charity Navigator in 2021, the Salk Institute has launched the *Campaign for the Future: Building a More Resilient World*—a bold, five-year, $500 million effort to attract the people and acquire the technology and space necessary to expand and accelerate Salk's critical research. At the center of this audacious goal is the plan to build the 100,000-square-foot Joan and Irwin Jacobs Science and Technology Center.

The first major commitment toward the construction of the Jacobs Center came from longtime Salk supporters Joan and Irwin Jacobs in the form of a match challenge. Between now and September 30, 2022, the Jacobs will contribute $1 for every $2 donated—up to $100 million, which would translate to a total of $300 million with matching funds—for gifts or pledges made toward the campaign.

Since 2002, Charity Navigator has used objective analysis to award only the most fiscally responsible organizations a four-star rating; only a quarter of charities rated receive this distinction. In 2011, Charity Navigator added to its ratings methodology 17 metrics, focused on governance, ethical practices and measures of openness. These Accountability and Transparency metrics, which account for 50 percent of a charity's overall rating, reveal which charities operate in accordance with industry best practices and whether they are open with their donors and stakeholders.

Salk promotes Kenta Asahina, Eiman Azim and Margarita Behrens

Assistant Professors Kenta Asahina and Eiman Azim were promoted to associate professor, and Associate Research Professor Margarita Behrens was promoted to research professor, each for their original, innovative and notable contributions to neuroscience.

KENTA ASAHINA

Asahina conducts research on the genetic and neural basis of social interactions as part of the Molecular Neurobiology Laboratory. To study the basis of animal social behavior, he uses the common fruit fly *Drosophila melanogaster* as a model organism for understanding the genes and brain cells that cause behavioral responses, such as aggression, escape and courtship. Asahina's discoveries include a molecule released from brain cells associated with aggressive behavior in *Drosophila*. This same molecule was linked to aspects of aggressive behavior in mammalian models, which suggests it may serve as a therapeutic target for alleviating some behavioral symptoms associated with mental and psychiatric disorders.

EIMAN AZIM

Azim, who holds the William Scandling Developmental Chair, conducts research in the Molecular Neurobiology Laboratory, where he studies how the nervous system guides movement. Understanding how movements are learned, planned, executed and corrected can teach us more about the ways our brains coordinate complex motions such as reaching, grasping and object manipulation. By dissecting the movement pathways one element at a time, Azim aims to pinpoint neural circuits and piece together the underpinnings of skilled motions. Dexterous movements of the arms and hands are critical functions often affected by neurodegenerative disease and injury, and Azim's work seeks to lay the foundation for better treatments and recovery of function.

MARGARITA BEHRENS

Behrens is a member of the Computational Neurobiology Laboratory, where she studies brain development and disruption. From birth to adulthood our brains activate or inhibit cells in response to our environments. However, this context-dependent regulatory mechanism may go awry in some individuals as they develop. Behrens focuses on the interplay between our environments and cellular processes to determine why some people develop brain disorders while others do not. She also investigates brain circuit formation and disruption within the regions responsible for planning, reasoning and decision-making. By charting how cells control gene activity and changes that occur during cell maturation, Behrens' work could lead to a better understanding of neuropsychiatric and neurodevelopmental disorders, such as depression, bipolar disorder, schizophrenia and autism. (For a full interview with Behrens, please visit page 24.)

Salk programs offer a range of ways to get involved. Learn about Salk science and support vital research.

DISCOVER SALK

EDUCATION OUTREACH
Salk offers a wide variety of programs to inspire—and launch—the next generation of scientists. The Education Outreach program includes a Mobile Science Lab, Heithoff-Brody Scholars curriculum and teacher training.

CHAIRMAN'S CIRCLE
Visionary donors in the Chairman's Circle provide the vital resources Salk researchers need to pursue breakthrough science.

SALK SCIENCE & MUSIC SERIES
Sunday afternoons bring together virtuosos from the worlds of science and music.

SALKEXCELLERATORS
Designed for young business professionals and community members committed to supporting Salk scientific discovery, Salkexcellerators offers a unique opportunity to support breakthrough research, while connecting with like-minded people.

