

04 | 16

WHERE CURES BEGIN.

insideSalk



AN INTERVIEW WITH SALK PRESIDENT
Elizabeth Blackburn



Dear Friends,

For those of you not yet acquainted with Salk's new president, I'm pleased and honored to introduce Nobel laureate Elizabeth Blackburn.

Elizabeth joins the Institute at a remarkable time in the history of biological research, an era when science is rapidly uncovering the underpinnings of health and disease. The future offers incredible promise, and she is the right person to lead Salk forward.

Her scientific accomplishments are extraordinary. She shared the Nobel Prize in Physiology or Medicine in 2009 for discovering the molecular nature of telomeres, the protective caps on chromosomes, and for co-discovering telomerase, an enzyme that maintains telomeres. Her discoveries launched an entire field of research into the aging process and may offer novel routes for managing age-related diseases such as cancer, heart disease, diabetes and dementia.

In addition to her Nobel Prize and numerous other prestigious scientific awards, Elizabeth won the respect of the international scientific community for her warm collegiality and abiding commitment to public service. Among her innumerable contributions, she was president of both the American Association for Cancer Research and the American Society for Cell Biology and served on editorial boards for influential journals such as *Cell* and *Science*.

Elizabeth once said in an interview that the best advice she ever received was to "put yourself in the very, very best environment where the best people are and best work is going on." I think she's done just that in joining us here at the Salk Institute and we couldn't be more optimistic about the future under her leadership.

A handwritten signature in black ink, appearing to read "Irwin Mark Jacobs".

Irwin Mark Jacobs, ScD
Chairman, Salk Board of Trustees



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ON THE COVER:

Salk President Elizabeth Blackburn

A FRESH LOOK FOR INSIDE SALK

With our new Salk president and updated website, it was time to give *Inside Salk* a makeover. We hope you'll enjoy the redesign of the Institute's flagship magazine. Let us know what you think at communications@salk.edu.

— *Inside Salk* staff

PRESIDENT'S LETTER

Dear Friends,

One thing that has become abundantly clear to me in my short time serving as Salk's president is that the Institute is continually reinventing itself—it is a wellspring of fresh ideas and surprising discoveries.

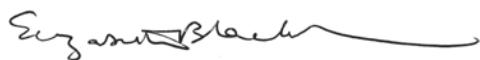
This is, of course, the result of Jonas Salk's vision for this wonderful place, which he built as a "crucible of creativity." The building itself is special: stunning architecture that inspires and enables the best science. So, too, is the Institute's unique culture. When Jonas Salk founded the Institute, he gathered together some of the world's best thinkers, and that ethos of collaborative genius has persisted through the decades.

Salk's scientists are now, as always, brilliant, inspiring and intensely curious. They have the generosity of mind and spirit to pursue biological knowledge for its own sake, while always keeping in mind the tremendous benefit such knowledge can have on improving lives.

Throughout history, we have witnessed time and time again the impacts of fundamental science on our understanding of the world and on human wellbeing. Jonas Salk's discovery of the polio vaccine stands as a shining example of this. As I look out to the future, there is a wonderful path that lies ahead of us. We have tremendous possibilities in science right now, thanks to a convergence of a critical mass of deep knowledge with the emergence of powerful new technologies.

Suddenly, we can ask questions we'd never dare to ask and formulate ideas that spur entirely new paradigms. It is a truly exhilarating time. I am honored to be a part of it and to lead the Salk Institute into a new era of biological inquiry and understanding.

Sincerely,

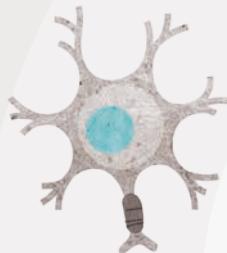
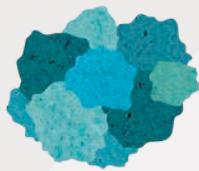


Elizabeth Blackburn
President, Salk Institute
Irwin M. Jacobs Presidential Chair



We have tremendous possibilities in science right now, thanks to a convergence of a critical mass of deep knowledge with the emergence of powerful new technologies.

DISCOVERIES



NEUROSCIENCE

New technologies are allowing us to explore the brain as never before. We are entering a new era in neuroscience where our knowledge of the brain is beginning to match the urgent need to prevent and treat diseases of the brain.



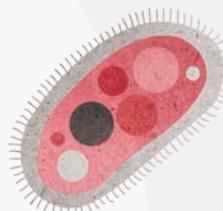
CANCER

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



GENETICS

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



MICROBIOME

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

RESEARCH AT SALK



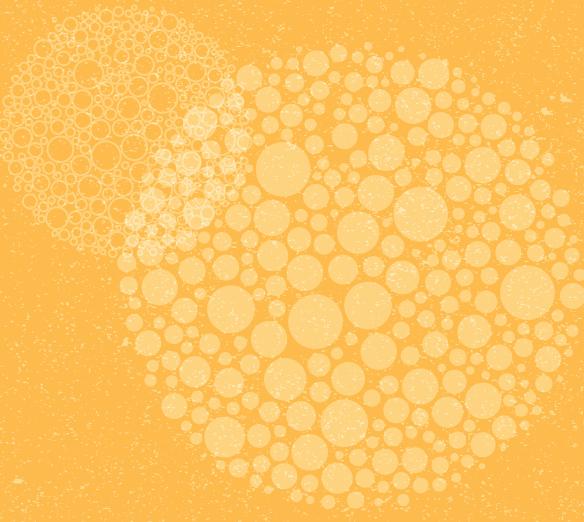
METABOLISM

We are working to understand human metabolism and what happens when this biological system breaks down. The problem is more important than ever, given the increasing burden that diabetes and other metabolic dysfunctions have on human health and society.

PLANT BIOLOGY

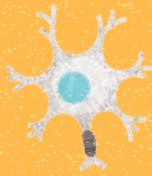
To match human population growth, world agricultural production must double over the next quarter century. At Salk, we study plants so that humans will have the food, clothing, energy and medicines they need now and in the future.

DISCOVERIES



In the last few months, Salk scientists have made breakthroughs in biology and health and have been published in prestigious journals, including *Science*, *Nature*, *Cell*, *PNAS* and *eLife*.

Discoveries gained local and global attention—most notably in *The New York Times* and dozens of other magazines, newspapers, TV channels and radio stations. Read on to see how Salk scientists are making a difference.



NEUROSCIENCE

SCIENCE 10/30/2015

Why brushing movements on our hairy skin make us scratch

Martyn Goulding and collaborators were able to show that the spinal neurons involved in the tingling sensation caused by a light touch are different from those transmitting pain. This is the first study that reveals the presence of a dedicated neural pathway for this particular sensation in the spinal cord. The new results lend insights into potential mechanisms of chronic itch, which can be caused by eczema, diabetic neuropathy, multiple sclerosis and certain types of cancers. It may also help explain why some people affected by itch are unresponsive to antihistamine drugs.

NATURE 10/28/2015

Bipolar patients' brain cells predict response to lithium

The brain cells of patients with bipolar disorder, characterized by severe swings between depression and elation, are more sensitive to stimuli than other people's brain cells, as revealed by Rusty Gage's lab. The discovery is among the first to show at a cellular level how the disorder affects the brain. The study found that cells from lithium responder patients showed weakened excitability after growing in the lithium while cells from patients who hadn't been helped by the drug remained hyperexcitable. The findings don't yet explain why lithium works for some patients and not others, but offer a starting point to better study bipolar disorder.

