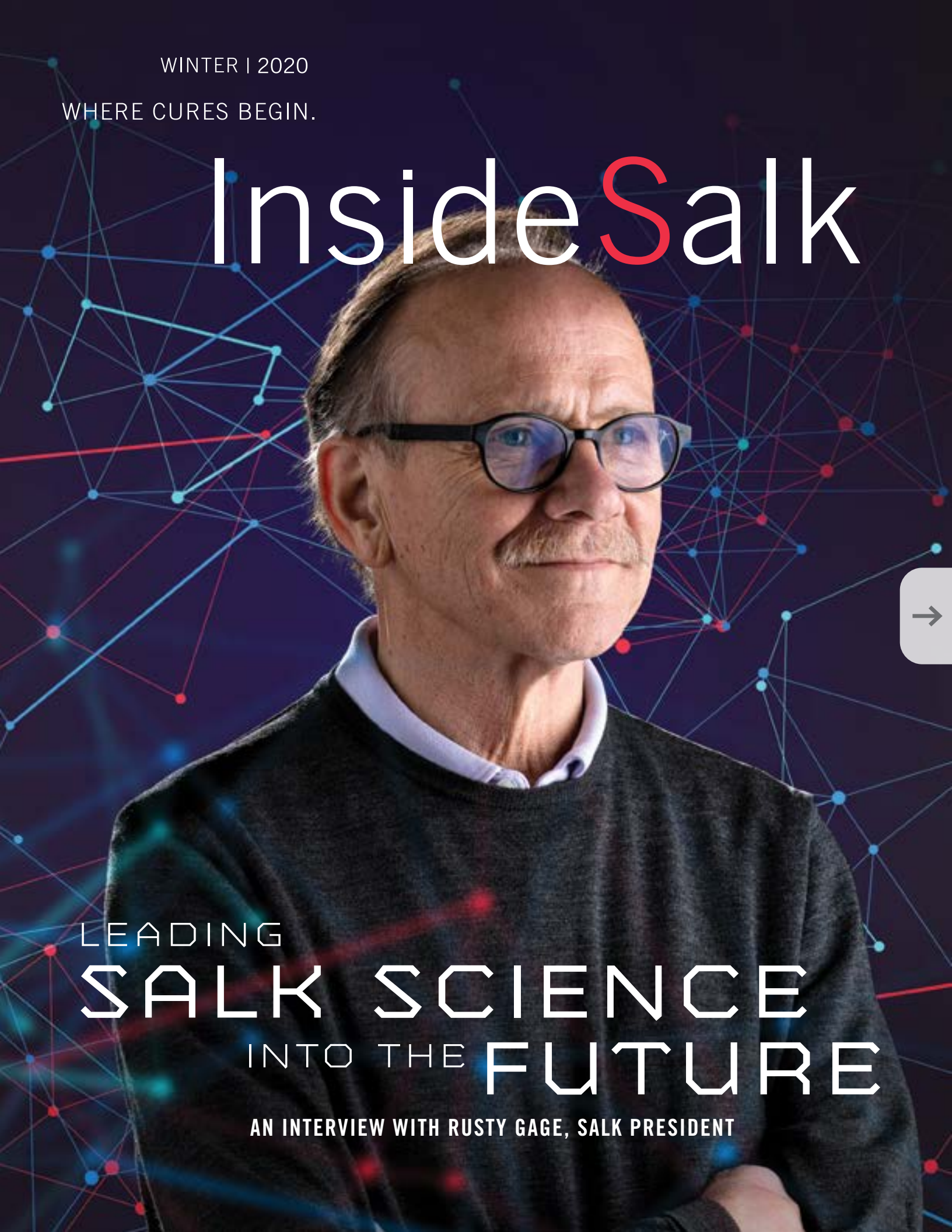
WINTER | 2020

WHERE CURES BEGIN.

InsideSalk



LEADING SALK SCIENCE INTO THE FUTURE

AN INTERVIEW WITH RUSTY GAGE, SALK PRESIDENT

CONTENTS

ON THE COVER:

Together with Salk's world-renowned researchers, Salk President Rusty Gage is leading the Institute in bold efforts to tackle climate change, cancer, Alzheimer's and much more.

EXECUTIVE LETTER

Dear Friends,

I hope this message finds you and your family safe and well during this unparalleled period in our history.

In ways large and small, the COVID-19 pandemic has changed our world and given us all an appreciation for many things we took for granted. This time last year, few of us could have imagined that a trip to the grocery store, a simple hug from a friend or a handshake would become a risk to our health.

This pandemic has also given us a renewed appreciation for the critical role scientific research plays in protecting our health and our way of life. As we anxiously await the distribution of effective vaccines, I take comfort knowing that the Institute's founder, Jonas Salk, faced a similar challenge with polio. Using basic science, he developed the first safe and effective vaccine, which helped halt polio epidemics. Science will once again prevail, this time over the novel coronavirus.

As 2020 comes to a close, I am filled with gratitude for the extraordinary efforts made by our faculty and administrative staff over the past year, which helped the Institute successfully navigate this pandemic. Under the leadership of President Rusty Gage, the Institute responded rapidly in March as the virus spread. A multidisciplinary team from across the Institute implemented strategies to protect our researchers and staff and allow for the safe pursuit of scientific research. And through this shared goal, stronger relations and new collaborations have been established among Salk staff, faculty, donors and trustees.

Salk is fortunate to have Rusty Gage as its leader. It is well known that Rusty is a brilliant neuroscientist whose work continues to be at the forefront of scientific discovery. But it is his generosity of spirit, humility and focus on the future that also make him such a strong leader for Salk. He is known for his ability to bring people together and collaborate to advance both the scientific and administrative goals of the Institute. It is this unique set of skills and experience that will help us build on Salk's 60 years of bold research and position the Institute for even greater success into the future. A look at how that future is poised to unfold at Salk is the focus of this issue.

In this edition of *Inside Salk* you will also find the 2020 Salk Donor Honor Roll, our annual acknowledgment and appreciation of those who have supported our work in the last fiscal year. Along with a summary report of the Institute's fiscal health, we acknowledge the more than 1,200 individuals, families, organizations and businesses who have supported Salk in the 2020 fiscal year (July 1, 2019 through June 30, 2020).

You will also discover how Salk scientists are pursuing their research and what makes them tick. Associate Professor Julie Law discusses how a chance event led her to devote her career to understanding the process of turning genes on or off. Staff Scientist Gerald Pao is at the forefront of scientific advancement, from studying the novel coronavirus to uploading brains to computers. And Postdoctoral Fellow Austin Coley not only conducts innovative brain research but also has a passion for advancing opportunities for greater diversity within the world of science.

The Institute's future is bright because of its dedicated supporters, leadership and the faculty and staff who embody the spirit of Jonas Salk's challenge to turn dreams into reality. On behalf of the Board of Trustees of the Salk Institute, I extend my deep appreciation for your support of Salk science. You have truly made a difference.

Sincerely,

Daniel C. Lewis
Salk Board of Trustees Chair

"As 2020 comes to a close, I am filled with gratitude for the extraordinary efforts made by our faculty and administrative staff over the past year, which helped the Institute successfully navigate this pandemic."

salk®

HARNESSING PLANTS INITIATIVE

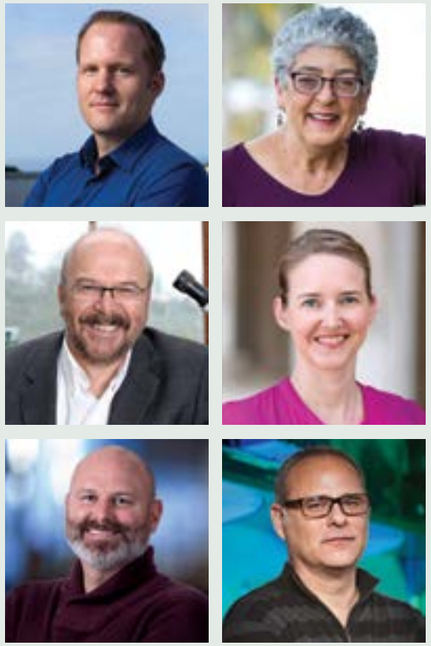
SALK'S HARNESSING PLANTS INITIATIVE (HPI) GARNERS WIDESPREAD SUPPORT

New grants are supporting the Institute's efforts to optimize plants' natural ability to store carbon and mitigate climate change. This support bolsters the ongoing HPI project focused on model plants that was funded through donations to The Audacious Project in 2019.

BEZOS EARTH FUND DONATES $30 MILLION TO SALK INSTITUTE FOR INNOVATIVE CLIMATE CHANGE RESEARCH

Salk's Harnessing Plants Initiative (HPI) received $30 million from the Bezos Earth Fund to advance efforts to increase the ability of crop plants, such as corn and soybeans, to capture and store atmospheric carbon via their roots in the soil. This work will explore carbon-sequestration mechanisms in six of the world's most prevalent crop species with the goal of increasing the plants' carbon-storage capacity. It complements an ongoing HPI project focused on identifying genes for increased carbon sequestration in model plants and then utilizing those genes to enhance carbon sequestration in crops.

The Bezos Earth Fund grant will enable Salk scientists to advance work in plant genetics, genomics, and biochemistry—and use the power of plant diversity—to develop global crops that will increase the amount of carbon removed from the atmosphere and store it deep in the earth's soil. Members of the HPI leadership team include Salk faculty Wolfgang Busch, Joanne Chory, Joseph Ecker, Julie Law, Todd Michael and Joseph Noel.



From top left: Wolfgang Busch, Joanne Chory, Joseph Ecker, Julie Law, Todd Michael and Joseph Noel.

SALK AND SEMPRA ENERGY ANNOUNCE PROJECT TO ADVANCE PLANT-BASED CARBON CAPTURE AND STORAGE RESEARCH

Salk and Sempra Energy (NYSE: SRE) announced a new project to advance plant-based carbon capture and sequestration research, education and implementation to help address the climate crisis. With its $2 million donation, Sempra will be the lead sponsor of the "Sequestering Carbon Through Climate Adapted Sorghum" project, part of the Institute's Harnessing Plants Initiative.

DIALING THE IMMUNE RESPONSE UP OR DOWN

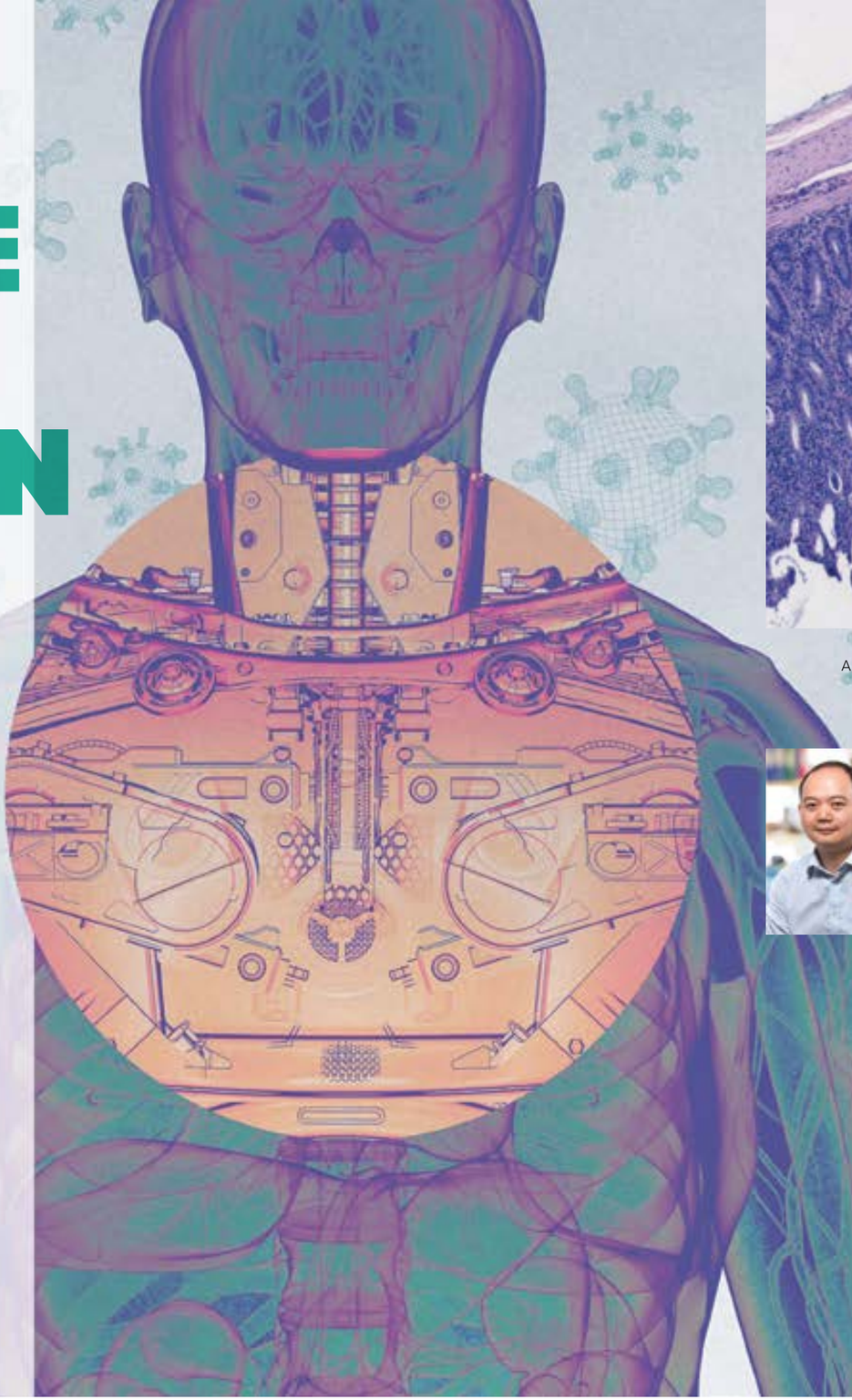
The immune system is a finely tuned machine. It must balance the release of its cellular army to deal with pathogens, such as the coronavirus, while reining in that army to stop the onslaught from attacking the body itself, which occurs in autoimmune diseases. Now, Salk researchers have made two new scientific discoveries about how the immune system functions to keep the body healthy.

