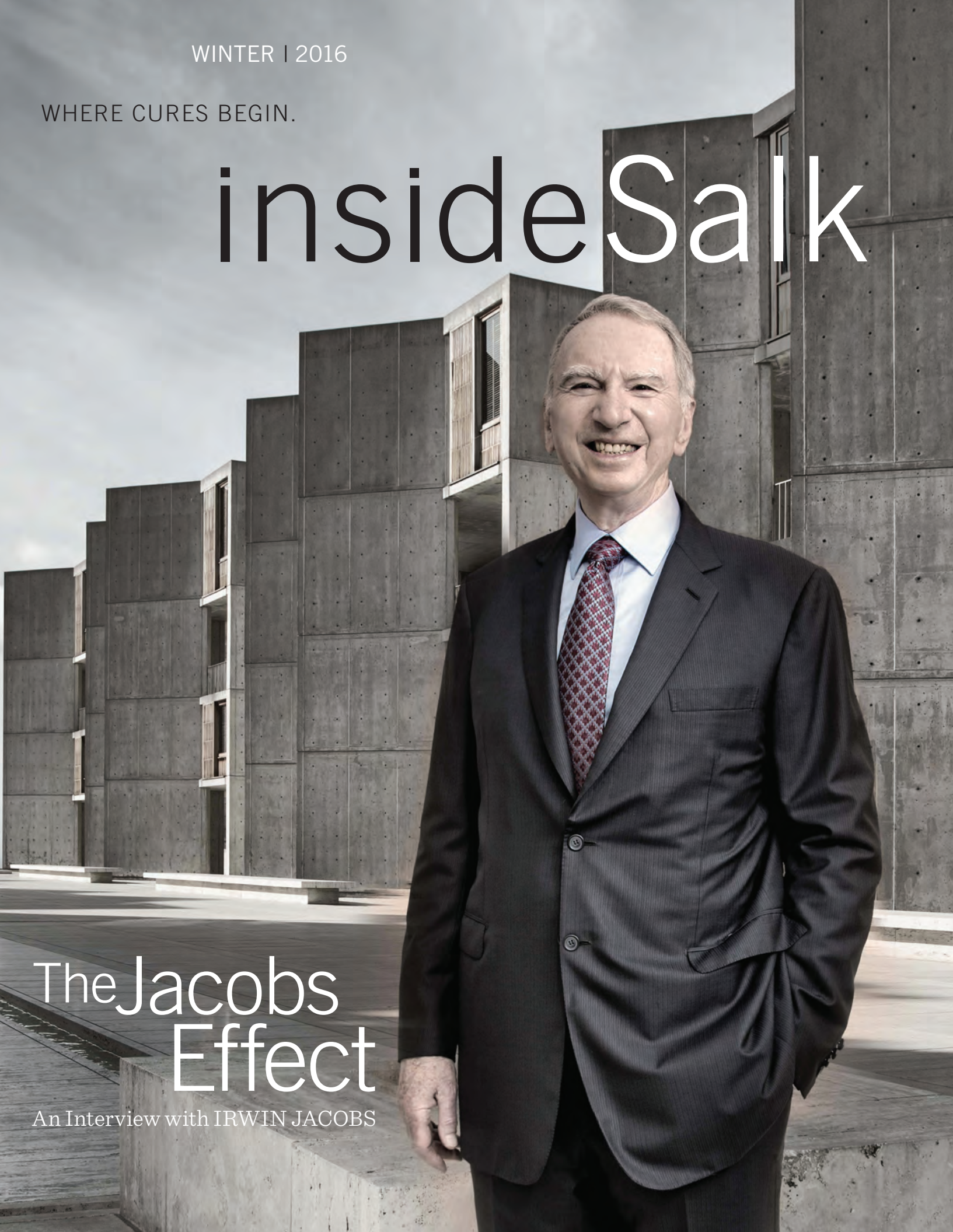
WINTER | 2016

WHERE CURES BEGIN.

inside Salk



The Jacobs Effect

An Interview with IRWIN JACOBS

CONTENTS

ON THE COVER:

Irwin Jacobs retires as the chair of Salk's Board of Trustees this year. The support and generosity of Jacobs and his wife, Joan, have enabled Salk scientists to push the boundaries of biomedical research and led to countless innovations.

PRESIDENT'S LETTER

Dear Friends,

Moving science forward requires partnerships. So in this season of giving thanks we highlight and thank our many partners, especially the donors who step up every year to fund important biological research at Salk. More than just money, though, these dedicated Salk supporters give of their time and their expertise. And for that we are particularly thankful.

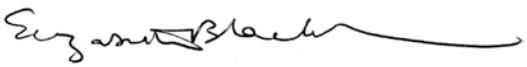
In this issue of *Inside Salk*, we feature our Innovation Grants Program, one Salk partnership program that propels the sort of high-risk, high-potential research that confirms the Institute's reputation as a world leader. This program enables ambitious scientists such as Clodagh O'Shea, Satchidananda Panda and Sreekanth Chalasani to pursue novel avenues of research that might otherwise have been orphaned due to a lack of traditional funding.

I'd like to point out that innovative partnerships are key to the Chan Zuckerberg Initiative, the $45 billion organization founded by Mark Zuckerberg and his wife, Priscilla Chan. In September, they announced plans to unite experts from around the world in virtual institutes dubbed "challenge networks" to tackle urgent scientific and medical problems. Such interdisciplinary collaboration has always been a tenet at Salk and I envision our Institute partnering with others within the framework of this new initiative.

Finally, on behalf of everyone here at Salk, I'd like to express our gratitude to two of our finest partners, Irwin Mark Jacobs and his wife, Joan. It is my honor to hold the Irwin M. Jacobs Presidential Chair, established in 2009 by Qualcomm, the San Diego-based telecommunications equipment company founded by Irwin. Over the course of a long and ongoing relationship with Salk, the Jacobses have helped create the Crick-Jacobs Center for Computational and Theoretical Biology, an interdisciplinary research unit providing unprecedented insights into the workings of the brain; they endowed two chairs recognizing Salk Nobel laureates Renato Dulbecco and Roger Guillemin; and they initiated a highly successful "chair challenge" in which they matched every gift of $2 million with an additional $1 million toward a goal of fully funding 20 endowed chairs. Now, after 10 years of astute leadership as chairman of the Salk Board of Trustees, Irwin is stepping down, even as he continues service as chair emeritus. What wonderful partners he and Joan have been—and continue to be—to Salk.

Read on to learn about all the amazing discoveries supported by our equally amazing partners. We appreciate each and every one of you, and I wish you a joyous holiday season.

Sincerely,



Elizabeth Blackburn
President, Salk Institute
Irwin M. Jacobs Presidential Chair

"More than just money, these dedicated Salk supporters give of their time and their expertise. And for that we are particularly thankful."

DISCOVERIES

In the last few months, Salk scientists have had groundbreaking work published in top journals and covered in notable media outlets. Read on to learn more.

READ	View the full news reports and more discoveries online at **www.salk.edu/news**

RESEARCH
AT SALK

NEUROSCIENCE

We are entering a new era in neuroscience where our knowledge of the brain is beginning to match the urgent need to prevent and treat diseases of the brain.

GENETICS

In many ways, we are our genes. At Salk, we explain the role of genes in everything from how tumors form to why certain people are at higher risk for neurological disorders.

MICROBIOME

We are not alone: The human body is home to trillions of bacteria. At Salk, we are exploring how this community of bacteria helps us stay healthy, and how we might help it fight disease.

AGING

Getting older doesn't have to mean getting sicker. We are committed to discovering the fundamental causes of aging and finding new ways to prevent and treat aging-related diseases.

METABOLISM

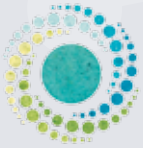
At Salk, we are working to understand human metabolism and what happens when this biological system breaks down. The problem is important as the burden of diabetes on society increases.

PLANT BIOLOGY

To match human population growth, world agricultural production must double over the next quarter century. We study plants so that humans will have the food, clothing, energy and medicines they need now and in the future.

CANCER

We are rapidly demystifying cancers and leading the search for the next generation of targeted cancer therapies. We see a future where every cancer and every patient has a cure.



REGENERATIVE MEDICINE

Many disorders and life-threatening diseases could be cured by replacing or fixing dysfunctional cells. We aim to uncover novel ways to provide new tissues and cells to the body while minimizing organ rejection.

IMMUNOLOGY

In a world full of dangers, from bacterial infections to cancer, our immune system is our fortress. We study the immune system to boost our ability to fight off numerous diseases.

FINDING A FIX FOR BROKEN NEURONS

The science of understanding neurodegeneration

SCIENTIFIC REPORTS
08/2016

Elevating brain protein allays symptoms of Alzheimer's and improves memory

The lab of Kuo-Fen Lee found that boosting levels of a specific protein in the brain alleviates hallmark features of Alzheimer's disease in a mouse model of the disorder. The protein, called neuregulin-1, has many forms and functions across the brain and is already a potential target for treating brain disorders, as detailed by Lee and first author Jiqing Xu on August 25, 2016 in *Scientific Reports*.

JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
08/2016

New mechanism discovered for Alzheimer's risk gene

Alan Saghatelian's lab identified a new connection between a gene called ApoE4 and protein build-up associated with Alzheimer's. Previous reports have suggested that ApoE4 may affect how the brain clears out protein clusters called beta-amyloid plaques, but what was happening at the molecular level wasn't clear. Saghatelian, first author Qian Chu and colleagues pinpointed how an enzyme, HtrA1, degrades ApoE4, which can let researchers better test hypotheses about ApoE4's role in Alzheimer's. The findings appear in the *Journal of the American Chemical Society*.

AGING AND MECHANISMS OF DISEASE
06/2016

Cannabinoids remove plaque-forming Alzheimer's proteins from brain cells

Salk Professor David Schubert, first author Antonio Currais and collaborators uncovered preliminary evidence that tetrahydrocannabinol (THC) and other compounds found in marijuana can promote the cellular removal of amyloid beta, a toxic protein associated with Alzheimer's disease. While these exploratory studies, detailed in *Aging and Mechanisms of Disease*, were conducted in neurons grown in the laboratory, they may offer insight into the role of inflammation in Alzheimer's and could provide clues to developing novel therapeutics for the disorder.

