InsideSalk

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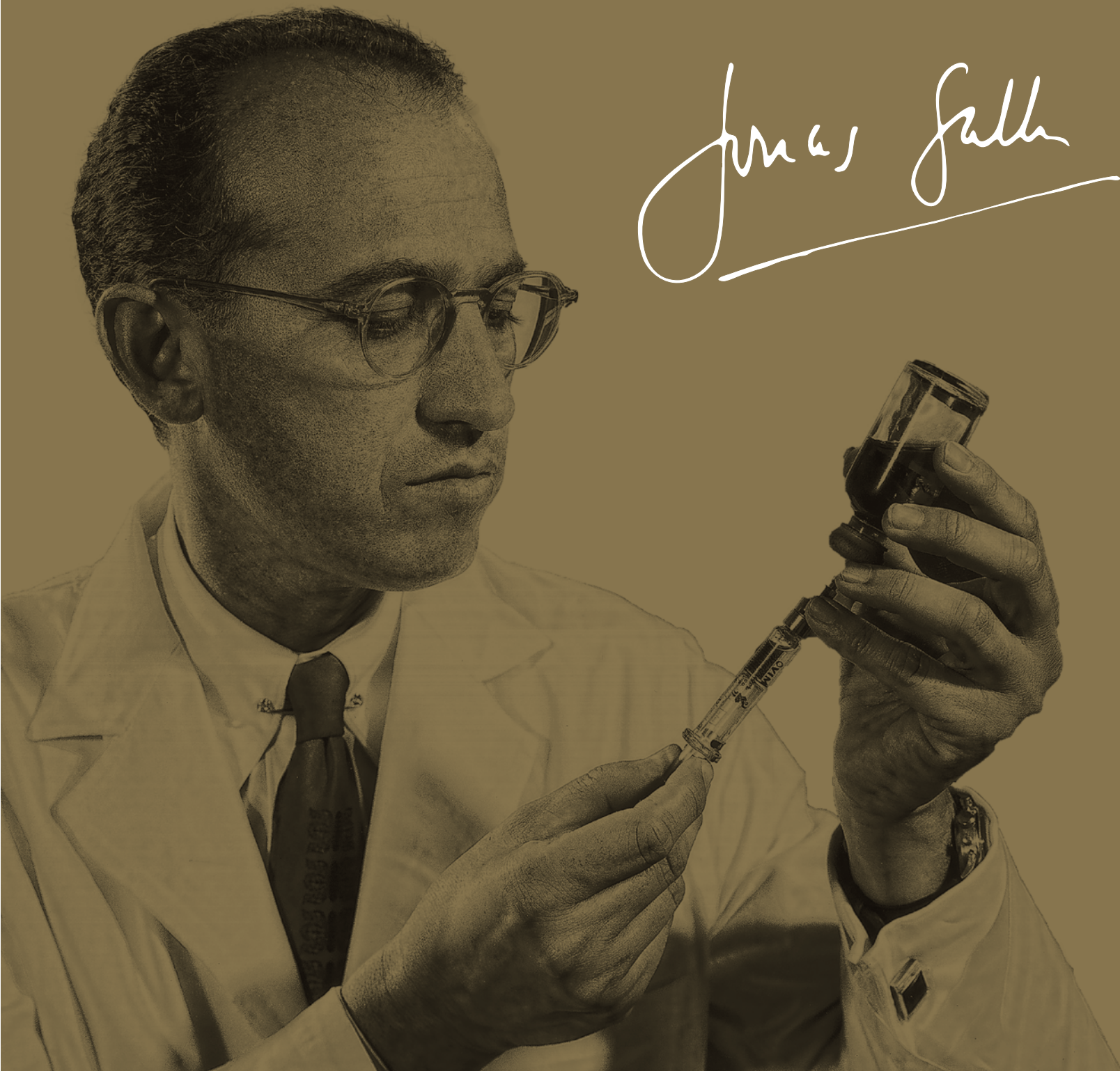
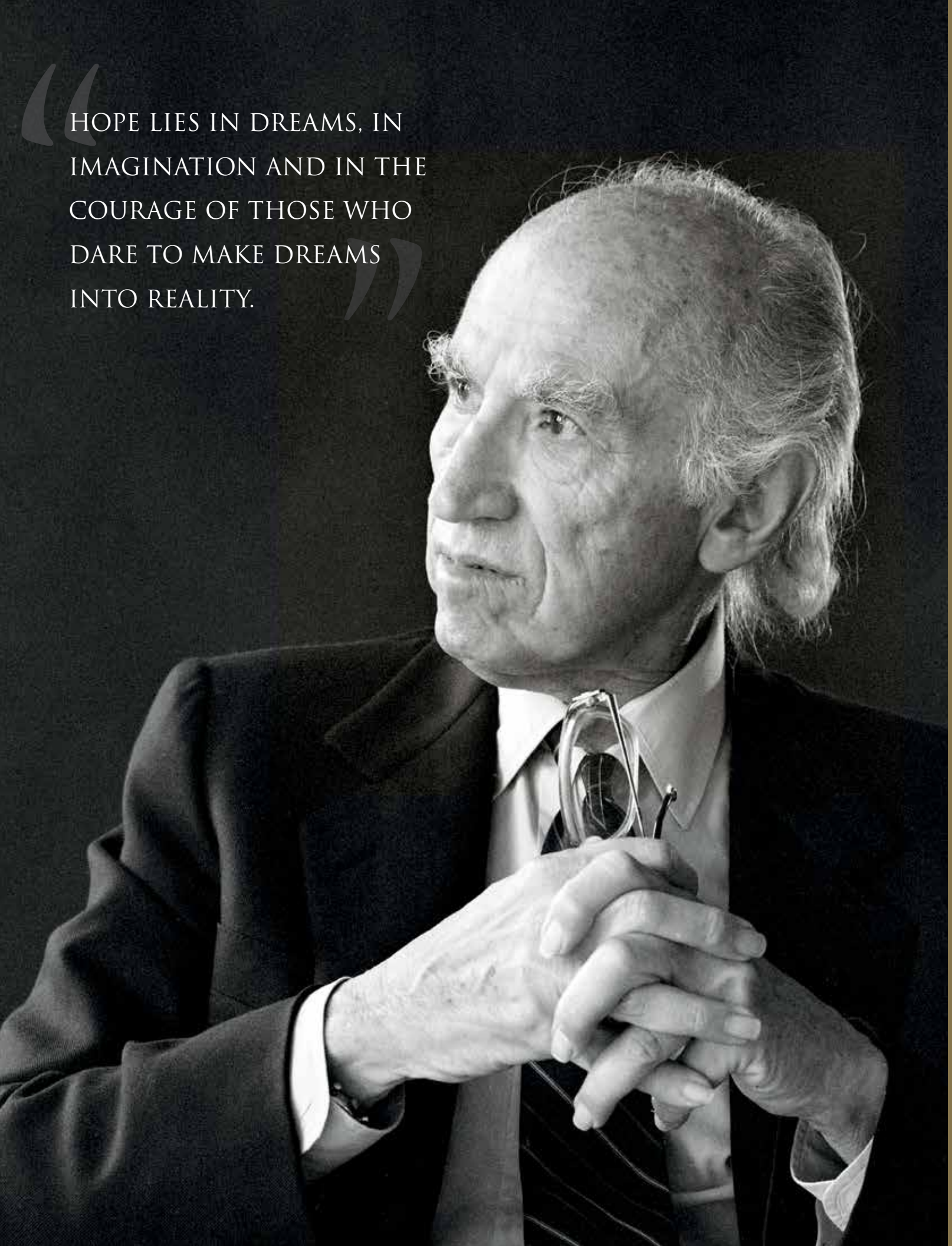
Salk Institute 08 | 14

THE SALK INSTITUTE COMMEMORATES



JONAS SALK

100 YEARS


“HOPE LIES IN DREAMS, IN IMAGINATION AND IN THE COURAGE OF THOSE WHO DARE TO MAKE DREAMS INTO REALITY.”


A Jaunty Sailor and Cautious Skier
Jonas Salk


AN ICON NAMED
SALK
Polio. It was the AIDS of the '50s. And then, 35 years ago this month, one man delivered us. For this he won the
TIME
THE WEEKLY NEWSMAGAZINE
THE INTREPID SCIENTISTS OF THE SALK INSTITUTE
Money's short, but the setting is superb—and so is the research
FIRST DAY OF ISSUE

August 2014
Inside Salk

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Next generation: Amy Firth

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Dear Friends,

William Brody

ONE HUNDRED YEARS AGO, ON OCTOBER 28, A CHILD WAS BORN in New York City. Bright and precocious, he rose from humble origins to enter college at age 15, and then enrolled in medical school. But along the way, he decided he'd rather help humankind more broadly and opted to become a medical researcher instead of a physician. By 1955, he had achieved his goal, discovering the polio vaccine and changing the course of history. Jonas Salk—for of course that's who I'm talking about—had defeated a disease that had struck dread into the hearts of people worldwide for over a century.

At that point, Salk could easily have rested on his laurels. But upon receiving the Congressional Medal for Distinguished Civilian Achievement in 1956, he said, "I feel that the greatest reward for doing is the opportunity to do more." And do more he did: in 1960, he established the research institute that bears his name.

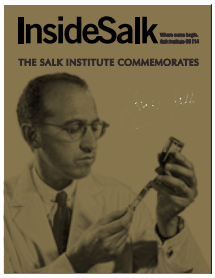
This issue of *Inside Salk* celebrates the centenary of Jonas Salk's birth and his extraordinary legacy as a scientist and a visionary. Although he died nearly two decades ago, his spirit remains vibrant here at the Salk Institute, where his commitment to breaking down barriers of all kinds is deeply embedded in our culture. The following pages are as much a reflection of Salk and his values as they are of the remarkable men and women whose careers and discoveries have been fostered at the "temple of science" he founded.

In addition to our cover story on Salk's legacy at the Institute, this issue introduces one of our newest faculty members, **Nicola Allen**, as well as a rising young star, postdoctoral researcher **Amy Firth**. We mark some milestones for our faculty, including the 65th birthdays of two accomplished scientists, plus promotions, awards and special events. Jonas Salk was deeply committed to nurturing future generations of scientists, which makes it especially apt that we are highlighting two brand new initiatives of our Education Outreach program. And our Discovery Roundup section features several recent findings by our faculty that have generated new insights in fields ranging from circadian rhythms to schizophrenia, from lung disease to memory storage, and from cancer to motor circuitry.

I hope you'll enjoy reading our retrospective on Salk and the latest news issuing from his creation. It is both an honor and a responsibility to steward his vision—a role that all of us at the Salk Institute enthusiastically embrace. As a friend and supporter of the Institute, you too share in Jonas Salk's vision and the scientific successes that vision has made possible. We are all most grateful.

William R. Brody

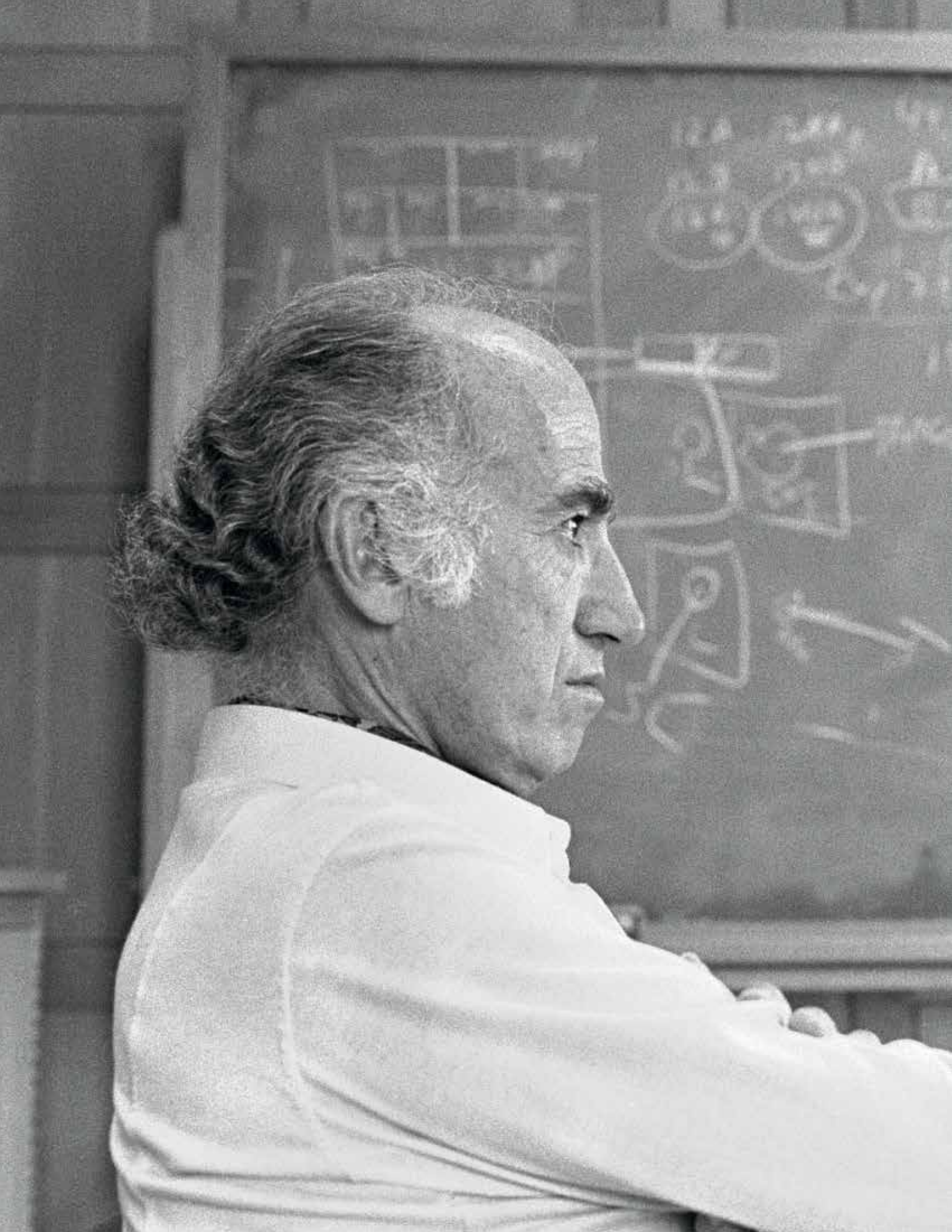
William R. Brody, MD, PhD
President, Salk Institute
Irwin Jacobs Presidential Chair



ON THE COVER

This issue commemorates the 100th anniversary of founder Jonas Salk's birthday.

Cover art based on a 1956 photo of Jonas Salk taken by Yousuf Karsh. Courtesy of the Estate of Yousuf Karsh.



The Legacy of Jonas Salk

100 years after Jonas Salk was born, his life is still changing the world.

ON OCTOBER 28, 1994, THE STAFF OF THE SALK INSTITUTE FOR BIOLOGICAL STUDIES gathered in the windy courtyard to celebrate what would be the 80-year-old founder's last birthday.

After his friends and colleagues had taken turns speaking to the assemblage, Jonas Salk, one of the most famous scientists in history, took the podium. Salk surveyed the attendees: staff and scientific luminaries, including several Nobel laureates, who had joined in his dream of collaborating across scientific boundaries to solve the world's problems.

"I express my gratitude for the opportunity I had to provide you with the opportunity to bring out the best in yourselves," said Salk, draped in a giant lei, a birthday gift from the chair of the Institute's board. "This is what the Institute was intended for."

It must have been a gratifying moment. Not only had Salk developed the first successful polio vaccine, making history by conquering one of the world's most terrifying diseases, he'd also lived to see the Institute, which he called his "experiment," grow into a research facility with an international reputation for cutting-edge biological work.

Heart failure led to Salk's death the following June. His influence on the world did not end then, however. Salk, who made *Time* magazine's list of the 100 most influential people of the 20th century, saved countless lives through the polio vaccine. And through the Salk Institute, he is still enabling some of the world's greatest thinkers to make life-changing discoveries.

Looking back, it is hard to pinpoint precisely what it was about Jonas Salk that led him to such tremendous success, not once, but twice. The recollections of those who knew the man—a philosophical, confident and soft-spoken scientist who eschewed publicity while relentlessly tackling global health issues—demonstrate a lasting legacy and positive influence on the future.