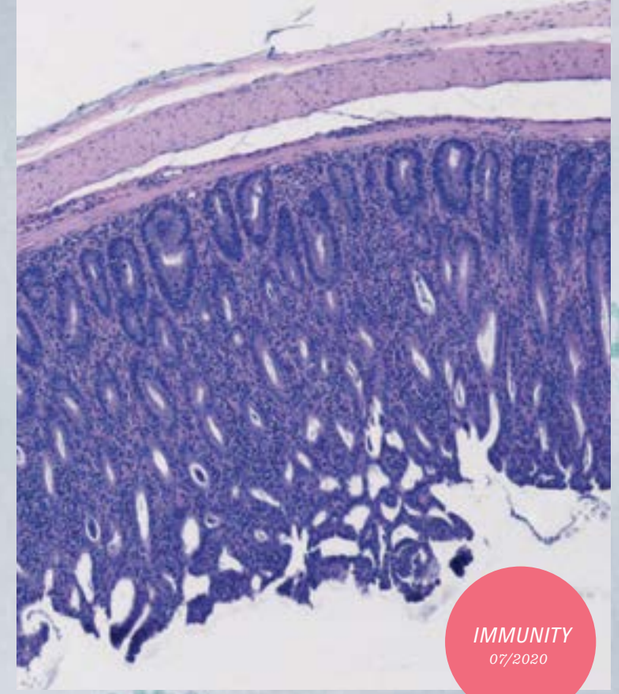
JOURNAL OF EXPERIMENTAL MEDICINE
06/2020

From left: Susan Kaech and Jun Siong Low.

Salk Professor Susan Kaech examined the immune cells in the lungs, a significant site of damage during the COVID-19 infection. When we are first exposed to bacteria or viruses, immune cells called killer T cells destroy the infected cells to prevent the spread of the disease. Killer T cells effectively provide long-term protective immunity against the invader, a fundamental concept behind vaccination. Kaech's team, including first author and then-graduate student Jun Siong Low, found that the cells responsible for long-term immunity in the lungs can be activated more easily than previously thought. The insight could aid in the development of universal vaccines for influenza and the novel coronavirus.

WATCH | www.salk.edu/kaech202012





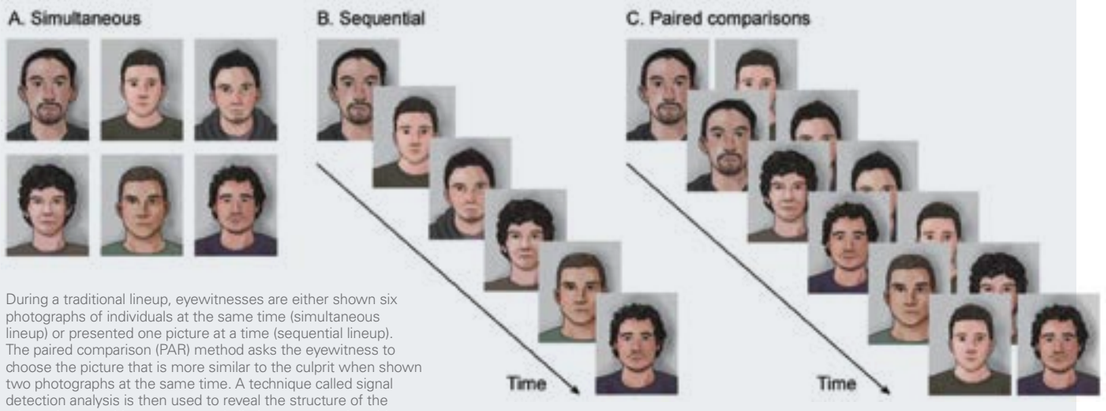
IMMUNITY
07/2020

A histology image showing inflammation in colon epithelium. Weakening of regulatory T cell function induces infiltration of immune cells (small blue dots) into colon epithelium (blue layer) and causes colitis.

From left: Ye Zheng, Eric Chin-San Loo, Jovylyn Gatchalian and Diana Hargreaves.

In the second advance, Associate Professor Ye Zheng, Assistant Professor Diana Hargreaves, co-first authors Jovylyn Gatchalian and Eric Chin-San Loo, and colleagues discovered a way to control regulatory T cells, immune cells that act as a cease-fire signal, telling the immune system when to stand down. Being able to increase or decrease regulatory T cell activity could one day help treat numerous diseases including rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease, lupus and even some cancers.

NEUROSCIENCE



During a traditional lineup, eyewitnesses are either shown six photographs of individuals at the same time (simultaneous lineup) or presented one picture at a time (sequential lineup). The paired comparison (PAR) method asks the eyewitness to choose the picture that is more similar to the culprit when shown two photographs at the same time. A technique called signal detection analysis is then used to reveal the structure of the witness's recognition memory and eliminate unconscious bias.

KEEPING INNOCENT PEOPLE OUT OF JAIL USING THE SCIENCE OF PERCEPTION

NATURE COMMUNICATIONS 07/2020

People wrongfully accused of a crime often wait years—if ever—to be exonerated. Many of these wrongfully accused cases stem from unreliable eyewitness testimony. Now, Professor Thomas Albright, Staff Scientist Sergei Gepshtein and colleagues have identified a new way of presenting a lineup to an eyewitness that could improve the likelihood that the correct suspect is identified and reduce the number of innocent people sentenced to jail.

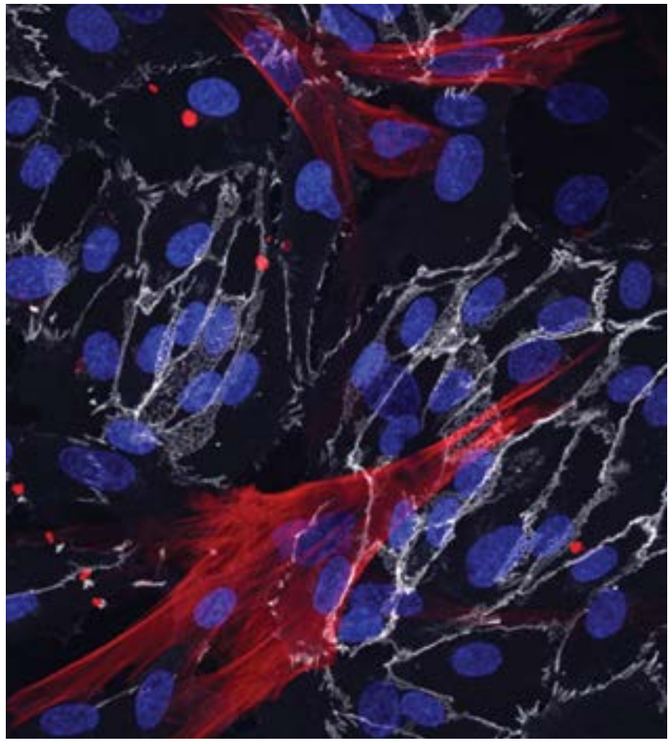
WATCH | www.salk.edu/albright202012

TRAVELING BRAIN WAVES HELP DETECT HARD-TO-SEE OBJECTS

NATURE 10/2020

Professor John Reynolds, Professor Terrence Sejnowski, co-first authors Zac Davis and Lyle Muller, and colleagues have uncovered details about the neural mechanisms underlying the perception of objects. They found that patterns of neural signals, called traveling brain waves, exist in the visual system of the awake brain and are organized to allow the brain to perceive objects that are faint or otherwise difficult to see.

AGING



Skin fibroblasts were successfully reprogrammed into the smooth muscle cells (red) and endothelial cells (white) that surround blood vessels. The cells' nuclei are shown in blue.
Credit: Bersini, Schulte et al. CC by 4.0

METHOD TO DERIVE BLOOD VESSEL CELLS FROM SKIN CELLS SUGGESTS WAYS TO SLOW AGING

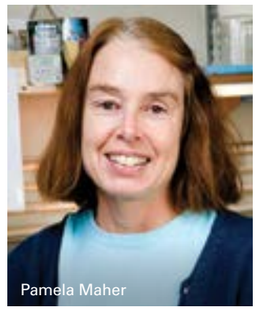
eLIFE 09/2020

Professor and VP/CSO Martin Hetzer, co-first authors Simone Bersini and Roberta Schulte, and colleagues have used skin cells called fibroblasts from young and old patients to successfully create blood vessel cells that retain their molecular markers of age. The team's approach revealed clues as to why blood vessels tend to become leaky and hardened with age, and lets researchers identify new molecular targets to potentially slow aging in vascular cells.

NEW MOLECULE REVERSES ALZHEIMER'S-LIKE MEMORY DECLINE

REDOX BIOLOGY 07/2020

A drug candidate developed by Senior Staff Scientist Pamela Maher and first author Gamze Ates of the Schubert lab, and previously shown to slow aging in brain cells, successfully reversed memory loss in a mouse model of inherited Alzheimer's disease. The new research also revealed that the drug, CMS121, works by changing how brain cells metabolize fatty molecules known as lipids.



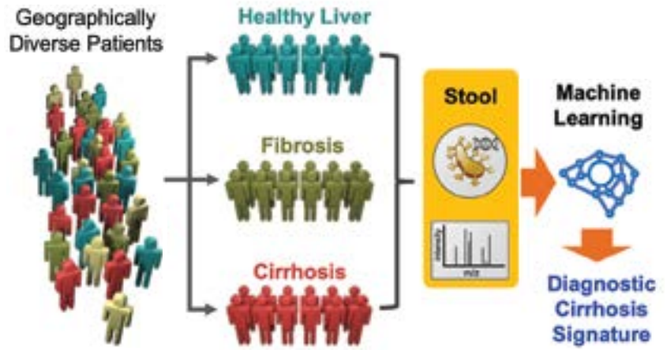
Pamela Maher

COMPUTATIONAL BIOLOGY

GIANT LEAP IN DIAGNOSING LIVER DISEASE

CELL METABOLISM 06/2020

Chronic liver disease represents a major global public health problem affecting an estimated 844 million people. A collaborative team of scientists, co-led by Salk Professor Ronald Evans and including first author Tae Gyu Oh and Senior Staff Scientist Michael Downes, have created a novel diagnostic tool based on the microbiome—a complex collection of microbes that inhabit the gut. The non-invasive method quickly and inexpensively identifies liver fibrosis and cirrhosis over 90 percent of the time and could lead to improved patient care and treatment outcomes.



Schematic showing how the microbiome signature from stool samples can be used to test for cirrhosis.

From left: Michael Downes, Tae Gyu Oh and Ronald Evans.

CANCER

LOCATION, LOCATION, LOCATION: THE CELL MEMBRANE FACILITATES RAS PROTEIN INTERACTIONS

THE PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES 05/2020

Many cancer medications fail to effectively target the most commonly mutated cancer genes in humans, called RAS. Now, Salk Professor Geoffrey Wahl, first author Yao-Cheng (Leo) Li and a team of scientists have uncovered details of how normal RAS interacts with mutated RAS and other proteins in living cells for the first time. The findings could aid in the development of better RAS-targeted cancer therapeutics.

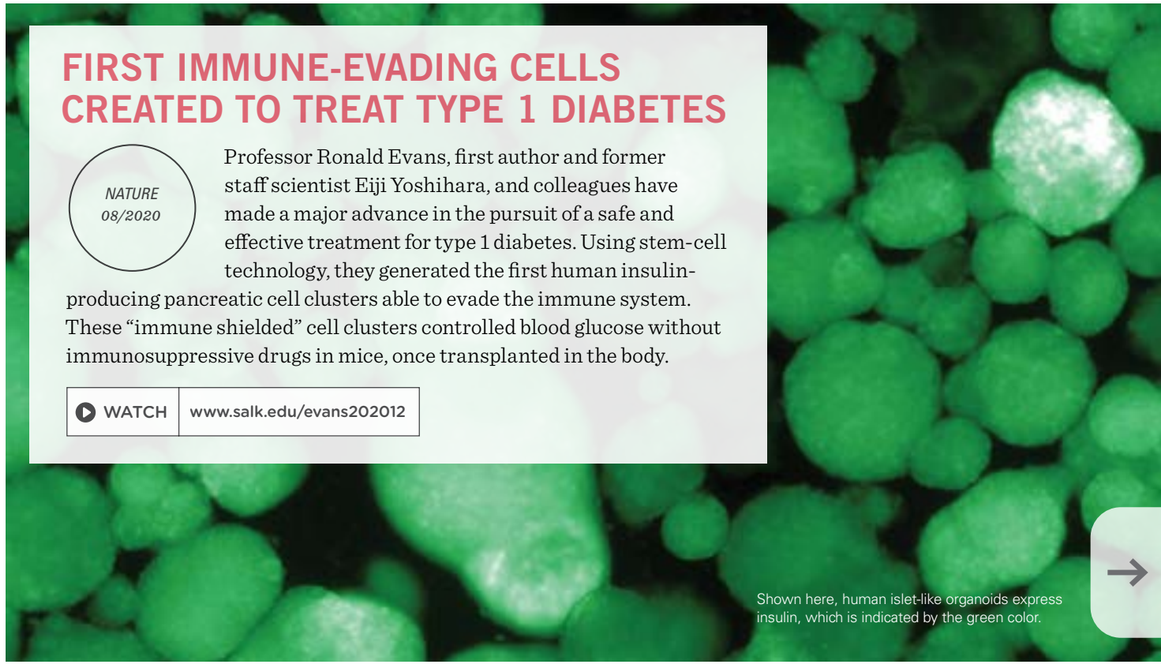
METABOLISM

FIRST IMMUNE-EVADING CELLS CREATED TO TREAT TYPE 1 DIABETES

NATURE 08/2020

Professor Ronald Evans, first author and former staff scientist Eiji Yoshihara, and colleagues have made a major advance in the pursuit of a safe and effective treatment for type 1 diabetes. Using stem-cell technology, they generated the first human insulin-producing pancreatic cell clusters able to evade the immune system. These "immune shielded" cell clusters controlled blood glucose without immunosuppressive drugs in mice, once transplanted in the body.