NEURON
08/2016

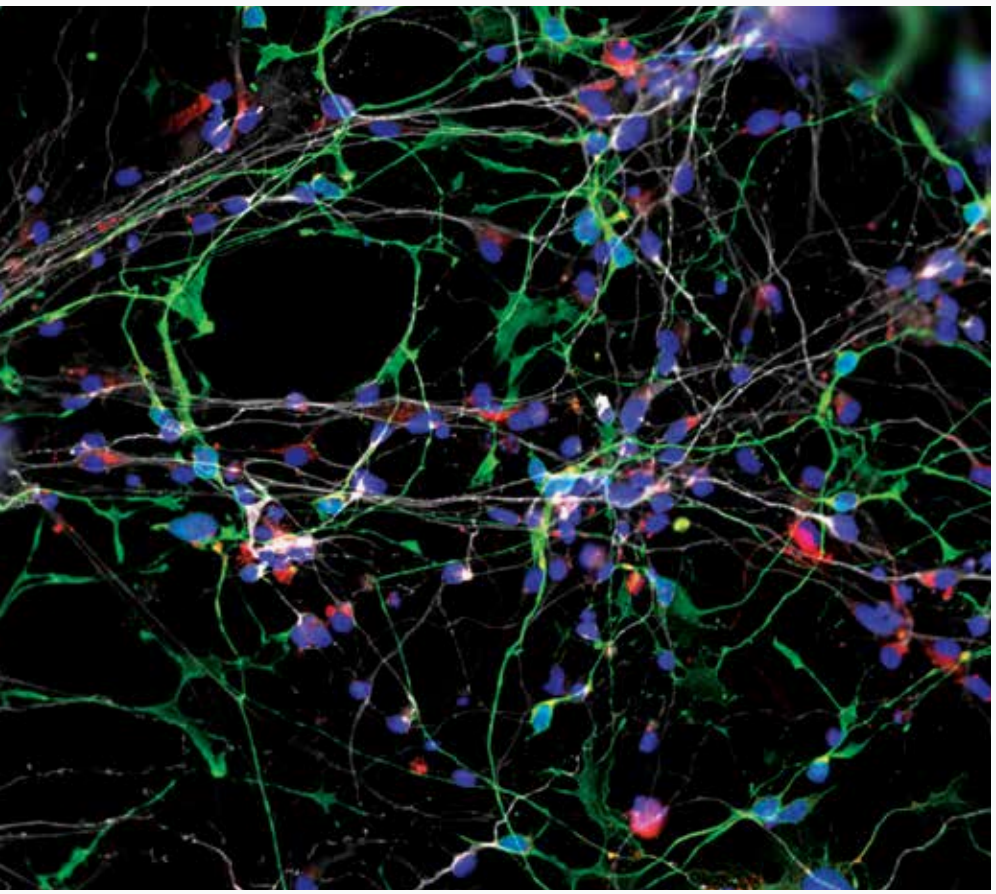
Salk scientists map brain's action center

Xin Jin and colleagues are using cutting-edge genetic, electrophysiological, and neural-tracing strategies to delve into the anatomy and function of lesser-known forms of organization in the brain. Jin, together with the paper's first authors Jared Smith, Jason Klug and Danica Ross, unraveled how particular cells in an area called the striatum receive a complex variety of information. This work, published in *Neuron*, could help better understand disorders such as Parkinson's disease, obsessive-compulsive disorder or addiction.

NEUROSCIENCE

NEURODEVELOPMENTAL MODEL OF WILLIAMS SYNDROME OFFERS INSIGHT INTO HUMAN SOCIAL BRAIN

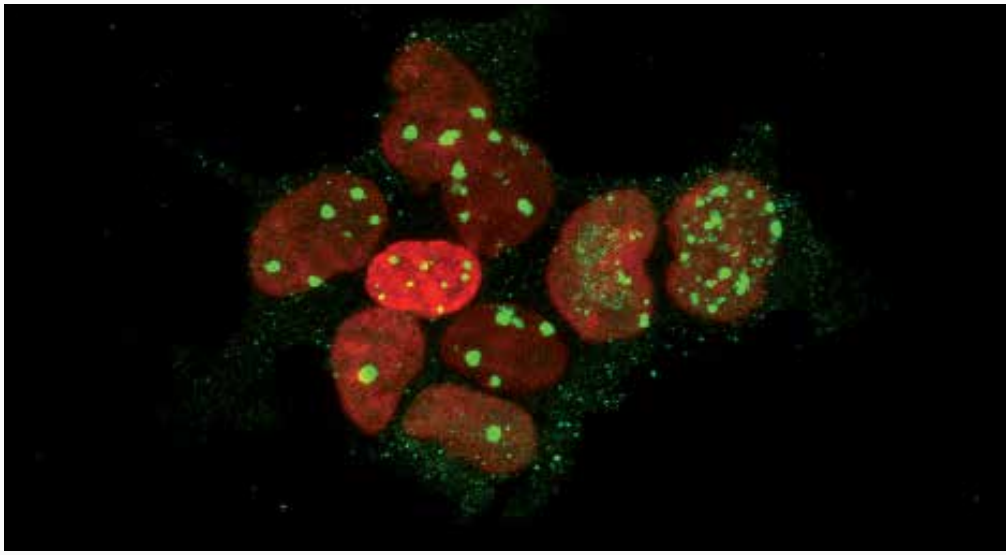
Rare genetic condition produces individuals with extremely sociable personalities but research may also shed light on biology and behavior of persons with autism and other social disorders.

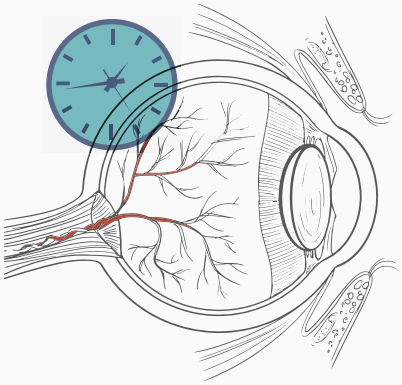


Researchers at the University of California, San Diego and the Salk Institute have created Williams syndrome-derived neurons in culture.
Credit: University of California, San Diego

In an August 2016 *Nature* paper spanning molecular genetics, stem cells and the sciences of brain and behavior, researchers at the University of California, San Diego and the Salk Institute have created a neuro-developmental model of a rare genetic disorder that may provide new insights into the underlying neurobiology of the human social brain. The disorder, called Williams syndrome (WS), is a rare genetic condition caused by deletion of one copy of 25 contiguous genes on chromosome 7, out of an estimated 30,000 genes in the brain. WS affects one in 10,000 people worldwide and an estimated 20,000 Americans. WS results in developmental delays, yet relative strengths in language use and face processing that result in a hyper-social predisposition. The labs of Ursula Bellugi and Rusty Gage in conjunction with UCSD were able to directly observe the behavior of cells with the genetic profile of WS. The cross-disciplinary research not only suggests potential new treatments for this behavioral syndrome but could also help scientists to better understand the fundamental biological processes underlying social interactions.

The "jumping gene" L1 cuts DNA in human cells to generate neuronal genomic diversity. Cells expressing L1 (genomic DNA shown in red) have high levels of DNA breaks as visualized by 53BP1 staining (green) which repairs broken DNA.



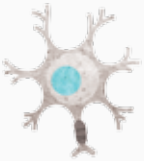


WHEN IT COMES TO RECOGNIZING SHAPES, TIMING IS EVERYTHING

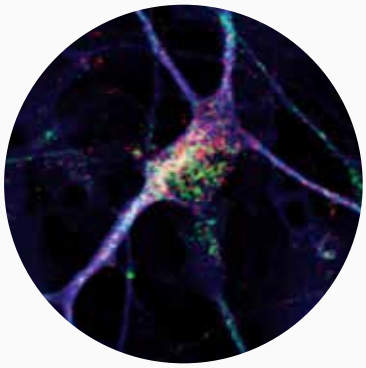
A *Neuron* study from John Reynolds' lab reveals more about how the brain processes vision, which could contribute to new therapies or visual prosthetics. Bursts in a neuron's electrical activity—the number of "spikes" that result when brain cells fire—make up the basic code for perception, according to traditional thought. But neurons constantly speed up and slow down their signals. Reynolds, first author Anirvan Nandy and colleagues found that being able to see the world relies on not just the number of spikes but the timing of those spikes as well. S

THE BRAIN'S STUNNING GENOMIC DIVERSITY REVEALED

Rusty Gage's lab showed how pieces of genomic material copy and paste themselves seemingly sporadically throughout DNA in brain cells. Gage, co-first authors Jennifer Erwin and Apuã Paquola, and collaborators, revealed that one type of jumping gene (called L1) can not only insert DNA but also remove large portions of it, resulting in much more genetic variation than previously thought. The team also examined how L1 variations influence a schizophrenia-associated gene called DLG2, providing insight into how these jumping genes could cause neurological diseases. The work was published September 2016 in *Nature Neuroscience.* S



NEUROSCIENCE

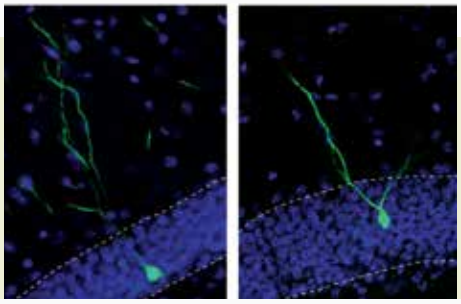


Neurons derived from cells of people with autism spectrum disorder show specific defects compared with those neurons derived from healthy people, including diminished ability to form excitatory connections with other neurons (indicated by red and green dots in the neuron).

NEW NEURONS REVEAL CLUES ABOUT AUTISM

The brains of some people with autism spectrum disorder grow faster than usual early on in life, often before diagnosis. In a study co-led by the Salk Institute, researchers found that stem cell-derived neurons made fewer connections in the dish compared to cells from healthy individuals. Furthermore, the scientists were able to restore communication between the cells by adding IGF-1, a drug currently being evaluated in clinical trials of autism.

In the journal *Molecular Psychiatry*, Salk Professor Rusty Gage, first author Carol Marchetto and colleagues show that it is possible to use stem cell reprogramming technologies developed in the past decade to model the earliest stages of complex disorders and to evaluate potential therapeutic drugs. S



MicroRNA miR-19 helps budding adult brain cells stay on track. Over-expressing miR-19 microRNA in neural progenitor cells in the adult brain of mice caused new neurons (green) to move and branch abnormally (right) compared to control neurons (left).