» View video: www.salk.edu/JonasSalk100/

A SMALL INSTITUTE, DREAMING BIG

How do you top coming up with the world's first effective polio vaccine? For many scientists, that would have been a sufficient, career-culminating event. But not for Jonas Salk. After his work on the vaccine, he was determined to fight other global health threats. The best way to do that, he reasoned, was to bring together thinkers from across fields of study in a space that supported scientific creativity—a space that didn't just provide laboratory equipment, but encouraged cross-disciplinary breakthroughs, too.

In 1960, Salk achieved the beginnings of his second legacy: he formally founded an ambitious, multidisciplinary institute in what was then a little-known area of San Diego, California. He envisioned establishing what he called a "crucible of creativity" that would encourage collaboration over competition, mutual appreciation over siloed departments, and a pervasive sense that everyone's work, in however small a way, contributed to bettering the human condition. To manifest this vision, he worked with famed architect Louis Kahn to design a space that reflected these ideals while recruiting some of the best minds in a variety of disciplines, including future Nobel Prize winners Francis Crick, Renato Dulbecco and Jacques Monod.

"He was not at all afraid to populate the Institute with scientists famous in their own right," says **Greg Lemke**, a professor in the Molecular Neurobiology Laboratory, whose accomplishments have led to a greater understanding of the immune and nervous systems. "There's a real danger for people with his level of fame to surround themselves with acolytes. Instead, he recognized that if you gather the brightest minds and give them a place to collaborate, new scientific findings would emerge. That is how he built a successful institute."

In her book, *Genesis of the Salk Institute*, professor emeritus **Suzanne Bourgeois** reflects on how Salk's vision attracted and inspired an impressive generation of scientific minds. And even when the Institute was securing funding in the early days, it "had assets more valuable than money: a reputation of distinction, a great building, and many loyal employees, both faculty and support staff, for whom the Salk Institute was not just a job, it was a dream," she wrote (pg. 180).*

Salk conveyed this dream not just through the conviction of his scientific endeavors, but also through a faith in intuition and an appetite for risk-taking, something he instilled in the Institute's culture. He inspired his colleagues to trust their guts, in both science and life, a philosophy that permeated many of his interactions at the Institute.

"The only advice I ever followed I got from Jonas: 'Do what makes your heart leap,'" says Bourgeois, who, along with future husband and founding fellow **Melvin Cohn**, now also a professor emeritus, were early recruits to the Institute. At Salk, Bourgeois accomplished pioneering work on the regulation of gene expression, while Cohn carried out seminal studies of the body's immune response.

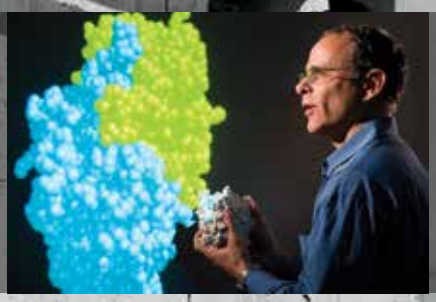
During his four decades at the Institute, **Inder Verma**, professor of genetics and one of the world's leading authorities on gene therapy, says that he received three pieces of advice from Jonas Salk that he has carried with him ever since. In addressing the entire faculty, Salk counseled them to be "good ancestors." To new faculty, he specifically called upon them to do what was good for the Institute. And to Verma himself, when Verma had lamented the lack of credit for a service he provided, Salk advised him to remember that the reward of work well done is to be asked to do it again.

"These became three of my defining guide-posts," says Verma, holder of the Irwin and Joan Jacobs Chair in Exemplary Life Science.

Salk illustrated this last piece of advice one day when Verma bumped into him in the Institute's courtyard. The visibly excited Salk said that he had just met an old acquaintance who had brought along a teenage grandson.

*Bourgeois, Suzanne. *Genesis of the Salk Institute.* Oakland: University of California Press, 2013

From left, clockwise:
Francis Crick, Edwin Lennox,
Jacques Monod, Jonas Salk,
Leslie Orgel, Melvin Cohn,
Salvador Luria, Jacob Bronowski,
Renato Dulbecco (1966)



When introduced to the man who conquered polio, the boy nonchalantly asked what polio was. The disease had been controlled so thoroughly in the country that the grandson had never heard of it, which Salk considered to be the ultimate triumph. "This is one of Jonas' gifts to me: a demonstration that reward is in the outcome, not the gratification of recognition," says Verma.

LOWERING WALLS ACROSS DISCIPLINES

Jonas Salk was particularly invested in the idea of lowering walls—literal and metaphorical—between fields of study, with a focus on bringing together the arts and sciences. The institute he designed with Kahn embodied this philosophy: not only is it visited by tourists from across the globe for its remarkable design, but its central open courtyard and unique absence of dividing walls between labs foster daily collaboration and interaction among scientists.

Within this structure, the Institute bridges disciplines of molecular, cellular, systems, behavioral and computational biology across a range of disease areas. Collaborations between Salk scientists are a direct result of the Institute's unique culture and physical structure, according to director of the Salk Institute Cancer Center **Tony Hunter**, whose groundbreaking research has led to new leukemia treatments. "To be successful, we have to collaborate and be greater than the sum of our parts," says Hunter, holder of the Renato Dulbecco Chair. "I believe that's how we've been able to achieve so much despite being a small institute."

It was crucial to work with people who had different interests and areas of expertise, in Salk's view. Some of Salk's early appointments emphasized his push for interdisciplinary efforts, including his decision to bring in faculty who weren't typical biologists, such as Salk Founding Fellow, mathematician and poet **Jacob Bronowski** and, in 1970, junior faculty member **Ursula Bellugi**, who later became a world-renowned expert on signed languages.

"He said to me, 'I love your research because it reveals how nature creates defects and the human mind overcomes them,'" says Bellugi, who is now director of the Laboratory for Cognitive Neuroscience.

Bellugi recalls that Salk frequently stopped by the lab to chat with study participants and their families. With his support, Bellugi and her lab eventually bridged linguistics and molecular studies to develop breakthrough insights into the neurobiological basis of language and a genetic condition known as Williams Syndrome.

Even today, despite not having a formal humanities program, the Institute is known for its deep appreciation of the arts. Every year, it hosts talks by renowned authors (most recently Jared Diamond and Michael Pollan), a classical music series and symphony concerts in the courtyard. Recent exhibitions by leading artists include the works of glass sculptor Dale Chihuly and painter—and Salk widow—Françoise Gilot.

Salk's ideas about breaking down the boundaries between labs extended to how an individual scientist defined his or her field of research. Salk professor **Fred Gage**, whose work has led to an abundance of critical new knowledge in genetics and neuroscience, says Salk promoted the idea that scientists should be able to go deep into an area of research but also be able to turn and move in a completely different direction without being constrained.

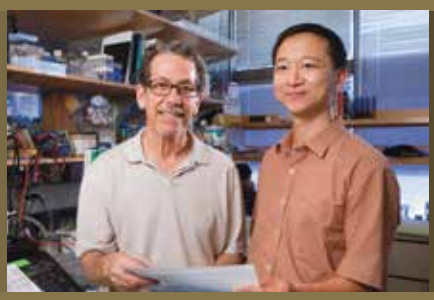
"This freedom," says Gage, holder of the Vi and John Adler Chair for Research on Age-Related Neurodegenerative Disease, "has allowed many very successful scientists to pursue multiple scientific directions in their careers at the Salk Institute. You can't do that in many places."

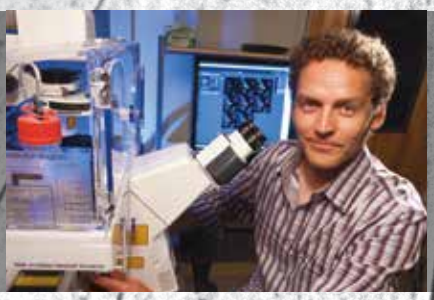
A RELUCTANT ICONOCLAST

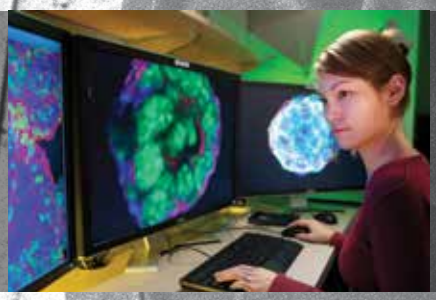
Jonas Salk never intended to be an iconoclast says his youngest son, Jonathan Salk, a psychiatrist based in Los Angeles. But when Jonas Salk believed something to be true—through a combination of logic and instinct—he followed it through to the end. His restless, unyielding drive led him not only to develop an inactivated virus vaccine for polio when others insisted it couldn't be done, but to found an institution that approached creativity in science from a multidisciplinary focus, a tactic increasingly common in research institutes today but fairly unusual at the time.

In the lab, Salk's approach was similarly unconventional as he explored promising concepts. Eldest son Peter Salk, a physician who worked with his father on cancer, multiple sclerosis and AIDS vaccine research, recalled that Jonas Salk would come into the lab on occasion with a new idea that would turn things "topsy turvy." This ability to look at things from a new angle also led him to create clear representations of complex data, which he called "making the invisible visible," says Peter Salk.

Jonas Salk often walked the halls to think and, during one walk, he told **Ronald Evans,** director of the Institute's Gene Expression Laboratory, that risks pay off in science as well as in life, a truism easy to say but one that Salk demonstrated in his two greatest legacies. "Jonas was a visionary who was not only brilliant but thought differently," says Evans, holder of the March of Dimes Chair in Molecular and Developmental Biology and a Howard Hughes Medical Institute investigator whose innovative







Peter Salk speaks about his father's legacy at a Salk Institute educational event.

A Legacy Beyond Science

AFTER DEVELOPING THE POLIO VACCINE, JONAS SALK HAD AN AMBITIOUS vision to bridge science and the humanities to solve major world problems.

Now, this aspect of his vision is the Jonas Salk Legacy Foundation's focus as part of an effort to address global issues through public health, policy and social lenses.

A prolific author as well as a world-renowned scientist, Salk set forth his ideas in books, articles and lectures that explored the human dimension underlying global problems—such as overpopulation—and suggested a way of thinking that might help solutions emerge. In his writings and his personal interactions, he encouraged a cautious optimism and faith in the power of creativity and collaboration across disciplines to tackle the broad array of challenges confronting humanity.

"Creating a polio vaccine and establishing the Salk Institute were enormous accomplishments," says Salk's eldest son, Peter, the Legacy Foundation's president. "My hope is that this foundation will complement the Institute and help bring the fullness of my father's dreams to fruition."

The foundation is helping to organize a series of conferences, symposia and public events around the globe to celebrate Jonas Salk's centennial period. (See www.jslf.org for further information.) Other foundation efforts include archiving and making publicly available historic lab materials; collaborating with the Mandeville Special Collections at the University of California, San Diego Library to facilitate online access to Jonas Salk's papers; supporting the worldwide eradication of polio; and promoting collaborative programs to tackle a range of public health and societal issues.

"One of my father's guiding principles was the notion that our capacity as human beings to think and act creatively gives us the ability to make the world a better place," says Salk's youngest son, Jonathan. "He had a passion for life, a joy in his work and a vision for a better future that I hope will be carried forward through this foundation."

work on hormones has led to more than half a dozen drugs for cancer and other diseases.

Salk also urged other scientists to take risks when their instincts prompted them to do so. For instance, he once asked Greg Lemke whether Lemke was a mutant. The two had been talking about an experiment involving mutant mice, and Lemke thought Salk was asking him about the mice. But in fact, Salk was using the term to distinguish between "evolvers" and "maintainers" of the status quo.

"There were things that became clear as Jonas explained this," said Lemke, who holds the Françoise Gilot-Salk Chair. "First, that Jonas considered himself as a mutant, and second, that he wanted this Institute to be populated by mutants. My answer today would be: I hope I am a mutant."

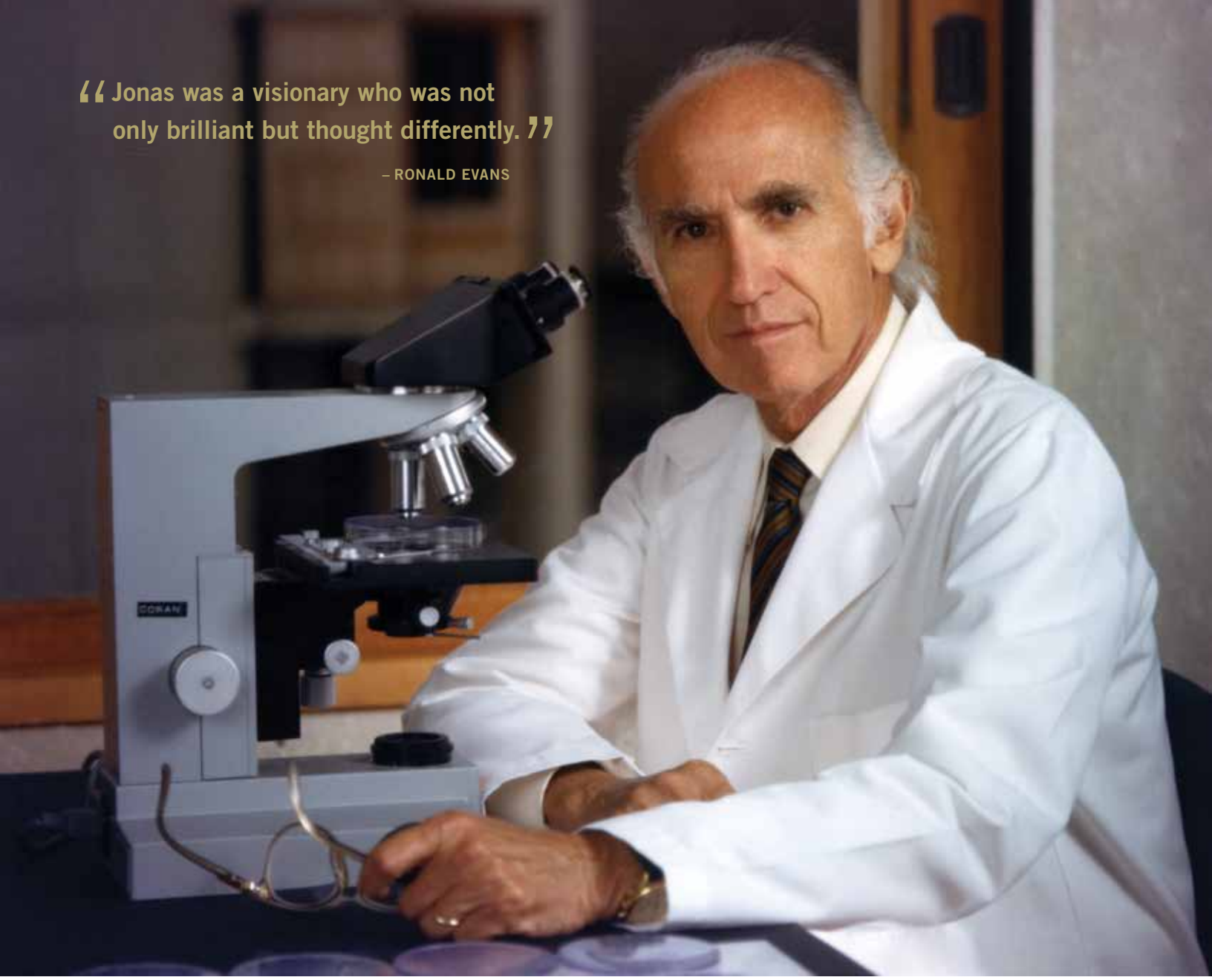
Like any public figure—particularly one who was a nonconformist—Salk had his disappointments. An intensely private man, he was not comfortable in the limelight, and the constant media attention aroused resentment from some in the scientific community. Salk was never inducted into the National Academy of Sciences, nor did he receive the Nobel Prize, a decision that some still say was unfortunate. Nevertheless, Salk seemed to take it in stride, an example of good faith for his colleagues.

"I often said to him that he should have received the Nobel Prize," says Distinguished Salk Professor **Roger Guillemin**, Nobel laureate, who joined the Institute in 1970. "He'd smile and say, 'Everyone thinks I did, so it makes no difference.'"