NATURE 10/21/2015

Targeting mutant proteins might be silver bullet for neurodegenerative diseases

Scientists have unraveled how mutant molecules damage the nervous system of people with Charcot-Marie-Tooth (CMT) disease, a group of disorders that hinder people's ability to move and feel sensation in their hands and feet, according to a paper co-led by Samuel Pfaff. The team used a range of neurogenetic, gene therapy, biochemical and structural biology research techniques to discover that the mutant GlyRS enzyme blocked molecular signals important for maintaining the health of motor neurons. The findings suggest a possible avenue for developing new therapies for CMT.

PORTRAITS OF

Heady science pain
of how the brain



THE MIND

It's a picture
that works



SCIENCE

12/18/2015

Loss of tiny genetic molecules could play role in neurodegenerative diseases

A tiny sliver of DNA—several thousand times smaller than a typical gene—produces a molecule that has crucial influence over whether people have control over their muscles. Samuel Pfaff and colleagues report that animals unable to produce just one type of many genetic molecules called microRNAs develop symptoms of devastating neurodegenerative diseases like amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease) and spinal muscular atrophy (SMA). The findings upend previous understanding of the role of microRNAs in the nervous system and may open a door to new avenues for treating neurodegenerative disorders.

MOLECULAR PSYCHIATRY

10/27/2015

Making serotonin-transmitting neurons in a dish

A team led by Rusty Gage has taken human skin cells and turned them into neurons that signal to one another using serotonin, a brain chemical crucial to mental wellbeing. Although serotonin neurons comprise only a small fraction of the brain's cells, these neurons are tied to debilitating disorders such as major depression, schizophrenia and autism. Depression is commonly treated using selective serotonin reuptake inhibitors, which heighten serotonin signaling in the small gaps between neighboring neurons. The new method of generating serotonin-transmitting neurons gives researchers a lens with which to study neurotransmitter mechanisms and how they may go awry in mental illness.

AGING

11/12/2015

Experimental drug targeting Alzheimer's disease shows anti-aging effects

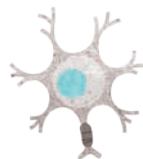
David Schubert's lab found that an experimental drug candidate aimed at combating Alzheimer's disease has a host of unexpected anti-aging effects in animals. His team expanded upon their previous development of a drug candidate, called J147, showing that it worked well in a mouse model of aging not typically used in Alzheimer's research. When these mice were treated with J147, they had better memory and cognition, healthier blood vessels in the brain and other improved physiological features.

CELL REPORTS

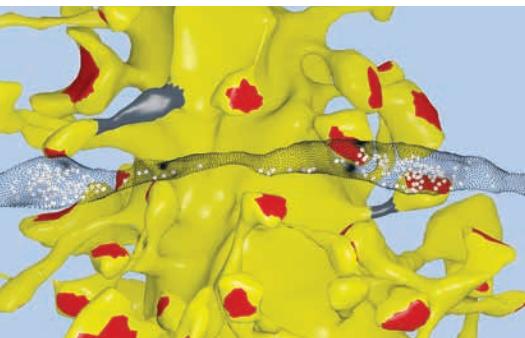
1/14/2016

Autism-linked protein lays groundwork for healthy brain

A gene linked to mental disorders helps lay the foundation for a crucial brain structure, according to research from Dennis O'Leary's lab. Researchers found that when the gene MDGA1 is disabled in early development, the neuron precursors in the cerebral cortex migrated to the wrong places in the brain and, without MDGA1, the cerebral cortex loses about half its neurons. These new results suggest that mutations in MDGA1 while the cortex is developing could produce snowball effects leading to the development of brain disorders.



MEMORY CAPACITY OF BRAIN IS 10 TIMES MORE THAN PREVIOUSLY THOUGHT



Scientists uncovered two synapses from the axon of one neuron (translucent black strip) forming onto a second neuron's dendrite (yellow). The synaptic contact areas (red), neck diameters (gray) and number of presynaptic vesicles (white spheres) of these two synapses differ only by about eight percent.

Terrence Sejnowski and colleagues published work in *eLife* in January 2016 demonstrating critical insight into the size of neural connections and putting the memory capacity of the brain far higher than common estimates.

A key part of brain activity happens when branches of neurons, much like electrical wire, interact at certain junctions, known as synapses. Neurotransmitters travel across the synapse to tell the receiving neuron to convey an electrical signal to other neurons. Synapses are still a mystery, though their dysfunction can cause a range of neurological diseases.

While building a 3D reconstruction of rat hippocampus tissue, the Salk team observed a single axon (output ‘wire’) from one neuron formed two synapses reaching out to a single dendrite (input ‘wire’) of a second neuron, signifying that the first neuron seemed to be sending a duplicate message to the receiving neuron. The team measured the difference in size between these two synapses in the hopes of gleaning insight into the range between synaptic sizes, which so far had only been classified as small, medium and large. They were surprised to find that the synapses differed by only eight percent.

Because the memory capacity of neurons is dependent upon synapse size, this eight percent difference turned out to be a key number the team could then plug into algorithmic models of the brain. This allowed them to measure how much information could potentially be stored in synaptic connections.

It was known before that the range in sizes between the smallest and largest synapses was a factor of 60 and that most synapses were simply classified as small. But armed with the knowledge that synapses of all sizes could vary in increments as little as 8 percent between sizes within a factor of 60, the team determined there could be about 26 categories of sizes of synapses, rather than just a few. In computer terms, 26 sizes of synapses correspond to about 4.7 “bits” of information. Previously, it was thought that the brain was capable of just one to two bits for short- and long-term memory storage in the hippocampus.

Aside from helping to better understand the brain, the discovery could also aid computer scientists in building ultraprecise—but energy-efficient—computers, particularly ones that employ “deep learning” and artificial neural nets, techniques capable of sophisticated learning and analysis. 

AS SEEN IN

SCIENTIFIC AMERICAN

BBC

Discover

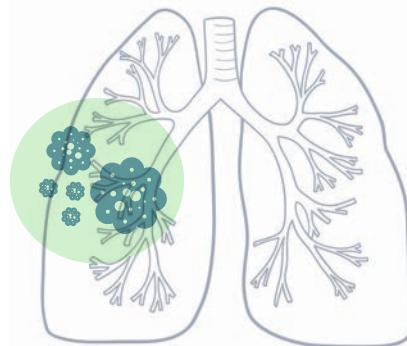
POPULAR SCIENCE



SCIENTISTS FIND KEY DRIVER FOR TREATMENT OF LETHAL BRAIN CANCER

A person diagnosed with the brain cancer glioblastoma multiforme typically survives 15 months, if given the best care. Inder Verma's lab discovered a key to how these tumor cells proliferate so quickly—and ways to turn this engine of tumor growth into a target for cancer treatment. The work was published January 8, 2016 in the journal *Science Advances*.

To study how glioblastoma multiforme spreads, Verma's team focused on a transcription factor called nuclear factor kB (or NF-kB). A transcription factor is a protein that binds to DNA and controls the fate of gene expression for a particular set of genes. Verma and colleagues ran a battery of tests to show how overzealous NF-kB activity pushed the cancer cells to proliferate, and how stopping NF-kB slowed cancer growth and increased survival in mice. The scientists fed mice a peptide (called NBD) that is known to block NF-kB activity when NF-kB is triggered by cytokines (proteins produced by the immune system). The NBD peptide easily traveled across the central nervous system and successfully penetrated glioblastoma tumor cells. Treating mice with the NBD peptide doubled their typical survival time compared to mice that didn't get the NBD peptide. **IS**



Salk scientists discovered a molecule called EphA2 that acts as a tumor suppressor in certain types of lung cancer.