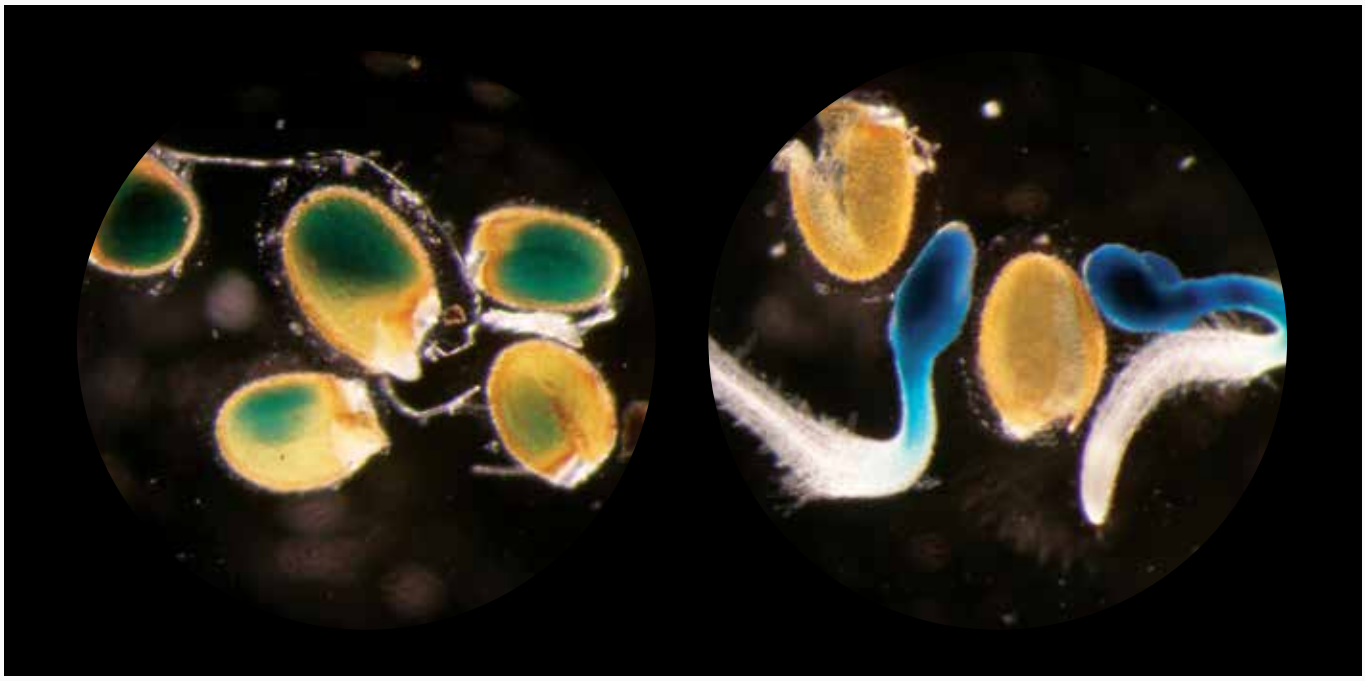
SMALL MOLECULE KEEPS NEW ADULT NEURONS FROM STRAYING, MAY BE TIED TO SCHIZOPHRENIA

A small stretch of ribonucleic acid called microRNA could make the difference between a healthy adult brain and one that's prone to disorders including schizophrenia.

Scientists at the Salk Institute discovered that miR-19 guides the placement of new neurons in the adult brain, and the molecule is disrupted in cells from patients with schizophrenia. The findings, published in the journal *Neuron* on July 6, 2016, pave the way toward a better understanding of how the adult brain controls the growth of new neurons and how it can go wrong.

Salk Professor Rusty Gage, first author Jinju Han and their colleagues found that levels of miR-19 changed more than levels of any other microRNA when precursors to new brain cells in these areas (called neural progenitor cells) were coaxed to become neurons in the adult brain. The researchers went on to show that when miR-19 was blocked in neural progenitor cells, levels of RNA corresponding to a gene called Rapgef2 were altered. Moreover, new neurons did not migrate to the correct areas of the brain.

Because the incorrect migration of new brain cells has been implicated in neuropsychiatric disorders like schizophrenia, Gage's group next analyzed the levels of miR-19 and Rapgef2 in neural progenitor cells that had been created by reprogramming skin cells from schizophrenic patients. Although the patients had no mutations in the gene for Rapgef2, they had high levels of miR-19 that corresponded with low levels of both the RNA and protein for Rapgef2. The team is now studying the role of miR-19 in mouse models of schizophrenia, as well as looking at cells from broader cohorts of human patients. S



The enzyme that degrades phaseic acid (blue) appears briefly in response to light during early seed germination. The picture on the left was taken one day after plant seeds were transferred from a dark environment to light; the picture on the right was taken on the second day.

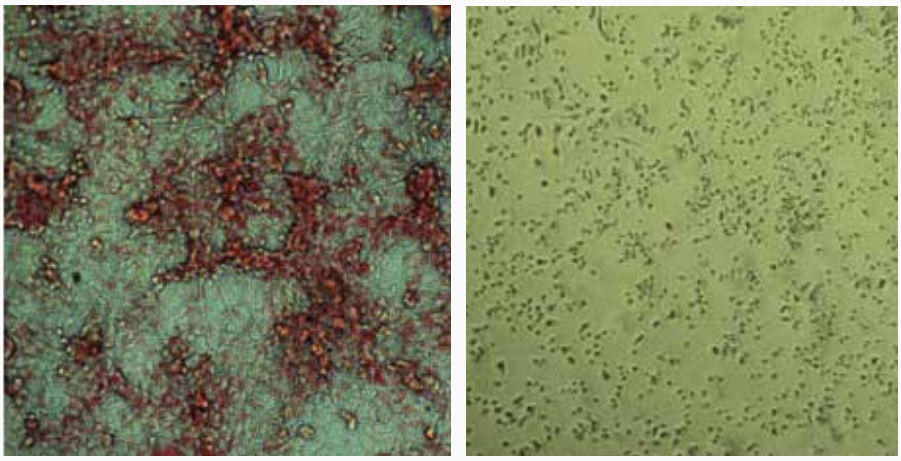
DISREGARDED PLANT MOLECULE ACTUALLY A TREASURE

Salk researchers discover that a plant molecule once regarded as a biological dead end now offers new leads into the development of hardier plants.

Research by Joseph Noel, first author Jing-Ke Wen and colleagues published August 2016 in the journal *Cell* reveals an unexpected role for a small, often overlooked molecule called phaseic acid, which has historically been cast as an inactive byproduct in plants. The new findings suggest that phaseic acid and its receptors probably co-evolved to become crucial for drought resistance and other survival traits and may inform the development of new, hardier crops that can weather natural disasters wrought by climate change.

The team used a commonly studied plant called *Arabidopsis thaliana* and obtained varieties that lacked the enzyme that processes phaseic acid, in effect accumulating large amounts of phaseic acid. To the group's surprise, the plants showed changes to the timing of seed germination and they survived without water for a longer period. This suggests that phaseic acid, rather than an inactive degradation product, could be a molecule that has its own capacity to cause changes like other plant hormones.

CANCER



Salk Institute researchers and collaborators developed a novel cancer treatment that halts fat synthesis in cells. Placebo-treated cells (left) have far more lipid (red) production compared to ND-646-treated cells (right).

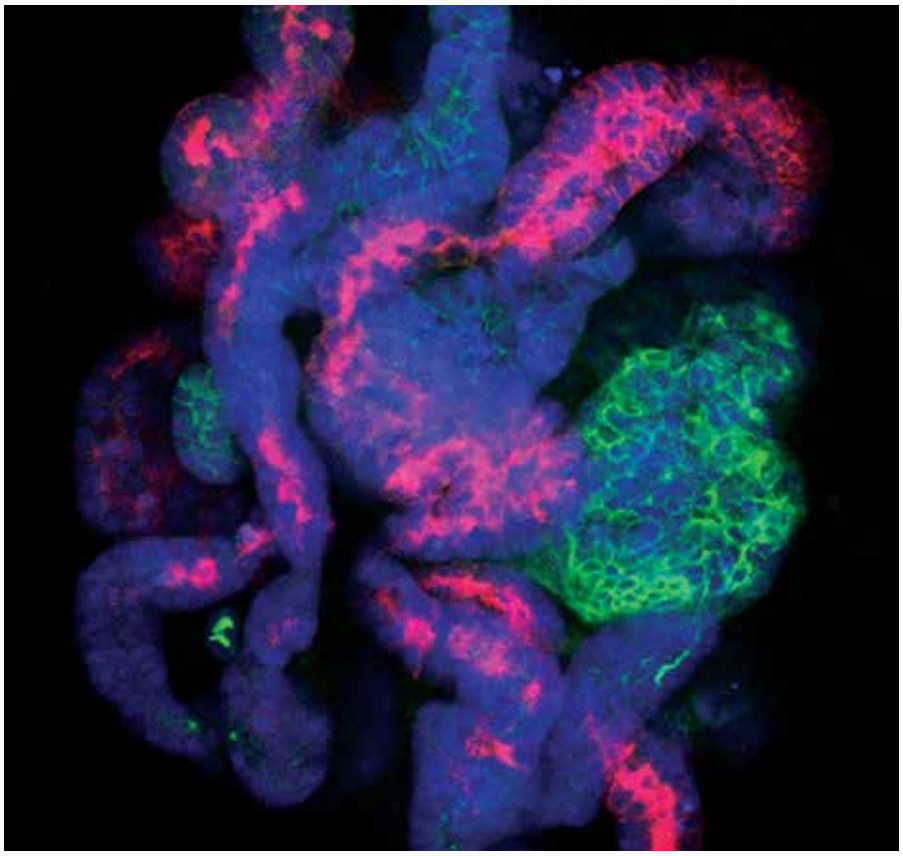
TARGETING FAT TO TREAT CANCER

Fat isn't just something we eat: it may lie at the heart of a new approach to treating cancer.

Cells create their own fat molecules to build critical cellular structures. Reuben Shaw's lab, along with academic and industry collaborators, has found a way to obstruct this instrumental process to stifle cancer's growth, detailed September 2016 in *Nature Medicine*. Like halting the delivery of supplies to a construction site, the approach stalls the molecular building blocks cancer needs to grow.