BEYOND THE LAB

In addition to encouraging innovations in science, Salk also saw the Institute as an incubator for the next generation of trailblazers in their fields. Even though it was never a degree-granting center, more than 3,200 postdoctoral fellows and graduate students have trained within its walls, and several have gone on to win Nobel prizes.

"Jonas saw the Salk Institute as an artists' colony for scientists, and the people who learn their trade here carry that ethos and creative inclination with them," says **William Brody**, president of the Institute. "When young scientists are exposed to our great thinkers and dynamic intellectual environment, it alters their perspective on what's possible."



> “Jonas was a visionary who was not only brilliant but thought differently.”
>
> – RONALD EVANS

But it wasn’t only scientists that Salk wanted to educate. Passing on knowledge to the public—especially the younger generations—to help them be “good ancestors” was especially important to him, maybe in part because he had seen the power of an educated public during the March of Dimes campaign to fundraise for development and testing of his polio vaccine, leading to its quick and widespread use.

Molly Hart Lebherz met Salk in the early 1990s at a group discussion on peace advocacy when she was working as a science education activist at what would later become the Foundation for Global Community. At first, she was star struck at meeting the person who had banished the “dark cloud” of fear of polio that she recalled from her childhood, but his kind demeanor soon put her at ease. Through their friendship, the Institute helped the foundation distribute the 1972 photo of Earth taken on the Apollo 17 mission to classrooms to serve as a visual teaching tool on conservation. Salk, she said, loved the idea and called the image the “best reference material.”

“He thought that there was nothing more important than impacting the next generation with a positive point of view. He wanted me to convey to them that humanity makes mistakes, but we can fix them,” Lebherz says, adding that she, professor emeritus **Walter Eckhart** and Salk often gathered, sometimes as frequently as once a month, to brainstorm new ways to reach students. “He asked me to stress to the children that their minds were the most important laboratory.”

Today, the Institute continues to communicate the importance of science outside the lab through four different elementary and high school science outreach programs. Each year, Salk’s Education Outreach program reaches about 3,000 middle and high school students in San Diego County with programs designed to inspire them to pursue studies and careers in science.

These outreach efforts are just one of the many ways Jonas Salk’s life continues to have an immeasurable impact on the world 100 years after he was born. His commitment to leave the world a better place drove his philosophical optimism, an optimism that inspired the people he knew and that is woven into the fabric of the institute he built.

“I took to heart an idea from Jonas that you get what you focus upon,” says Eckhart. “For Jonas, I think his goal was always for science to do something helpful for humanity.”

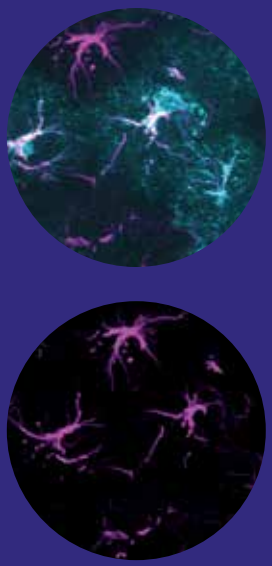
One on one with…
Nicola Allen

Nicola Allen is a neuroscientist, but she doesn't focus on the superstar of the brain, the neuron. Rather, she studies astrocytes, star-shaped cells once thought to be "filler," but recently shown to be crucial to brain function—the producer, director, stage designer and supporting cast to the neurons.

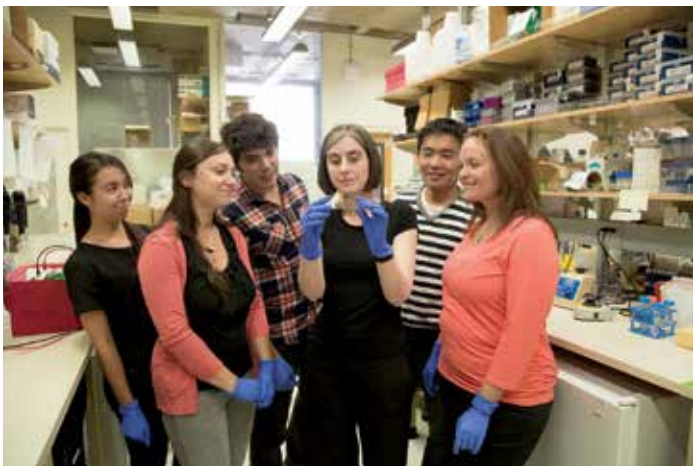
These mysterious brain cells have only recently edged into the field of neurobiology as a viable research area and they have significant potential for helping to understand neurodevelopmental and degenerative diseases like autism, epilepsy, schizophrenia, stroke and Alzheimer's disease. These prolific cells are, Allen says, a major player in the brain, despite their longtime obscurity.

Named for their multi-armed shapes—where long branches extend from a single cell body to touch over 100,000 neural connections known as synapses—astrocytes do more than provide the support system and scaffolding for the brain. While the bushy astrocytes don't transmit electrical signals of their own, they use chemical signaling to affect nearby neurons, setting the stage for complex neural messaging. And, like neurons, astrocytes exist in a variety of forms found in different configurations throughout animals' brains, increasing in number roughly proportional to the brain's size.

To better untangle the role of these enigmatic cells, Allen's lab investigates astrocyte protein families that appear to be crucial in neural development, operation and adaptation.



Astrocytes, shown above, surround neurons and assist with nerve growth and function.



From left to right: Catriona Lewis, Isabella Farhy, Matthew Boisvert, Nicola Allen, Tongfei Liu, Cari Dowling

What drew you to start researching the brain?

Growing up, my all-girls' grammar school in England had great biology classes and teachers. I thought I'd be a vet or a doctor, but I realized that fundamental research drew me the most because you're finding out what's really going on, whereas in medicine, you're at the end phase of new discoveries. The brain is the most mysterious of all the organs, so I wanted to learn more.

I was the first in my immediate family to receive a PhD, which focused on the cellular mechanisms that go wrong during stroke. Neurodegenerative diseases interested me the most because they are so enigmatic. My mom's always telling me to hurry up and cure Alzheimer's—hopefully, our findings will help lead to that someday.

Why are astrocytes overlooked in conventional neurobiology?

Cell types like astrocytes are understudied even though they have huge implications for quality of life and aging. Traditionally, researchers thought that studying neurons would tell us what we need to know about the brain because they are the cells that are sending electric signals, making decisions and relaying messages. Now, we think that astrocytes are just as useful to study—not only do they make up about 50 percent of the brain, but they are actively instructing the neurons on how to connect with each other as the brain develops. And in adult brains, astrocytes are modulating ongoing neuronal activity, which will completely change the output of the neurons. Astrocytes are involved in every stage of development and likely have different roles as one ages, so they are incredibly important.

What are the implications for astrocytes in disease?

Other researchers have done experiments in the last few years showing that, in mice with genetic predispositions to developmental disorders that model autism, the introduction of astrocytes actually rescues the defective neurons. New astrocytes don't completely cure the mice, but their presence increased the growth of neurons' branched projections and alleviated a lot of symptoms, such as breathing difficulties.

Similarly, introducing mutant astrocytes to normal neurons is enough to make the neurons defective. So there is this real, constant interaction between cell types that is setting up the right connections in the brain and the number of connections.

So could a better understanding of astrocytes lead to "new and improved" brains?

The long-term goal of studying astrocytes is to learn how to repair damaged circuits by prompting neurons to reform synapses in a controlled way. By reintroducing astrocyte factors to a damaged brain, you could, in theory, encourage neurons to create new connections and improve brain function.

Previous work showed that bringing astrocytes from young animals into old animals gave the old animals a new plasticity in the brain—that is, they were more easily able to make connections that improve cognition—while bringing in old astrocytes had no effect. Studies done in 2013 found that introducing human astrocytes into mice resulted in an enhanced ability in behavioral learning in the mice, potentially because the larger, human astrocytes could interface with more synapses.

We want to understand these special features of young astrocytes that enable the brain to be flexible and create new connections. However, in eventual therapeutic applications, you wouldn't want to introduce too much plasticity, or the brain would forget everything it learned instantly. We want to manipulate those features in a controlled way.

What are the big questions your relatively new lab at the Salk Institute aims to tackle?

Astrocytes secrete many proteins that affect synapses. Before I began my research, it was already known that one class of proteins the astrocytes secrete establishes normally structured synapses between

» View video: www.salk.edu/allen

neurons. However, those synapses were silent—they didn't have any electrical activity. I discovered a second class of proteins that is responsible for affecting the ability of the neuron to respond to neurotransmitters and communicate with its neighbors. This isn't the whole story—this class only establishes an immature connection between neurons—so we are looking for an additional class of proteins that strengthens synapses later in mature brains. We also know that astrocytes secrete classes of proteins that make inhibitory connections between neurons, but we don't know what these proteins are yet.

There are a lot of myths about the brain. Which, as a neurobiologist, would you most like to dispel?

The myth that we only use 10 or 20 percent of our brains still persists in culture even though it's been discredited. In truth, nearly all of our brain areas are active at some time over a given day.

What advice do you convey to new scientists?

I think the most important thing for a scientist is a sense of perseverance and, along with that, a positive attitude. Also, being open to new ideas is crucial. Even though science is about being inquisitive, sometimes it's easy to get stuck in one way of thinking. Scientists should be receptive to new ideas, able to look at findings and follow up across disciplines if needed.

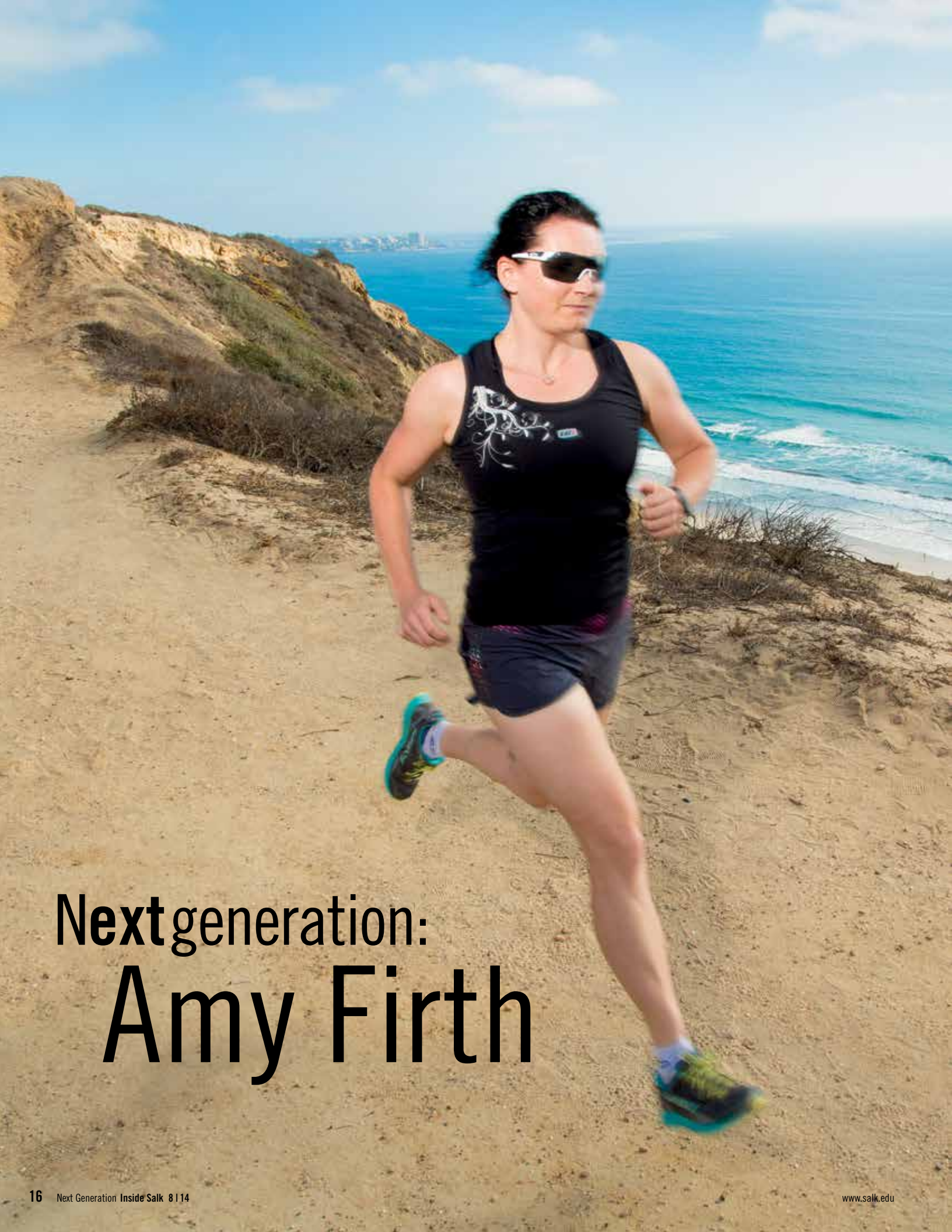
That is what's great about the Salk Institute. I believe very strongly in the mission of the Institute in that we're doing research to understand basic biology, but in the long term this research will likely have a tangible effect for people. So much of what we study has the strong potential for therapy. Having the flexibility to follow questions and develop collaborations will help us reach that knowledge faster.

What would people be most surprised to find out about you?

I spent six months traveling before doing my PhD, backpacking through Fiji, New Zealand, Australia, Indonesia, Singapore, Malaysia and Thailand. While in New Zealand, I went skydiving, which was fantastic. After that I did another backpacking trip with my brother to Vietnam and China for two months. I've been scuba diving in Malaysia, Thailand and Vietnam. Next, I'd love to go to the Galápagos Islands.

What do you do in the little free time you have between setting up a lab and research?

My boyfriend and I kayak, snorkel, watch wildlife and frequently visit the San Diego Zoo. If I really need a break, I watch British crime series, particularly PBS Masterpiece Mystery: Inspector Lewis, Prime Suspect, Sherlock and others.



Next generation:
Amy Firth

Amy Firth tests the limits in the lab and on the playing field.

AMY FIRTH DOESN'T BELIEVE IN LEAVING WELL enough alone. She has an affinity for demanding sports—she's competed in two Ironman triathlons and a 50-kilometer trail run, and she trained for the six-day TransRockies Run that took place earlier this month, a 120-mile trail race through the mountains of Colorado. And that's not to mention the high-level horse competitions that were her passion when she was younger.

"I always like to test how far I can push myself," says Firth, a postdoctoral researcher in the lab of Salk professor **Inder Verma**. "Once I've done one thing, I have to go to the next level and do the next crazy thing."

She could just as easily be describing her career in science, which has taken several twists and turns on its upward trajectory. Firth, who grew up on a farm in Yorkshire, England, was always interested in science because she loved animals and wanted to become a veterinarian.

» View video: www.salk.edu/firth

But she soon realized that in order to treat her patients, she would need to have an understanding of drugs and how they worked. So when she got to the University of Bath, she focused instead on pharmacology—the study of drug interactions with the body.

It was during her final year of college, as part of a three-month capstone project, that the course of her career changed yet again. Landing in the lab of Sergey Smirnov, she learned to record currents across cells that were isolated from the pulmonary artery.

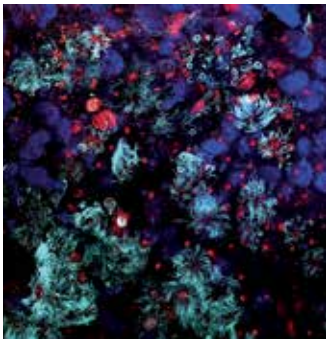
"And that," she says, "was the start of my interest in lungs."

Firth remained at the University of Bath to earn her PhD, and when it came time for her to find a postdoctoral position, she was keen for a placement in a world-renowned lab studying pulmonary hypertension. She ended up at University of California, San Diego, working with Jason Yuan, who was studying ion channels and pulmonary disease pathogenesis. "It was a good transition forward to continue what I was doing and apply it to disease pathogenesis," she says.

UC San Diego, renowned for its clinical program in chronic thromboembolic pulmonary hypertension (CTEPH), provided Firth with unique access to surgically removed lung tissues. Usually blood clots in the lungs, or pulmonary embolisms, resolve without treatment or are broken up through medication. When a clot doesn't dissipate, or clots recur frequently, however, harmful vascular changes can take place in the lungs and can result in pulmonary hypertension. Pulmonary hypertension is associated with high morbidity and mortality due to right-sided heart failure. Although rare, CTEPH is often misdiagnosed because its symptoms can be similar to those of more common conditions, and it may occur in patients with no overt history of pulmonary embolism.