MOLECULAR “BRAKE” STIFLES HUMAN LUNG CANCER

By testing over 4,000 genes in human tumors, Inder Verma's team found an enzyme responsible for suppressing lung cancer, which affects nonsmokers as well as smokers and is the leading cause of cancer-related deaths worldwide. This enzyme, called EphA2, normally polices a gene responsible for tissue growth. But when EphA2 is mutated, the Salk team discovered, cellular systems can run amok and quickly develop tumors. The research, published the week of November 2, 2015 in *PNAS*, suggests that EphA2 could be a new target for a subset of lung cancer. **IS**



SALKEXCELLERATORS *revved into 2016*

A talented trifecta of Salk cancer researchers—Geoffrey Wahl, Amy Rommel and Reuben Shaw (above, from left)—drew 75 attendees to the Salkxcellerators program in January at the Institute. The scientists spoke of their groundbreaking work pursuing the origins of cancers and better understanding the tumor suppressor P53 and glioblastoma. Also announced was a \$20,000 grant from Merck to help fund early career scientists.

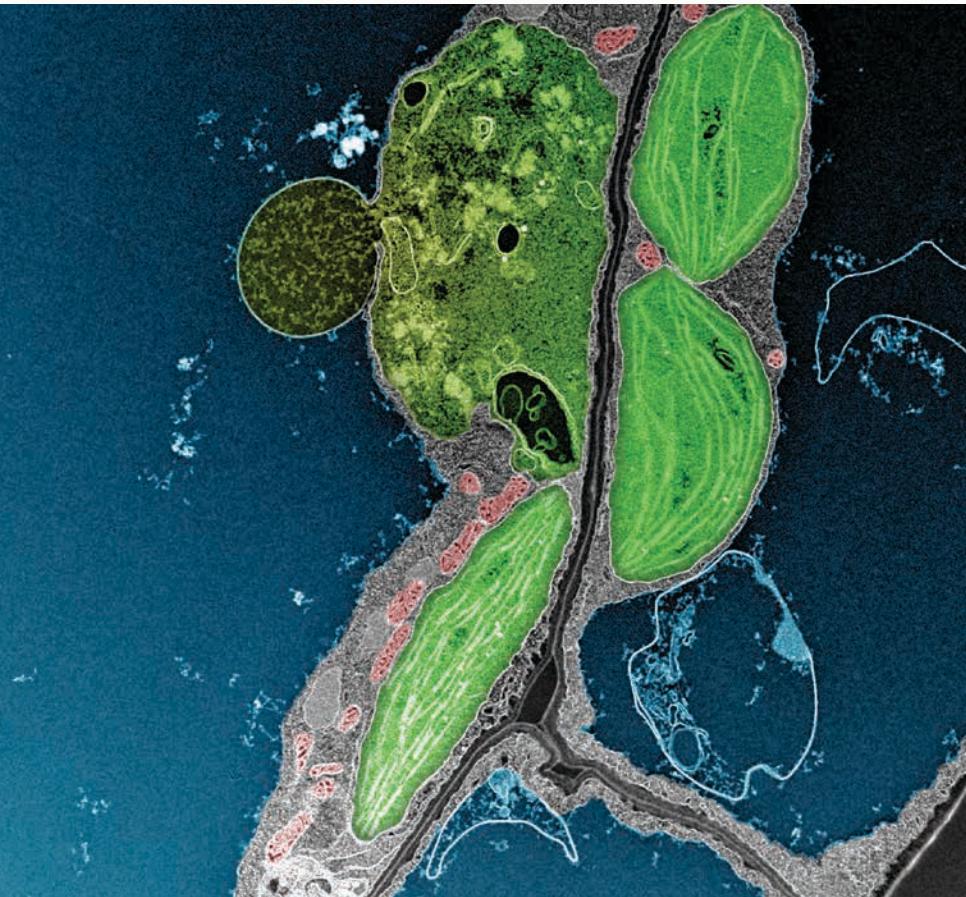
Salkxcellerators, the next generation of community members committed to supporting scientific discovery at Salk, meets throughout the year.

To learn more:

Contact Jane Rhett,
director of Annual Giving
(858) 453-4100 x1521
jrhett@salk.edu
www.salk.edu/salkxcellerators



In plant cells, most of the chloroplasts (green) and mitochondria (red) appear healthy. However, cells degrade dysfunctional chloroplasts (such as in the top left of this image) so material can be reused in the cell.



CELLULAR DAMAGE CONTROL SYSTEM HELPS PLANTS TOUGH IT OUT

The command center of the cell, the nucleus, occasionally sends out signals to destroy all of the 50-100 chloroplasts in the cell, such as in autumn when leaves turn brown and drop off.

New research from Joanne Chory's lab, published in *Science* on October 23, 2015, reveals details into a fundamental mechanism of how plants manage their energy intake. This new mechanism could potentially be harnessed to improve crop yield.

Plants have cellular organelles akin to tiny solar panels in each leaf. These microscopic structures, called chloroplasts, convert sunlight into chemical energy to enable the plant to grow. The command center of the cell, the nucleus, occasionally sends out signals to destroy all of the 50-100 chloroplasts in the cell, such as in autumn when leaves turn brown and drop off. However, the Salk team found out how the plant nucleus begins to degrade and reuse the materials of select, malfunctioning chloroplasts—a mechanism that had been suspected but never shown until now.

The team found that the cells in the *Arabidopsis* plant marked damaged chloroplasts for degradation with a protein tag called ubiquitin, which is used in organisms from yeast to humans to modify the function of a protein. Under closer investigation, the team observed that a protein called PUB4 was initiating the tagging.

While PUB4 had been tied to cell death in other work, the Salk team showed that this protein starts the degradation of chloroplasts by placing ubiquitin tags to mark the organelle for cellular recycling. Uncovering biological mechanisms such as these leads researchers a step closer to controlling chloroplasts and designing crops that are more resistant to stressors. ■

AS SEEN IN

The New York Times

HERE COMES THE SUN: CELLULAR SENSOR HELPS PLANTS FIND LIGHT

Despite seeming passive, plants wage wars to outgrow each other and absorb sunlight. If a plant is shaded by another, it becomes cut off from essential sunlight it needs to survive. Scientists in Joanne Chory's lab have discovered a way by which plants assess the quality of shade to outgrow menacing neighbors, a finding that could be used to improve the productivity of crops. The work, published December 24, 2015 in *Cell*, shows how the depletion of blue light detected by molecular sensors in plants triggers accelerated growth to overcome a competing plant.

The work upends previously held notions in the field. It was known that plants respond to diminished red light by activating a growth hormone called auxin to outpace its neighbors. However, this is the first time researchers have shown that shade avoidance can happen through an entirely different mechanism: instead of changing the levels of auxin, a cellular sensor called cryptochrome responds to diminished blue light by turning on genes that promote cell growth. This study is the first to show how cryptochromes promote growth in a shaded environment. **IS**

A graft between two genotypes of *Arabidopsis thaliana* is shown in a confocal microscopy image. One genotype has plasma membranes marked in yellow, and the other marked in red.