Researchers had previously hypothesized that interrupting cells' lipid assembly line could disable cancer, but it was only recently that they were able to disrupt the process and test this theory. Shaw, first author Robert Svensson, and colleagues partnered with Nimbus Therapeutics to test a molecule that shuts off a critical player in lipid synthesis, an enzyme called Acetyl-CoA Carboxylase, or ACC. In large-scale tests in animal models of cancer and in transplanted human lung cancer cells, the novel ACC inhibitor led to tumor masses shrinking by roughly two-thirds compared to untreated animals. And when the team paired this new drug with one of the common treatments for non-small lung cancer (carboplatin), the anti-tumor response was even greater: a dramatic 87 percent of tumors were suppressed, compared to 50 percent with the standard treatment alone, pointing to a promising drug candidate for lung cancer as well as liver and other types of cancer. S

WATCH | www.salk.edu/insidesalk/1216/shaw



Above: Salk researchers created kidney progenitor cells that survive in the lab using a 3D culture and a mix of supporting molecules.

Right: Salk scientists created a new method to develop an endless supply of kidney precursor cells. Pictured are long-term cultured nephron progenitor cells (red) incorporating and becoming part of the kidney after being transplanted into a developing kidney.

NEW METHOD CREATES ENDLESS SUPPLY OF KIDNEY PRECURSOR CELLS

The lab of Juan Carlos Izpisua Belmonte has discovered the holy grail of endless youthfulness—at least when it comes to one type of human kidney precursor cell. Previous attempts to maintain cultures of the so-called nephron progenitor cells (NPCs) often failed, as the cells died or gradually lost their developmental potential rather than staying in a more medically useful precursor state.

But by using a three-dimensional culture and a new mixture of supporting molecules, Izpisua Belmonte and co-first authors Zhongwei Li, Toshikazu Araoka, and Jun Wu have successfully suspended the cells early in their development. These NPCs, at least in humans, normally only exist during a brief stage of embryonic development. The cells go on to form nephrons, the functional units of the kidney, responsible for filtering the blood and excreting urine. But adults have no remaining NPCs to grow new kidney tissue after damage or disease. Generating NPCs in the lab, scientists believe, will offer a new way to study kidney development and eventually treat kidney diseases. The work appeared in *Cell Stem Cell* in August 2016.

An interview with the outgoing chairman of Salk's Board of Trustees, Irwin Jacobs

Perhaps it's his humble nature that prompts tech titan and philanthropist Irwin Jacobs to credit good luck to his life of wild successes. But to everyone else it's clear that the lucky ones are the many people who have benefited from the vision, service and incredible generosity of Jacobs and his wife, Joan. The Salk Institute and those helped by the Institute's biomedical research have been particularly fortunate that Jacobs served as chairman of Salk's Board for 10 years and that he and his wife have supported Salk science for even longer.

As a co-founder of Qualcomm in 1985, Jacobs redefined how the world thinks of telecommunications and information technology, including developing and commercializing Code Division Multiple Access (CDMA) in wireless networks.

The Jacobs


visionary
tech
Effect

Joan and Irwin Jacobs

Jacobs at his 80th birthday symposium on unraveling biological complexity and invigorating research through innovation, leadership and philanthropy (top left) and introducing Symphony at Salk (top right).

Bottom image: Standing between his wife, Joan (left), and Salk President Elizabeth Blackburn, Irwin Jacobs posed with Salk senior faculty members who received chairs as part of the Joan Klein Jacobs and Irwin Mark Jacobs Senior Scientist Endowed Chair Challenge.

The Jacobs have long been generous supporters of the San Diego Symphony, the Museum of Contemporary Art, San Diego, the La Jolla Playhouse, and the University of California, San Diego (UCSD), including the Jacobs School of Engineering and the new UCSD Jacobs Medical Center. They first became involved with the Salk Institute in 2004 when they helped establish the Crick-Jacobs Center for Computational and Theoretical Biology, which uses computer modeling to study how the brain processes information.

Following his retirement from Qualcomm, Jacobs was elected chairman of the Salk Institute's Board of Trustees in 2006, and for the past decade has overseen hiring two of the Institute's presidents and the successful Campaign for Salk, the Institute's first capital campaign.

Along the way, the Jacobs have been tireless and generous supporters of Salk science, as well as inspiring others to join them in advancing the Institute's mission of changing lives through high-risk, high-reward science. Among other things, they established a challenge grant to encourage donors to endow 20 chairs for senior scientists. For every $2 million that a donor contributes toward an endowed chair at the Institute, Joan and Irwin Jacobs added $1 million to achieve the $3 million funding level required to fully endow a chair for a Salk senior scientist. All 20 chairs have been established.

They also launched Salk's Innovation Grants Program, a donor-funded mechanism for supporting riskier, but potentially very rewarding, projects that would otherwise be orphaned (see page 18). The program has supported dozens of projects and resulted in groundbreaking results reported in high-impact journals such as *Science, Cell, Nature, PNAS* and *Neuron*. As Jacobs prepared to step down as Salk chairman in November 2016, *Inside Salk* asked some parting questions.

You had a long and successful career in academia and later in industry at Linkabit and Qualcomm. Some people would have kicked their feet up in retirement on a beach somewhere. Why have you and Joan devoted so much of your time and resources to service and philanthropy?

I enjoyed a very fulfilling academic experience at MIT and UCSD, followed by a most rewarding business career, co-founding and leading Linkabit in 1969 and Qualcomm in 1985. During that period I was fortunate to work with very good people on exciting projects, translating new ideas into useful products. I have always enjoyed learning about new areas, particularly in engineering and science. When I retired, Joan and I decided to continue family tradition and focus on using our time and resources to support interesting nonprofit institutions. We choose areas that have the potential to impact many, including research, education from K-12 to university, social and community needs, and cultural activities. We enjoy working with projects that have well-defined goals and good leadership.

You have been involved in many philanthropic endeavors. What attracted you to Salk?

The presence of the Salk Institute in La Jolla was one important factor in our decision to move here from Boston in 1966. Then, following retirement from Qualcomm, I became interested in learning more about biology and Salk, of course, was very attractive for its world-renowned research program. But I think what convinced me to later

When I retired, Joan and I decided to continue family tradition and focus on using our time and resources to support interesting nonprofit institutions.

Top image: Jacobs (right) tours Salk's new central power plant, which was completed in 2012.

Bottom image: Jacobs (left) with renowned glass sculptor Dale Chihuly during a 50th anniversary celebration of the Institute.

become involved was a lunch I had at Salk in March 2003. Francis Crick, Sidney Brenner, Rusty Gage, Chuck Stevens and Terry Sejnowski were there and the discussion was fascinating. I found that neuroscience had connections back to my work in information theory and communications which could be pursued. In June 2005, I attended an International Council Meeting at Chateau Margaux, heard many stimulating lectures, and that sealed the deal.

Is there anything from your tenure as chairman of Salk's Board that you are particularly proud of?

A lot of exciting things happened during my tenure as chair. Perhaps foremost, we selected two new presidents for the Institute. That was a bit of a challenge, and I ended up being happy with the outcome in both cases. For the first, I was given a notebook full of names, and did a lot of research. I came across Bill Brody's name and thought he'd be ideal if we could lure him away from Johns Hopkins. Luckily that all worked out and he served six years as a very successful president at Salk. When Bill retired, we began a broad search, but when we learned that Elizabeth Blackburn would consider such a step in her career, we focused on attracting her to Salk. I am very pleased that we succeeded. Another significant event occurred early in my time as chair and that involved guiding Salk into becoming one of the founding members in the Sanford Consortium for Regenerative Medicine which continues to play a significant impact on science on the Mesa.

Are there particular areas of Salk research or projects that you've found most intriguing?

All of the areas of research are progressing well, often yielding surprising results. Neuroscience, because of its

breadth, because it does have a connection to information theory, and because of increasing progress in understanding the brain at many levels, is perhaps most intriguing. Brain research also requires substantial engineering effort to be able to sense what is happening in the brain. Indeed, the National Academy of Engineering chose reverse engineering of the brain as one of its Grand Challenges. That is rather an ambitious challenge but quite intriguing. Of course, the allure of the Salk is its broad and innovative approach to science. We've made great progress in learning the biology of many cancers, leading to personalized treatments based on sequencing an individual's tumors. From a scientific and even an artistic point of view, it's exciting to see the work in biophotonics, allowing us to visualize life at a level previously impossible.

Looking around your house, clearly you and Joan have a love of art. Is there something that art and science share that draws you to both?

We enjoy being surprised by new ideas and forms. Artists and scientists are interested in innovative outlooks on our world and are willing to experiment and take risks – and they must have persistence. We are often intrigued by the simplicity of the end results masking the many approaches explored along the way.

I noticed your house is very modern. What was your first reaction when you saw the architecture of Salk?

During a trip to San Diego in 1965, Joan and I had a chance to explore the region and discovered the Salk Institute. I still remember it as a "wow" moment. Although the architecture first appeared brutal, it appealed very much to our personal aesthetic. It is so contemporary, so well sited and so beautifully thought through and functional. When we considered moving to La Jolla, the Salk Institute and the opportunity to teach and help form a brand new university became deciding factors. However, it took one additional incident to sway our decision. It's funny how small things do change the course of life. When I was first offered the job at UCSD, I turned it down, with family, friends and career all on the East Coast. But for the next two days, we questioned our decision. Returning home the second day, soaked from a major rainstorm, Joan read me a description of a contemporary home that was for sale. I said, "Let's go see it tomorrow." She said, "There's only one problem, it's in La Jolla." And so here we are.

Has the unexpected played out in other ways in your life?

Entering a business career provides another example. When we moved to San Diego, I didn't really plan on going into business. However, I had co-authored a textbook on digital communications at MIT. As a result, I received many more requests for consulting from companies in California than I could handle. I mentioned this to two faculty friends at UCLA and they suggested we should start a company to share the consulting. And that's how Linkabit, my first company, began. It began to grow, so I took a one-year leave from UCSD to get it organized, found the technology business great fun, and in 1972 became a dropout from academia. The digital communication theory that I had been teaching proved very useful in business and Linkabit was a great success. I sold it in 1980 and remained until 1985. Six persons who had worked with me at Linkabit suggested starting another company. Although we did not have any products in mind when starting, the unexpected occurred again and Qualcomm became another success driven by innovative products.