In studying how blood clots in CTEPH become fibrotic and solid, completely blocking the lungs, Firth began to look at what cell types contribute to the condition. What she found was that cells capable of developing into multiple types of tissues seemed to be involved in the progression of the disease.

And from there, her research began to focus on stem cells. Since joining Verma's lab four years ago for her second postdoctoral appointment, Firth has been modeling the respiratory tract—specifically, airways. Taking skin cells from patients with lung disease, she has reprogrammed the cells to become induced pluripotent stem cells (iPSCs), then coaxed them to become lung cells in order to study them in a dish. Her method circumvents some of the limitations inherent in existing methods of studying lung disease. Mice, for instance, develop lung disease very differently from humans and don't manifest it to the same extent, which makes translating information from mouse models to humans difficult. And human lung tissue



This image shows induced pluripotent stem cells that have been coaxed to change into epithelial cells which line the airways of the lung. The blue stain indicates the cells' nuclei. Clusters of basal bodies (red) enable the cells to generate hundreds of hair-like projections called cilia (light blue). These ciliated cells beat to propel mucus out of the airways and protect from infection.

Amy Firth competing in her first 3-day horse trials event in 1996, pictured here during the cross country jumping portion with her horse, "The Nightwatchman."

> **"Amy is fearless, exciting and demands the best from herself and her colleagues. I can always count on her to deliver."**
>
> **– INDER VERMA**

is especially perishable, providing only a brief window before starting to deteriorate.

"I wanted to find a way to study human disease in a reproducible way, and having iPSCs basically gave me a pool of cells with the capacity for indefinite growth and generation of any cell in the body," she explains.

Once she has guided the iPSCs into becoming lung cells, Firth can use gene editing techniques to remove a mutated gene and replace it with a corrected one. Or, conversely, if donated patient tissue is unavailable, she can remove a normal gene and insert a mutation.

"It gives us a reproducible way of looking at the role of mutations in disease and looking at what the downstream signaling pathways are that occur after you have a mutation," she says. "The nice thing about the system is that with little tweaks here and there, I can essentially use it to model nearly any lung disease, and I can take this wherever I want."

Her research was published in March in the prestigious *Proceedings of the National Academy of Sciences*. But Firth is quick to caution that her technique is still in the early stages and needs some refinement. She's hoping it can eventually be used for high-throughput screening to identify new drugs, as well as to uncover the underlying mechanisms for diseases where the mechanisms aren't well known.

"Everyone asks me if I'm trying to regenerate a lung in a dish," she says, "but I think being able to put cells back and remodel a lung is a ways off." That said, she's begun forging collaborations with other scientists, using the cells she generates to begin exploring that possibility. Her expertise in lung stem cells also led to an invitation last year to edit a book on the subject, which is slated for publication this fall.

"Amy is fearless, exacting and demands the best from herself and her colleagues," says Verma, who holds the Irwin and Joan Jacobs Chair in Exemplary Life Science. "I can always count on her to deliver."

As if all this isn't demanding enough, Firth continues to test the limits outside the lab, as a Category 2 bicycle racer for the South Bay Wheelmen in Los Angeles, as well as racing for the Rehab United Elite triathlon team in San Diego. Her biggest extracurricular challenge may lie ahead, however. She recently joined her lab's softball team, which has left this diehard fan of Britain's Tottenham Hotspur soccer team a bit out of her element but game to learn.

"They were having so much fun, I decided to join them," she says. So every Monday, she dons a baseball glove and takes her place behind the infield, ready for whatever the players, science and life bat her way.

BESTSELLING FOOD WRITER MICHAEL POLLAN

MAKES EXCLUSIVE APPEARANCE AT THE SALK

NEW YORK TIMES **BESTSELLING AUTHOR** and journalist Michael Pollan paid a visit to La Jolla on March 19 to take part in a thought-provoking discussion at Salk. Pollan is the author of the bestsellers *In Defense of Food: An Eater's Manifesto* and *The Omnivore's Dilemma: A Natural History of Four Meals*, which was named one of the ten best books of 2006 by the *New York Times* and *Washington Post*. Salk professor **Ronald Evans** posed a series of questions to Pollan, who responded by covering topics ranging from how he got his start writing about food, agriculture and the environment, to his thoughts about America's obesity epidemic and the food movement. The discussion was followed by a Q&A session with the audience and a reception.

As the grandson of a produce distributor and wholesaler, Pollan developed an interest in food and gardening at an early age. He grew his first garden at the age of eight and returned to gardening in his late twenties. It was these experiences that sparked his interest in the relationship between humans and nature.

"It was my mishaps in that garden that really launched me," he says. "I thought, this is my subject; I'm going to write about nature in these messy places where humans and the natural world have to engage with one another."

Over the past 25 years, Pollan has written books and articles about the perils of the industrial food chain. In *The Omnivore's Dilemma* he traces four food chains—industrial, big organic, local farm and hunter-gatherer—and examines how what we eat affects our health and the environment. Pollan says that writing *The Omnivore's Dilemma* changed his eating habits.

"I eat very differently," he says. "What I've learned about nutrition and health has changed my behavior." In particular, he has focused on fresh and local foods.

Pollan has long warned of the dangers behind industrial farming and has become a leading advocate for reforming the nation's agricultural policies. He traces the start of America's obesity epidemic to agriculture subsidy policies enacted in the 1970s. The subsidies favored some foods over others, with corn and soybeans taking the lead.

"Certain kinds of calories got really cheap," he says, noting the importance of policies in shaping food trends.

At the conclusion of his talk, Pollan was asked what he believes is the secret to longevity. His advice was simple: everything in moderation and a focus on fresh foods. "Nutrients are still very confusing," he says, adding that maybe someday scientists can design food intakes to maximize health but "in the meantime, we should focus on eating real food."

Step into Discovery

walk for salk explore salk

Where cures begin Tours, activities, talks

Second annual **Step into Discovery** brings the community to the Salk

ON SATURDAY, APRIL 12, THE SALK INSTITUTE INVITED THE SAN Diego community onto campus and more than 1,100 people came out for a day of fun and learning at the second annual Step into Discovery.

More than 600 walkers participated in the 5K Walk for Salk, arriving as early as 8 a.m. to pick up T-shirts and goodie bags and enjoy a gluten-free breakfast from Escondido-based GNI Bakery. After the walk, visitors had a chance to browse sponsor booths and a steady stream of budding scientists filtered through the Kids' Discovery Zone to learn about the brain, plants, disease modeling and cancer.

Visitors were also treated to talks by Jonas Salk's son, Dr. Peter Salk, and two of the Institute's faculty members, **Sreekanth Chalasani** and **Janelle Ayres**. More than 500 people participated in Explore Salk tours, getting a peek inside the Institute's laboratories and technology core facilities. In all, 15 labs and three cores opened their doors to the tours.

Many volunteers and staff helped make Step into Discovery 2014 an enjoyable and educational event for the community, while sponsors, including title sponsor Rudolph and Sletten, ensured that the day was a tremendous success.

Backward glances at **Back to Basics** lecture

Back to Basics
LECTURE SERIES at the SALK INSTITUTE

THE THEME WAS SALK HISTORY ON March 25, when **Suzanne Bourgeois**, professor emerita and founding director of the Regulatory Biology Laboratory, addressed an audience of more than 100 about the early years of the Institute. The author of *Genesis of the Salk Institute: The Epic of Its Founders*, Bourgeois was the featured attraction at the spring Back to Basics lecture, held in the Institute's Conrad T. Prebys Auditorium. She discussed the book, which was published last summer by the University of California Press, and shared archival photographs and inside stories about the founding of the Salk. Her talk sparked an animated Q&A session that continued into the reception and book signing following the lecture, and all copies of the book on hand sold out.

Back to Basics is a free biannual lecture series that is open to anyone interested in learning more about Salk science. The next installment will be held Tuesday, September 23, and will feature **Ronald Evans** from the Gene Expression Laboratory, who will talk about his latest research. For more information, contact Jennifer Rothrock, at 858-453-4100 ext. 2068, or jrothrock@salk.edu.

Salk microflora researcher Janelle Ayres named Searle Scholar

JANELLE AYRES, ASSISTANT PROFESSOR IN THE NOMIS FOUNDATION LABORATORIES for Immunobiology and Microbial Pathogenesis, has received the prestigious Searle Scholar award, which each year is given to only 15 researchers in the chemical and biological sciences. The scholarship provides each recipient with $300,000 to support scientific research over the next three years. This year, 172 applications were considered from recently appointed assistant professors, nominated by 120 universities and research institutions.

Ayres' work focuses on the trillions of bacteria that live in intestines and are responsible for health and wellness. Many diseases occur when that microbial system is thrown out of whack and "bad" bacteria take over. Using antibiotics to fight infections has limitations: besides not working for all diseases, antibiotics also kill good bacteria and contribute to multi-drug-resistant harmful bacteria ("super bugs"). Ayres focuses on an entirely new approach to therapeutics by investigating how helpful microflora could be leveraged to combat the effects of harmful bacteria in place of or in addition to antibiotic treatment. Rather than attempting to eliminate the bad bacteria directly, she is using beneficial bacteria to target and control the damage generated during infections (for example, diarrhea and rapid weight loss), thereby giving an organism's immune system time to clear out the infection. Studying how to engineer microbes that can colonize the intestine while providing beneficial effects could lead to new treatments for infectious and inflammatory diseases and pathologies associated with cancer and aging.

SEARLE SCHOLARS PROGRAM

Ronald Evans, director of the Gene Expression Laboratory, holder of the March of Dimes Chair in Molecular and Developmental Biology and a Howard Hughes Medical Institute investigator, received an honorary doctorate for outstanding scientific research from the University of Groningen, one of the oldest and largest universities in the Netherlands. The university created a mini-documentary featuring Evans as one of "10 Extraordinary Scientists."

San Diego developer Donald Cohn elected to Salk Board of Trustees

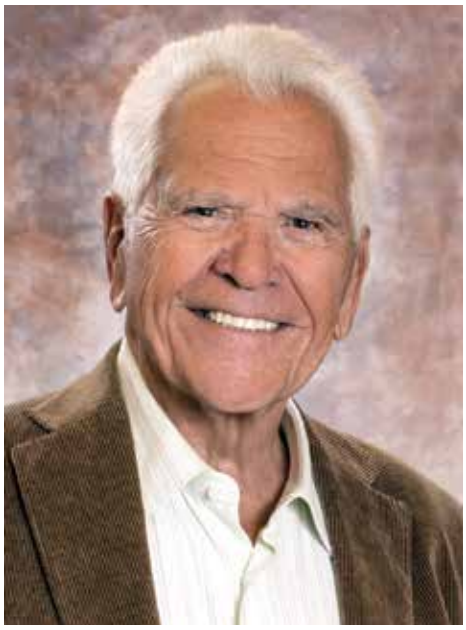
IN APRIL, LONGTIME SAN DIEGO REAL estate developer and community builder Donald Cohn became the newest member of the Salk Institute Board of Trustees.

"Donald's success as a businessman, philanthropist and community volunteer make him a vital asset to our board," says chairman **Irwin Jacobs**. "We are greatly pleased to have him join our Board of Trustees."

Cohn established his business career in San Diego in 1961. From then through 1979, he was active in the development of over 3,000 residential units, both as a builder and investor. In 1980, he founded DataQuick Information Systems, serving as CEO and managing its growth as it became the largest real estate information provider in the United States; it was sold to Acxiom Corporation in 1995. Subsequently, he was founder and CEO of DTS Communications until its sale to a New York Stock Exchange firm in 1997. Since that time, he has been an investor in other business ventures and continues to manage his real estate portfolio.

Cohn is a past chair of the Old Globe Theatre and director of the Plaza de Panama Committee (Balboa Park project). In 2006, he and his wife, Karen, gave $5 million to the Old Globe to establish the Karen and Donald Cohn Education Center, the theater's first dedicated space for education and outreach programs.

The Cohns have also supported the San Diego Opera; San Diego Symphony; The Bishop's School; University of California, San Diego; University of San Diego; and the Museum of Contemporary Art San Diego.



Left upper: Fei-Fei Dong, Right upper: Clodagh O'Shea

Lower left: Marc Montminy, Lower right: Karen Joy Davis and Sean Lee

Spectacular first season of Salk

Science & Music Series

concludes; lineup announced for next year

ON MAY 18, THE INAUGURAL SALK SCIENCE & MUSIC SERIES concluded with a remarkable performance by pianist Fei-Fei Dong and a fascinating scientific talk by Salk associate professor **Clodagh O'Shea**. The six-part series, which began in October, brought together virtuosos from the worlds of both music and science. Because of its resounding success, the series will return for a second season beginning in the fall.

The seed for the Salk Science & Music Series was planted when Salk president **William Brody** envisioned a continuation of the Salk tradition of combining science and art in imaginative ways. Observing the many parallels between art and science, he knew that attracting music lovers to the Salk would naturally tie in with the creative approaches scientists employ in their research. Each concert features performances by some of the hottest established and emerging classical and jazz musicians, along with talks about the latest discoveries by the Institute's world-renowned scientists.

"The combination of science and music is in keeping with Jonas Salk's original vision for the Institute, which is to merge science and art," he explains.

Longtime Salk supporter and former trustee Conrad Prebys generously donated a magnificent Steinway concert grand piano, which anchors the series. Concert pianist Karen Joy Davis served as executive producer.

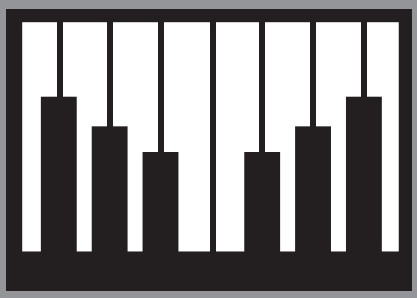
"The gift of the Steinway concert grand inspired the creation of the series," Davis says. "A great piano needs to be played and enjoyed! I think the Salk's amazing history of discovery and its iconic architecture make it the perfect setting for combining music and science."

Using her extensive contacts in the classical music world, Davis was able to attract the world-class talent that marked the first season. Once the program came to life, it was quickly embraced by the San Diego community.

A stellar lineup has already been slated for the upcoming second season of the Science & Music Series, which will open in November with jazz piano phenom Eldar Djangirov and his trio and conclude with the Brubeck Brothers Quartet in June. Other performances will include pianist Sean Chen, 2013 Van Cliburn Crystal Award winner; Karen Joy Davis and Rachel Kudo in a duo piano concert; Ching-Yun Hu, winner of the 2008 Arthur Rubinstein International Piano competition; and pianist Giuseppe Mentuccia.

For a complete schedule of the second Salk Science & Music Series and information about tickets, please visit http://music.salk.edu/. President's Club members receive admission and premier seating to all Salk Science & Music Series concerts, as well as an invitation to a post-concert reception. For information about joining the President's Club, visit http://www.salk.edu/support/presidentsclub.html or call (858) 453-4100, ext.1405.