Credit: Charles Melnyk at The Sainsbury Laboratory, Cambridge University



GRAFTED PLANTS' GENOMES CAN COMMUNICATE WITH EACH OTHER

Agricultural grafting dates back nearly 3,000 years. By trial and error, people from ancient China to ancient Greece realized that joining a cut branch from one plant onto the stalk of another could improve the quality of crops. Now, Joseph Ecker and collaborators have combined this ancient practice with modern genetic research to show that grafted plants can share epigenetic traits, according to a paper published the week of January 18, 2016 in *PNAS*.

The work showed that epigenetic information in the form of tiny molecules called sRNAs is transferred between the two plants and can change one another's gene expression. sRNAs contribute to a gene silencing process called DNA methylation, where molecular markers bind along DNA to block the cell's machinery from expressing the genes under the markers. It turns out that thousands of sites along the *Arabidopsis thaliana* genome were silenced by transferred sRNAs. The team plans to continue to explore the epigenetic effects of mobile RNA in other plants, pursuing revelations that could eventually help growers better manipulate crops. **IS**



When mitochondria are under attack, cells send an emergency alert instructing mitochondria to break apart.



HOW THE CELL'S POWER STATION SURVIVES ATTACKS

Mitochondria, the power generators in our cells, are essential for life. When they are under attack—from poisons, environmental stress or genetic mutations—cells wrench these power stations apart, strip out the damaged pieces and reassemble them into usable mitochondria. Now, Reuben Shaw's lab has uncovered an unexpected way in which cells trigger this critical response to threats, offering insight into disorders such as mitochondrial disease, cancer, diabetes and neurodegenerative diseases—particularly Parkinson's disease, which is linked to dysfunctional mitochondria. The work was published January 15, 2016 in *Science*.

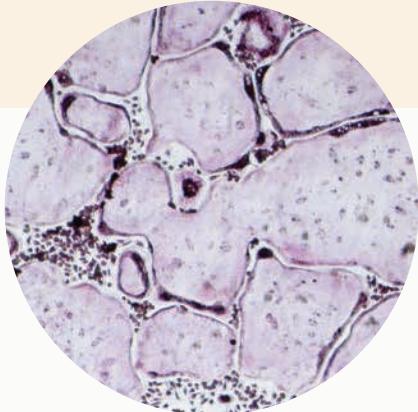
The team found that when cells are exposed to mitochondrial damage, a central cellular fuel gauge, the enzyme

AMPK, sends an emergency alert to mitochondria instructing them to break apart into many tiny mitochondrial fragments. Drilling down further, the researchers found that AMPK actually acts on two areas of a mitochondrial receptor, called mitochondrial fission factor (MFF), to start the process. MFF calls over a protein, Drp1, that binds and wraps around the mitochondrion like a noose to twist and break it apart.

Interestingly, AMPK is activated by the widely used diabetes therapeutic metformin, as well as exercise and a restricted diet. The new findings suggest that some of the benefits from these therapies may result from their effects in promoting mitochondrial health. **IS**

Scientists found that cholesterol affects a protein in osteoclasts (pictured), large cells in the bone that help break down and repair bone tissue.

Credit: UT Southwestern Medical Center

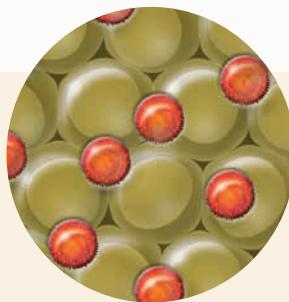


NEW TIE BETWEEN CHOLESTEROL AND BONE DENSITY

Alan Saghatelian and collaborators at the University of Texas Southwestern Medical Center uncovered how lipid metabolism is involved in maintaining bone health. Using a method developed in the Saghatelian lab, the team discovered that cholesterol can bind to a protein called estrogen-related receptor alpha that regulates bone density. This finding, published in *Cell Metabolism* on January 14, 2016, suggests that drugs commonly used to manage cholesterol levels also impact bone density and points to newer and better drugs to treat bone diseases. **is**

BLOCKING IMMUNE CELL TREATS NEW TYPE OF AGE- RELATED DIABETES

Diabetes is often the result of obesity and poor diet choices, but for some older adults the disease might simply be a consequence of aging. New research has discovered that diabetes—or insulin resistance—in aged, lean mice has a different cellular cause than the diabetes that results from weight gain (type 2). And the findings point toward a possible cure for what the co-leading scientists, Ronald Evans and Ye Zheng, are now calling a new kind of diabetes (type 4). In mice with age-related disease, the labs found abnormally high levels of immune cells called T regulatory cells (Tregs) inside fat tissue. Mice with obesity-related diabetes, on the other hand, had normal levels of Tregs within the tissue, despite having more fat tissue. When Tregs were blocked from accumulating in the fat, mice no longer developed type 4 diabetes in old age. The work was published November 18, 2015 in *Nature*. **is**



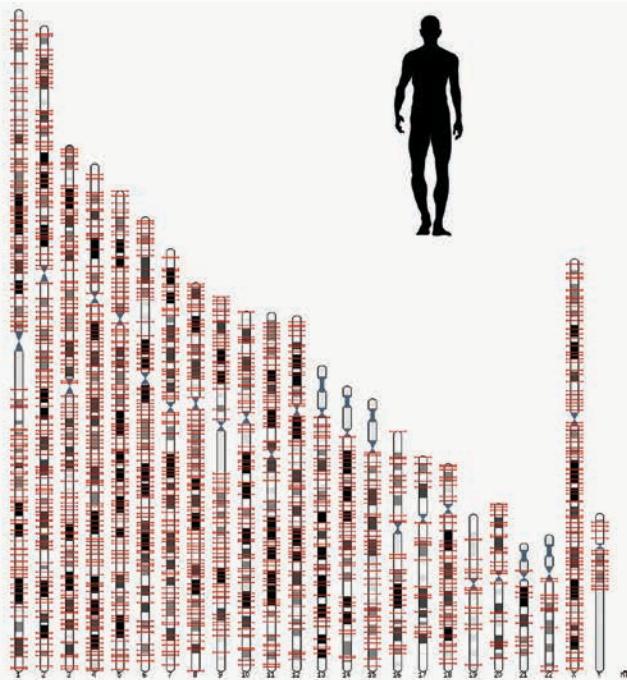
In aged mice with diabetes, Tregs are overexpressed in fat tissue and trigger insulin resistance. When Tregs are blocked, the fat cells in mice become insulin sensitive again.

FIGHTING LIVER FIBROSIS, THE WOUND THAT NEVER HEALS

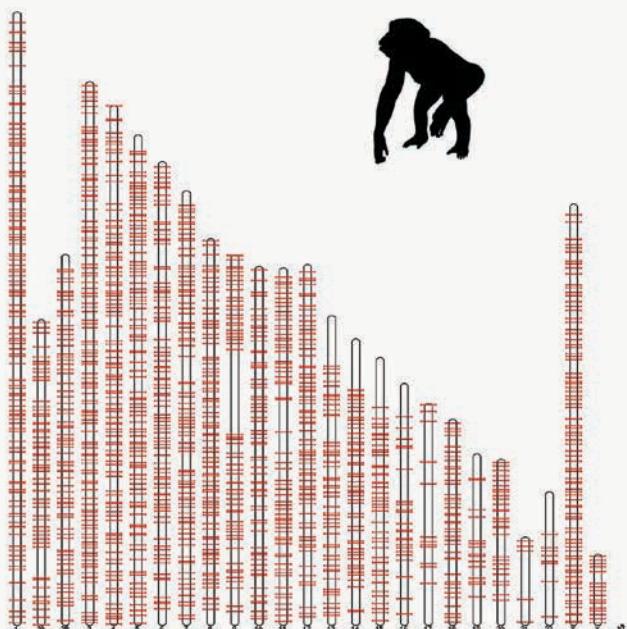
Chronic damage to the liver eventually creates a wound that never heals. This condition, called fibrosis, gradually replaces normal liver cells—which detoxify the food and liquid we consume—with more and more scar tissue until the organ no longer works. Scientists led by Ronald Evans have identified a drug that halts this unchecked accumulation of scar tissue in the liver. The small molecule, called JQ1, prevented as well as reversed fibrosis in animals and could help the millions of people worldwide affected by liver fibrosis and cirrhosis, caused by alcoholism and diseases like hepatitis. These results were published in *PNAS* the week of December 7, 2015. **is**



A



B



Salk researchers discovered a new genetic component, called ORFO, spread throughout the DNA of humans, chimps and most other primates. This image shows the locations of ORFO on human (A) and chimp (B) chromosomes.