PRESIDENT'S CLUB
The President's Club helps recruit top-tier scientists, acquire cutting-edge technology and embark on innovative research initiatives.

INSTITUTE COUNCIL
This group of highly engaged individuals focuses on advancing Salk's scientific initiatives and supporting groundbreaking discoveries.

SALK WOMEN & SCIENCE
Showcasing the achievements of Salk's women of science, this program welcomes community and business leaders interested in inspiring women to embrace scientific research personally and philanthropically.

PARTNERS IN RESEARCH
Partners in Research invest in the future of cancer, aging, Alzheimer's disease and diabetes research by incorporating their philanthropic support for Salk in their estate plans.

SYMPHONY AT SALK
This annual concert under the stars features the incredible San Diego Symphony and a guest artist, while supporting the Institute's world-renowned research and award-winning education outreach programs.

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EVENTS

"I never thought of myself as a trailblazer, but I did want to change the dialogue regarding women in leadership roles, whether as philanthropists, professional fundraisers or anyone pursuing a nontraditional career path."

REBECCA NEWMAN

NEWEST TRAILBLAZER AWARD RECIPIENT REBECCA NEWMAN

Rebecca Newman, Salk's recently retired vice president of External Relations, was honored with the Ursula Bellugi Trailblazer Award at the July 14 Salk Women & Science event. Newman's ability to establish strong relationships with leading philanthropists and some of San Diego's biggest employers in the biotech industry has been key to her success as a fundraiser. Prior to joining Salk, she served for six years as associate vice chancellor of development at UC San Diego, where she successfully led the university's capital campaign and exceeded its $1 billion goal.

Newman joined Salk in 2008, where she has led the entire fundraising program, including strategic planning and campaigns, as well as donor relation- and event-related activities and communications. She successfully launched and exceeded the Institute's first major fundraising campaign to support scientific research, which secured more than $360 million in 2015. In addition, Newman oversaw 14 years of Symphony at Salk and created countless outreach programs, including the Salk Women & Science program, which she established in 2011 to raise the profile of women in science through historic fundraising and community engagement.

The Ursula Bellugi Trailblazer Award recognizes outstanding achievements made by women in their

SALKEXCELLERATORS

On May 25, Assistant Professor Christina Towers shared with the Salkexcellerators how she is using a combination of DNA-editing techniques, light-based genetic manipulation (optogenetics), three-dimensional miniature organs (organoids) and detailed imaging to uncover how cancer cells survive by recycling both their own nutrients and the power-generating structures called mitochondria. Her goal is to work with local clinicians to develop targeted cancer therapies that can block the cancer cell recycling pathways that allow these cells to survive. Towers' research could lead to methods to reduce cancer recurrence and improve outcomes for patients with cancer. Salkexcellerators are the next generation of community members who support scientific discovery at Salk and engage with scientists through a full schedule of activities.

CHRISTINA TOWERS

fields. Recipients have pioneered changes within their disciplines as innovators, leaders, collaborators and mentors. They are dedicated to making significant advances in both their professional and personal lives. Trailblazers forge their own paths to achieve their visions. Past award recipients include Distinguished Professor Emerita Ursula Bellugi, Professor Emerita Catherine Rivier and Professor Joanne Chory.

"Receiving the Trailblazer Award was both surprising and humbling," Newman says. "It is intimidating to stand in a group with the late Ursula Bellugi, as well as the extraordinary Catherine Rivier and Joanne Chory, all of whom are icons not only for the great accomplishments of their science but also for their humanity, work ethic and generosity of spirit.

"It is also validating to have the recognition that true impact results from people of many different skill sets working together to achieve great results. I never thought of myself as a trailblazer, but I did want to change the dialogue regarding women in leadership roles, whether as philanthropists, professional fundraisers or anyone pursuing a nontraditional career path. I tried to lead by working hard and mentoring both women and men I supervised to have confidence in their abilities, to trust their instincts and to value the skills they bring to every endeavor—their success has been my greatest gift."