SALK & SCIENCE MUSIC SERIES



PLEASE JOIN US AS WE CONTINUE THIS EXCITING JOURNEY INTO OUR SECOND SEASON

Sunday, November 2, 2014

ELDAR TRIO
Jazz pianist virtuoso, Eldar Djangirov, returns to San Diego to perform with his Trio

"His command of the instrument is beyond staggering." —*Bob Doershuk: Downbeat Magazine*

TERRY SEJNOWSKI
Professor and Laboratory Head
Computational Neurobiology Laboratory

Sunday, December 7, 2014

RACHEL KUDO & KAREN JOY DAVIS
Duo piano concert, featuring Tchaikovsky's Nutcracker Suite

"Kudo is an extraordinary artist who promises to become a legend." —*El Nuevo Herald*

"Ms. Davis' performance was unique and assured...displayed sparkling brilliance and technical accuracy." —*The London Times*

TOM ALBRIGHT
Professor and Director,
Vision Center Laboratory

Sunday, January 25, 2015

GIUSEPPE MENTUCCIA
Winner of the 2006 Vittoria Prize from the Accademia Nazionale di Santa Cecilia

"This young pianist has warmth, musical intelligence and an innate electricity." —*Talk in New York*

TONY HUNTER
Professor, Molecular and Cell Biology Laboratory

Sunday, February 22, 2015

SEAN CHEN
Pianist, 2013 Van Cliburn Crystal Award winner

"Sean Chen has the rare ability to combine poetic musical sensibilities and dazzling technical prowess." —*Paula Edelstein, LA Music Examiner*

INDER VERMA
Professor, Laboratory of Genetics

Sunday, April 26, 2015

CHING-YUN HU
Winner, 2008 Arthur Rubinstein International Piano competition

"Ching-Yun Hu possesses the soul of Chopin." —*Chopin International Festival, Duszniki-Dzroj, Poland*

JUAN CARLOS IZPISUA BELMONTE
Professor, Gene Expression Laboratory

Sunday, June 7, 2015

BRUBECK BROTHERS QUARTET
Tribute to Dave Brubeck concert

"Once again the Brubeck Brothers Quartet attains that rarefied level where music is both relaxed and expressive." —*All About Jazz*

SATCHIN PANDA
Associate Professor,
Regulatory Biology Laboratory

Scientific symposia mark milestone birthdays for **Ronald Evans** and **Geoffrey Wahl**

TWO OF THE INSTITUTE'S MOST distinguished senior scientists recently celebrated landmark birthdays, Salk style. Daylong scientific symposia for **Geoffrey Wahl**'s and **Ronald Evans**' 65th birthdays paid homage to their remarkable careers, featuring tributes by colleagues and presentations by speakers who had played important roles in their professional lives. Family members and friends also put in guest appearances, and the proceedings were leavened with liberal doses of good-natured ribbing. Each symposium ended with remarks by the honoree, followed by a reception.

The festivities began April 4 with the symposium marking Wahl's 65th birthday, although it was nearly a year late, rescheduled to coincide with the 2014 annual meeting of the American Association for Cancer Research (AACR), which was held in San Diego. (Wahl served as president of the organization in 2006.) Guest speakers included 2007 Nobel laureate Mario Capecchi of the University of Utah, who had been Wahl's doctoral advisor; George Stark, from the Cleveland Clinic's Lerner Research Institute, his postdoctoral mentor; Peter Jones, from USC's Norris Comprehensive Cancer Center, also a former president of the AACR; Arnie Levine from the Institute for Advanced Study; Gigi Lozano from the M.D. Anderson Cancer Center; and Dan Von Hoff from TGen (the Translational Genetics Institute) in Phoenix, Arizona. As a sabbatical visitor in Wahl's lab, Von Hoff got him interested in both translational research and the AACR.

Evans' 65th birthday symposium, held June 2, featured his postdoctoral advisor, James Darnell of Rockefeller University; Leslie Anne Leinwand from the University of Colorado; Bert O'Malley, a colleague from

Colleagues and friends join Ronald Evans in celebrating his 65th birthday.

Baylor College of Medicine; Pierre Chambon of IGBMC in France, a "friendly competitor" who shared the 2004 Lasker Prize with Evans; former postdocs David Mangelsdorf of the University of Texas Southwestern Medical Center; Katja Lamia from The Scripps Research Institute; and 1985 Nobel laureate Joseph Goldstein of the University of Texas Southwestern Medical Center.

Following the formal part of each program, the honoree was presented with a walker and other gag gifts. Salk's senior illustrator **Jamie Simon** created humorous posters for the symposia–Wahl's, a take-off of *Dr. Strangelove*, and Evans', a play on *A Beautiful Mind*—establishing a tone that was equal parts serious science and lighthearted homage to two world-class investigators.

Whimsical posters announcing the birthday symposia for Ronald Evans (left) and Geoffrey Wahl (right).

salk women & science
Where cures begin.

Janelle Ayres

Salk Women & Science continues to gain momentum

MORE THAN 100 FEMALE BUSINESS AND community leaders gathered at Salk on March 5 for a Women & Science event featuring a talk by **Janelle Ayres**, of the Nomis Center for Immunobiology and Microbial Pathogenesis. Ayres' talk, "Good bugs vs. bad bugs: Using the intestinal microbiota to treat infectious diseases," was an overview of her research into the defense strategies that enable a host to survive when interacting with microbes, and she explained how understanding these mechanisms can lead to new treatments for infectious and inflammatory disease.

Salk chief operating officer and executive vice president **Marsha Chandler** welcomed guests to the event, and **Greg Lemke**, a professor in the Molecular Neurobiology Laboratory and holder of the Françoise Gilot-Salk Chair, introduced Ayres' talk.

Salk Women & Science was launched in July 2012 to engage the community in biological science and technology and ultimately support the advancement of women in science. Three Women & Science events are offered annually, as well as small private dinners hosted by female faculty. The next event will take place in October. For more information about Women & Science, visit www.salk.edu/womenandscience.

From left to right: Marsha Chandler, Greg Lemke, Julie Law

From left to right: Meredith Counce, Sam Pfaff, Clodagh O'Shea, William Brody, Charlotte Jones Anderson, Ronald Evans, Rebecca Newman, Inder Verma

FOUNDATION LEADERS BRUSH UP ON TAX LAWS AND FOUNDATION MANAGEMENT AT THE 42ND ANNUAL TAX SEMINAR FOR PRIVATE FOUNDATIONS

A SERIES OF NATIONALLY KNOWN LECTURERS AND AUTHORS provided insights on foundation law, management, finance and governance on May 14-16 at the Salk Institute's 42nd annual Tax Seminar for Private Foundations. Sixty foundation leaders from across the country were in attendance at the event, which was held at the Lodge at Torrey Pines.

"Beyond the excellent presentations and La Jolla's summer-like weather, the conference offered several special events," notes tax seminar chairman Edwin Hunter, president of Hunter, Hunter & Sonnier, LLC.

Many community members joined seminar participants for the keynote address by Charlotte Jones Anderson, executive vice president of the Dallas Cowboys and chair of NFL Charities. Her presentation, titled "How passion and compassion have shaped the Dallas Cowboys," focused on the synergy between the private philanthropy of the Jones family and the Dallas Cowboys brand, offering a fascinating perspective on philanthropy as a dynamic part of a family business.

Attendees also heard scientific updates from Salk scientists **Inder Verma**, **Janelle Ayres** and **Terrence Sejnowski**. Dr. Peter Salk, son of Institute founder Jonas Salk, spoke about his father's legacy and the global impact of his work.

"The seminar continues to be an extremely useful forum for trustees to learn about the latest developments in tax law and to interact with tax experts and foundation peers," says **Rebecca Newman**, Salk's vice president of external relations.

Whether covering the complexities of changes in tax law or offering new ideas and perspectives, the seminar provides a wealth of resources for foundation leaders.

From left to right: Elaine Marshall, Susie Spanos, Pierce Marshall, Charlotte Jones Anderson

Geoffrey Wahl elected to Academy of Arts and Sciences Class of 2014 for outstanding scientific work

LAST APRIL, THE AMERICAN ACADEMY OF ARTS AND SCIENCES (AAAS) elected **Geoffrey Wahl**, a professor in Salk's Gene Expression Laboratory and holder of the Daniel and Martina Lewis Chair, to its distinguished membership. The society's ranks include Nobel laureates, Pulitzer Prize recipients and Oscar winners, as well as intellectual luminaries dating back to the founding of the United States. George Washington and Benjamin Franklin were members, as was Albert Einstein. Wahl joins 13 other Salk professors as members of the organization.

Wahl seeks to determine how cancers originate and progress and why tumors become resistant to even the most powerful anti-cancer drugs. His goal is to translate the knowledge gained from basic research into the development of new treatment strategies to manage all types of cancer more effectively.

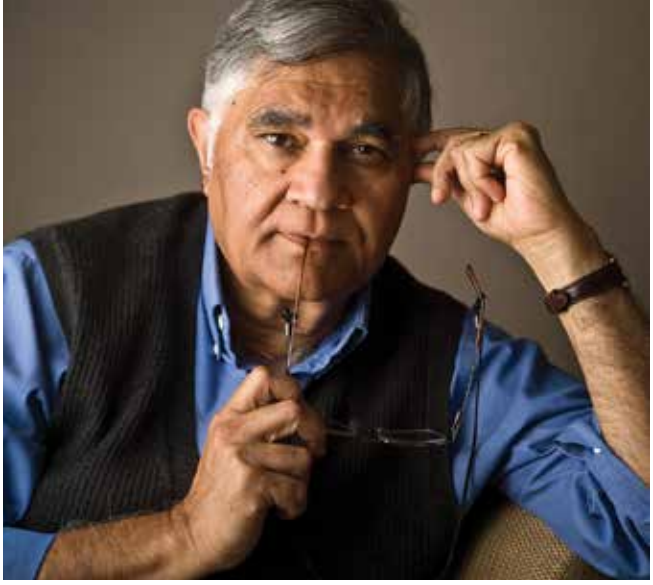
"It has been my privilege to call Geoff a colleague and a dear friend," says **Inder Verma**, a professor in Salk's Laboratory of Genetics and American Cancer Society Professor of Molecular Biology. "His work in understanding cancer has been critical to the field, and he is highly deserving of this honor." Verma, along with Carol Prives, a professor at Columbia University, nominated Wahl for membership in the academy; both are AAAS members themselves.

"I am humbled by the honor and privilege of being included as a member of this academy and deeply grateful to those who nominated and supported me," says Wahl. "I have been fortunate to work with students, postdoctoral scholars and collaborators whose efforts, insights and intellect were vital to my work."

The academy is one of the country's oldest and most prestigious honorary learned societies and a leading center for independent policy research. The current membership includes more than 250 Nobel laureates and more than 60 Pulitzer Prize winners. Other members elected in 2014 include authors John Irving and E. Annie Proulx, cartoonist Jules Feiffer, actor Al Pacino, political economist Robert Reich, former Paramount CEO Sherry Lansing and oceanographer Robert Ballard, along with a host of illustrious scientists, mathematicians, engineers, economists, historians, social scientists, educators, philanthropists, artists and more.

Salk Board of Trustees tours the Waitt Advanced Biophotonic Center with assistant professor **Axel Nimmerjahn** and staff on April 10.

Salk Trustees Ernest and Evelyn Rady, Linda Chester, Ben Lewis, Alan Gold and Fred Dotzler visit the laboratory of Salk professor Axel Nimmerjahn.



Inder Verma

Ronald Evans

Two faculty inducted into the 2014 elected class of fellows of the American Association for Cancer Research Academy

THE AMERICAN ASSOCIATION FOR CANCER Research (AACR), the world's oldest and largest professional society dedicated to advancing cancer research, inducted Salk professors **Ronald Evans** and **Inder Verma** into its 2014 class of elected fellows in April.

The AACR Academy recognizes scientists who have made exceptional contributions to cancer research or cancer-related biomedical science and whose work has had a major impact in their fields. The fellows are elected through a peer-review process that evaluates individuals on the basis of their innovative and influential scientific achievements in cancer research.

Verma, who is holder of the Irwin and Joan Jacobs Chair in Exemplary Life Science and American Cancer Society Professor of Molecular Biology, is renowned for developing innovative gene therapy techniques that have led to a better understanding of tumors, cancer stem cells and cancer-related genes.

Evans, director of the Gene Expression Laboratory, is the March of Dimes Chair in Developmental and Molecular Biology and a Howard Hughes Medical Institute investigator. Evans is a leading authority on hormone signals, many of which he discovered are primary targets in the treatment of leukemia and pancreatic, breast and prostate cancers.

Cancer metabolism expert Reuben Shaw promoted to full professor

REUBEN SHAW, A MEMBER OF THE MOLECULAR and Cell Biology Laboratory and a Howard Hughes Medical Institute early career scientist, has been promoted from associate professor to full professor after a rigorous evaluation process by Salk senior faculty, non-resident fellows and scientific peers.

"We are pleased to recognize Professor Shaw's original, innovative and notable contributions to biological research in pathways that underlie the development of cancer and metabolic disorders," says Salk president **William Brody**.

While investigating one of the most commonly mutated genes in lung cancer, Shaw discovered an energy-sensing pathway that shuts down cell growth and reprograms metabolism when nutrients are scarce. His lab went on to molecularly decode a number of new components of this biochemical pathway, which connects nutrition and exercise to suppression in both cancer and diabetes.

This biochemical circuit, the AMPK pathway, is activated by exercise and caloric restriction and tells cells to lower their glucose, lipids and growth. The pathway halts the growth of tumor cells, which have an aberrant revved-up metabolism, but also restores normal function to the liver and other tissues in diabetics. Shaw's lab recently followed up on a prediction from its previous studies to test whether drugs widely used to treat type 2 diabetes could work as cancer treatments. The team found specific efficacy in some forms of lung cancer for which there are currently no good therapies.

Researchers in Shaw's lab also use genetic mouse models to further examine the connections between cancer and metabolic diseases and to tease out the precise role of each component of the signaling pathway. In the past five years at Salk, the lab's studies have led to the discovery of new therapies for both cancer and type 2 diabetes.

Salk's Dona Mapston leads students in science-focused activities as part of the Institute's Education Outreach program.

Education Outreach

launches innovative programs to promote science education

IF PAST HISTORY IS ANY INDICATION, SALK'S award-winning Education Outreach program may be poised to garner a few new accolades in the not-too-distant future. Not only has it introduced a brand-new program that promotes virtual interactions between Salk scientists and elementary school students, but it recently received one of just seven pilot grants awarded by the American Academy of Arts and Sciences (AAAS) through the organization's new STEM (Science, Technology, Engineering and Mathematics) Volunteer Program. Add these groundbreaking initiatives to Education Outreach's existing High School Scholars program, March of Dimes High School Science Day and Mobile Science Lab, and it's an even stronger formula for success in attracting young people to science studies and careers.

SciChat, the program for elementary students, uses Skype to enable students at Del Mar Hills Academy of Arts and Sciences in Del Mar, California, to ask Salk scientists general questions about their research and what it's like to work in the field. The project's goal is to let the students interact with scientists so they can picture themselves in similar roles someday.

"We are thrilled to have this new opportunity for young students to meet and talk with our scientists," says **Ellen Potter**, director of the Education Outreach program. "We are now able to bring the Salk to the students when the students can't come to us. It is a great way to extend our outreach and share our excitement for scientific discovery."

The first SciChat took place February 11, when **Abby Buchwalter**, a postdoctoral fellow in **Martin Hetzer**'s lab, described her research to nearly 30 fourth-, fifth- and sixth-grade students during their lunch break. Seven more SciChats took place over the next four months, and plans call for the popular program to continue into the next academic year.

The AAAS grant will fund a pilot initiative at Salk called New Frontiers in Science Education. The program will bring San Diego-area high school science teachers together with Salk scientists to develop curricula based on the state-of-the-art research taking place at the Institute. **Ronald Evans**, an HHMI investigator, holder of the March of Dimes Chair in Molecular and Developmental Biology and an international authority on hormones who has long been committed to fostering relationships with local educators, sponsored the proposal on behalf of Salk.