PROTEIN FACTORIES HIDDEN IN HUMAN JUMPING GENES

In a paper published October 22, 2015 in *Cell*, Rusty Gage's lab reported a previously unknown wellspring of genetic diversity in humans, chimps and most other primates. This diversity arises from a new component of itinerant sections of mobile genetic code known as jumping genes.

Gage and colleagues found human and chimp DNA peppered with sequences of genetic code they dubbed ORFO, which spreads throughout the genome on jumping genes. The ORFO sequences may produce hundreds or even thousands of previously unknown proteins. The abundance of ORFO instances in the human genome suggests that it played—and still plays—an important role in evolutionary diversity and flexibility by serving as a mechanism for generating novel proteins. The discovery of these mobile protein factories may also shine light on the origins of genetic mutations responsible for cancer and other diseases.

The scientists plan to next determine how many of the instances of ORFO actually code for proteins and to investigate what function those proteins serve. They are also interested in exploring ORFO's role in neurological disorders such as schizophrenia, where previous studies have suggested jumping genes may be involved. **IS**



MICROBIOME

'SUPERHERO' MICROBIOME BACTERIA PROTECT AGAINST DEADLY SYMPTOMS DURING INFECTION

As concerns over deadly antibiotic-resistant strains of 'superbug' bacteria grow, Janelle Ayres and colleagues are offering a possible solution to the problem: 'superhero' bacteria that live in the gut and move to other parts of the body to alleviate life-threatening side effects caused by infections.

In a paper published October 30, 2015 in *Science*, Ayres' lab reported finding a strain of microbiome *Escherichia coli* bacteria in mice capable of improving

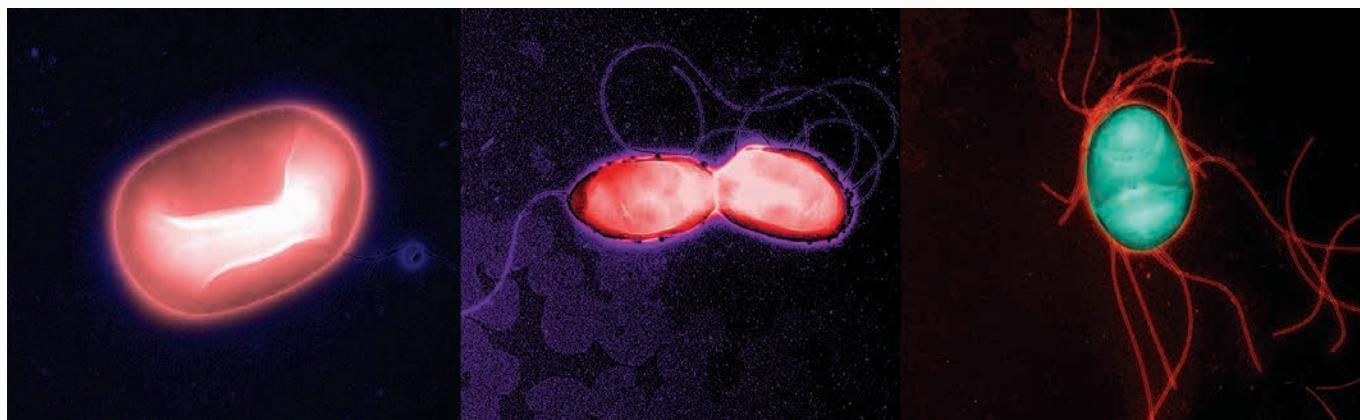
the animals' tolerance to infections of the lungs and intestines by preventing wasting—a potentially deadly loss of muscle tissue that occurs in serious infections. If a similarly protective strain is found in humans, it could offer a new avenue for countering muscle wasting, which afflicts patients suffering from sepsis and hospital-acquired infections (many of which are now antibiotic resistant).

The Salk team identified a population of laboratory mice that appeared resistant to muscle wasting. By comparing the makeup of the intestinal microbiomes of these mice to mice that lacked resistance, the team identified a strain of *E. coli* that was present only in the wasting-resistant mice. When normal mice were given an oral treatment of

this beneficial *E. coli* strain, they gained the ability to maintain their muscle and fat mass during intestinal infections and pneumonia.

Collaborating with the laboratory of Ronald Evans, the scientists discovered that during an infection by the pathological bacteria, the *E. coli* left the gut and moved into the fat tissues to induce protective responses that nourish the muscles. Normally, mice with lung and intestinal infections see a drop in a hormone known as insulin-like growth factor 1 (IGF-1), a molecule that signals the body to retain muscle mass. But the protective *E. coli* activated the IGF-1 pathway in the fat tissues, preserving normal IGF-1 levels and maintaining the animal's muscle in spite of the pathogenic infections. The team will investigate how long this *E. coli* strain can hold off the pathogens; whether the body's immune system will eventually eradicate the harmful bacteria completely; and if such a microbe exists in humans. **IS**

Salk scientists found a strain of *E. coli* bacteria (left) that was able to stop muscle wasting in mice infected with either *Salmonella Typhimurium* (center) or *Burkholderia thailandensis* (right).



OBSE

RVATIONS

AN INTERVIEW WITH SALK PRESIDENT

Elizabeth Blackburn



Born in Hobart, Tasmania

1948



UNIVERSITY OF
CAMBRIDGE

Earns PhD in molecular biology,
University of Cambridge



Berkeley
UNIVERSITY OF CALIFORNIA

Joins University of California, Berkeley
as assistant professor



With Carol Greider, co-discovers telomerase,
an enzyme that restores telomere ends

1977

1978

1984

When Jonas Salk announced the discovery of the polio vaccine in 1955, Elizabeth Blackburn was six years old and busy collecting tadpoles and ants a world away in her native Tasmania. She couldn't have known it then, but science, discovery and Jonas Salk would all play important roles in her future.

After his vaccine discovery, Salk went on to found the Salk Institute for Biological Studies and Blackburn went on to a distinguished career as a pioneering molecular biologist whose research would eventually earn her a Nobel Prize.

This January, Blackburn began serving as the new president of the Salk Institute, taking the helm of Jonas Salk's world-renowned scientific enterprise and leading an elite cadre of scientists as they push the frontiers of discovery in fields such as cancer, neuroscience, aging and plant biology.

"Few scientists garner the kind of admiration and respect that Dr. Blackburn receives from her peers for her scientific accomplishments and her leadership, service and integrity," says Irwin M. Jacobs, chairman of Salk's Board of Trustees. "Her deep insight as a scientist, her vision as a leader and her warm personality will prove invaluable as she guides the Salk Institute on its continuing journey of discovery."