From left: Gerald Joyce, Kay Tye, Carol Gallagher and Marna Whittington.

SALK WOMEN & SCIENCE PROGRAM LEADING THROUGH THE PANDEMIC AND BEYOND

During a special Women & Science event on July 14, a panel of speakers discussed the unique challenges faced by women leaders in science and industry during the COVID pandemic, new research opportunities and lessons learned, the importance of supporting women leaders, and the future of the Salk Institute. The event opened with remarks by Director of Donor Relations Betsy Collins and President Rusty Gage. Senior Vice President and Chief Science Officer Gerald Joyce moderated the panel, which featured Board Chair Marna Whittington, Trustee Carol Gallagher and Professor Kay Tye.

The event was dedicated to the late Professor Emerita Ursula Bellugi and her pioneering roles in science, at Salk and in the Institute's Women & Science program. (Learn more about Bellugi on page 28.)

GERALD JOYCE

INSTITUTE COUNCIL MEETING

Members of the Institute Council gathered at Salk on June 1 for the group's seventh annual meeting. Salk leaders shared details of the Institute's vision for the future, including plans to build the new Joan and Irwin Jacobs Science and Technology Center on the east side of campus. The program included presentations from faculty members, executive and administrative leaders, and concluded with a special cocktail reception in the West Courtyard.

POWER OF SCIENCE LECTURE SERIES

On April 6, Professor Greg Lemke delivered a presentation titled "21st Century Salk: Building a More Resilient World" as part of Salk's Power of Science Lecture Series. A Salk researcher since 1985, Lemke described how our understanding of biology and the way research is conducted have changed dramatically since the Institute's founding. He also shared his thoughts on how science—and the Institute—will continue to evolve through the next decade and beyond.

WATCH | https://www.salk.edu/powerofscience202204

LOUIS VUITTON FASHION SHOW

Institute founder Jonas Salk understood that art and science come from the same creative source, and it was his intention that his Institute become a place where scientists and artists could both find inspiration. In keeping with Salk's vision, on May 12 the Institute was proud to host French luxury fashion house Louis Vuitton and guests for a private fashion show presenting the brand's Cruise 2023 collection. "The show was fantastic because it introduced the fashion community to the Salk Institute and its science," says Greg Lemke, professor and Françoise Gilot-Salk Chair. "Bringing creative people with very different interests to the Institute is an important cross-fertilization. They were able to experience our iconic buildings and hear about our work firsthand."

INTERNATIONAL WOMEN'S DAY

In recognition of International Women's Day, on March 22 a diverse panel discussed their own personal experiences with gender and other biases and shared thoughts on how to improve equity and inclusion in science. The program included an overview of this year's theme, #BreakTheBias, and participants shared how the Salk community is working toward that goal. The panel featured Dannielle Engle, assistant professor; Mallory Zaslav, vice president of Equity and Inclusion; Talmo Pereira, Salk fellow; Kurt Marek, executive director of Grants Development; and Ying Sun, postdoctoral fellow.

CHANELLE JIMENEZ

From Left: Ying Sun, Talmo Pereira, Mallory Zaslav, Dannielle Engle and Kurt Marek.

Photo by PATRICK T. FALLON/AFP via Getty Images

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CLIVE GREENSMITH

SALK SCIENCE & MUSIC SERIES

The eighth season of the Salk Science & Music Series wrapped on June 12 with the beautiful music of pianist **Sean Chen**, and **Professor Martyn Goulding** gave a presentation on current work in the Molecular Neurobiology Laboratory.