During the first year of the project, three teachers and Salk scientists, including Evans, will take part in focus groups and workshops

> "We are now able to bring Salk to the students when students can't come to us. It is a great way to extend our outreach and share our excitement for scientific discovery." – ELLEN POTTER

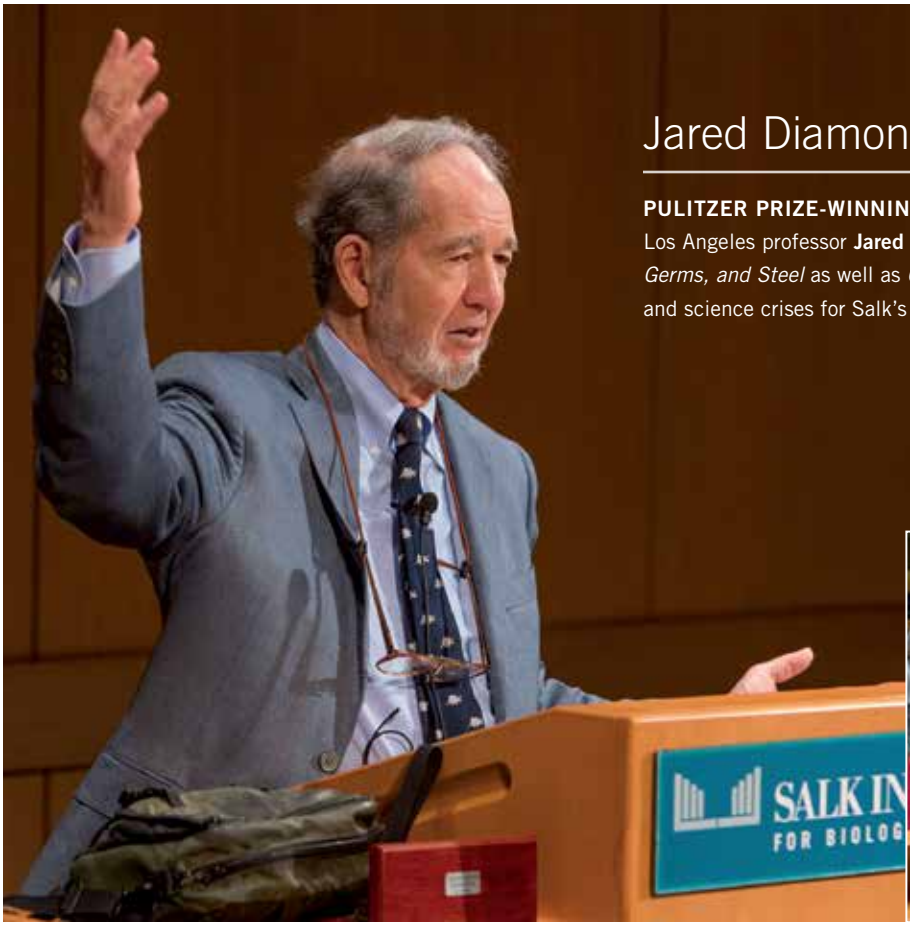
Students gather in the Salk courtyard with Salk scientists and staff during March of Dimes High School Science Day.

to identify specific areas of Salk research that lend themselves to adaptation for the classroom. Working collaboratively, the scientists and teachers will then develop appropriate curriculum and support materials that incorporate elements of state and national science standards. Local high school teachers will be recruited to participate in the second year of the grant, and during the summer, the teachers will also have opportunities to spend time in the laboratory with a volunteer research scientist to observe how actual research is carried out.

"This is an extraordinary opportunity to leverage the scientific expertise of Salk investigators and the enthusiasm and classroom experience of the participating teachers," says **Dona Mapston**, Education Outreach specialist. "It will be fascinating to see what comes out of the process."

March of Dimes High School Science Day ignites interest in future scientists

MORE THAN 230 HIGH SCHOOL STUDENTS FROM 23 CAMPUSES throughout San Diego County converged on the Salk March 1 for the 2014 March of Dimes High School Science Day. The half-day science immersion program exposed participants to a variety of experiences, with the aim of sparking their interest in the field. In the morning, following welcoming remarks by Salk president **William Brody**, Salk employee volunteers shepherded groups of students to labs across the campus where they took part in hands-on science experiments under the direction of postdocs and graduate students. Following lunch, attendees enjoyed a talk by **Sreekanth Chalasani**, an assistant professor in the Molecular Neurobiology Laboratory, who spoke about *c. elegans* as a model organism. All students left with a logoed string backpack and new perspectives on science and the possibilities of science careers.



Jared Diamond visits the Salk

PULITZER PRIZE-WINNING AUTHOR AND UNIVERSITY OF CALIFORNIA, Los Angeles professor **Jared Diamond**, whose bestselling works include *Guns, Germs, and Steel* as well as *Collapse*, spoke to a packed auditorium on social and science crises for Salk's Francis Crick Lecture in April.

AMERICAN SOCIETY FOR MICROBIOLOGY

Salk scientist Vicki Lundblad wins accolades

VICKI LUNDBLAD, A PROFESSOR IN the Molecular and Cell Biology Laboratory, has been awarded the Becky and Ralph S. O'Connor Chair in recognition of her excellence in the field of molecular and cell biology. Ralph O'Connor, who serves on the Salk Board of Trustees, and his wife, Becky, generously created the chair as an "investment that has the potential for maximum impact on human health."

Lundblad has also been elected a 2014 Fellow of the American Academy of Microbiology for her pioneering work in telomere biology. Fellows are elected annually through a highly selective process based on significant contributions to the field of microbiology, a field that boasts the names of Louis Pasteur, Jonas Salk and many others responsible for some of the greatest achievements in biomedical history.

Lundblad's research has defined a key molecular mechanism that is critical in both aging and cancer. She found that the ends of chromosomes, known as telomeres, shorten over time, acting as a "molecular clock" that counts down the number of times a cell can divide. She has also shown that a telomere-dedicated enzyme called telomerase can help reset the clock and increase cell division. Figuring out how to control this molecular clock suggests the tantalizing possibility of both halting cancerous cells and promoting healthy aging. Toward that end, Lundblad's lab is currently teasing out the pathways that either promote or inhibit telomerase inside cells.

Fred Gage and Kristen Brennand

New stem cell research points to early indicators of schizophrenia

CURRENTLY, OVER 1.1 PERCENT OF THE world's population has schizophrenia, with an estimated 3 million cases in the United States alone. The economic cost is high: in 2002, Americans spent nearly $63 billion on treating and managing the disability. The emotional cost is higher still: 10 percent of those with schizophrenia are driven to commit suicide.

Yet, scientists still know little about its underlying causes and do not know which cells in the brain are affected and how. Previously, it had only been possible to study schizophrenia by examining the brains of patients after death, but age, stress, medication or drug abuse had often altered or damaged the brains, making it difficult to pinpoint the disease's origins.

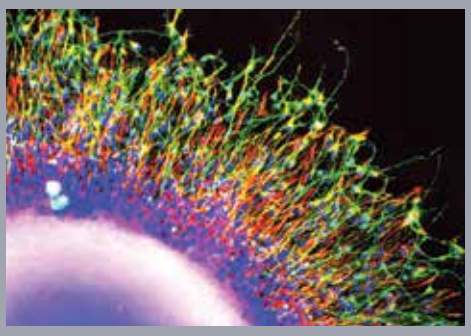
Using new stem cell technology, scientists in the lab of **Fred Gage** have shown that neurons generated from the skin cells of people with schizophrenia behave strangely in early developmental stages. The findings of the study, published in *Molecular Psychiatry*, are consistent with a prevailing theory that events during pregnancy can contribute to schizophrenia, even though the disease doesn't manifest until early adulthood.

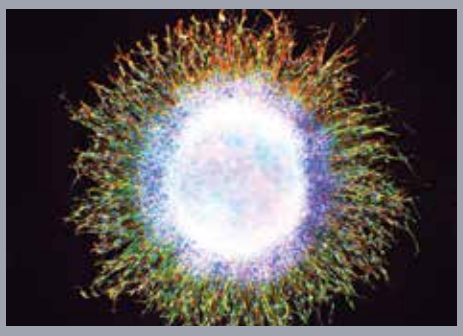
"This study aims to investigate the earliest detectable changes in the brain that lead to schizophrenia," says Gage, who heads Salk's Engman Laboratory for Schizophrenia Research. "We were surprised at how early in the developmental process defects in neural function could be detected."

Taking skin cells from patients, Gage's team coaxed the cells to revert back to an earlier stem cell form and then prompted them to grow into very early stage neurons (dubbed neural progenitor cells or NPCs), which are similar to the cells in the brain of a developing fetus. They generated NPCs from the skin cells of four patients with schizophrenia and six people without the disease, then tested the cells in two types of assays. On both tests, the researchers found that NPCs from people with schizophrenia differed in significant ways from those taken from unaffected people.

Kristen Brennand, the paper's first author and now an assistant professor at the Icahn School of Medicine at Mount Sinai, said the researchers were surprised that the skin-derived neurons remained in such an early stage of development. "We realized they weren't mature neurons but only as old as neurons in the first trimester," she says. "So we weren't studying schizophrenia but the things that go wrong a long time before patients actually get sick."

According to Gage, the study hints that there may be opportunities to create diagnostic tests for schizophrenia at an early stage. The research was supported in part by the Robert and Mary Jane Engman Foundation.





These images show the movement of patient-derived neural progenitor cells from a sphere of neurons in a migration assay. How far and how quickly the neurons move indicates whether they may behave atypically in the brain.

> "We really never expected that we would be able to decouple the sleep-wake cycle and the eating cycle, especially with a simple mutation."
>
> – SATCHIDANANDA PANDA

Genes discovered linking circadian clock with eating schedule

FOR MOST PEOPLE, THE URGE TO EAT A MEAL OR SNACK COMES at a few predictable times during the waking part of the day. But for those with a rare syndrome, hunger comes at unwanted hours, interrupts sleep and causes overeating. A team in the lab of **Satchidananda Panda** recently discovered a pair of genes that normally keeps eating schedules in sync with daily sleep rhythms. In mice with mutations in one of the genes, eating patterns are shifted, leading to unusual mealtimes and weight gain. The results were published in *Cell Reports*.

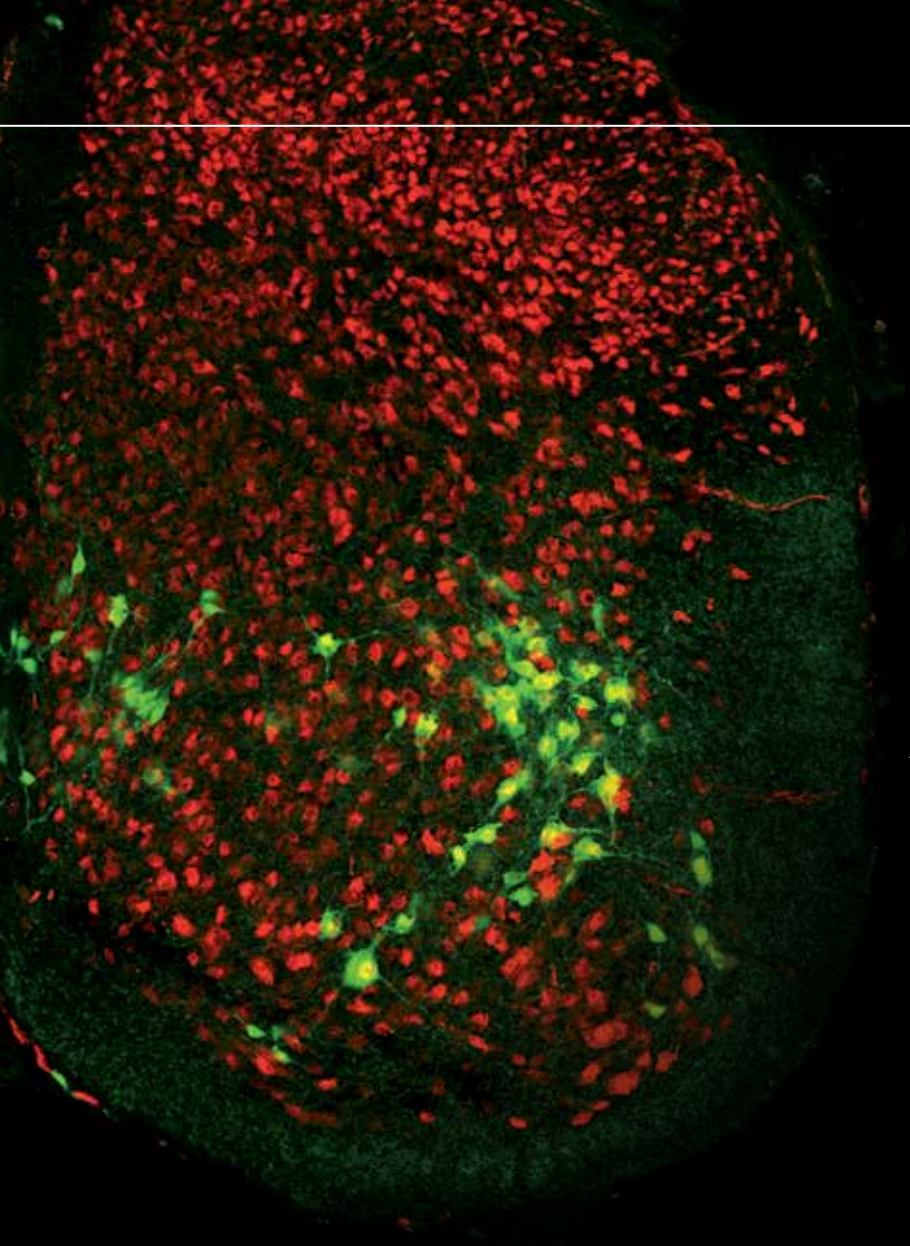
"We really never expected that we would be able to decouple the sleep-wake cycle and the eating cycle, especially with a simple mutation," says Panda, whose work is supported in part by the Joe W. and Dorothy Dorsett Brown Foundation. "It opens up a whole lot of future questions about how these cycles are regulated."

More than a decade ago, researchers discovered that individuals with an inherited sleep disorder often carry a particular mutation in a protein called PER2, in an area of the protein that can be phosphorylated—the ability to bond with a phosphate chemical that changes the protein's function. Humans have three PER, or period, genes, all thought to play a role in the circadian clock and all containing the same phosphorylation spot.

Panda's lab joined forces with a Chinese team led by Ying Xu of Nanjing University to test whether mutations in the equivalent area of PER1 would have the same effect as those in PER2. They bred mice to lack the mouse period genes and added in a human PER1 or PER2 with a mutation in the phosphorylation site. As expected, mice with a mutated PER2 had sleep defects, dozing off earlier than usual. The same wasn't true for PER1 mutations, though.

Mice with the PER1 phosphorylation defects ate earlier than other mice. The defect caused them to awaken and snack before their sleep cycle was over, and eat more food throughout their normal waking period. When researchers looked at the molecular details of the PER1 protein, they found that the mutated PER1 led to lower protein levels during the sleeping period, higher levels during the waking period and a faster degradation of protein whenever it was produced by cells. Panda and his colleagues hypothesize that normally, PER1 and PER2 are kept synchronized, but a mutation in one of the genes could break this link and cause off-cycle eating or sleeping.

When the team restricted access to food, providing it only at the mice's normal meal times, they found that even with a genetic mutation in PER1, mice could maintain a normal weight. Over a ten-week follow-up, these mice—with a PER1 mutation but timed access to food—showed no differences compared to control animals. This tells the researchers that the weight gain caused by PER1 is entirely caused by meal mistiming, not other metabolic defects.



V2b interneurons, responsible for a key locomotion circuit, appear as green with yellow nuclei in a spinal cord while all other neurons are red.

Discovery reveals circuitry of fundamental motor circuit

THE SPINAL CORD CONTAINS A NETWORK OF NEURONS THAT ARE able to operate largely in an autonomous manner, thus allowing animals to carry out simple rhythmic walking movements with minimal attention—giving us the ability, for example, to walk while talking on the phone. These circuits control properties such as stepping with each foot or pacing the tempo of walking or running.

Recently, a team of researchers led by **Martyn Goulding** identified for the first time which neurons in the spinal cord are responsible for controlling a key output of this locomotion circuit, namely, the ability to synchronously activate and deactivate opposing muscles to create a smooth bending motion (dubbed flexor-extensor alternation). The findings were published in *Neuron*.

Motor circuits in the spinal cord are assembled from six major types of interneurons—cells that interface between nerves descending from the brain and nerves that activate or inhibit muscles.

Goulding and his group had previously implicated one class of interneurons, V1, as being a likely key component of the flexor-extensor circuitry. When V1 interneurons were removed, however, the team saw that flexor-extensor activity was still intact, leading them to suspect that another type of cell was also involved.

To determine what other interneurons were at play in the flexor-extensor circuit, the team looked for other cells in the spinal cord with properties similar to those of the V1 interneurons and began to focus on another class of neuron whose function was not known—V2b interneurons. Using a specialized experimental setup that allows one to monitor locomotion in the spinal cord itself, the team saw a synchronous pattern of flexor and extensor activity when V2b interneurons were inactivated along with the V1 interneurons.

"Our whole motor system is built around flexor-extension; this is the cornerstone component of movement," says Goulding, who holds Salk's Frederick W. and Joanna J. Mitchell Chair. "If you really want to understand how animals move, you need to understand the contribution of these switching cells."