WATCH | www.salk.edu/evans202012



Shown here, human islet-like organoids express insulin, which is indicated by the green color.

From left: Reuben Shaw and Jeanine Van Nostrand.

COMMON DIABETES DRUG REVERSES INFLAMMATION IN THE LIVER

GENES & DEVELOPMENT 09/2020

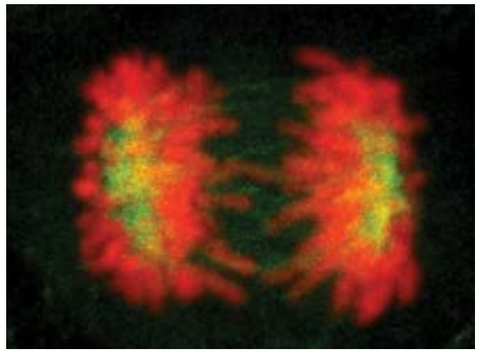
The diabetes drug metformin has been prescribed to hundreds of millions of people worldwide as the frontline treatment for type 2 diabetes. Now, Professor Reuben Shaw, first author Jeanine Van Nostrand and colleagues have shown the importance of specific enzymes in the body for metformin's function. In addition, the new work showed that the same proteins, regulated by metformin, controlled aspects of inflammation in mice, something the drug has not typically been prescribed for. Apart from clarifying how metformin works, the research has relevance for many other inflammatory diseases.

GENETICS

HOW CELLS SOLVE THEIR IDENTITY CRISIS

GENES & DEVELOPMENT 06/2020

Cancer is often the result of DNA mutations or problems with how cells divide, which can lead to cells "forgetting" what type of cell they are or how to function properly. Professor and VP/CSO Martin Hetzer, first author Hyeseon Kang, Assistant Professor Jesse Dixon and colleagues have now provided clarity into how new cells remember their identity after cell division. These memory mechanisms could explicate problems that occur when cell identity is not maintained, such as cancer.



A cell dividing into two cells during the process of mitosis. The microtubules (green) are shown pulling the chromosomes (red) to the opposite sides of the cell.

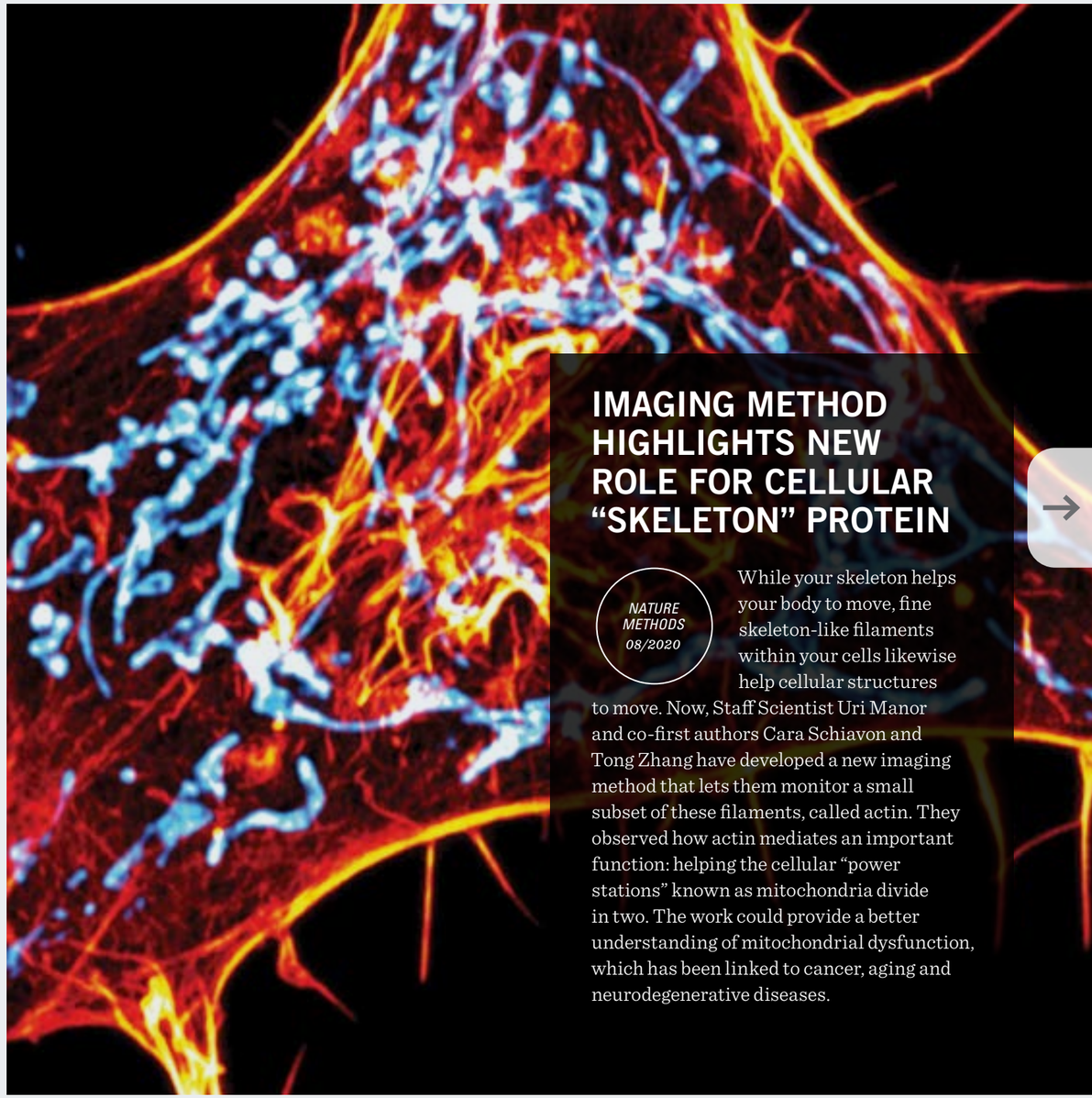
NEW MAPS OF CHEMICAL MARKS ON DNA PINPOINT REGIONS RELEVANT TO MANY DEVELOPMENTAL DISEASES

NATURE 07/2020

In research that aims to illuminate the causes of human developmental disorders, Professor Joseph Ecker, first author Yupeng He and colleagues have generated 168 new maps of chemical marks on strands of DNA—called methylation—in developing mice. The data can help narrow down regions of the human genome that play roles in diseases such as schizophrenia and Rett syndrome.

WATCH | www.salk.edu/ecker202012

PROTEIN INTERACTIONS



IMAGING METHOD HIGHLIGHTS NEW ROLE FOR CELLULAR "SKELETON" PROTEIN

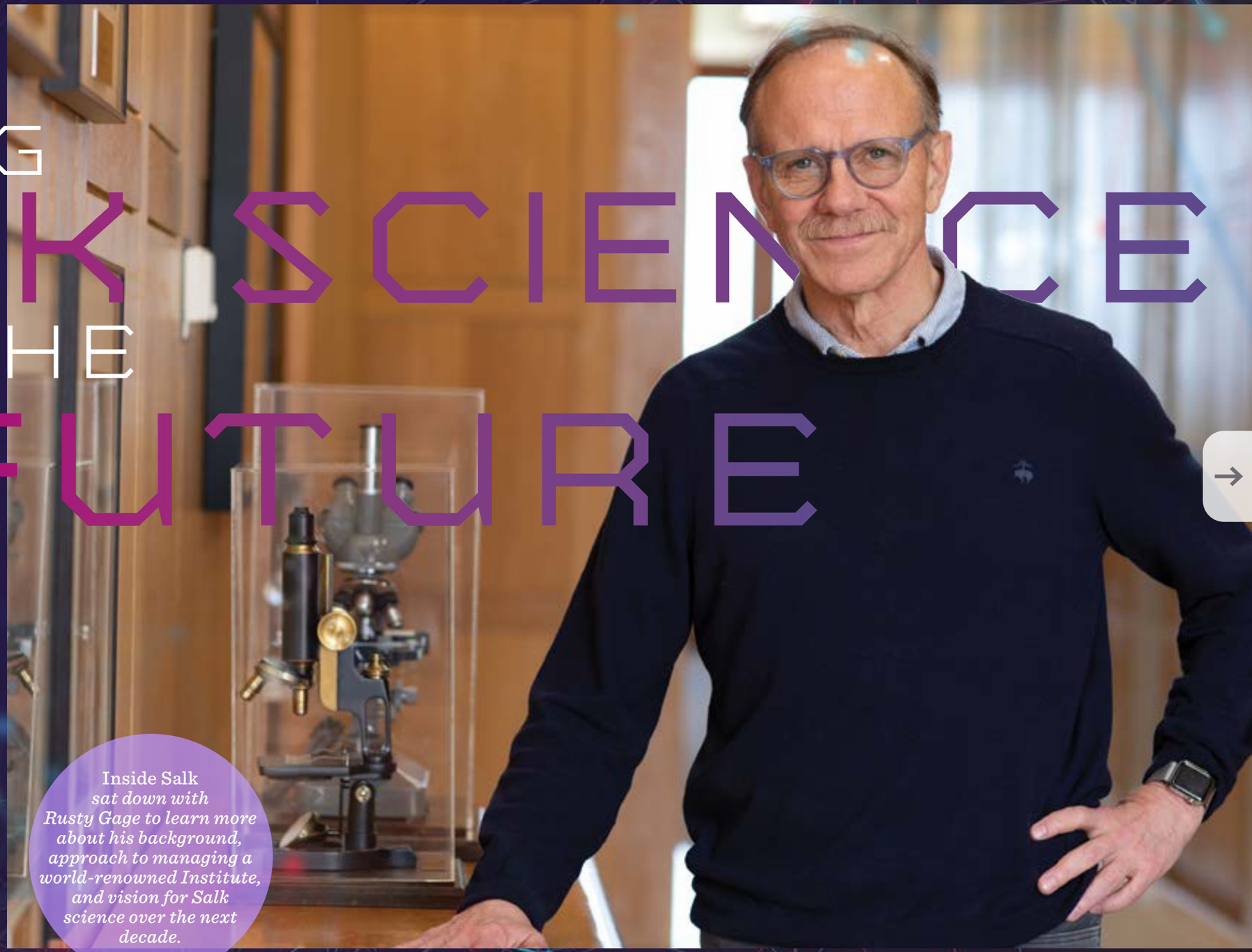
NATURE METHODS 08/2020

While your skeleton helps your body to move, fine skeleton-like filaments within your cells likewise help cellular structures to move. Now, Staff Scientist Uri Manor and co-first authors Cara Schiavon and Tong Zhang have developed a new imaging method that lets them monitor a small subset of these filaments, called actin. They observed how actin mediates an important function: helping the cellular "power stations" known as mitochondria divide in two. The work could provide a better understanding of mitochondrial dysfunction, which has been linked to cancer, aging and neurodegenerative diseases.

Two decades into the 21st century, the way science is conducted is changing dramatically. The Salk Institute, built with the implicit understanding that science is ever-evolving and institutions must adapt, is changing too.

LEADING SALK SCIENCE INTO THE FUTURE

To understand the future of Salk science, one only needs to look to its leader, current President and longtime faculty member Rusty Gage. From managing the COVID-19 crisis that threw the world into disarray, to advancing efforts in support of equity and inclusion, Gage has been agile and collaborative, responsive and engaged. Even as he leads Salk's response during these difficult and uncertain times, he balances a robust scientific research portfolio. From his lab to the President's office, Gage has his eyes on the future of science at Salk, and on the significant shifts poised to transform the world of basic scientific research. His success lies largely in his approach: he pairs a disciplined and astute habit of observation with a deeply collaborative nature, where he seeks to lift diverse voices across the Institute to inform his daily decisions while working strategically to advance scientific initiatives; recruit a new generation of brilliant Salk scientists; and build the financial and scientific resources necessary to move Salk into future.