WATCH | www.salk.edu/insidesalk/1216/jacobs

FRONTIERS

"PROVIDING BRIGHT AND ORIGINAL MINDS THE OPPORTUNITY TO QUICKLY PURSUE A NEW IDEA DOES FREQUENTLY RESULT IN UNEXPECTED AND OCCASIONALLY FUNDAMENTAL BREAKTHROUGHS."

IRWIN JACOBS Chairman, Salk Board of Trustees

SPARKS OF INNOVATION

Supporting risky ideas can lead to **phenomenal science**

SHREK CHALASANI
Salk Associate Professor

The tiny worms from Sreekanth "Shrek" Chalasani's laboratory are media darlings. Among other notable media outlets, they've made headlines in the *Guardian, Scientific American* and *The New York Times*—not to mention the stir they've caused in the technical scientific literature.

The worms' fame stems not from their own merits, but from the fact that they are the first organisms whose brains and behaviors can be controlled using sound waves. The technique for exerting this control, dubbed sonogenetics, was first developed in Chalasani's laboratory at Salk, and represents a prime example of how supporting a scientist's creative, if unorthodox, idea can lead to surprising and important innovations.

"Turning specific neurons on and off with sound offers a noninvasive method for studying the brain and opens the door to replace invasive clinical procedures like deep brain stimulation," says Chalasani, an associate professor in the Molecular Neurobiology Laboratory.

This discovery was made possible by a new kind of support: the Innovation Grants Program, launched in 2006 as the brainchild of Salk Board of Trustees chair and philanthropist Irwin Jacobs. Jacobs and his wife, Joan, committed $8 million to fund out-of-the-box ideas through this program, with the goal of supporting theories based on solid science but with no data yet to suggest success. Such proposals might sound risky in terms of achievement but, if they pan out, have the potential to lead to groundbreaking technologies and discoveries. Too often, scientists' most creative ideas aren't explored because they are difficult to fund, but the Innovation Grants Program has turned a number of "wacky" ideas into enviable cutting-edge research programs.

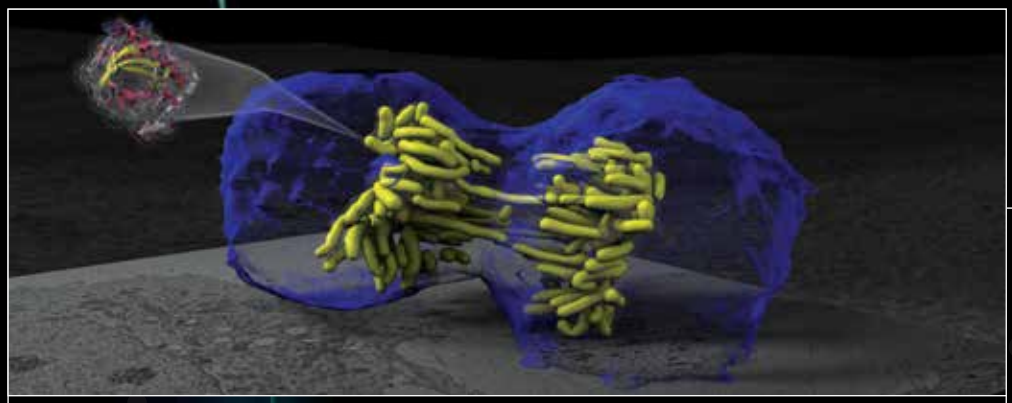
Chalasani's idea of using ultrasonic waves to manipulate neurons was funded by two Innovation Grants in 2011 and 2015. In September 2015, Chalasani's team reported early success with the unprecedented approach in *Nature Communications*, which garnered media attention for his lab.

"Without the Innovation Grants, this project might have never happened. I had no data to even think that sound could be used in this manner," says Chalasani. "It was a pie-in-the-sky idea in some ways. But the grants helped us to test our idea. More than just funding, the grants gave me the confidence to pursue this novel idea."

SONOGENETICS

"TURNING SPECIFIC NEURONS ON AND OFF WITH SOUND OFFERS A NONINVASIVE METHOD FOR STUDYING THE BRAIN AND OPENS THE DOOR TO REPLACE INVASIVE CLINICAL PROCEDURES, LIKE DEEP BRAIN STIMULATION."

SHREK CHALASANI Salk Associate Professor



"THE INNOVATION GRANT WAS LIKE A STEPPING STONE FOR MY LAB TO GET ENOUGH DATA TO HAVE A SENSE THAT THE TECHNOLOGY MIGHT WORK."

CLODAGH O'SHEA Salk Associate Professor

CHROMATIN & DNA

The grants, Jacobs says, are meant for Salk scientists—all trailblazers in their respective fields—to test a notion or idea so unexpected and new that traditional funding sources, such as government grants, would not typically take on the financial risk. The effort grew, gaining additional supportive donors (the Rose Hills Foundation, James Melcher and April Benasich, Fondation Ipsen, and Elizabeth Keadle) and funding 76 awards averaging $120,000 each to date. Though donors have often supported new scientific research at Salk, the program has helped ensure that bold and creative scientific ideas based on excellent science receive immediate funding.

"This program is intended to provide resources for early, innovative, and often high-risk scientific research, and to do so with minimal delay. We have been very pleased with the originality and success of the funded projects," says Jacobs. "Providing bright and original minds the opportunity to quickly pursue a new idea does frequently result in unexpected and occasionally fundamental breakthroughs, substantially supporting progress in solving our most pressing science and medical problems." For example, now Chalasani's work to expand his technique into mammals has garnered two major grants, one from the Keck Foundation and one from the National Institutes of Health's BRAIN Initiative, announced in October 2016, to further develop the technology and test the process in mammalian cells, with the hopes of moving to human therapies.

Allowing this unfettered exploration of ideas has resulted in a number of impressive innovations in the last few years alone. Salk Associate Professor Clodagh O'Shea was the recipient of one such grant in August 2013 to explore new technologies related to the complex packaging of DNA and proteins (called chromatin) within a cell's nucleus. The configuration of chromatin is one that has confounded scientists but holds clues to understanding health and disease. How tucked away and thereby inaccessible genetic material is within chromatin determines whether or not certain genes—such as ones that suppress tumors—are active.

The Innovation Grant helped O'Shea to explore new imaging and sequencing technologies to visualize the structure and function of DNA in time and space—work which has the potential to reveal the structural code that determines if a gene is in an "on" or "off" state in diseases such as cancer. Aside from better understanding chromatin, O'Shea is also using this knowledge to design synthetic viruses and genetic

CLODAGH O'SHEA
Salk Associate Professor

SATCHIDANANDA PANDA
Salk Professor

machines that can infiltrate the nuclei of cancer cells, for example, and selectively destroy tumors.

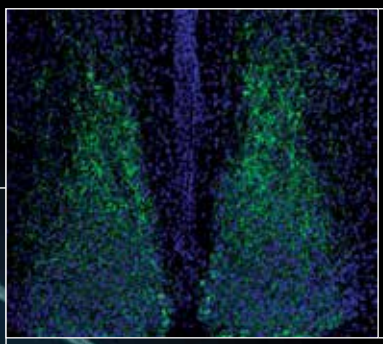
The work eventually led to O'Shea receiving a 2014 Keck Foundation award in partnership with the University of California, San Diego for $1 million. The next year, she was also one of the recipients of a $120 million, 5-year multi-institute initiative by the NIH to understand the cell's nucleus.

"The Innovation Grant was like a stepping stone for my lab to get enough data to have a sense that the technology might work," says O'Shea, holder of Salk's William Scandling Developmental Chair and an HHMI Faculty Scholar. "The problem with disruptive technologies is that people say it's never been done before so it won't work and they won't fund it. But something like the Innovation Grants allows us to get an inkling that an idea could be possible and gather data for a proof-of-principle to get more funding to then take the research further."

In another example of cutting-edge science finding traction through Innovation Grants, Salk Professor Satchidananda Panda received support to examine how eating and lifestyle activities affect daily biological cycles (circadian rhythms) and, by extension, health and illness. His Innovation Grant backed a study into the ebb and flow of genes tied to circadian patterns in baboons in Kenya. Through the research, which has been extended with additional funding from the U.S. Department of Defense, Panda aims to chart daytime and nighttime patterns of gene activity and reveal cellular "switches" that could help reset or control circadian rhythms.

Panda's line of research could have vast implications for treating jet lag, sleep disorders, shift work and overall health. For example, he has published data demonstrating that mice which eat within a set amount of time (12 hours) resulted in slimmer, healthier mice than those who ate the same number of calories in a larger window of time, indicating that when one eats in relation to circadian rhythms may be as important as what one eats. Additionally, his research has uncovered that circadian rhythms even mediate the immune system, suggesting that genes and molecules involved in the circadian clock could be drug targets for conditions linked to inflammation, infections or cancer.

"The Innovation Grant's support was critical to explore this novel idea which now has been gaining traction in the field



"IT APPEARS THAT CIRCADIAN RHYTHMS CAN HAVE PROFOUND EFFECTS ON EATING DISORDERS, DIABETES, OBESITY AND OTHER HEALTH AILMENTS."