Goulding's discovery may pave the way for new therapies for spinal cord injuries or other motor impairments related to disease.

Michal Krawczyk and Beverly Emerson

Salk scientists identify novel regulator of key gene expression in cancer

THE COX-2 GENE MEDIATES INFLAMMATION, which in most cases helps our bodies eliminate pathogens and damaged cells. But inflammation also has a dark side: it aids growth and spread of tumors in the early stages of cancer. By learning more about how COX-2 is affected, scientists may be able to provide a potential target for future cancer treatment.

Now, a team in the lab of **Beverly Emerson** has identified a key genetic switch, a string of nucleotides dubbed a long non-coding RNA (lncRNA), that acts as an on/off switch for the COX-2 gene. The function of lncRNAs is not well understood, but evidence increasingly points to their role in regulating gene expression, as they are found overexpressed in esophageal, colorectal and breast cancers.

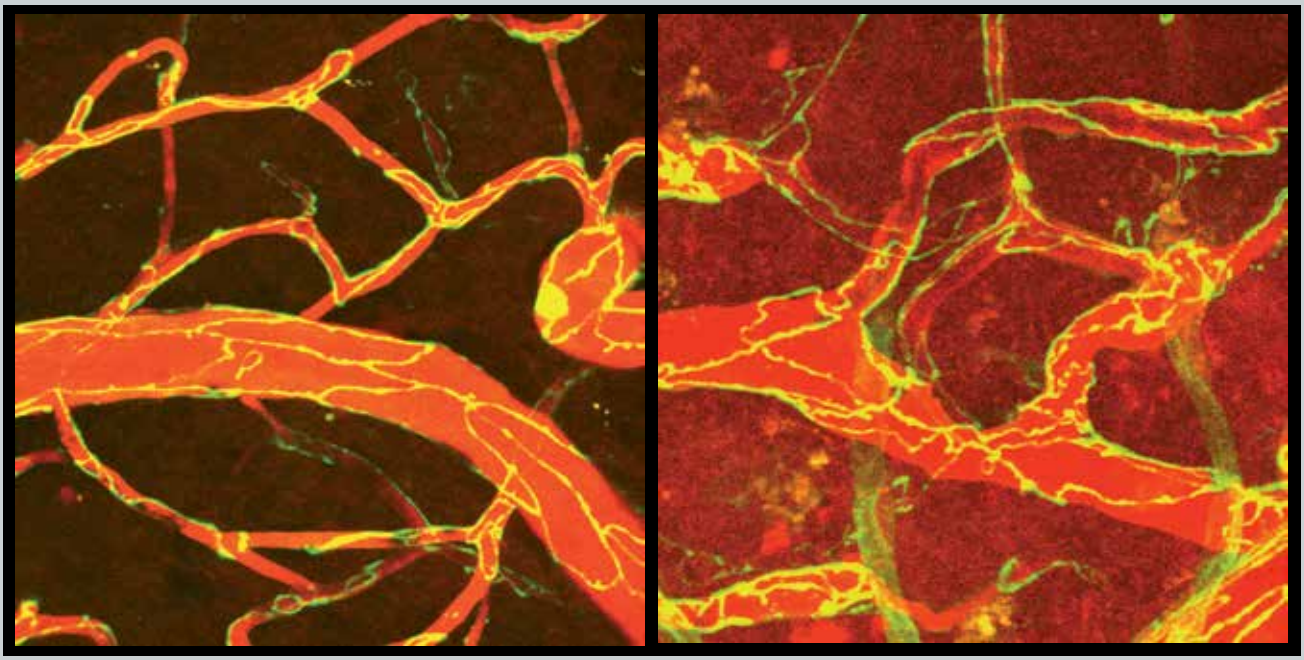
"Deciphering the mechanism of COX-2 gene regulation is of great clinical interest," says Emerson, holder of the Edwin K. Hunter Chair. "COX-2 is instrumental in the development of several types of cancer, including colon, breast and prostate cancer. Strategies that specifically modulate COX-2 activity could be an attractive treatment approach."

Using human mammary epithelial cells, Emerson and senior scientist **Michal Krawczyk** discovered that an lncRNA called PACER kicks a molecule called p50 off the COX-2 gene, causing COX-2 to go into overdrive. This is the first time scientists have shown that non-coding RNAs must be activated in order to squelch the activity of p50, a gene repressor. In turn, says Krawczyk, blocking p50 promotes the assembly of molecular activators of gene expression, which ramp up COX-2 activity.

The scientists were also surprised to note an additional potential role for PACER-induced COX-2 activation in cancer. Early in the disease process, instead of activating the immune system to clear malignant cells from the body, COX-2 aids the growth and spread of tumors. In later stages of disease, however, Krawczyk says cancer cells often shut off COX-2 activity, as if at that stage COX-2 is no longer beneficial for tumor growth because it exposes spreading tumor cells to the immune system. That presents the opportunity to trigger COX-2 expression via PACER in late-stage cancers to aid immune system clearance of metastatic cells.

"This could be a potential treatment for late-stage cancers," says Krawczyk. "We could possibly use small molecules to reactivate COX-2 activity, or perhaps even supply PACER itself, to fight the disease."

The findings of the study were published in *eLife*.



The microscope image on the left shows brain blood vessels (red) with intact junctions (yellow lines) between cells that compose the vessel walls. The image on the right shows blood vessels and junctions two days after a stroke. Blood material has entered the brain (dark red background). Scientists from the Salk Institute and UC Irvine showed that early blood material leakage (within 6 hours after stroke) is due to increased carrier protein transport through the cells of the vessel walls and not through gaps at the junctions, as previously thought.

Researchers identify new cause of brain bleeding immediately after stroke

STROKE IS NOT ONLY A COMPLEX AND DEVASTATING NEUROLOGICAL condition; it's the fourth-leading cause of death and primary reason for disability in the United States. It results in severe blood-brain barrier damage, which allows entry of blood-borne material into the brain, contributing to cellular death and permanent cognitive and movement impairments.

Researchers in the lab of **Axel Nimmerjahn**, collaborating with Dritan Agalliu, an assistant professor of developmental and cell biology at UC Irvine, have discovered a new mechanism that allows blood to enter the brain immediately after stroke, revealing a possible means to create new therapies that may reduce or prevent stroke-induced damage in the brain. In their research, Nimmerjahn and Agalliu developed a novel transgenic mouse strain in which they used a fluorescent tag to see the barrier-forming tight junctions between the cells that make up the blood vessels in the nervous system. This allowed them to image dynamic changes in the barrier during and after stroke in living animals.

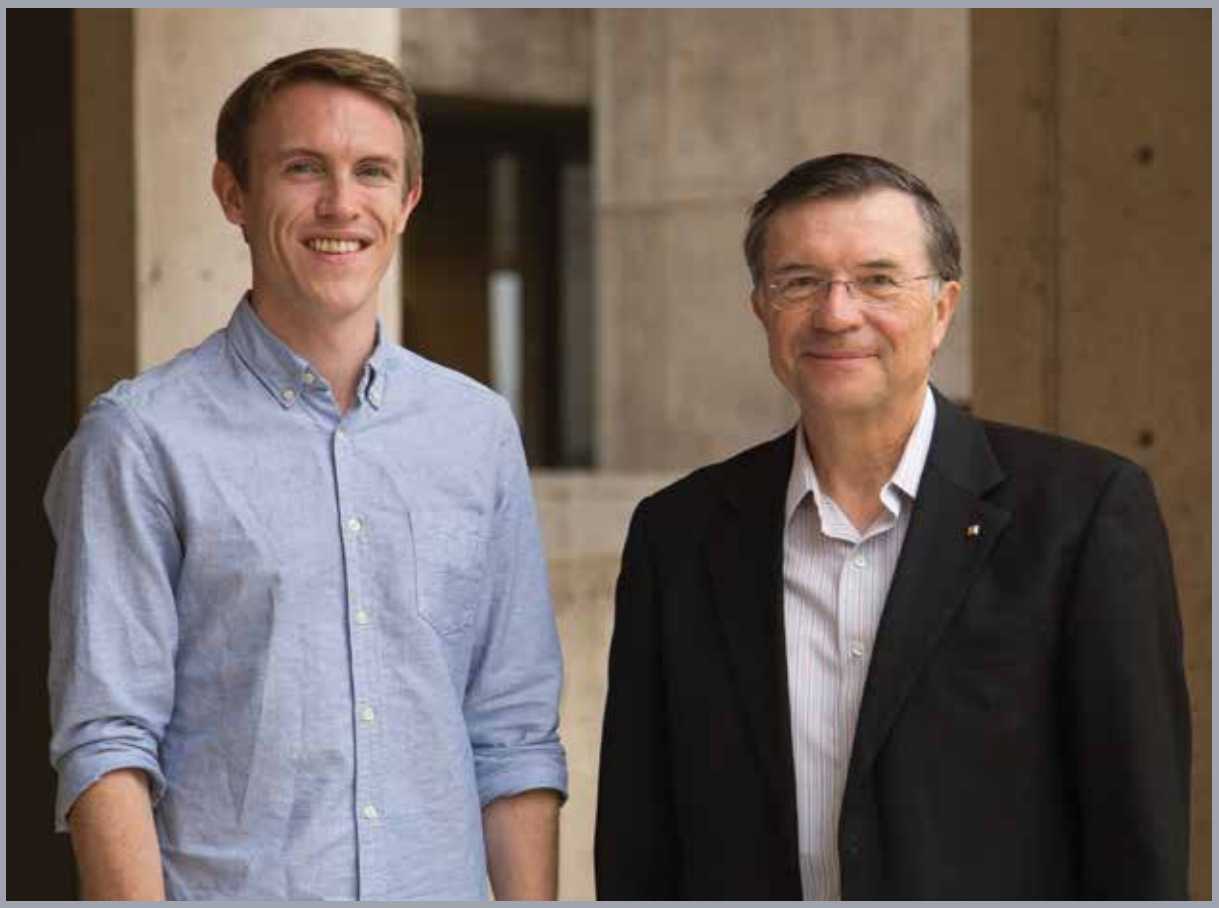
While seeing that the barrier function was rapidly impaired after stroke (within six hours), they unexpectedly found that this early barrier failure is not due to the breakdown of tight junctions between the blood vessel cells, as had previously been suspected, because tight junction breakdown did not occur until two days after the injury. Instead, they reported dramatic increases in carrier proteins, called serum albumin, flowing directly into brain tissue. These proteins travel through the cells that make up the blood vessels, called endothelial cells, using a specialized transport system that normally operates only in non-brain vessels or immature vessels within the central nervous system (CNS). This finding suggests that the transport system underlies the initial failure of the barrier, allowing entry of blood material into the brain within six hours of a stroke.

Early regulation of the specialized transport system in the CNS following stroke may spur development of imaging methods or biomarkers in human studies to identify the initial stages of stroke and thereby prevent damage as early as possible.

Plus, says Nimmerjahn, "Our new transgenic mouse strain and imaging approaches may also allow mechanistic insight into other CNS disorders associated with blood-brain barrier dysfunction, such as brain infection, amyotrophic lateral sclerosis or vascular cognitive impairment." His laboratory is currently developing and applying new light microscopic tools to uncover how CNS immune cells respond to injury, mediate repair and influence nervous system function and behavior.

Results of the stroke study appeared in *Neuron*.

> "Our new transgenic mouse strain and imaging approaches may also allow mechanistic insight into other CNS disorders associated with blood-brain barrier dysfunction, such as brain infection, amyotrophic lateral sclerosis or vascular cognitive impairment."
>
> – AXEL NIMMERJAHN



Cian O'Donnell and Terrence Sejnowski

Explaining how memories stick together

OVER THE PAST FEW DECADES, NEUROSCIENTISTS HAVE REVEALED much about how long-term memories are stored. For significant events—for example, being bit by a dog—a number of proteins are quickly made in activated brain cells to create the new memories. Some of these proteins linger for a few hours at specific places on specific neurons before breaking down. This series of biochemical events allows us to remember important details about that event—such as, in the case of the dog bite, which dog, where it was located and so on.

One problem scientists have had with modeling memory storage is explaining why only selective details and not everything is strongly remembered. Now **Terrence Sejnowski** and his group have created a new model of memory that explains how neurons retain select memories a few hours after an event. This new framework provides a more complete picture of how memory works, which can inform research into conditions such as Parkinson's, Alzheimer's, post-traumatic stress disorder and learning disabilities.

"Previous models of memory were based on fast activity patterns," says Sejnowski, a Howard Hughes Medical Institute investigator and holder of Salk's Francis Crick Chair. "Our new model of memory makes it possible to integrate experiences over hours rather than moments."

By incorporating data from previous literature, Sejnowski and postdoctoral researcher **Cian O'Donnell** developed a model that bridges findings from both molecular and systems observations of memory to explain how this memory window works. Using computational modeling, they showed that despite the proteins being available to a number of neurons in a given circuit, memories are retained when subsequent events activate the same neurons as the original event. They found that the spatial positioning of proteins at both specific neurons and at specific areas around these neurons predicts which memories are recorded.

The new model, reported in *Neuron*, also provides a potential framework for understanding how generalizations from memories are processed during dreams. While much is still unknown about sleep, research suggests that important memories from the day are often cycled through the brain, shuttled from temporary storage in the hippocampus to more long-term storage in the cortex. Researchers observed most of this memory formation in non-dreaming sleep. Little is known about if and how memory packaging or consolidation is done during dreams. O'Donnell and Sejnowski's model, however, suggests that some memory retention does happen during dreams, and by applying their findings, they came up with a theoretical model for how the memory abstraction process might work during sleep.

> "Our new model of memory makes it possible to integrate experiences over hours rather than moments."
>
> – TERRENCE SEJNOWSKI

Inder Verma and Amy Firth

Salk lab turns skin cells into human airway tissue

STUDYING DISEASES THAT AFFECT THE lungs and nearby airways has been limited by the ability to collect diseased tissue from patients and by the complexity of organs. Multiple cell types make up airway tissue, so studying how a disease changes just one cell type in the lab may not be an accurate reflection of the full impact of the disease.