Inside Salk *sat down with Rusty Gage to learn more about his background, approach to managing a world-renowned Institute, and vision for Salk science over the next decade.*

Leading with vision and collaboration

When Rusty Gage, the Vi and John Adler Chair for Research on Age-Related Neurodegenerative Disease, assumed the presidency of Salk in 2018, he had decades of pioneering neuroscience papers to his credit. Since then, he has balanced two equally demanding full-time jobs: president of an elite, world-renowned institution that conducts innovative science, and leader of a distinguished neuroscience laboratory.

Gage is one of the world's preeminent neuroscientists, known for overturning longstanding scientific dogma that the brain does not make new neurons, with a 1998 study revealing that "neurogenesis" does, in fact, occur in select areas of the brain.

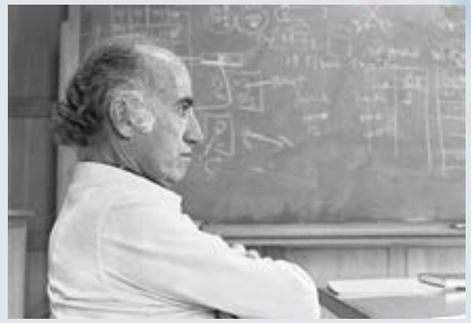
Since 2014, he has consistently been named one of science's most highly cited researchers by Clarivate, indicating that his work has been repeatedly judged by his peers to be notable for its significance and usefulness. And his lab, one of Salk's largest, routinely delivers cutting-edge methodologies and ground-breaking discoveries to find better ways to understand and treat conditions of the brain, such as Alzheimer's, depression, autism, bipolar disorder and schizophrenia.

"In this new paradigm, you not only read the literature, but you aggregate data sets from all over the world and build a theoretical model of the concepts you're interested in, so you can decide what scientific questions to pursue."

RUSTY GAGE

Raised in a military family stationed abroad, Gage went to high school in Italy before attending college at the University of Florida and graduate school at Johns Hopkins University. He married his high school sweetheart and the couple moved to Sweden, where Gage completed a Fulbright fellowship and held a faculty position at Lund University. He joined the faculty at UC San Diego in 1985, and the family settled in San Diego, where his mother was raised and went to college. A dedicated mentor, he delights in the Gage lab reunions held every few years for alumni who travel back to Salk from around the world to share their research with their former colleagues and their former advisor.

As President of Salk, Gage brings a scientific approach to leading: much like gathering data to test a hypothesis, he seeks input from a diverse group of stakeholders and synthesizes it into a coherent picture to help guide the Institute. Gage—who arrived at Salk while founder and polio vaccine developer Jonas Salk was still



Gage worked alongside notables, such as Jonas Salk (pictured above).

TECHNOLOGY

MARTIN HETZER
Vice President and Chief Science Officer
Jesse and Caryl Philips Foundation Chair
Professor, Molecular and Cell Biology Laboratory

"Salk's future successes and breakthroughs, like our deep history of scientific discovery, will be the result of the teamwork of postdoctoral researchers, students, staff scientists and exceptional faculty—all critically supported by the research centers, shared core facilities and animal research department. Bold and collaborative science is the hallmark of the Institute, and the CSO office intends to bring that spirit to all future endeavors, both at Salk and with local and international partnerships."

The Office of the Chief Science Officer provides leadership in developing and implementing Salk's overall scientific strategy, as well as overseeing research operations in support of this strategy.

IMMUNOBIOLOGY

SUSAN KAECH
NOMIS Chair
Professor and Director, NOMIS Center for Immunobiology and Microbial Pathogenesis

"The future of immunobiology, both at Salk and beyond, holds a great deal of promise. Not only are we learning more every day about the fundamentals of immunity, but we are also discovering how to harness the immense power of the immune and cooperative defense systems and the microbiome to target cancer, autoimmune diseases and infections, to help people live longer, healthier lives."

Salk's NOMIS Center for Immunobiology and Microbial Pathogenesis is working to delineate the mechanisms that cause infectious diseases, understand the body's response to injury or infection, and explore why inflammatory processes spin out of control under some circumstances.

AGING

JAN KARLSEDER
Donald & Darlene Shiley Chair
Professor, Molecular and Cell Biology Laboratory
Director, Paul F. Glenn Center for Aging Research

"Understanding the complexity of the aging process and extending the human health span have become top priorities of the Salk Institute, and will remain so in the future. Neurobiology, cell and molecular biology, systems biology and computational biology will synergize to clarify complex age-associated pathologies such as Alzheimer's disease, hearing loss, cardiovascular disease, diabetes and cancer. The collaborative nature of Salk will allow a uniquely cooperative approach through our Optimizing Aging Initiative, which takes advantage of the widespread expertise of Salk faculty."

GERALD SHADEL
Audrey Geisel Chair in Biomedical Science
Professor, Molecular and Cell Biology Laboratory
Director, San Diego Nathan Shock Center

"Aging is a complex process and not everyone ages the same way, so researchers have to study its basic biology from many different angles and in many different types of cells. The San Diego Nathan Shock Center will provide critical infrastructure to help researchers with their studies into aging, as well as pilot grants for experiments and support and encouragement for new researchers to enter the field of aging research."

Aging is the greatest risk factor for many diseases. Salk researchers seek to discover the fundamental causes of aging, so that everyone can live longer, healthier lives.

CANCER

REUBEN SHAW
William R. Brody Chair
Professor, Molecular and Cell Biology Laboratory
Director, Salk Cancer Center

"Cancer is a complex and ever evolving foe, which is why Salk researchers are joining forces to attack it from many different angles—metabolic therapies, immunotherapies, targeted therapies, epigenetics and more. Working across scientific fields, we have continued to discover new and unexpected therapeutic lines of attack to conquer cancer."

The Salk Cancer Center, one of seven National Cancer Institute (NCI)-designated basic research cancer centers, recently launched the Conquering Cancer Initiative to harness new strategies against five deadly cancers: pancreatic, ovarian, lung, brain (glioblastoma) and triple negative breast.

present—brings a deep respect for the Salk ethos of fostering collaboration between disciplines to encourage new discoveries. Thus, with the concurrence in 2020 of Gage's 25th year at Salk with the Institute's 60th anniversary and the heightened interest in scientific research catalyzed by the COVID-19 pandemic, we felt it was a fitting time to take a deeper look at his vision for the future of science at Salk. (*Inside Salk*'s summer issue covered how the Institute is responding to the pandemic, including launching almost two dozen new research projects devoted to tackling COVID-19.)

Looking Ahead

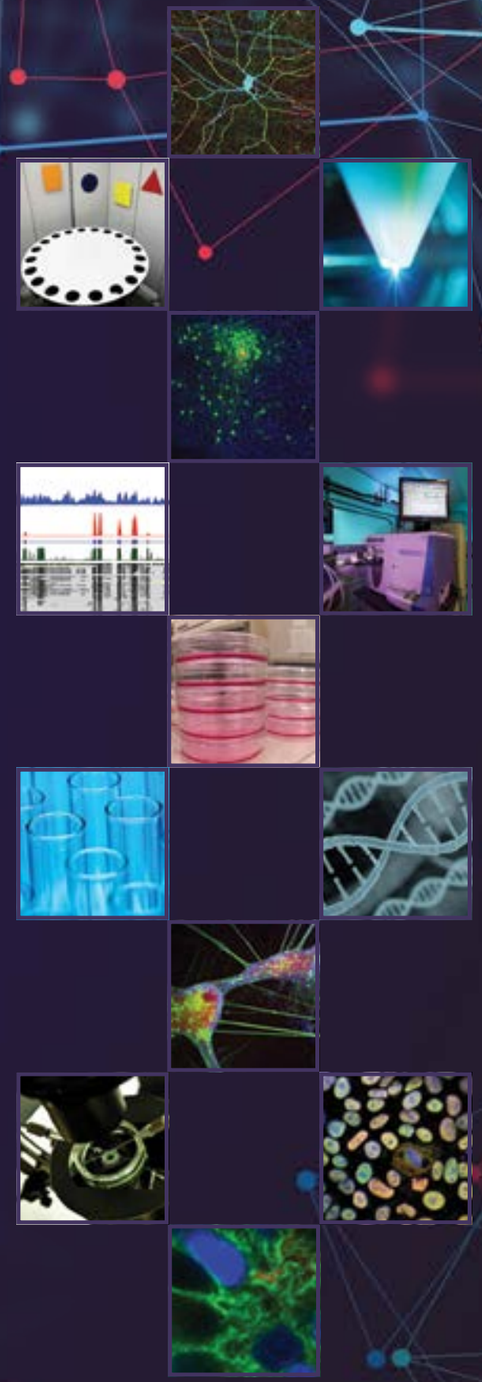
"The way science is done is changing," Gage says. "The traditional way scientists conducted life-science research was to base their scientific inquiries around what skill sets they had. So, scientists formulated experiments that they could address in their labs. Then they looked at whatever results they got and, again, tried to solve the next question in terms of their own experience."

Now, Gage explains, biological research is undergoing a fundamental shift. The latter part of the 20th century saw the dawn of the information age, and by the turn of the millennium, computing power coincided with the generation of massive amounts of biological data; the era of big data has been launched, when vast quantities of information too unwieldy for human calculation can be manipulated and analyzed for meaningful patterns using computer algorithms (see *Inside Salk* Winter 2019). The charge for the 21st century, then, is to make sense of these massive quantities of biological data scientists are now able to collect. And this, Gage contends, means conducting life-science research in a whole new way.

Salk's collaborative ethos means scientists in different areas are accustomed to working across disciplines, not just within the Institute, but also across the world.

"We are beginning to see a new biology that incorporates computation, mathematics and engineering," says Gage. "In this new paradigm, you aggregate data sets from all over the world and build a theoretical model of the concepts you're interested in, so you can decide what scientific questions to pursue. Here, the model is helping guide you to where the really critical questions are, and answering those questions is not dependent entirely on your personal experience, skills or equipment. It may involve building a new instrument, for example, so engineering becomes a big part of it. It may point you in a therapeutic direction, so translation may be a part. Additional computation and refining of theoretical models may also be necessary."

This new way of doing biological research plays to many of Salk's strengths. The Institute's emphasis on collaboration is exemplified by the research cores—shared facilities that give Salk scientists access to cutting-edge technologies and staff with expertise that individual labs may not have. Salk has 13 of these cores, including biophotonics (advanced imaging), next generation sequencing and stem cells, to name just a few. Salk's collaborative ethos means scientists in different areas are accustomed to working across disciplines, not just within the Institute, but also across the world. Many Salk faculty already have national and international collaborations in progress. Locally, Salk's faculty works closely with the UC San Diego Supercomputer Center, School of Engineering, School of Medicine and Moores Cancer Center and other organizations.



Above and below: Renderings of the new facility that will be built on the original campus. It will include hubs for bioengineering, computation and translation.

"...the idea that science is changing all the time, and the building space has to fit the science."

RUSTY GAGE

A Glimpse of the Future

Gage imagines that, in the near future, the Institute will have new hubs for bioengineering, computation and translation. He envisions an additional research facility, in close proximity to the iconic original campus, to house incoming researchers specializing in these new directions; their work will complement and contribute to established research areas for which the Institute is already known (see Sidebars: Research Areas). The original plans for the Institute envisioned such future buildings, in keeping with Jonas Salk's understanding that science changes and the needs of science change. To accomplish these ambitious goals for facilities, centers and recruitment, Salk will undertake a campaign next year.

Part of the Institute's mission is training the next generation of scientists, and Gage is looking forward to adding more early career researchers to the ranks of Salk's outstanding current junior faculty, who are just as brilliant and driven as their predecessors in asking bold questions about cancer, genetics, metabolism, plant biology and the immune system. Of particular importance to Gage is building on Salk's culture of respect, diversity and inclusion. Gage firmly believes that the creativity and skills necessary for bold scientific discovery require researchers with a diversity of ideas and experiences. One of his first acts as president in 2018 was to establish an Office of Equity and Inclusion, and Gage continues to champion efforts that advance this strategic goal.

Asked what Jonas Salk might think of this vision, Gage pauses for a long moment before responding. "I think there's two parts of this vision for the future Jonas would appreciate. One is the cooperation aspect, people of different backgrounds working together on big questions. He had an idea that we should be serving deep scientific knowledge, but with a humanistic perspective. The other is the idea that science is changing all the time, and the building space has to fit the science. I think he would embrace both ideas."

Like Jonas Salk, who over 60 years ago had a vision for how the world would benefit from an institution devoted to basic scientific research, Gage has a vision in which the future of science—Salk style—will be every bit as exciting as its past. S

PLANTS

JOANNE CHORY
Howard H. and Maryam R. Newman Chair in Plant Biology
Professor and Director, Plant Molecular and Cellular Biology Laboratory
Co-Director, Harnessing Plants Initiative

WOLFGANG BUSCH
Professor, Plant Molecular and Cellular Biology Laboratory & Integrative Biology Laboratory
Co-Director, Harnessing Plants Initiative

"Humanity is at a crossroads due to a warming planet. Society can no longer conduct business as usual, and Salk's plant biologists have a unique contribution to make. The next 10 years will be critical for climate change, and within that time we expect the Harnessing Plants Initiative to have made significant inroads in an effort to enhance the natural ability of plants to draw down CO2 to help to restore natural balance."

The Salk Institute's highly ranked plant program recently launched the Harnessing Plants Initiative, a plant-based approach to drawing down carbon dioxide from the atmosphere and storing it stably in the roots of crops.