Inside Salk sat down for a conversation with Blackburn as she settled into her new office overlooking the coast of La Jolla.

Did you ever consider a career outside of science?

When I was a teenager, I had classical music lessons all through school. I really loved music and I played competently. I thought, 'Wouldn't it really be great to be someone whose life is really all about music?' But another part of me was very realistic. Being competent at piano playing is a far cry from being a real performer and to love music isn't to mean you can make a career out of it.

So I had the wistful dream of being a musician. But I also knew I loved science, even as a teenager. For over 50 years—most of my life!—I have been front and center a laboratory scientist. Science, to me, was the best thing that I could do. I do still noodle on the piano, mostly just for my own relaxation. We have a piano in our house in San Francisco, and my husband and son would make themselves scarce when I'd play. The only one who would put up with it was our parakeet, that had no means of escape and would chirp away merrily along with various sonatas and other piano pieces I play.

Any other enduring passions besides science and music?

For years, I read every spy book and mystery book I could. More recently I've become fascinated by twentieth century history, especially the earlier part of that century, when the world went through such major events and transitions. Now I'm really enjoying biographies, because people are so interesting. I've recently been reading a fascinating book called *Jonas Salk: A Life* by Charlotte DeCroes Jacobs. He was really an extraordinary person. The house we are renting here in La Jolla just happens to be next to his house, which is intriguing.

When I was young, I read a biography on Marie Curie and that moved me very much, because I loved how she took on science. She had two kids whom she home schooled in physics. I loved the picture of this person who was so dedicated to science but was also a devoted mother. Her daughter who wrote the biography clearly adored her. That book really captivated my imagination about being a scientist.



Joins University of California, San Francisco
as full professor



1990

2001

2006

What made you decide to accept the position as president of Salk?

Because it's Salk! It's such a special place. Your heart does a little leap every time you first step into the courtyard. The architecture is so extraordinary; it makes you wonder what it does for creativity. There has to be some amazing synergism that neuroscientists will have to figure out. There's always been that special feeling about the place, and the science is really something special as well. So, when the possibility of becoming president came along, I got really excited. I told myself it would pass—but of course it didn't. [laughs] I really kept thinking about it, the next day and the next day, and I began to think, this could be real. A big part of my excitement was knowing the Institute as a non-resident fellow and having such an admiration for the scientists and the science that happens here and the ways it happens.

Will you miss running a lab and being engaged in your own research?

We have chapters in our lives. Even my scientific career went through many chapters. At different stages you could have called me a biochemist, a molecular biologist, a geneticist, a parasitologist, an RNA biologist, an enzymologist, somebody who works in cell biology, cancer and aging, and then a collaborator in clinical and human studies. All of those phases were different but always in some way focused on scientifically thinking about a central question: 'How do these ends of chromosomes work?' Which became: 'How does it relate to human lives?' I've really had my fun in the lab. Now the question is how to foster other people's scientific careers. I've mentored graduate students and postdocs all throughout my career, but always as part of my own research program. As president of Salk, I now have the opportunity and the responsibility to pursue that mission at a larger scale and especially to grow younger people's careers and successes in science.

Do people have misconceptions about science?

There is a visual stereotype of the lone scientist wearing a white coat—and the coat hangs very straight indeed. It somehow suggests that the work is rigid, boring and solitary. In fact, science is probably one of the most social things on the planet. It's all about ideas going viral among science communities. Scientists

think deeply much of the time but if they don't communicate what they did, in one sense it didn't happen. If you're doing a biological experiment and you don't write down what you did in a notebook or publish it in a paper, that experiment never existed, right? If it never makes it out of your mind, it doesn't advance science. So it's an incredibly social and communal kind of enterprise. Science also has this interesting dynamic of balancing rigor with creativity. It's a lot like art. You look at Picasso, and you think he's creating very free-form, simple-seeming works. But Picasso was taught early on how to draw in the most classic styles and he mastered those completely. His more creative work could launch from this rigorous training. The scientist's lab coat is an emblem of the rigorous platform that launches the real creativity in science.

The biological sciences have moved so rapidly in the past 60 years. What's left to learn?

I wonder in biology if we aren't where physics was in the nineteenth century. We know so much about the molecules, cells and cellular signaling and other fundamentals about how things work at one level, and yet, at another level we don't know a lot. We're very mystified by the complexity of the whole organism. We look at all of the elements and say, 'Gosh, how did this actually turn into a human who is functional for 70, 80, 90 or even 100 years?'

There was great confidence in nineteenth century physicists and a feeling that they had a handle on how things worked, but there were universes they hadn't even dreamed of. We're at this stage of justifiable pride in all we know about biology, and yet, we know it's still very tough. In a hundred years, scientists may look back and say, 'They knew a lot of great rigorous biology, but boy, they were so naïve.' We've already had a few surprises. For instance, how important RNA molecules are in many of the functions we thought proteins dominated. There are probably other worlds in biological systems that we've never imagined.

How is technology changing biological sciences?

Technology is letting us do remarkable things like study single cells and single molecules, and suddenly people are framing questions in ways that they never could before. There was no point in asking those questions in the past because there was no way to experimentally verify them. Technologies are now revealing



Included in *Time* magazine's list of world's 100 top influencers

2007

“You have to always be asking what makes a scientific community greater than the sum of its parts. At Salk, everybody is committed to this idea that doing science—great science—is not only the most exciting thing they do but also that this is what will make a lasting impact on human wellbeing.”

things that you couldn't see before, and suddenly you can visualize what's actually going on. This is opening up new understandings of biology—and therefore of disease. We can now ask questions about our biological complexity, about what makes things work so well, much better than would be expected. The more we understand these systems the better we will understand the diseases that disrupt them.

As president of Salk, what are your aspirations for your time at the Institute?

We can start with one very clear mission: to have great science thrive at Salk. So what does that mean? We'll need funding, of course, that's always critical, but money isn't enough. You can have all the money in the world, but if you don't have the right kind of environment that inspires people to do great science there's no point. You have to always be asking what makes a scientific community greater than the sum of its parts. At Salk, everybody is committed to this idea that doing science—great science—is not only the most exciting thing they do but also that this is what will make a lasting impact on human wellbeing. The important thing is making sure that we have a community of people devoted and enabled to do that. It's also important that people who train at Salk leave the Institute with not only the skill set to do rigorous, creative science, but with a passion to do really great science. ■



Awarded Nobel Prize in Physiology or Medicine for telomere discoveries

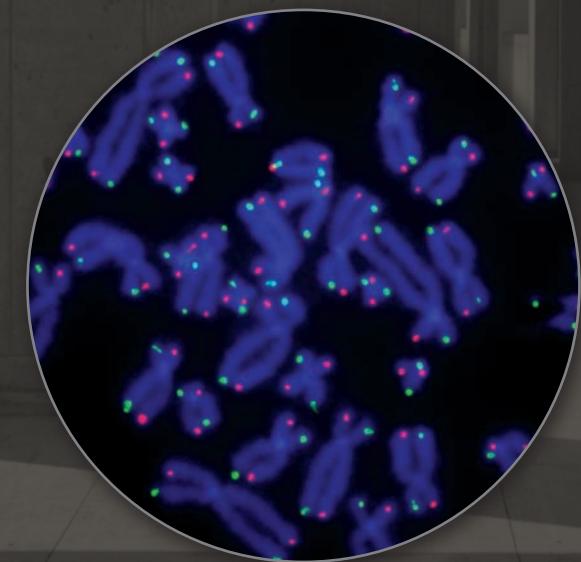


Named president of the Salk Institute

2009

2016

Telomeres: Keeping Genetic Time



Elizabeth Blackburn shared the Nobel Prize in Physiology or Medicine in 2009 for discovering the molecular nature of telomeres and for co-discovering telomerase, an enzyme that maintains telomere ends. The huge amount of the genetic material in the form of DNA in the cells of living organisms is physically compacted into minuscule bundles called chromosomes. Telomeres protect DNA by capping the ends of chromosomes and may act as sensors of aging as they shorten, marking a cell's age and possibly changing its genetic programming over time. Telomeres have recently emerged as a unifying regulator and read-out of human aging and may well be a major coordinator and link between various age-associated diseases.