Using reprogrammed skin cells, researchers in the lab of **Inder Verma** have for the first time used stem cell techniques to grow fully functional assemblies of the cells that line airways leading to the lungs. The lab-grown airway tissue can now be used to study the molecular basis of lung diseases—from rare genetic disorders to common afflictions like asthma and emphysema—and to test new drugs to treat the diseases. The results of the study, a collaboration with **Fred Gage**, were published in *Proceedings of the National Academy of Sciences.*

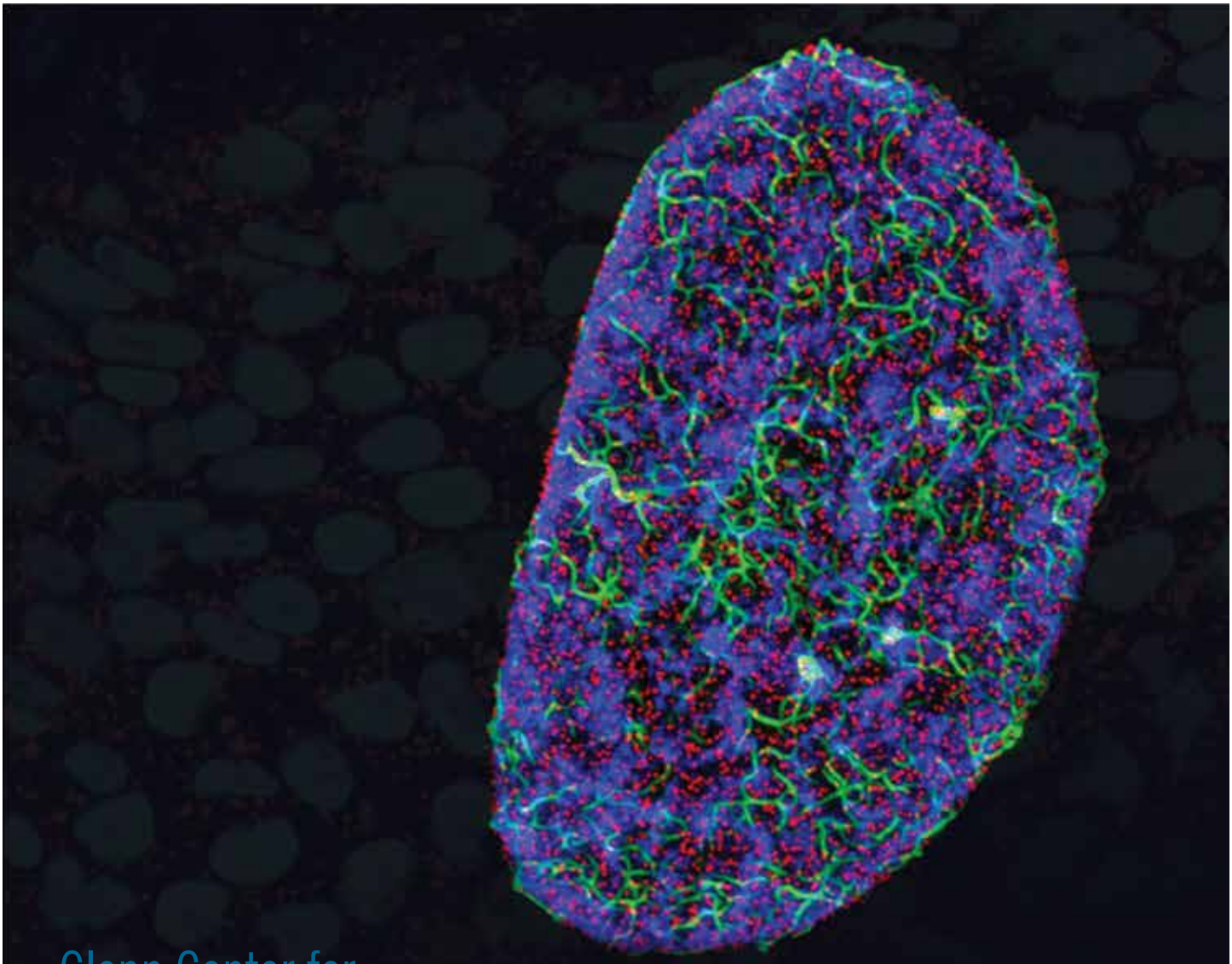
In the new work, the researchers developed the complex airway tissue, composed of four different cell types, by reprogramming skin cells into stem cells, then exposing the stem cells to a unique recipe of chemicals that steered them down a particular airway-specific developmental path. Since skin cells contain the same master set of genes as lung cells, any airway tissue grown from a patient's skin cells will have the disease-causing gene mutation in them.

"The ability to generate a variety of cells that compose a fully mature lung is the first step to understanding the molecular mechanisms of many lung diseases," says Verma, who holds the Irwin and Joan Jacobs Chair in Exemplary Life Science and is also an American Cancer Society Professor of Molecular Biology.

While the grown cells aren't identical to those found in all parts of the lung, similar procedures could pin down how to grow tissue from other sections of the respiratory system. Already the new protocol can be used to develop cell populations to study rare diseases, such as primary ciliary dyskinesia, known to affect the cilia lining airways. In addition, new treatments or genetic therapies could be tested on lab-grown airway tissue derived from an affected patient's cells.

"It will hopefully become possible one day to correct the genetic mutations in these tissues and engraft them back into the airways of a patient," says **Amy Firth**, a postdoctoral researcher in Verma's lab and first author of the paper (see Next Generation, p.16).

Airway tissue grown in the lab could also reveal how pollutants or nicotine exacerbate symptoms of diseases not only affected by genetics but by the air a person breathes.



This image from the Hetzer laboratory is being used to investigate how the organization and the architecture of the nucleus influence gene activity.

Glenn Center for Aging Research receives additional $3 million from the Glenn Foundation for Medical Research

THE INSTITUTE'S INVESTIGATIONS INTO THE BIOLOGY OF normal human aging and age-related diseases have received a significant boost, thanks to a recent $3 million gift from the Glenn Foundation for Medical Research. The gift will support Salk's Glenn Center for Aging Research, which was established in January 2009 with a $5 million gift, also from the Glenn Foundation. The center draws from 11 of Salk's leading laboratories specializing in genetic analysis, stem cell biology and metabolism research.

"The biology of aging underlies all the major human diseases," Glenn Foundation president Mark Collins says. "To understand the fundamental aging process and to intervene is to delay the onset of disease, to extend the healthful years of life and reduce costs to society."

The foundation's support positions the Glenn Center to rapidly advance aging research and shed light on ways to stave off a multitude of age-related diseases, such as cancer, cardiovascular disease, diabetes and Alzheimer's disease. The center, which focuses on whole systems biology, organ biology and cellular aging biology, was the third of eight institutions to join the Glenn Consortium for Research in Aging, which also includes Harvard Medical School, MIT's Department of Biology, Princeton University and the Stanford University School of Medicine.

Salk Institute receives $25 million gift from former Salk trustee Conrad T. Prebys

IN JUNE, THE SALK INSTITUTE RECEIVED a milestone gift: $25 million from San Diego philanthropist and former Salk trustee Conrad T. Prebys, to support cutting-edge biological research on a wide range of diseases. The gift is the single largest ever to the Institute's endowment, and in honor of Prebys' generosity, the Salk Institute auditorium, which regularly hosts talks by some of the world's most prominent scientists, has been named the Conrad T. Prebys Auditorium.

"The scientists at Salk are diving deep into understanding how our bodies operate at the molecular level and what happens when we get sick," says Prebys, a prominent real estate developer and stalwart supporter of San Diego institutions. "It is vital work that must be done before we can really conquer disease. We need this foundational science to lay the underpinnings for new therapies and cures. I'm honored to play a role in supporting this important research."

A native of South Bend, Indiana, Prebys was raised in a neighborhood where most of the residents worked in local factories. Encouraged by an inspirational teacher, he was the first of five brothers to graduate from a university. He went on to found Progress Construction Company, a developer of real estate enterprises in California and Texas.

When he was a child, Prebys' brother contracted polio, and he saw the power of scientific research to cure disease when Jonas Salk developed the first polio vaccine.

Prebys has long been a supporter of the Salk Institute and previously served on the Institute's Board of Trustees. Earlier, he gave $2 million to establish the Conrad T. Prebys Endowed Chair in Vision Research for **Thomas Albright**, one of the Institute's neuroscientists. He has also been a longtime supporter of Symphony at Salk, the Institute's annual gala.

His latest gift contributes to the Campaign for Salk, the Institute's first-ever fundraising campaign, and will help grow the Institute's unrestricted endowment—one of the priorities of the campaign. Funding from unrestricted endowment allows the Institute to address its most critical research needs by providing flexibility in how the funding is used.

The Campaign for Salk was launched publicly in January 2012, with the goal of raising $300 million by July 2015. Prebys' gift brings the total raised so far to more than $275 million.

"Mr. Prebys is renowned for his remarkable generosity and his vision in boosting San Diego by supporting its pillar institutions," says Salk president **William Brody**. "His gift to Salk's unrestricted endowment provides the financial flexibility for Salk to adapt and thrive as technology, science and human needs evolve, leaving a lasting legacy."

> "Mr. Prebys is renowned for his remarkable generosity and his vision in boosting San Diego by supporting its pillar institutions."
>
> – WILLIAM BRODY

Salk Science Leads to Discoveries.

IMPACTING HUMAN HEALTH BEGINS AT THE SALK.

Scientific discovery at the Salk Institute is made possible through annual contributions from individuals, organizations, corporations and foundations. Your support will accelerate the pace of breakthroughs in understanding disease and pave the way to new drug therapies. To learn more, please visit **www.salk.edu/support** or call 858.453.4100 x1405.

Get Involved

FRIENDS OF SALK

Unrestricted gifts, in any amount, provide funding where it is most needed and allow our scientists to conduct critical early-stage research. Contributors up to $2,500 receive *Inside Salk* magazine and invitations to annual events.

SALKEXCELLERATORS

The Salkexcellerators program is focused on making Salk science accessible to a younger generation of business professionals, entrepreneurs and volunteers. Donors receive *Inside Salk* magazine and invitations to private receptions and lectures with Salk's renowned scientists. Salkexcellerators meet in La Jolla and New York City, and engagement ranges from $500 to $5,000.

PRESIDENT'S CLUB

President's Club donors fulfill a central role for the Institute and provide the flexibility to respond to Salk's greatest needs. Contributors of $2,500 – $25,000 enjoy unique opportunities to interact with our scientists in the lab and receive Salk publications.

CHAIRMAN'S CIRCLE

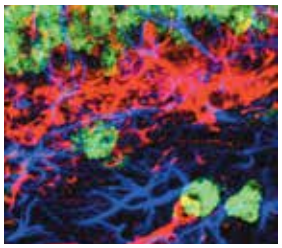
Chairman's Circle visionary donors support the Institute's mission with unrestricted annual gifts of $25,000 and above. Their generous support fills a vital need for the Institute by providing the world's finest minds in science with the resources to pursue discoveries at the frontier of human knowledge. Donors are invited to exclusive lab tours and special events with senior researchers that provide opportunities to discuss specific areas of interest. Donors receive Salk publications and individual reports on the impact of their gifts.

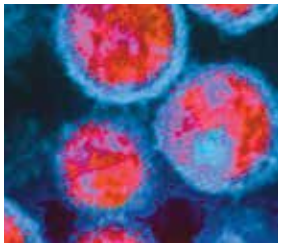
SPECIAL PROJECTS

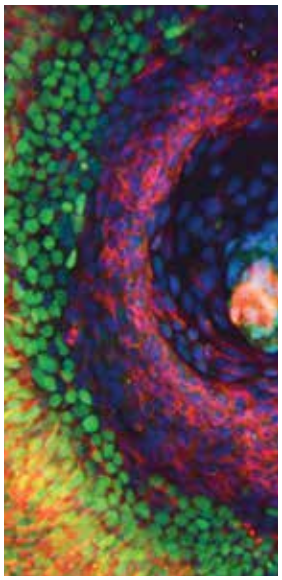
If you have a special interest in one of Salk's areas of research, such as cancer, aging, diabetes, neuroscience, genetics, vision or plant biology, you may designate your gift to support investigations in that field. You may also elect to support the work of a young scientist with a fellowship or Salk's education outreach programs. You will be privy to exclusive updates and invitations.

PARTNERS IN RESEARCH

Salk's legacy society, Partners in Research, welcomes those who have included Salk in their estate plans. Charitable gift planning is a powerful way of ensuring your legacy lives on, and it can maximize tax and other financial benefits to you, your family, and the Institute. Partners in Research members receive special communications and are invited to events throughout the year.







Insider's View

William R. Brody, MD, PhD
President, Salk Institute
Irwin Jacobs Presidential Chair

BENJAMIN FRANKLIN, PERHAPS THE WISEST OF OUR nation's founders, wrote the oft-repeated adage: *"An ounce of prevention is worth a pound of cure."* But even the wise and practical Mr. Franklin made mistakes where prevention was concerned.

Around the time Franklin wrote these words, a deadly smallpox epidemic was sweeping across the United States and the rest of the world. The smallpox inoculation technique of the time had originated in Africa. An African servant of the clergyman Cotton Mather in Boston explained to Mather the use of smallpox inoculation in West Africa. Mather noted this down and convinced a local doctor, Zabdiel Boylston, to try this method during the Boston smallpox outbreak of 1721.

At the time, inoculation used a string that had been drawn through the pustule of a smallpox victim and then was dried and saved. For inoculation, an incision was made, and the string was drawn through it to infect the recipient with attenuated smallpox. During that period, the recipient would be contagious to others but would more often get a milder form of smallpox with a lower risk of death. The mortality rate was 2 percent for inoculated people versus 15 percent for non-inoculated people.

Unfortunately, the Franklin brothers' Boston newspaper was critical of the 1721 smallpox inoculation, and Franklin decided not to inoculate his children, with disastrous consequences.

"In 1736, I lost one of my sons," Franklin would later write, "a fine boy of four years old, by the smallpox taken in the common way. I long regretted bitterly and still regret that I had not given it to him by inoculation."

Following the Boston outbreak, inoculation became the state-of-the-art treatment until Dr. Edward Jenner's discovery of the more effective and lower-risk cowpox vaccination, which was published in 1798. (Recipients of Jenner's vaccine were not contagious to others, an important improvement.)

Despite being one of the leading thinkers of his time, Franklin made a tragic miscalculation about the importance of inoculation. Judging from his famous quip about prevention, he seems to have learned from his mistake, yet it is a mistake that continues to plague individuals and societies—one that finds its roots in popularized misinformation.

When Jonas Salk introduced his vaccine in 1955, using killed polio virus particles, the vaccine encountered significant scrutiny in the press, including an article by the muckraking columnist Walter Winchell, who claimed the use of the Salk vaccine would kill thousands of children. It was suspected that inflammatory journalism was being pushed sotto voce by Salk's rival, Dr. Albert Sabin, who was developing an oral vaccine using live attenuated polio virus.

The United States switched to the oral polio vaccine (OPV), but it was eventually abandoned in favor of the Salk vaccine because there were isolated cases of polio that occurred in children who had been inoculated with the OPV.

The philosopher Georg Wilhelm Friedrich Hegel wrote, *"We learn from history that we do not learn from history."* And on the eve of what would have been Jonas Salk's 100th birthday were he living today, I have to wonder if Hegel wasn't right—even as I hope he wasn't. Despite the remarkable discovery of the Salk vaccine, we've learned recently that polio has not been eradicated worldwide. Even more profound, skepticism about the potential dangers of polio and other vaccines in our country has led to increasing abandonment of vaccinations, and we are beginning to see the reemergence of diseases like measles and whooping cough that can be effectively prevented by the use of vaccines.

While the work of Salk scientists doesn't necessarily lead them to develop vaccines, many of their discoveries about cells, bacteria, viruses and immunology lay the foundation for future vaccine development for diseases like malaria, Ebola and, perhaps one day, HIV. But these preventives, like those of Franklin's time and those available today, will only be effective if they are used.

Franklin's own poignant experience only serves to emphasize that the route to wellness and healthy aging is to avoid encountering a disease to the best extent possible, or at least to defer as long as possible the onset of a debilitating illness.

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7 **Salk Women & Science**

22 **San Diego Salkexcellerators**

NOVEMBER

2 **Salk Science and Music Series featuring the Eldar Trio**

DECEMBER

7 **Salk Science and Music Series featuring Rachel Kudo and Karen Joy Davis**

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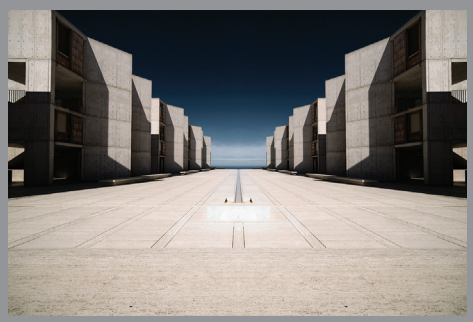

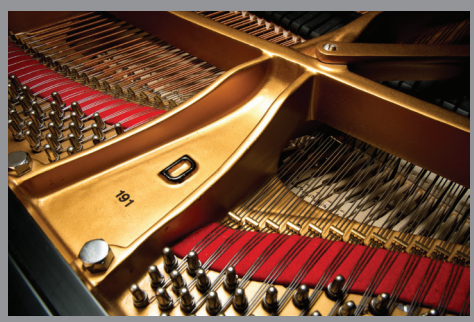

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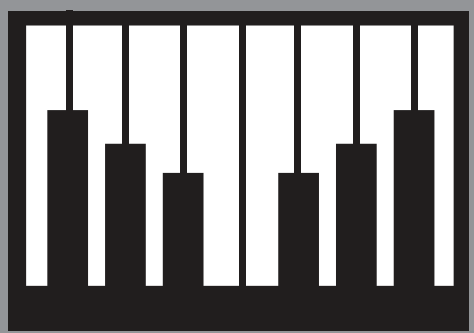

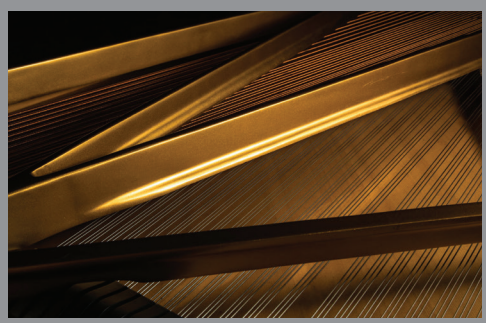

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