Back in person for the entire season for the first time in more than two years, the Salk Science & Music Series provided audiences with four remarkable Sunday afternoons featuring virtuosos from the worlds of science and music. The concerts in the series included performances and talks by the following musicians and scientists:

MARCH 20, 2022

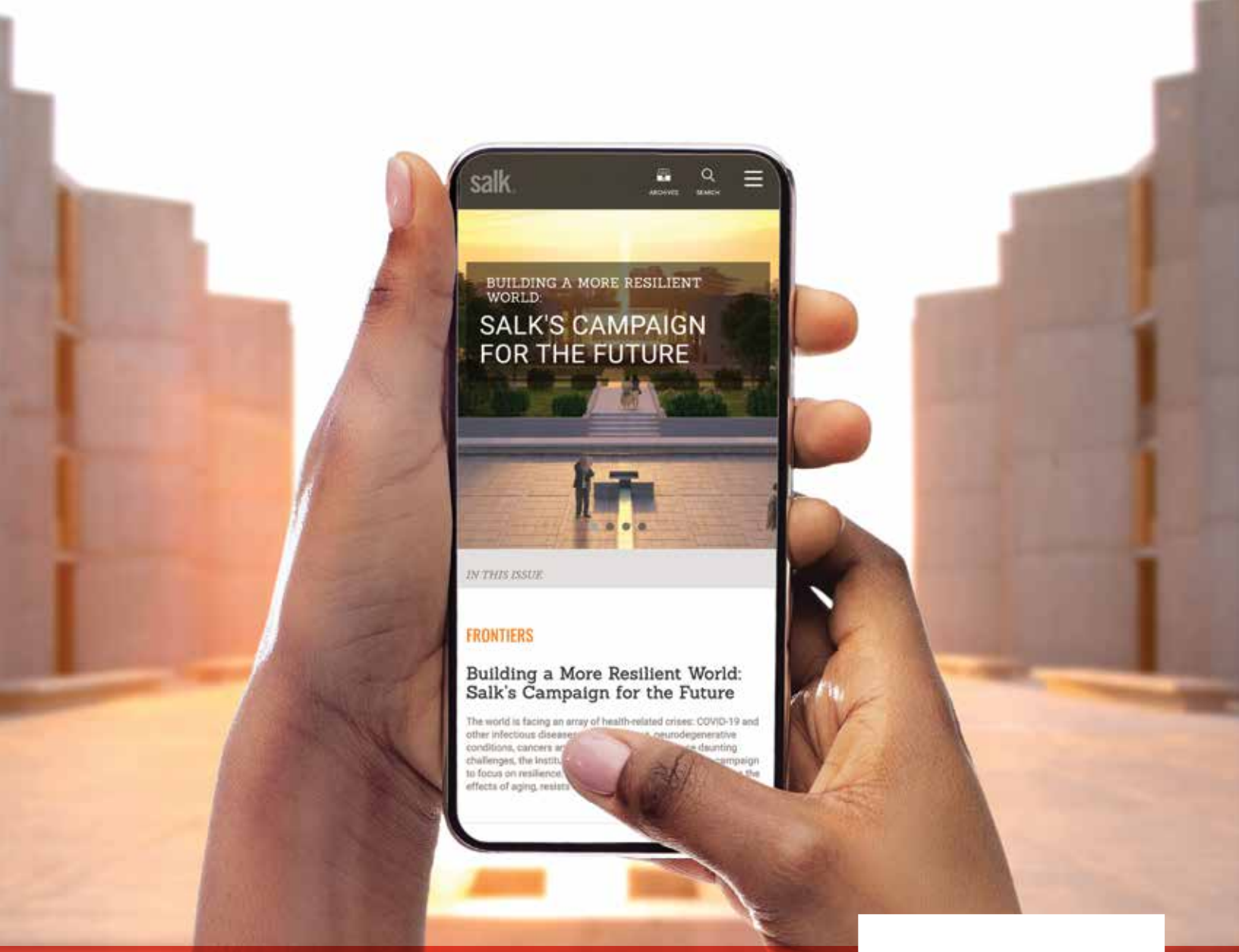
Clive Greensmith, cello, and
Karen Joy Davis, piano
Scientific presentation by
Assistant Professor Dannielle Engle,
Regulatory Biology Laboratory

APRIL 24, 2022

Benjamin Beilman, violin, and
Roman Rabinovich, piano
Scientific presentation by
Research Professor Todd Michael,
Plant Molecular and Cellular Biology
Laboratory

MAY 15, 2022

Zlata Chochieva, piano
Scientific presentation by
Assistant Professor Pallav Kosuri,
Integrative Biology Laboratory



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