COMPUTATIONAL BIOLOGY

TERRENCE SEJNOWSKI
Francis Crick Chair
Professor and Laboratory Head, Computational Neurobiology Laboratory
Director, Crick-Jacobs Center for Theoretical and Computational Biology

"It has become routine to sequence all the genes in single cells and it is now possible to record simultaneously from tens of thousands of neurons engaged in behavior. Computational tools such as machine learning and new engineering approaches are essential for analyzing these data and developing new theories for the complex functions of cells and brains. The Crick-Jacobs Center will expand to take on these challenges over the next decade."

Salk's Crick Jacobs Center brings together life scientists, computational scientists and engineers to develop the instrumentation and analytical tools that will be needed to tackle some of the biggest questions in science.

JULIE LAW

Revealing RNA

Although Associate Professor Julie Law began college thinking she was going to become a physician, a summer job in a lab introduced her to the rewards of scientific research. She earned a bachelor's degree in biochemistry and biophysics, as well as a doctoral degree in biochemistry (studying parasites), and she conducted postdoctoral research into the chemical tags on DNA that are known as methylation. As a member of the plant biology faculty at Salk, Law studies gene regulation.

Inside Salk ***sat down with Law to find out about the common themes underlying her research and to discuss what motivates her both in and out of the lab.***

What is the "big picture" description of your research?

JL: In biology, there's what's known as the central dogma about the flow of genetic information. All the information is hardwired in the DNA code, and then it has to be translated into other languages for the cellular machinery to understand. And RNA is one of those intermediary translation steps. But over several decades of research, it's been realized that RNA plays a really fundamental role in a diverse set of processes outside of that initial translation of information. So, since my graduate school days, my research interests have been grounded in trying to understand the different roles that RNAs—short copies of DNA segments—play in connection to gene regulation, which, essentially, is the process of turning genes on and off.

We hear a lot about DNA and genes, but we don't really hear much about gene regulation. What is it, and why is it important?

JL: Every cell within an organism has nearly identical genetic information, yet not all cells look or act the same. In mammals, a heart cell isn't the same as an immune cell, for example, even though they share the same genetic blueprint. The way you get cellular diversity is by controlling which genes are turned on and which ones are turned off, which is dictated by various types of chemical modifications. These modifications [also called the epigenome] can include chemical tags that attach to DNA, or the proteins that bundle DNA into a package that fits in the cell. And just as mistakes in the DNA code of a gene can result in disease, problems with gene regulation can also cause disease.

You referred to mammalian cells, but you work with plants. Can you explain why?

JL: I would say the strengths of studying gene regulation in plants are twofold: First, you can get viable genetic mutants, which allows you to manipulate the processes. You can figure out, for example, if you tweak this gene, what goes wrong in the context of a living organism. In mammalian systems, these kinds of tweaks can be lethal, making it very hard to understand the causes or consequences of particular changes. And second, plants have a very short life span, which allows us to look at things over multiple generations and collect a large amount of information over a short time.

> *"Plants have a very short life span, which allows us to look at things over multiple generations and collect a large amount of information over a short time."*
>
> JULIE LAW

Speaking of plants, at Salk one of the things you're working on is the Harnessing Plants Initiative, which seeks to mitigate global warming by using plants' natural ability to capture and store carbon. How does your work fit into the initiative?

JL: The Harnessing Plants Initiative involves all of the plant biology faculty at Salk. We've banded together to use our collective expertise to address a globally important problem, which, of course, is climate change. We want to identify or generate plants that can shuttle more carbon—from CO_2 in the atmosphere—into very long-lasting carbon-storage molecules in plant roots and the soil. But we don't want to have to recreate the wheel; engineering every step in the process, from taking in the CO_2 to generating these carbon-rich molecules, would be very difficult. So we want to understand how the plant normally turns on the machinery necessary to do that process and then turn it up. My work involves identifying the gene regulatory machinery that will allow us to do that turning up.

Were you always interested in science?

JL: I was always interested in science and math. When I was in my second year in college, I had the opportunity to do a summer internship in a lab. That opened my mind to all kinds of different possibilities, and it's what convinced me to switch from premed to the biochemistry/biophysics degree. I was addicted to the lab from the start, and I had this realization that you could work in a research lab, making new discoveries, and get paid for it!

Are there any other scientists in your family?

JL: Yes, on both sides. My mother is a microbiologist and worked in a hospital lab until she retired recently, and her work was my first exposure to science. My father and two of his three brothers are in STEM as well. My dad is an electrical engineer, and my two uncles are chemical engineers, so it's safe to say I had a lot of exposure to science growing up.

How did you end up at Salk?

JL: Salk is a really special place on many levels. For me, the huge drawing points were the strength of both the plant biology program and the program studying gene regulation and epigenetics. A lot of places independently study those processes, but very few bring them together across a diverse set of species and organisms. So it was a unique opportunity to join a world-renowned plant biology institute but also be surrounded by people studying the role of epigenetics in cancer and the roles of genome structure in genome stability.

Not coming from a plant biology background, I was drawn to the idea that studying processes from different angles and in different organisms can give you a great perspective on science. And having a place that values that kind of diversity was really attractive to me.

Right now, due to the COVID-19 pandemic, you're not able to work much in the lab. Are there things you miss?

JL: Definitely. Before all the working from home, it was quite exciting to get in, in the morning, seeing what people were doing and seeing what the day was going to bring. You never quite knew what new experiments you were going to get to do.

The pandemic is probably also affecting what you can do outside of the lab, but under normal circumstances, what do you like to do for fun?

JL: I grew up in Oregon, camping, doing a bunch of sports, riding a motorcycle. I don't do as many of those things anymore, but I still like hiking and being outdoors.

You rode a motorcycle? That sounds pretty adventurous!

JL: I guess I just grew up doing it, so I didn't think about it as being so adventurous, but—yeah. I ran into a tree once, with a lot of people watching, so that was pretty embarrassing at the time. But it's a good memory now. S

INSIGHTS

From studying the novel coronavirus to downloading brains to computers, Staff Scientist Gerald Pao is at the forefront of scientific advancement. For Pao, being a staff scientist gives him the freedom to explore a broad range of risky scientific endeavors that could yield pioneering results.

"A staff scientist can be an incredibly enabling position, where I can pursue a greater variety of topics that are difficult to approach in more traditional positions—and I have a lot of interests!" says Pao.

Gerald Pao

Pushing the limits in science and in life

PATH TO SALK

Pao grew up in Spain, Germany and the United States. He had a keen interest in science from an early age, and when he was in middle school, he asked his biology teacher to teach him about gene expression and the genetic code. The teacher refused, telling Pao that he was too young, so Pao begged his father to help him find a mentor in molecular biology.

His father obliged, and at the age of 12, Pao began spending time at the Center for Molecular Biology at the Universidad Autónoma de Madrid, where he learned about gene expression in the model system *Drosophila melanogaster*, a fly. A few years later, at the urging of Professor Gines Morata, Pao decided to attend the University of California San Diego (UC San Diego) due to the strength of molecular biology programs both there and at the Salk Institute, across the street.

For his undergraduate degree in molecular biology, Pao explored the evolution of tyrosine kinases—enzymes that serve as on/off switches—and the complex nature of protein interactions. In his sophomore year, Pao connected with Salk Professor Tony Hunter, whose seminal discovery of tyrosine phosphorylation (the mechanism behind the on/off switches) led to the development of an entire class of anticancer drugs called tyrosine inhibitors, one of which is the leukemia drug Gleevec.

"Tony has an amazing, encyclopedic breadth of knowledge and excitement for science," says Pao. "He is like the wise man on the mountain that you can consult about any scientific query."

Pao completed his PhD in molecular biology jointly at UC San Diego and Salk, and he now works as a staff scientist in Hunter's lab.

DAY-TO-DAY

Prior to the COVID-19 pandemic, Pao spent many months of every year in Japan, taking skin samples from ocean-dwelling bigfin reef squid for his research. Squid have special proteins, called reflectins, that allow them to camouflage themselves by tuning the amount of light reflected by their skin—manipulating what scientists call the optical density. Pao is trying to hack these reflectins so that scientists can more easily view internal processes, such as the activity of the brain.

Although the pandemic has made his squid project more difficult to pursue, Pao has numerous other scientific endeavors to keep him busy, including his research involving the novel coronavirus.

COVID-19 RESEARCH

At Salk, Pao and colleagues have engineered a fake virus that has the exterior of the coronavirus, allowing them to study a mutation in the spike protein; the protein is what enables the virus to pull itself inside the host cell. "We're interested in a mutation in the spike protein that makes the virus possibly more infectious," says Pao. "When we introduced the mutated virus into human cells in the lab, we observed that the cells became infected five times more efficiently than with the nonmutated virus." Although these findings are preliminary and were conducted using a virus that mimics the novel coronavirus, they could help guide vaccine design for specific coronavirus strains.

Pao is also working on creating fluorescent fake viruses that light up, which will allow scientists to determine whether viruses stick to surfaces, such as face masks, or how the viruses move in air-conditioning systems.

LEISURE TIME

In his free time, Pao likes to play volleyball and surf. He also enjoys rock climbing and has been known to sneak up to Yosemite for a weekend of big wall climbing on El Capitan.

FUN FACTS

Pao paid for college by working as a professional model in Europe. He modeled in commercials for athletic brands and walked the runway for fashion brands, such as Benetton. Pao also speaks German, English, Mandarin, Cantonese and Spanish fluently.

FUTURE PROJECTS

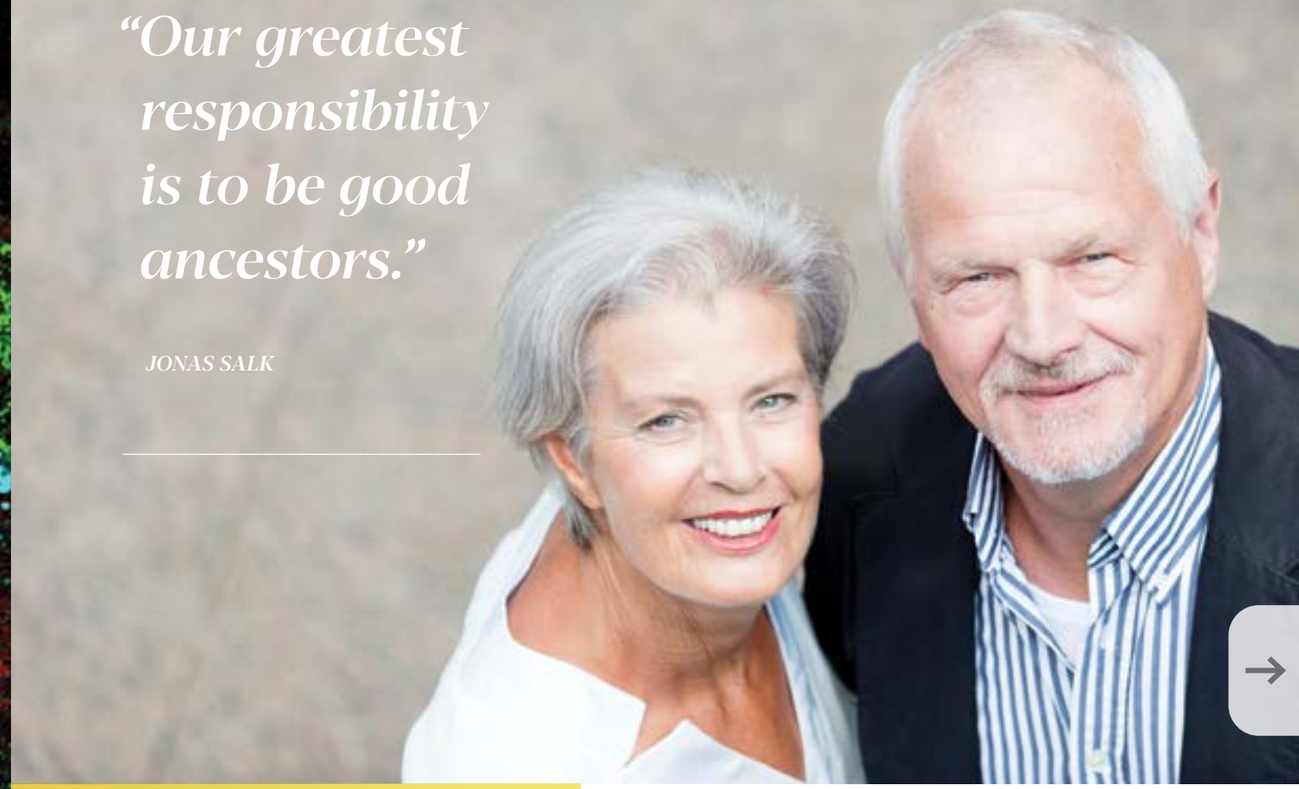
Pao and colleagues are working on a new project that allows neural data from the brain to be downloaded to a computer. The researchers are taking the data from fly and fish brains and converting it into a computer model to create a program that behaves like a real fly or fish.

"Essentially, we are downloading a fly brain onto the computer," explains Pao. "It's not just science fiction. We want to create artificial intelligence that is based on real biology."

In recent work from the Kaech lab, researchers demonstrated that long-term immunity in the lungs can be more easily activated than previously thought—a finding that could help address infections like influenza or COVID-19. This defense is mounted in lung tissue (green) by specialized immune cells, called killer T cells (blue), surrounded by other lung immune cells (red). (See Discoveries to learn more.)