FRONTIERS IN regenerative medicine

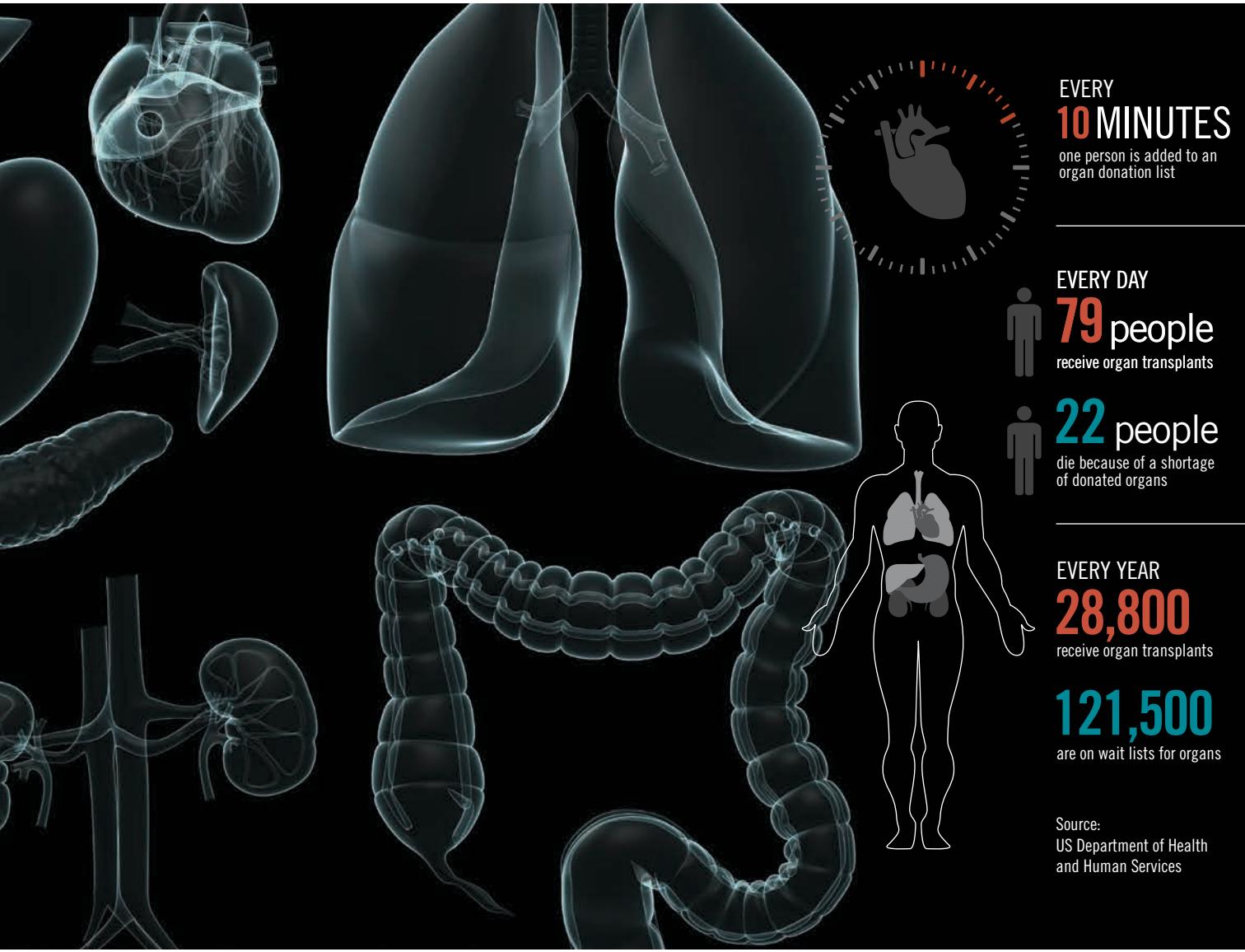
Human stem cell growth in animal hosts might provide a new source of transplantable tissue.



When Juan Carlos Izpisua Belmonte and his team at Salk made global news headlines last fall for developing a technique for growing human stem cells within a mouse embryo, it no doubt puzzled the average reader. They may have asked: What's the point?

For the thousands of people waiting for life-saving organ transplants, the question would have been different:

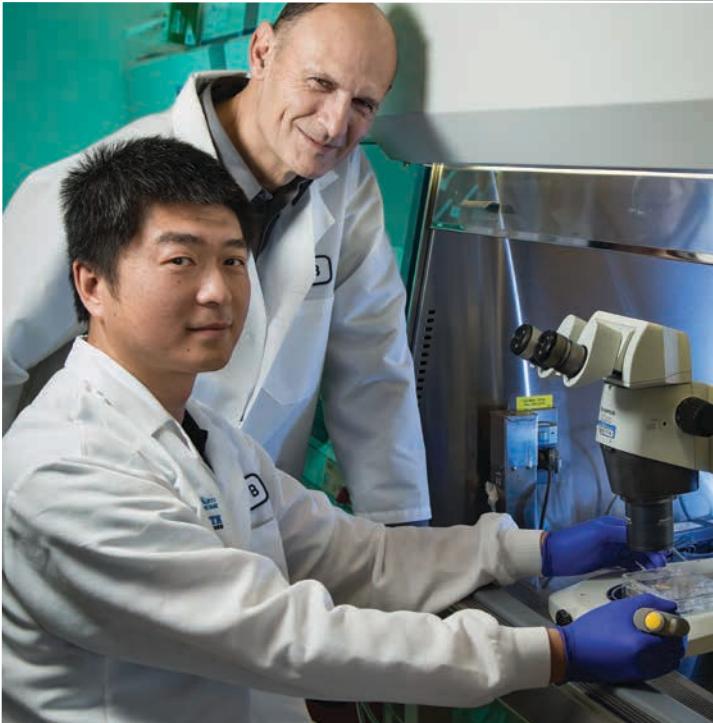
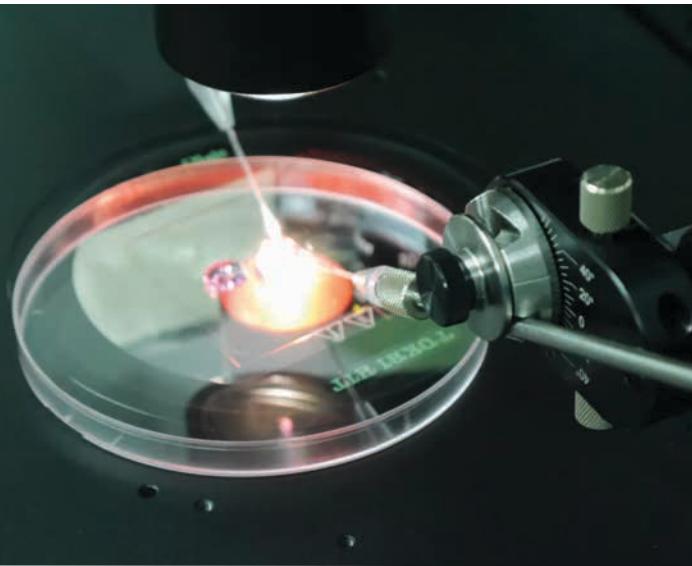
When will this work?