SATCHIDANANDA PANDA Salk Professor

CIRCADIAN RHYTHM

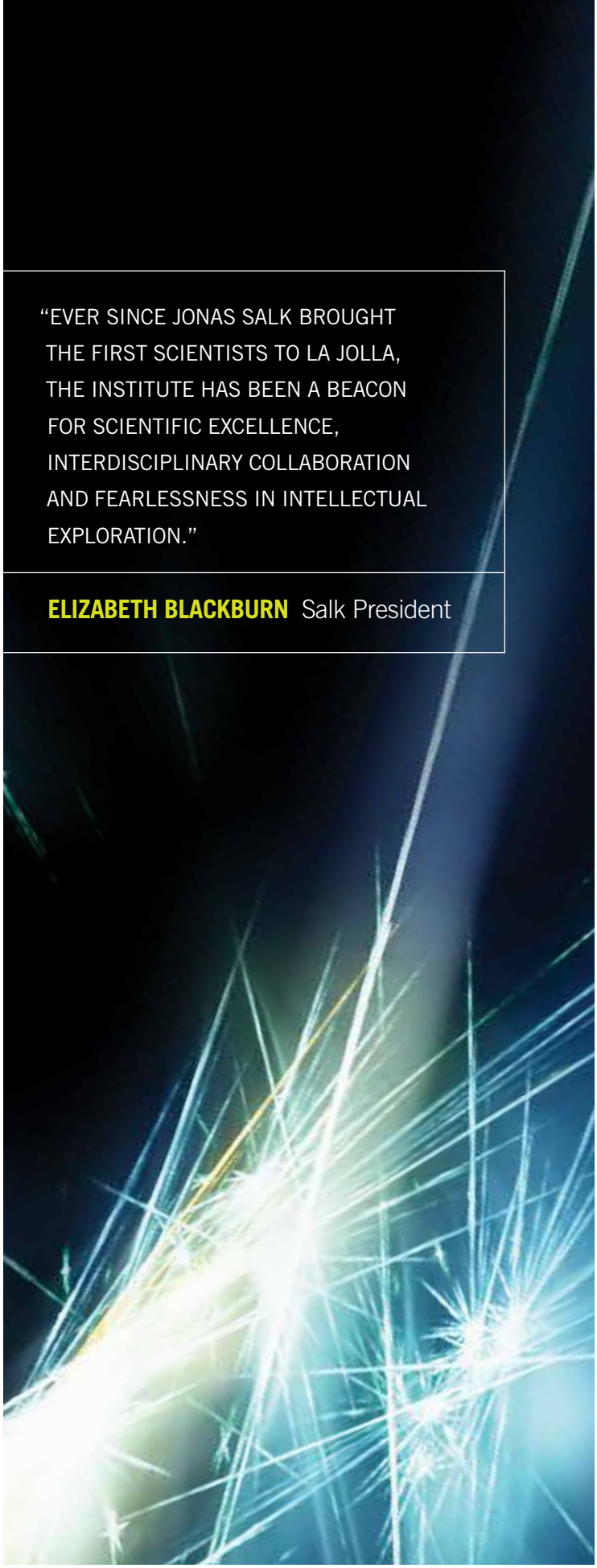
and in the press," says Panda. "It appears that circadian rhythms can have profound effects on eating disorders, diabetes, obesity and other health ailments."

The list of innovations since the program's inception continues across labs. Of the awards granted, about 30 to 50 percent of the projects have successful results—an exceedingly promising success rate for ideas that may originally be viewed as far-fetched. "Support like the Innovation Grants is one of the few ways big-risk—and big-reward—scientific endeavors happen," says Salk Research Development Director Michael Nunn, who oversees the Innovation Grants process. "The program is one of the things that keeps Salk at the cutting edge."

The Innovation Grants aren't just for early career scientists. This support allowed Salk Professor Tony Hunter to develop new tools to study the role of a little understood chemical process (histidine phosphorylation) and Salk Professor Vicki Lundblad to dig into what happens at the ends of chromosomes, called telomeres, which are tied to a cell's health and an organism's lifespan. Both scientists received additional support from federal grants to continue their research. In another success story, Salk Professors Martyn Goulding and Ed Callaway made dramatic inroads in tracing neural circuits and optogenetics—the more mature cousin of sonogenetics.

"We have been able to push the boundaries of neuroscience thanks to the Innovation Grants," says John Reynolds, a Salk professor who received Innovation Grants along with Salk Professor Kuo-Fen Lee to develop a new mammal research model based on the marmoset to better understand gene activity, neurobiology and vision. After initial promising results, Lee and Reynolds are exploring other avenues of funding to continue research in this area. "We are optimistic about receiving additional support to explore new aspects of neurodegenerative disease, in particular Alzheimer's, in the marmoset model," says Lee.

"Ever since Jonas Salk brought the first scientists to La Jolla, the Institute has been a beacon for scientific excellence, interdisciplinary collaboration and fearlessness in intellectual exploration," says Salk President Elizabeth Blackburn. "By developing programs like the Innovation Grants and others to offer unfettered support for big-thinking and brilliant science, we are able to ensure an emergence of the most creative science discoveries."

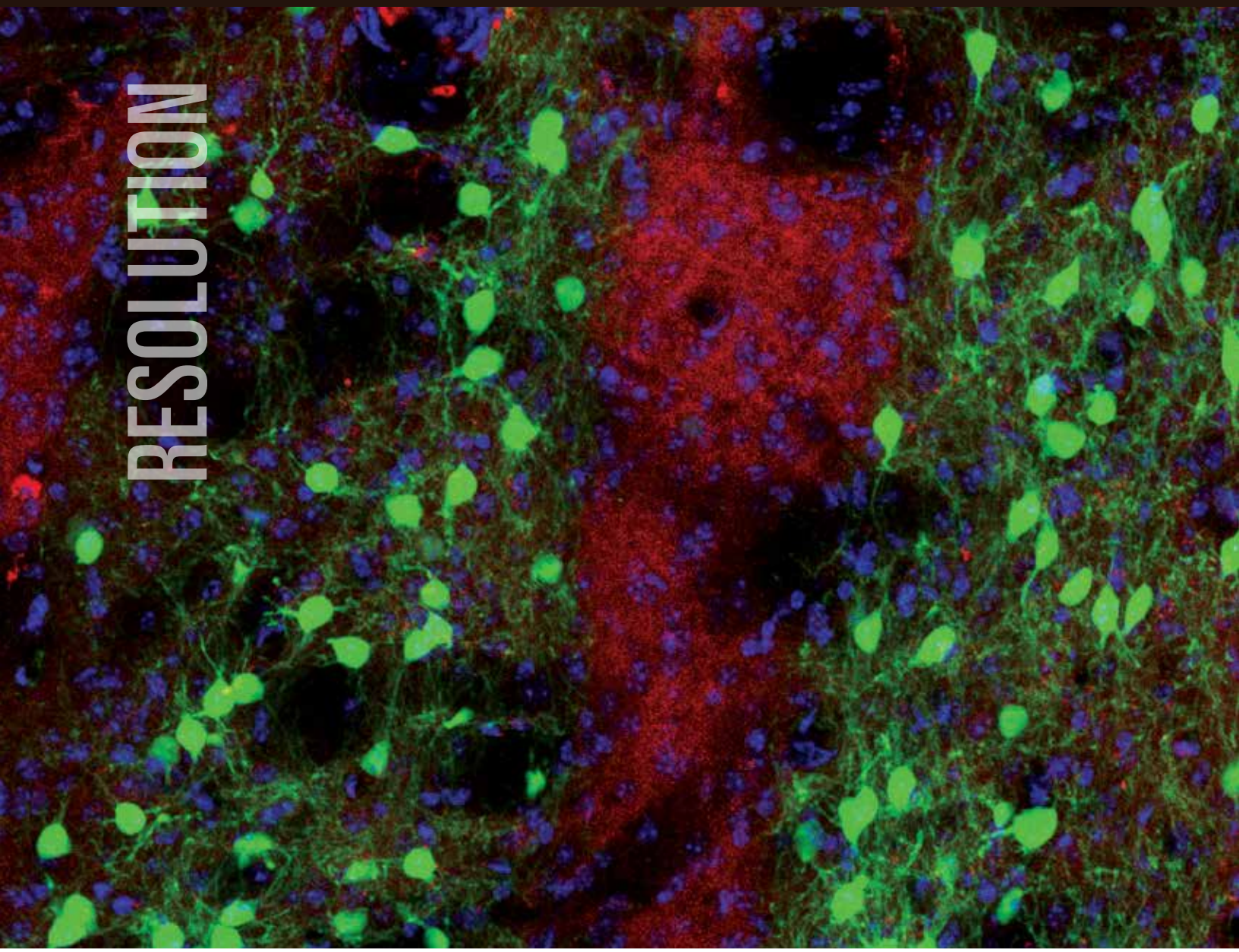


"EVER SINCE JONAS SALK BROUGHT THE FIRST SCIENTISTS TO LA JOLLA, THE INSTITUTE HAS BEEN A BEACON FOR SCIENTIFIC EXCELLENCE, INTERDISCIPLINARY COLLABORATION AND FEARLESSNESS IN INTELLECTUAL EXPLORATION."

ELIZABETH BLACKBURN Salk President

mapping connections

Salk Institute researchers in the lab of Salk Assistant Professor Xin Jin employed novel genetic tools to map the connectivity of neurons within a part of the brain, called the striatum, that controls movement toward a goal or reward. The matrix neurons, highlighted in green, appear to avoid the patch neurons (in red), which are smaller clusters of neurons in the striatum.



UNRAVELING THE MYSTERIES OF LIFE

with Abby Buchwalter

NEXTGEN

On a rainy summer afternoon in suburban New York, a bored 12-year-old Abby Buchwalter found her calling for biology through, of all things, a telephone. Taking apart an old rotary dial phone unearthed in a friend's basement, she analyzed its "tiny bits and bobs" to determine how it came together to make a machine. She remembers it as a defining experience that made her want to figure out how things work.

As a staff scientist in Martin Hetzer's Molecular and Cell Biology Laboratory, Buchwalter now figures out how things work on a cellular level. She focuses on the nucleus, the command center of cells. She first studied the nuclear pore complex, an assembly of proteins that act as gatekeepers on the outside of the nucleus, granting only some molecules access to the DNA housed inside. Halfway through her postdoctoral fellowship, she wanted to shift directions, and with Hetzer's support, did a reboot.

For the past two years, Buchwalter has been working on another part of the nucleus called the nuclear lamina. Akin to a skeleton, the nuclear lamina provides structural support and helps organize the nucleus. Buchwalter initially was interested in the lamina's function, stability and lifespan. When she found it constantly reassembles and remodels while the nucleus remains intact, she then wondered how it might change in disease. That led her to Hutchinson-Gilford progeria syndrome, a rare genetic disorder characterized by premature aging and death.

The lamina is mutated in the disease, and Buchwalter found that this mutation alters some regulatory processes in the nucleus, particularly the production of proteins. The prematurely aged cells make too many ribosomes, the cellular machines that build proteins. As a result, the cells produced too much protein, resulting in their using up their energy stores too fast. At the cellular level, patients with progeria are, simply put, living fast and dying young. The disease has proven to be a research model for normal aging processes.

Away from the bench, Buchwalter is active in Salk's Education Outreach program and helped develop SciChats, video interactions between Salk scientists and local students interested in research. She also participates in Reuben H. Fleet Science Center's "Two Scientists Walk Into a Bar," a community outreach that places scientists in a local bar and invites the public to ask them anything.