"Our greatest responsibility is to be good ancestors."

JONAS SALK



NEXT GEN

Shaping academia for future scientists

Austin Coley

"Exposure is the best thing to change attitudes. People need to see that there are successful Black scientists in academia."

Austin Coley, though only at Salk since 2019, has already taken an active role in everything from conducting innovative research around the brain to spearheading a wide variety of outreach activities.

Raised by a single mother, Coley grew up in multiple towns in New Jersey as his family moved to seek better opportunities and avoid troubled neighborhoods. He was a star football player in high school, but the summer after his senior year he experienced a life-altering injury.

"My first love was football," says Coley. "But I wrecked my hamstring, so I could no longer play. My entire life changed."

Outside of football, Coley had always enjoyed biology and anatomy classes. "Understanding how the body worked and how diseases affected the body fascinated me," he says. So, he started exploring university biology programs.

The historically Black college and university (HBCU) North Carolina Central University caught his attention, as it offered a brand-new science complex and enthusiastic faculty. Once there, despite his excitement for biology, Coley struggled with his first exams.

"I had come to college to study science, yet I failed my first round of biology and chemistry exams. I was scared," he shares. "I decided that I would learn how to study and really apply myself for the next exams. This would be my last shot. If I failed again, I would drop out of the major."

Coley threw himself into his academics. He spent his days in the library, deciphering chemical equations and memorizing biological definitions. He aced his next exams.

After undergrad, Coley went on to complete his master's degree in cell physiology at Case Western Reserve University but was disappointed with the lack of support, encouragement and representation of Black scientists in his program. When he applied for his PhD in neurobiology at Drexel University College of Medicine, Coley knew he wanted to be in a lab that championed minorities in science. Professor Wen-Jun Gao welcomed Coley into his lab to work on the molecular components involved in schizophrenia.

"When I was growing up, my uncle was diagnosed with schizophrenia, but I had no idea. We didn't talk about his condition in my family, as there is a stigma around mental health in the Black community," says Coley. "I want to uncover the neural mechanisms of schizophrenia to improve our understanding of the disease, mental health awareness and outcomes."

In his third year in graduate school, Coley came to San Diego to attend the Society for Neuroscience annual conference, where he learned about a new award to fund minority researchers on their path to full-time faculty positions: the NIH Blueprint Diversity Specialized Predoctoral to Postdoctoral Advancement in Neuroscience Award. Coley was the perfect fit.

Winning the award jump-started Coley's career, as it funded the last two years of his PhD and provided funding for his entire postdoctoral studies. With independent funding, Coley could choose nearly any scientist in the country to work with for his postdoc, and he chose renowned neuroscientist and Salk Professor Kay Tye.

"Kay offered to support not only my scientific interests, but also my social justice activities outside of her lab. It was clear that she believed in me," says Coley.

In the Tye lab, Coley is now studying the populations of neurons that are affected in anhedonia, the inability to experience pleasure, which is a core symptom of schizophrenia and depression. He is using calcium imaging techniques to examine the neurons in the frontal lobe of the brain, called the prefrontal cortex. His goal is to see if manipulating certain neurons in the prefrontal cortex helps alleviate symptoms of schizophrenia and depression.

Outside of the lab, Coley is also an active member of Salk's community. Currently, he is co-chairing the newly formed Black Association at Salk (BAS), which aims to unite and support Black employees through social hours, speakers and professional development opportunities. He is also working with Salk's Diversity and Inclusion Task Force to invite more Black speakers to the weekly seminar series.

"Exposure is the best thing to change attitudes. People need to see that there are successful Black scientists in academia," says Coley. "I would love to be a quiet scientist, focus on my work and go home, but right now I need to do everything I can to improve the scientific ecosystem for the next generation of Black scientists."

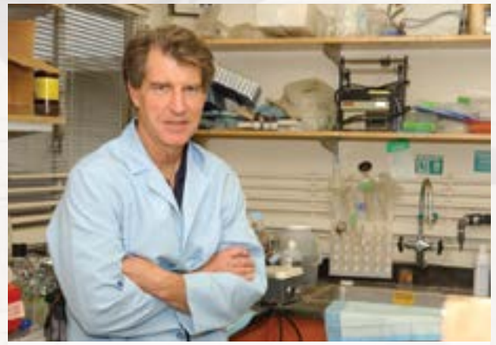
LONGTIME SALK PROFESSOR DAVID SCHUBERT PASSES AT THE AGE OF 77

Renowned cell biologist and Salk Professor David Schubert passed away on August 6, 2020, at the age of 77 in La Jolla, California. He was known for the development of novel screening techniques that allowed his team to identify naturally occurring chemicals that can slow or prevent the neurological damage that occurs in neurodegenerative disorders, such as Alzheimer's disease.

"We are deeply saddened by Dave's passing. He was one of the earliest graduate students at Salk and spent close to 55 years of his scientific career here," says Salk President Rusty Gage. "Dave will be greatly missed and we are forever thankful for his contributions to our research community."

Jan Lewerenz, a senior physician at Ulm University Hospital, in Germany, and one of Schubert's former postdoctoral researchers, adds, "I will remember Dave as one of the best human beings I had the privilege to know. Without him my life would have been different … The world, now more than ever, is in desperate need of people like Dave."

Schubert was born in 1943 in Indianapolis, Indiana, and earned his BA in chemistry from Indiana University in 1965. He first came to Salk later that year as a graduate student in the lab of late Salk professor and immunologist Melvin Cohn, while working on his PhD in cell biology at the University of California San Diego. Schubert then moved to the Pasteur Institute, in Paris, for his postdoctoral fellowship under the direction of Nobel Laureate François Jacob before returning to Salk in 1970 as a member of the faculty. He established the first neurobiology laboratory at the Institute. In that capacity, he developed and characterized a large number of nerve, glial and muscle cell lines that have served as the basis for numerous important discoveries by labs around the world. Schubert served as a professor and the head of the Cellular Neurobiology Laboratory until his passing.



> *"THE WORLD, NOW MORE THAN EVER, IS IN DESPERATE NEED OF PEOPLE LIKE DAVE."*
>
> **JAN LEWERENZ**
> SENIOR PHYSICIAN, ULM UNIVERSITY HOSPITAL

Schubert's diverse body of work includes research on various factors influencing the health and development of nerve and muscle cells, on a type of cancer called neuroblastoma, and on genetically modified crops.

In recent years at Salk, Schubert and his wife, Salk Senior Staff Scientist Pamela Maher, developed a novel screening technique to test for naturally occurring chemicals that can prevent the type of nerve cell death found in neurodegenerative diseases. This led to the establishment of the first medicinal chemistry lab at Salk, where he worked to make derivatives of neuroprotective natural products that have much-improved medicinal, chemical and pharmacological properties over the parent compounds. For example, the lab found that fisetin, which naturally occurs in strawberries, prevents memory and learning deficits in mouse models of Parkinson's and Alzheimer's diseases. A synthetic derivative of fisetin is now undergoing the studies necessary for moving into clinical trials. Additionally, they found that a synthetic derivative of the curry spice curcumin, called J147, improves behavioral and pathological symptoms associated with Alzheimer's, traumatic brain injury and stroke. This compound is currently in a phase 1 clinical trial for the treatment of Alzheimer's.

Schubert also believed in giving back to the local San Diego community and served as a member of the County of San Diego Scientific Advisory Board as well as the National Water Reuse Panel for San Diego County.

Between his graduate work and faculty appointments, Schubert spent close to 55 combined years at the Salk Institute. He passed away due to B cell lymphoma and is survived by his wife, Pamela Maher, his son, Bruno Schubert, and his three grandchildren.

SALK MOURNS TWO LONGTIME DONORS

Glenn and Simner will be deeply missed. Their partnerships enabled the type of scientific discoveries that change the world for the better and the Institute's science is stronger today because of them.

PAUL F. GLENN

Longtime Salk donor Paul F. Glenn passed away on September 29, 2020, at his home in Montecito, California. He was an attorney by education, and had a fruitful career as a commodities trader. Glenn founded the Glenn Foundation for Medical Research in 1965. His philanthropic focus was ahead of its time: to fund research that would lead to treatments and therapies to extend the quality of a person's health during their lifetime.

Due to his generous financial support, Paul F. Glenn Centers for the Biology of Aging Research were established not only at the Salk Institute, but also at Harvard, Stanford, MIT, the Mayo Clinic, Princeton, Einstein College of Medicine, University of Michigan and the Buck Institute. The Glenn Foundation has funded more than $100 million in basic research since its inception. Salk's Glenn Center was established in January 2009 with a $5 million award from the Glenn Foundation and the award has been extended three times since then.

The Salk Institute extends its heartfelt condolences to the Glenn family and the Glenn Foundation.

TINA SIMNER

Committed Salk donor Tina Simner passed away on October 4 at her home in La Jolla. Her support and leadership over the years, especially of the Salk Women & Science program, cannot be overstated.

Simner moved to the San Diego area from New York, where she'd run a fashion accessories business with her late husband for 25 years. She began her support of Salk by way of Symphony at Salk, the Institute's main fundraising event, held every summer.

In addition to her generous giving, Simner played an instrumental role in recruiting Chef Jeffrey Strauss for the event, an accomplishment she took great pride in.

In recent years, Simner turned her focus to supporting the Salk Women & Science program, generously donating to the program and lending her skills to fundraising events. She also provided her fashion industry expertise, chairing the Design and Discovery Fashion Showcase in 2017 along with Salk Professor Janelle Ayres.

Simner had a love for life, was an accomplished artist, a devoted friend and generous to those less fortunate than herself.

The Institute extends its deepest condolences to the Simner family.

SALK WELCOMES TOP SCIENTISTS IN CANCER BIOLOGY AND BIOPHYSICS

Over the summer, the Salk Institute hired two new assistant professors in the fields of cancer biology and biophysics, respectively. Daniel Hollern and Pallav Kosuri will bring fresh perspectives to advance an understanding of, and find new treatments for, breast cancer and heart disease.

"We are elated to bring on two highly accomplished early-career scientists," says Salk President Rusty Gage. "Daniel and Pallav represent the bright future of the Salk Institute, and we are excited to see what innovations and collaborations stem from their research endeavors here at Salk."

Pallav Kosuri

Assistant Professor Pallav Kosuri joins Salk from Harvard University, where he was a postdoctoral fellow in the lab of Xiaowei Zhuang. At Salk, he will join the faculty of the Integrative Biology Laboratory. His work aims to better understand the physics of biological machines—from muscles contracting, to enzymes reading and editing DNA. Specifically, he is developing technologies to visualize and measure the movements of single molecules and map their organization in tissues, in order to create an integrated theory of how mechanical movement gives rise to biological function. He will apply this knowledge to examine heart disease in order to better understand why the heart experiences mechanical failure and to point the way to innovative new treatments.

Originally from Sweden, Kosuri completed his PhD in biochemistry and molecular biophysics at Columbia University. He currently holds two patents for his technologies, along with numerous accolades including the Titus M. Coan Prize for Excellence in Basic Research, the Columbia University distinction award for doctoral defense and a Fulbright Scholarship.

Daniel Hollern

Assistant Professor Daniel Hollern comes to Salk from the University of North Carolina at Chapel Hill, where he was a postdoctoral fellow in the lab of Charles Perou. Hollern joins Salk's NOMIS Center for Immunobiology and Microbial Pathogenesis as well as its renowned NCI-designated Cancer Center to pursue research that can improve the treatment of cancer patients. In particular, his lab will focus on triple-negative breast cancer (one of the five deadly cancers being researched in Salk's Conquering Cancer Initiative), where management of advanced disease is very challenging. Hollern takes a multi-disciplinary approach to investigate responses to cancer therapies, immune cell dynamics and the mechanisms controlling tumor growth. In order to improve treatment strategies for cancer patients, he will leverage functional genomics and experimental biology to study the anti-tumor immune response.

Hollern earned his PhD in cell and molecular biology from Michigan State University and holds numerous awards including the Joseph S. Pagano Award, consecutive NIH Ruth L. Kirschstein National Research Service Awards (NRSA) and the Aitch Foundation Award.

CONSORTIUM LED BY SALK TO RECEIVE EXPECTED $5 MILLION FOR NEW CENTER TO STUDY CELLULAR AGING IN HUMANS

Gerald Shadel

Rusty Gage

Martin Hetzer

Tatyana Sharpee

Aging is the most significant risk factor for human disease. Human cells and tissues age at different rates depending on their intrinsic properties, where they are in the body and environmental exposures. Yet, scientists do not fully understand this variability and how it contributes to overall human aging, risk for disease or therapeutic responses.

The Salk Institute will establish a world-class San Diego Nathan Shock Center (SD-NSC), a consortium with Sanford Burnham Prebys Medical Discovery Institute and the University of California San Diego to study cellular and tissue aging in humans. The Center will be funded by a grant from the National Institute on Aging of the National Institutes of Health and is expected to total $5 million over the next 5 years.

Salk Professor Gerald Shadel led the successful grant proposal and will be director of the center. Professors Rusty Gage, Martin Hetzer and Tatyana Sharpee will lead several of the key research and development core facilities.

The SD-NSC will be one of a network of eight Nathan Shock Centers nationwide, which are named after Nathan Shock, Director of the Gerontology Research Center at National Institutes of Health for nearly 35 years and regarded by many as the “father of gerontology.”