For total relaxation, Buchwalter likes to knit, a craft she learned from her mother. On Saturday afternoons she can be found knitting with friends at Station Tavern in South Park, keeping her hands busy and her mind free to unravel the mysteries of life. S

LISTEN | www.salk.edu/insidesalk/1216/buchwalter

SPOTLIGHT

Martin Hetzer named Vice President and Chief Science Officer

Martin Hetzer

The Board of Trustees approved the appointment of Martin Hetzer, a professor in the Molecular and Cell Biology Laboratory and holder of the Jesse and Caryl Philips Foundation Chair, to the position of Vice President and Chief Science Officer (VP-CSO). Under the direction of the Institute president, and in conjunction with the Research Advisory Committee (RAC), Hetzer will provide leadership in developing and implementing Salk's overall scientific strategy, as well as overseeing research operations in support of this strategy. He will continue to serve as principle investigator of his lab.

SALK INSTITUTE AMONG TOP 25 NORTH AMERICAN SCIENTIFIC "STARS" IN *NATURE INDEX*

According to a new report by Nature Publishing Group, the Salk Institute ranks as one of the leading scientific "stars" in North America with high-quality output that has grown particularly fast.

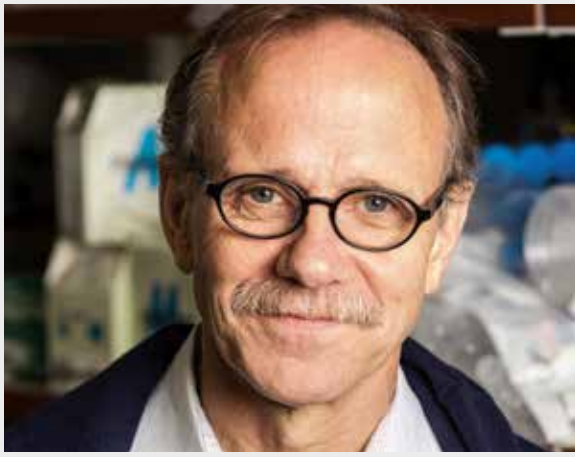
The data use a series of metrics to evaluate over 8,000 scientific institutions across the globe. The index, designed to be a tool for assessing research performance, charts which countries and institutions are the most efficient at producing high-quality results based on publications in top-tier journals. The Salk Institute is listed among the top 25 institutions in all of North America in the "Regional Stars" section of the index.

MYCIRCADIANCLOCK APP

Satchidananda Panda, a professor in the Regulatory Biology Laboratory, has created a new smartphone app to get an understanding of when, what, and how much we eat, sleep, and move. With enough subjects, he hopes to test the benefits of time-restricted feeding under different conditions of sleep, activity, and disease. Download it with the QR code or explore it at mycircadianclock.org.

RUSTY GAGE TO CO-LEAD $15 MILLION MENTAL HEALTH INITIATIVE

Rusty Gage, a professor in the Laboratory of Genetics and holder of the Vi and John Adler Chair for Research on Age-Related Neurodegenerative Disease, along with Johns Hopkins researchers, is spearheading a multi-institutional effort to develop new ways of studying and screening drugs for schizophrenia and bipolar disorder. The consortium, which is funded by the National Institute of Mental Health, will use samples from patients to improve upon induced pluripotent stem cell technology and observe how specific types of brain cells are affected by the diseases and how they respond to drug candidates.



Rusty Gage

SALK WELCOMES NEW TRUSTEE

Eric Sagerman, a strategic advisor with broad financial, technology and health care experience, joined the Salk Institute Board of Trustees in August. A former CEO and president of the medical records company Universata, Sagerman served as a managing director and Head of Strategy and Strategic Marketing for Allianz Global Investors after spending 16 years with American Express in a number of marketing and business management posts, both domestically and internationally. As senior vice president, he was involved in many growth and restructuring initiatives, including launching the Global Network Services business, the Corporate Card business and the Centurion "Black" Card. Sagerman currently serves on the board of Teach for America, San Diego, and is a member of the Salk Institute Investment Committee. He earned a BA in economics from Tufts University and an MBA from the Amos Tuck School, Dartmouth College. He and his wife, Jane, live in La Jolla.

Eric Sagerman

Clodagh O'Shea

hhmi | Howard Hughes Medical Institute

CLODAGH O'SHEA WINS COMPETITIVE GRANT FROM FACULTY SCHOLARS PROGRAM

Clodagh O'Shea, an associate professor in the Salk Institute's Molecular and Cell Biology Laboratory, is among the first recipients of a grant from the Faculty Scholars Program, a new partnership of Howard Hughes Medical Institute (HHMI), the Bill & Melinda Gates Foundation and the Simons Foundation for early career researchers whose work shows the potential for groundbreaking contributions in their fields. O'Shea is one of 84 Faculty Scholars who will receive $100,000–$400,000 per year over five years to support their pursuit of innovative research. The grant will support her cutting-edge technologies to design synthetic viruses and other genetic devices that are able to selectively target cancer cells.

THE TELOMERE EFFECT

Salk President Elizabeth Blackburn's new book, *The Telomere Effect*, will hit bookshelves in early 2017. Co-authored with Elissa Epel, health psychologist and founder and director of UCSF's Center on Obesity Assessment, Study, and Treatment, the book features Blackburn's work on telomeres, telomerase, and their role in the aging process, as well as specific lifestyle habits to protect them and slow down disease.

Preorder the book on **Amazon.com**.

EDUCATION OUTREACH DIRECTOR ELLEN POTTER RETIRES

When neurobiologist Ellen Potter launched Salk's Mobile Science Lab in 1996 in conjunction with the County Office Of Education, her mission was clear: Use state-of-the-art laboratory activities to show San Diego's middle schoolers that science is understandable, it can be a career, and above all, it's fun.

Potter retires this month after 38 years at the Salk Institute. She leaves a rich tradition of educating and exciting the next generation of scientists, having provided thousands of students with the knowledge and skills needed to pursue basic research, as well as unparalleled exposure to Salk's world-class faculty.

"Ellen's exceptional dedication to education has left its mark at Salk and in the wider community," says Salk President Elizabeth Blackburn. "Countless students and members of the public have discovered a love and appreciation of science thanks to Ellen's verve, infectious enthusiasm and highly effective efforts."

Under the direction of Potter and Co-Director Dona Mapston, the Education Outreach department has grown to offer several signature programs that expose students to genetics and biotechnology, including the March of Dimes High School Science Day and the eight-week Heithoff-Brody Scholars Program for high school students every summer. Last year, Salk invited 300 girls from the San Diego Unified School District for a "Women in Biotech" presentation as part of a STEAM Leadership Series, and in 2014, Education Outreach developed SciChats—Skype tours and talks between researchers and students—as well as video curriculum for teachers. "Ellen made it possible for Salk scientists like me to learn how to share what we do with the broader world," says Abby Buchwalter, a staff scientist in Martin Hetzer's lab and an Education Outreach volunteer. "I have always admired the passion that drove her to start Education Outreach. The outreach community that she built has greatly enriched my training period here—a sentiment I'm sure many other past and present Salk scientists share."

In recognition of Potter's efforts to enhance K-12 science education in San Diego, the inaugural "Research Connections for Teachers Symposium" held at Salk this fall was named in her honor. The symposium for middle and high school teachers featured Salk scientists describing the latest trends in biological research on topics including cancer, diabetes and epigenetics. "Bringing techniques like DNA extraction, gel labs and fruit fly phenotyping to my students through Salk's Education Outreach program is absolutely amazing and could not be more relevant to the world we live in," says James King, a science teacher at Monroe Clark Middle School in San Diego.

Ellen Potter

Other accolades for Potter's work have been the 2009 Partnership Award by the San Diego Science Alliance and the San Diego Unified School District's 20-year Partner in Education award in 2012. "Ellen has been an inspiration and driving force behind our Education Outreach program," says Walter Eckhart, professor emeritus in Salk's Molecular and Cell Biology Laboratory. "Her enthusiasm and dedication touched the lives of many young people."

Her collaborative spirit extends to other institutions throughout San Diego, including UCSD's Biobridge program, The Scripps Research Institute, Birch Aquarium and the San Diego County Office of Education. She serves on the Educational Steering Committee for BIOCOM, a life science industry association representing more than 500 members.

A native of La Cañada Flintridge, California, Potter studied biology at the University of California, San Diego before joining the Salk Institute in 1978 as a research assistant in the Regulatory Biology lab, and in 1991 received her PhD in pharmacology from UCSD under the mentorship of Wylie Vale. She is married to Salk Professor Ronald Evans of the Gene Expression Laboratory and they have a daughter, Lena.

EVENTS

From left: Lt. Col. Bob Sulier, John Reynolds, Geoffrey Wahl and Sally Ganley.

PATRIOTIC PROFESSORS

Salk faculty Geoffrey Wahl and John Reynolds received a Patriotic Employer award in recognition of their support of Salk research administrative assistant Sally Ganley's service in the United States Army Reserve. As a reservist, Ganley, who works in the labs of both Wahl and Reynolds, attends a Battle Assembly one weekend a month and annual training. Lt. Col. Bob Sulier of the Army Reserve thanked both professors and lab colleagues for supporting Ganley's military service.

LEADING SCIENCE

Salk Women & Science's fall program showcased the Institute's core facilities and the innovation and technology they provide to support breakthrough science. More than 200 people filled the Conrad T. Prebys Auditorium in October to hear Manching Ku, Carolyn O'Connor and Sarah Dunn talk about how their work in these cores contributes to the future of human health and well-being.

Pictured from left: Manching Ku, Carolyn O'Connor and Sarah Dunn.

From left: Elizabeth Blackburn, Sa Chen, Karen Joy Davis, Greg Lemke and Catherine Rivier.

High school participants in the flagship Heithoff-Brody Scholars Program.

FUTURE SCIENTISTS OF AMERICA

This summer, an elite group of high school students made Salk their home as they participated in the eight-week Heithoff-Brody Scholars Program, the flagship offering of Salk's Education Outreach. Working side-by-side with Salk scientists in their labs, the teen scholars performed experimental work in plant biology, integrative genomics and computational neurobiology, to name a few research areas.

FOURTH SCIENCE & MUSIC SERIES UNDERWAY

The Salk Institute introduced the fourth season of its popular Science & Music Series in October with a concert by Sa Chen, one of China's most celebrated classical pianists, and a presentation by Greg Lemke, Salk professor. In November, violinist Asi Matathias and pianist Karen Joy Davis paired with Martin Hetzer, Salk professor and chief science officer. Remaining concerts will be: January 22, February 12, March 12 and April 30.

To learn more, visit www.salk.edu/music or call (858) 587-0657.