SALK INSTITUTE AND BRIDGEBIO PHARMA COLLABORATE TO ADVANCE THERAPIES FOR GENETICALLY DRIVEN DISEASES

The Salk Institute and BridgeBio Pharma, Inc., announced a three-year collaboration to advance cutting-edge academic discoveries in genetically driven diseases toward therapeutic applications. Under the partnership, BridgeBio will help fund research programs from Salk’s world-renowned innovative cancer research, with the eventual goal of developing new therapeutics for patients in need.

November 2019

FIVE SALK RESEARCHERS AWARDED 2020 PADRES PEDAL THE CAUSE GRANTS

A record $3.1 million was raised by last year’s Padres Pedal the Cause event, funding cancer research at five San Diego facilities, including the Salk Institute.

Salk Professors Ronald Evans, Tony Hunter, Susan Kaech and Reuben Shaw, and Assistant Professor Dannielle Engle, were among the collaborative mix of researchers and medical professionals to receive funding this year.

An all-time-high number of participants—nearly 3,000—took part in the sixth-annual Pedal the Cause event on November 16, 2019, which included multiple cycling courses, a 5K, spin classes and kid-friendly activities. Proceeds from the event support innovative cancer projects with a major emphasis on collaborative, translational research that offers a clear path to clinical trials.

Padres Pedal the Cause provides grants to cross-institutional teams of scientists and physicians at the Salk Institute, Sanford Burnham Prebys Medical Discovery Institute, Moores Cancer Center at UC San Diego Health and Rady Children’s Hospital. The annual event has raised more than $13 million to fund 62 cancer research projects since its inception.

This year’s Padres Pedal the Cause event, originally scheduled for November 1, 2020, has been moved to spring 2021.

REWARDING OUT-OF-THE-BOX IDEAS: **THE 2020 SALK INNOVATION GRANT AWARDS**

Every year, the Salk Innovation Grants Program awards fund out-of-the-box ideas from Salk labs that hold significant promise but may not yet have the track record to attract attention from more traditional funding sources.

Awarded semi-annually by a competitive peer-review process, this program is critical to catalyze emerging science with the power to redefine the future and has led to a host of impactful discoveries since its launch in 2006 by the forward-thinking minds of then-Board chair Irwin Jacobs and his wife, Joan, who have supported the program every year since its existence.

Congratulations to all of the 2020 winners!

COLLABORATION GRANTS

These collaborative grants provide seed funding to large, ambitious ideas involving three or more Salk investigators.

JOHN REYNOLDS
JUAN CARLOS IZPISUA BELMONTE
RUSTY GAGE

Professors John Reynolds, Juan Carlos Izpisua Belmonte and Rusty Gage will examine the hallmarks of aging in animal models to determine whether mobile DNA elements, called LINE1 retrotransposons, can be manipulated to slow or reverse aging to create an innovative healthy aging intervention.

MARTYN GOULDING
AXEL NIMMERJAHN
SUNG HAN

Professor Martyn Goulding, Associate Professor Axel Nimmerjahn and Assistant Professor Sung Han will investigate how sensory signals from the skin, the biggest sensory organ, are processed as they travel to the brain. The project will potentially reveal new targets for sensory dysfunction, which can occur with chronic pain and autism spectrum disorders.

ROSE HILLS GRANT

DANNIELLE ENGLE

Assistant Professor Dannielle Engle was named The Rose Hills Foundation's 2020-2021 Innovator Grant Program awardee. The award provides $100,000 for Engle to investigate how the sugar CA19-9 makes pancreatic cancer more aggressive, increases metastatic spread, and interacts with metastatic sites. As most pancreatic cancer patients are diagnosed with metastatic disease, blocking CA19-9 interactions may intercept metastatic spread.

2020 INNOVATION GRANTS

SATCHIN PANDA

One of the holy grails of circadian biology research is to understand what determines whether an animal is active during the day (diurnal) or during the night (nocturnal). To begin to answer this question, Professor Satchin Panda will measure changes in hormones and gene activity as two species of animals—the night monkey and mouse—switch between diurnal and nocturnal lifestyles. One potential outcome of this work will be strategies for improving the health and life quality of shift workers, a growing fraction of the worldwide workforce.

EDWARD STITES

The RAS protein is frequently mutated in some of the most difficult-to-treat cancers, including lung and colon. To better understand the contribution of RAS to cancer, Assistant Professor Edward Stites will activate a particularly deadly version of RAS in the microscopic worm *C. elegans*, a widely used model organism. Subsequent genetic and chemical screens will help to reveal new drugs and therapeutic strategies for treating RAS-associated cancers.

SUSAN KAECH

Cancer cells are metabolically greedy, which often leads to nutrient depletion within and around a tumor. Professor and Director of the NOMIS Center for Immunobiology and Microbial Pathogenesis Susan Kaech hypothesizes that this lack of nutrients starves immune cells that might otherwise recognize and eliminate the tumor. The team will map the nutrient landscape of different tumors, with the goal of identifying specific nutrients (metabolites) that boost immune cell effectiveness. Results will help to improve current anti-cancer immunotherapies.


Joanne Chory

JOANNE CHORY RECEIVES PEARL MEISTER GREENGARD AWARD

Howard Hughes Medical Institute Investigator and Professor Joanne Chory, who is the Howard H. and Maryam R. Newman Chair in Plant Biology and director of the Plant Molecular and Cellular Biology Laboratory at Salk, has been awarded the 2020 Pearl Meister Greengard Prize, a preeminent international award recognizing outstanding women scientists. The award recognizes Chory for fundamentally changing researchers' understanding of plant growth and development, and for her groundbreaking efforts to combat climate change. The Pearl Meister Greengard Prize was founded by the late Nobel Prize-winning neuroscientist Paul Greengard, in honor of his mother.

RONALD EVANS RECEIVES NOMIS AWARD

Professor Ronald Evans, director of Salk's Gene Expression Laboratory and March of Dimes Chair in Molecular and Developmental Biology, has been awarded a 2020 NOMIS Distinguished Scientist and Scholar Award by the NOMIS Foundation, a Swiss foundation that supports high-risk basic research. The award, which totals $2.5 million, recognizes scientists for their "outstanding contributions to the advancement of science and human progress through their pioneering, innovative and collaborative research," according to NOMIS. The award will enable Evans to decode how different parts of the body, including the brain, endocrine glands, gut, liver, immune cells and the microbiome, cooperate to maintain health.

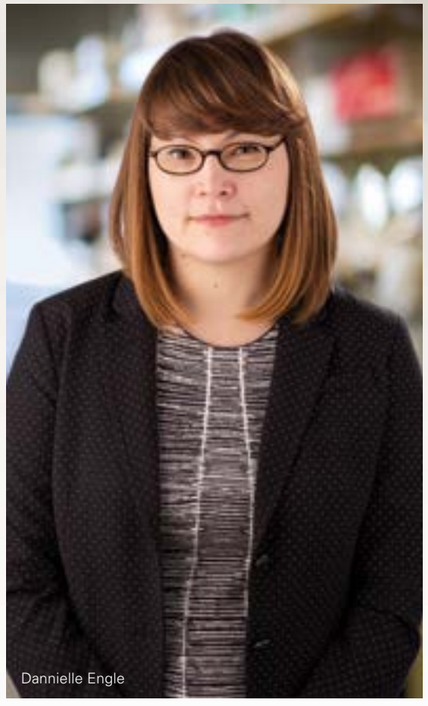

Ronald Evans


Edward Stites

EDWARD STITES RECEIVES NIH DIRECTOR'S NEW INNOVATOR AWARD

Assistant Professor Edward Stites has been named an NIH Director's New Innovator for 2020 as part of the National Institutes of Health's High-Risk, High-Reward Research Program. The award "supports unusually innovative research from early career investigators," according to the NIH and provides $1.5 million for a 5-year project. For his project, Stites will use mathematical and biological approaches to identify strategies to convert failed therapeutics into effective agents.

DANNIELLE ENGLE WINS NEW INVESTIGATOR AWARD


Dannielle Engle

Assistant Professor Dannielle Engle has been awarded a New Investigator Award from the Tobacco-Related Disease Research Program (TRDRP) to examine how tobacco use promotes cellular changes that lead to pancreatic cancer. Engle will receive more than $1 million over 3 years to develop new models for examining how tobacco carcinogens (cancer-causing substances) lead to tumor development and metastasis.

EDUCATION OUTREACH GOES VIRTUAL

When the COVID-19 pandemic closed local schools this past year, Salk's Education Outreach department had to get creative to continue its mission of teaching and inspiring students to pursue careers in science. They quickly adapted and rolled out virtual options for popular programs, to great success.

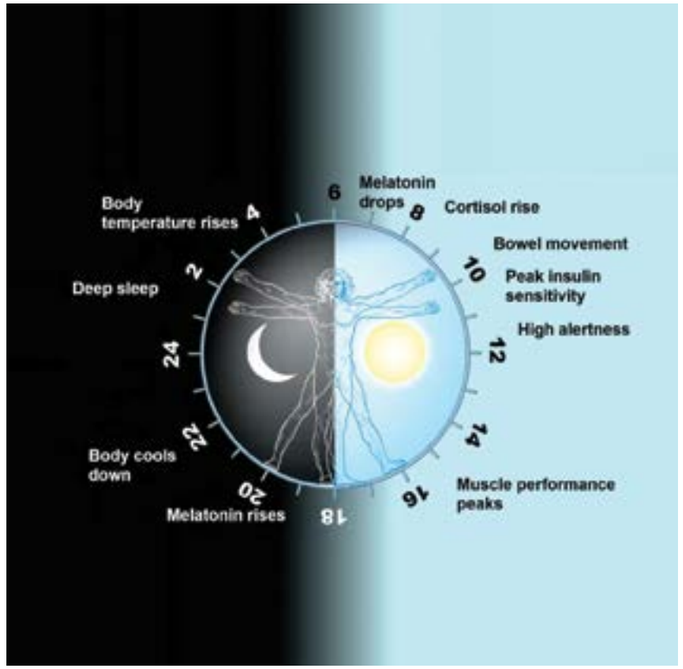
The Heithoff-Brody High School Summer Scholars program normally accepts 10 to 12 students each year to intern at Salk. Because the program had to go virtual, it was modified to the Introduction to Research Science and Communication Virtual Program and accommodated 76 students from 40 different schools, selected from a pool of over 400 applicants hailing from 10 states and two additional countries (Mexico and India). Over four weeks, these high school students completed virtual lab simulations, learned about common laboratory practices, and were provided professional development opportunities. After completing the program, 93.4% of students said they were interested in pursuing a career in STEM (science, technology, engineering and math).

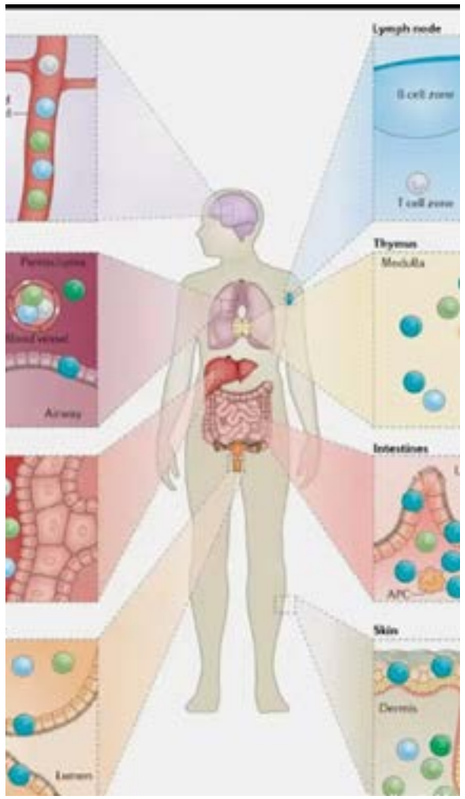
Additionally, the Institute's popular Mobile Science Lab was transformed into a virtual experience. It brought volunteer scientists into distance-learning classrooms to conduct a combination of minds-on and hands-on biotechnology activities, including a DNA extraction, with middle school classrooms all over San Diego. The Virtual Mobile Science Lab is on pace to reach more than 770 students from more than 20 schools in nine different San Diego zip codes by the end of the calendar year.

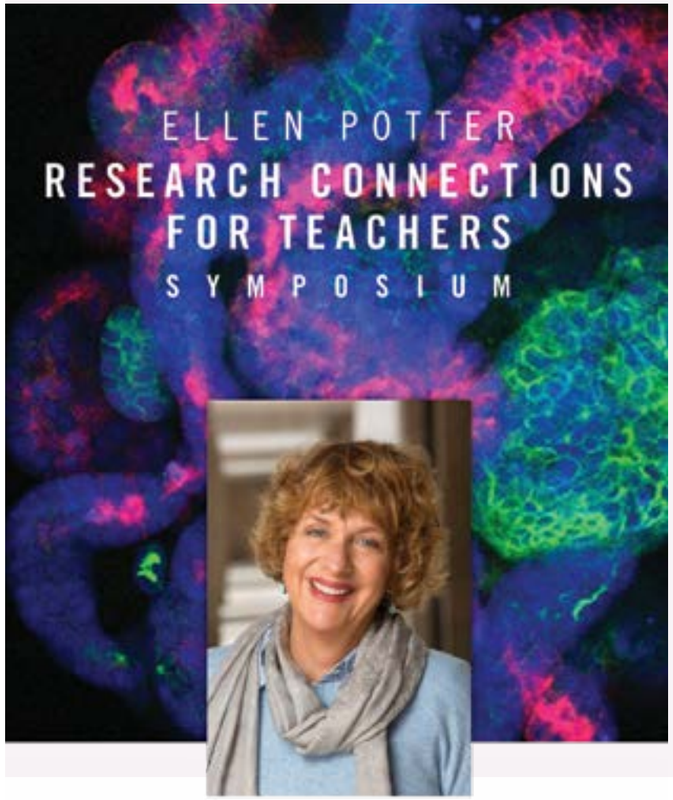
Finally, both the Summer Scholars program and the Virtual Mobile Science lab took advantage of SciChats, an additional EO program. The interactive sessions allowed students to learn over Zoom from volunteer scientists about their research and what it's like to be a scientist. By the end of 2020, 53 SciChats will have been held, compared to an average of six in previous years.

To learn more about Education Outreach, as well as access virtual tools for learning, visit **www.salk.edu/education**

EVENTS







ELLEN POTTER SYMPOSIUM GOES VIRTUAL

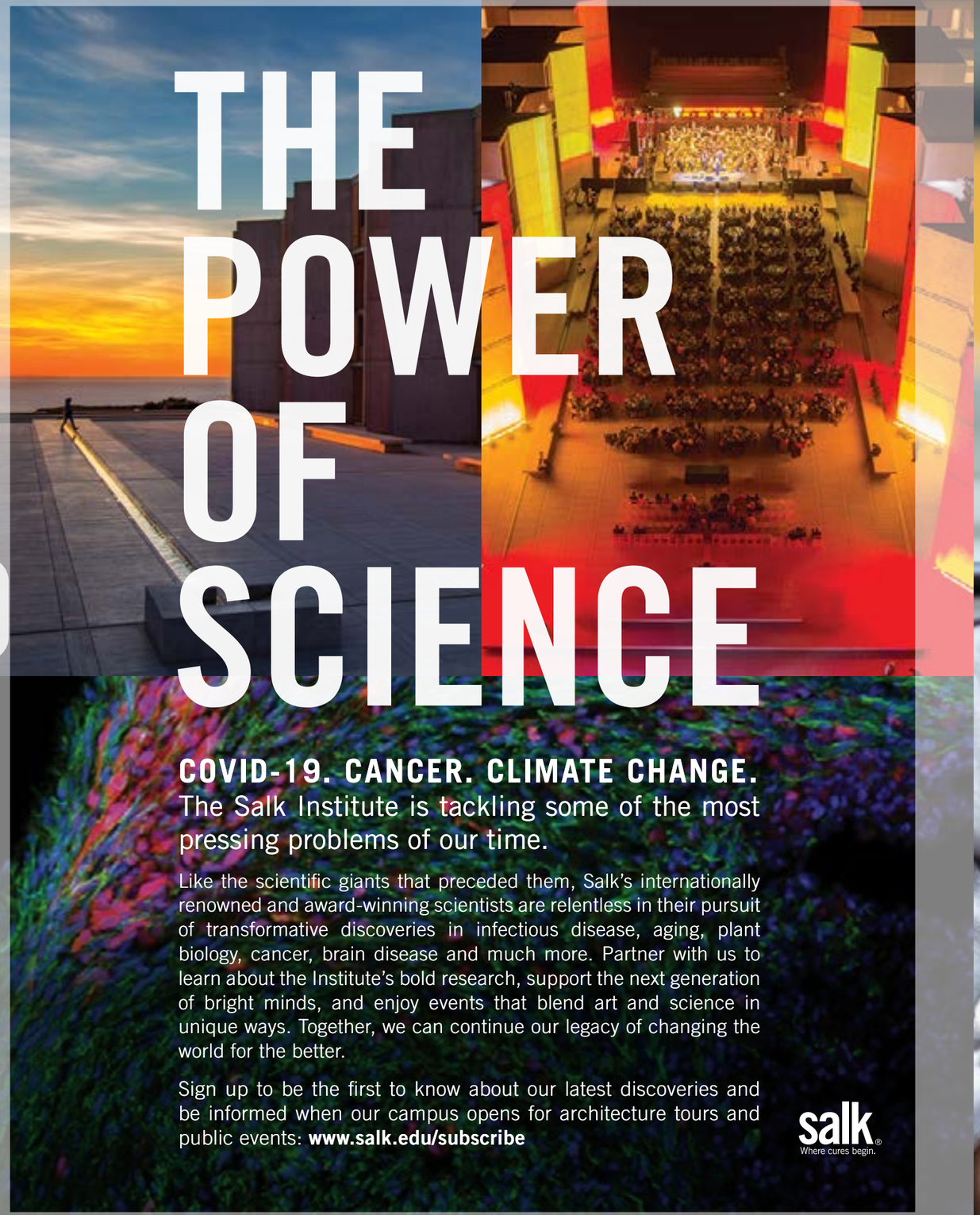
On October 24, Education Outreach held its annual Ellen Potter Symposium, featuring Uri Manor, director of Salk's Advanced Biophotonics Core. Each fall, teachers are invited to Salk to hear from Salk faculty and researchers in a seminar environment, then collaborate with colleagues to apply what they have learned to their lesson plans.

SALK JOINS VIRTUAL WELLBEING PANEL

On October 28, Susan Kaech, Salk Professor and Director of the NOMIS Center for Immunology and Microbial Pathogenesis, joined a panel of speakers hosted by Union Bank entitled "Women, Wealth and Health: Connecting Well-Being and Philanthropy in the Age of COVID." She joined Jennifer Alcorn, deputy director of Philanthropic Partnerships for the Bill and Melinda Gates Foundation; and Eric Verdin, president and CEO of the Buck Institute for Research on Aging, in discussing health and aging research, community involvement and health-related philanthropic efforts.

UnionBank[SM]


Susan Kaech



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Molly Matty, postdoctoral fellow, in Season 2, Episode 12.

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The podcast is available on **iTunes**, **Google Play** and anywhere you listen to podcasts.

To learn more, visit **www.salk.edu/podcast**

SEASONS 1 & 2 (AVAILABLE NOW)
SEASON 3 (COMING EARLY 2021):

Thomas Albright *on using neuroscience to make eyewitness identification more accurate*

Ronald Evans *on discovering the key to how hormones affect gene activity*

Julie Law *on defining the epigenome and why it's important in health and disease*

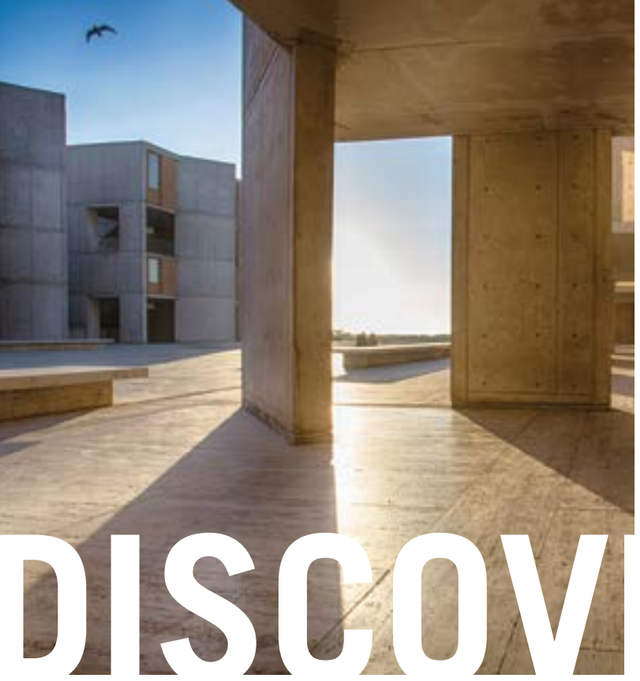
Dmitry Lyumkis *on researching how coronavirus proteins are assembled and bind to promote viral infection*

Satchin Panda *on the benefits of staying in sync with your biological clock*

Staff scientist perspective: **Gerald Pao** *on examining how the novel coronavirus spreads and exploring the transparency of squids*

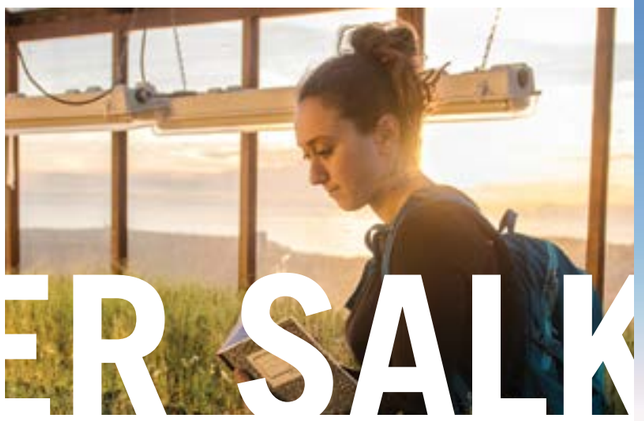
Postdoc profile: **Nikki Lytle** *on making scientific advances in pancreatic cancer*

And more!



DISCOVER SALK

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



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.

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

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.

SALKEXCELLERATORS
Designed for young business professionals and community members committed to supporting Salk scientific discovery, Salkexcellerators offers a unique opportunity to support cutting-edge 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.

ARCHITECTURE TOURS
The Salk Institute has been described as one of the most significant architectural sites in the United States and has garnered accolades for its design and preservation.

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.

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

EXPLORE SALK
The Institute's free open house allows the community to see Salk science up close through fascinating talks, interactive booths, a self-guided tour and a kids' discovery zone.

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.

INSTITUTE COUNCIL
This group of highly engaged individuals focuses on advancing Salk scientific initiatives.

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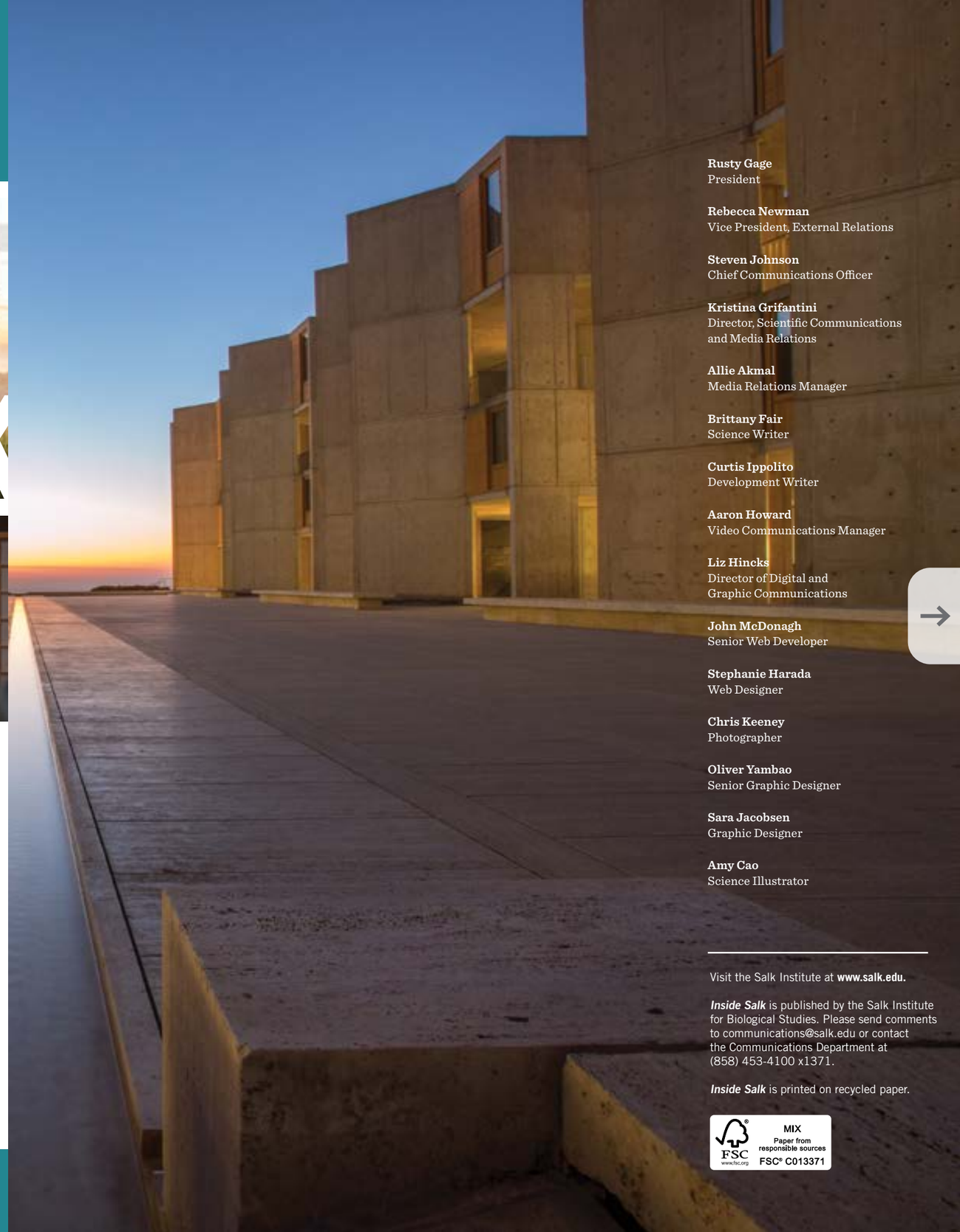

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