EVENTS

Kelli O'Hara

LOVE WAS IN THE AIR

The Salk Institute celebrated its 21st annual Symphony at Salk with a love-themed program performed by Broadway luminary Kelli O'Hara and the San Diego Symphony led by guest conductor Maestro Thomas Wilkins.

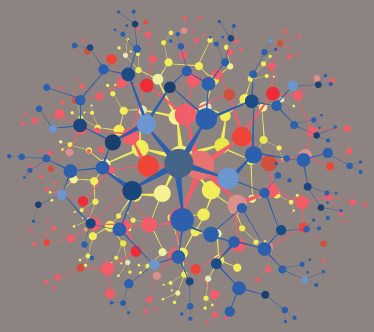
More than 700 donors and community supporters gathered in the courtyard to dine and hear melodies from Bernstein's *West Side Story* to Tchaikovsky's *Sleeping Beauty Waltz*. O'Hara ended the evening with *I Could Have Danced All Night* from Lerner and Loewe's *My Fair Lady*. La Jolla's quintessential summer event raised more than $1.1 million for Salk's mission of research and discovery.

From left: Leon Furth, Rochelle Carson-Begley, Ed Begley, Jr., Liz Keadle and Al Gore.

DISCOVER SALK

EVERY CURE BEGINS WITH YOU.

You don't need a science degree to make a big difference at Salk.

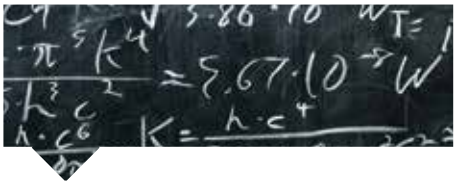


Learn more about the many options for joining the Salk community by visiting **www.salk.edu/support or calling (858) 453-4100 x1201.**

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

GIVING PROGRAMS

EDUCATION OUTREACH

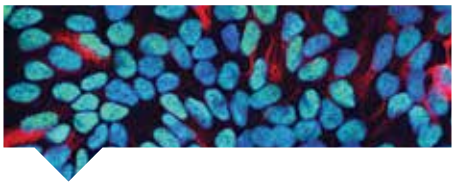


Offering nearly half a century of programs to inspire—and launch—the next generation of scientists, Salk's Education Outreach includes a Mobile Science Lab, High School Scholars curriculum and SciChats@Salk.

SALK WOMEN & SCIENCE

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

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.

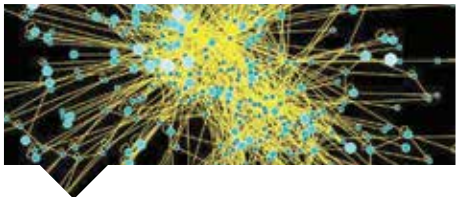
PARTNERS IN RESEARCH

Invest in the future of cancer, aging, Alzheimer's disease and diabetes research by incorporating philanthropic support for Salk into your estate plans.

PRESIDENT'S CLUB

Fuel Salk's ability to recruit top-tier scientists, acquire cutting-edge technology and embark on innovative research initiatives by joining the President's Club.

CHAIRMAN'S CIRCLE



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

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PERSPECTIVE

The Power of **Emergent Creativity**

When Jonas Salk began his polio vaccine work in a cramped, underequipped basement lab in Pittsburgh, he faced a daunting disease that terrorized the world. There were no guarantees he would find success, but the times demanded that he try.

In a world facing unprecedented challenges, such as how to augment human health and well-being, and global climate change, we must continue to prioritize both the root of courageous basic research and its blossom, scientific collaboration. Once again, the times demand it.

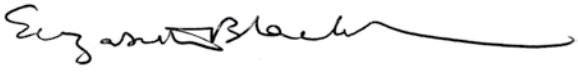
Every day, all around us, we see living examples of the advantages of basic research. In 2006, when UC Berkeley biochemist Jennifer Doudna met with a geobiologist colleague to offer ideas about the purpose of strange, repetitive DNA sequences in microbes called CRISPRs, the repeats' function was still being determined. The following year, a new postdoc joined Doudna's lab to study the CRISPR system and, while Doudna thought his work on CRISPR-associated genes (called Cas) would further scientific understanding, she didn't have any expectations of where it would lead.

And so, today, we are in the midst of yet another biotechnology revolution. This one was catalyzed by the development of a DNA-cutting tool based on the CRISPR-Cas system, which we now know to be part of a microbe's immune defenses. Many scientists are using the tool to edit DNA with greater precision than ever before. Among them are Helmsley-Salk Fellow Patrick Hsu, who develops CRISPR to be ever crisper, all the better to use it to reverse engineer cellular processes. One of Patrick's goals is to uncover the mechanisms behind neurodegenerative diseases. And Salk Professor Juan Carlos Izpisua Belmonte recently made headlines when his lab re-engineered CRISPR's molecular scissors to recognize and cut up HIV. Salk Professor and Cancer Center Director Reuben Shaw employs the tool to understand how knocking genes out of cells' energy-regulating pathways impacts anti-cancer pathways.

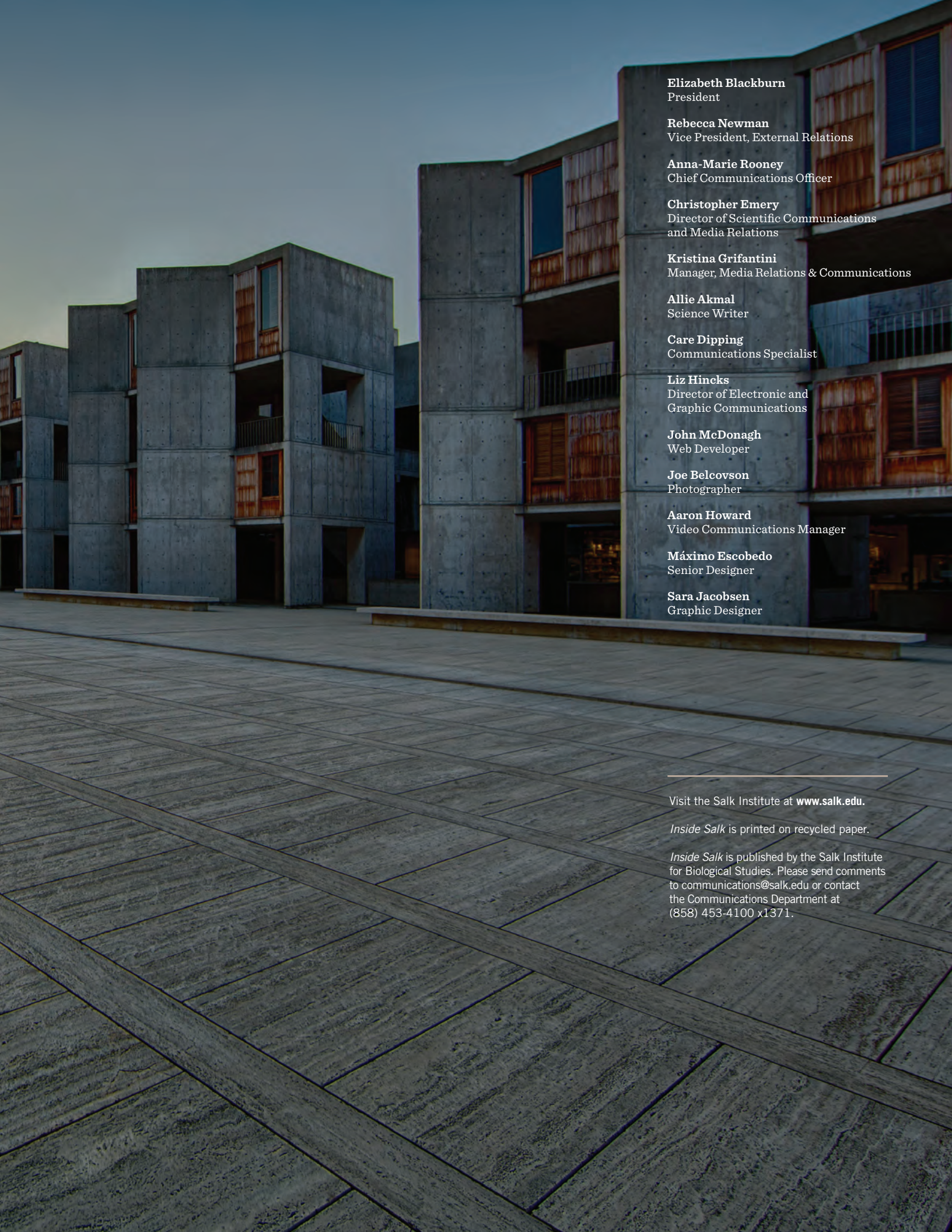
The beauty of basic research is that we never know where it will lead. If we have the courage to face its risks, it can lead to great rewards. The therapeutic use of penicillin is the result of basic research. So is almost every medicine in clinical use.

Yet another compelling reason for why the CRISPR story has already become the stuff of legend is that it illustrates the power of basic research plus scientific collaboration to drive innovation. Initially, members of Doudna's lab followed their curiosity and took a risk. Later, their work built on that of scientists who discovered CRISPR's immune functions, and still others who identified a whole slew of related Cas genes. This snowballing and cross-pollination of knowledge in the scientific community led to what I think of as "emergent creativity," where the nexus of many discoveries produces an innovation of surprising importance. The sum, in terms of impact, is far greater than the parts. At Salk, that ethos of emergent creativity is played out in wonderful and unpredicted ways every day, week, month and year. Emergent creativity is in our Institute's very DNA.

As I approach the end of my first year as Salk's president, I couldn't be prouder of how all the science community at Salk combine a deep commitment to innovation through basic research with a true spirit of scientific generosity and, yes, true creativity.



Elizabeth Blackburn
President, Salk Institute
Irwin M. Jacobs Presidential Chair



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Inside Salk is published by the Salk Institute for Biological Studies. Please send comments to communications@salk.edu or contact the Communications Department at (858) 453-4100 x1371.

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CALENDAR

JANUARY

22 Salk Science & Music Series
featuring Amit Peled with Noreen Polera
with Assistant Professor Kenta Asahina

FEBRUARY

12 Salk Science & Music Series
featuring Sean Chen and Karen Joy Davis
with Assistant Professor Saket Navlakha

MARCH

12 Salk Science & Music Series
featuring Zlata Chochieva
with Assistant Professor Eiman Azim

29 Salk Women & Science

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