Source:
US Department of Health
and Human Services

That's because Izpisua Belmonte's discovery was a proof of concept for a potentially new source of transplantable organs, and for many patients that resource can't come soon enough. Tens of thousands of people around the world receive organ transplants every year. But while the medical know-how for transplanting organs has expanded rapidly, the availability of donated organs has lagged. Due to the lack of donors and the risk of organ rejection, in the United States alone, an average of 22 people die each day while waiting for an organ donation.

Even for people who don't require an immediate organ transplant to survive, chronic diseases can cause secondary health issues that could be prevented by replacing the damaged or diseased organ—for instance, the difficulty of managing insulin and blood sugar levels can result in diabetics going blind and losing limbs to amputation.

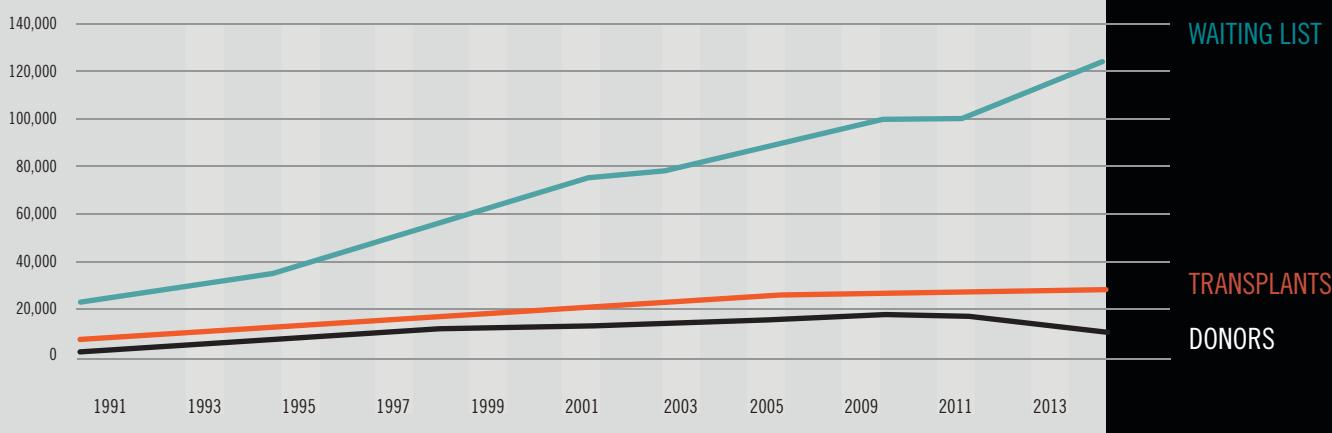


Researchers can now take a person's skin cells, use chemicals to revert them back into what's called induced pluripotent stem cells (iPSCs), and then coax those reprogrammed stem cells to turn into desired tissue-specific cells, such as those of the brain, muscle or pancreas.

Counterclockwise from top right: team of scientists at Agropor field laboratory, Spain; Human stem cells being inserted into a pig blastocyst; Salk researchers Juan Carlos Izpisua Belmonte and Jun Wu; another angle of stem cell insertion; human stem cells grown in pig blastocyst; pigs at Agropor facility.

GROWING NEED

Every year, the gap between the number of people waiting for organ donations and the number of donors widens.



Source: US Department of Health and Human Services

Against this backdrop, the rapid pace of stem cell science in recent years has provided a ray of hope. Scientists around the world have been exploring ways to use stem cells—cells still in nascent stages of development—to grow new tissues in the laboratory. Growing functional organs in the lab has, however, proved daunting. When a heart or a kidney forms in an animal during early development, it happens within the fetus, a complex environment that's very difficult to recreate in a petri dish.

"We're working every day on this problem of how to grow organs in the lab, but we're still a long way away," says Izpisua Belmonte. "But animals grow perfect organs all the time. It gave us the idea of using an animal as a host to grow a human organ."

In a paper published in the journal *Nature*, the scientists reported they had been able to integrate human stem cells into early-stage mouse embryos so that the human stem cells began the first stages of differentiation—meaning they appeared to begin the process of generating precursors of the body's various tissues and organs.

Since then, with support from the Moxie Foundation, the Salk team has been exploring whether the same technique might allow pigs to be used as hosts for growing human organs. A key part of their approach is developing ways to precisely target the human cells to become specific organs needed for transplant. The Salk scientists have teamed up with experts in pig biology at the University of California, Davis; two universities in Spain, the Catholic University of Murcia and the University of Murcia; and the Spanish agricultural company, Agropor.

If their technique pans out, it could help overcome a major hurdle to organ transplants: the risk that the recipient's body will reject the new organ. Several attempts have been made at transplanting whole animal organs into humans—the most famous of which was an American infant girl known as "Baby Fae," who received a baboon's heart—but patient immune systems inevitably reject the animal organs.

The Salk researchers think they may be able to get around this with advances in generating stem cells from patient cells that have already developed into a specific type of tissue, such as skin. Researchers can now take a person's skin cells, use chemicals to revert them back into what's called induced pluripotent stem cells (iPSCs), and then coax those reprogrammed stem cells to turn into desired tissue-specific cells, such as those of the brain, muscle or pancreas. If a person's iPSCs were used to grow an organ in an animal, the organ might pose less risk for rejection because the cells have the same DNA as the original patient skin cell.

"If we can tell the human iPSCs in an animal host to develop into a kidney or pancreas or eye, it could provide an entirely new source for transplant tissues," says Izpisua Belmonte. "We're still in the initial stages of determining if this is even possible and whether human cells can participate in the early formation of tissues in the host animal and become part of their development. We have a long and exciting scientific problem ahead of us." **is**



NEXTGEN KATZ/ZACH

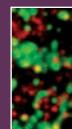
NEXTGEN

VISUALIZING NATURE INSIDE THE LAB AND OUT

Zachary Katz is a visual person: from insect-devouring plants to bustling cells, he strives to see what happens in nature. While growing up in Arizona and then Florida, Katz and his brother gathered specimens of rocks and plants (particularly of the carnivorous variety). Katz took up photography to catalog his collections, leading to his interest in another method for visualizing the natural world, microscopy.

In the lab, Katz creates new kinds of microscopes to observe single immune cells, the body's first responders to threats. Immune system sentries called T cells rapidly summon a swarm of defensive cells when they detect intruders. But when T cells aren't operating correctly, they can mistakenly ignore deadly threats (like cancer) or attack the body and cause autoimmune or immune-deficiency disorders, such as allergies and type 1 diabetes.

T cells malfunction when proteins on their outside membrane confuse safe cells with sick ones. By building tools to observe which—and where—molecules are interacting with those membrane proteins, Katz can find ways to control T cells. To catch the motion of these fleeting interactions, Katz programs strobe lasers to light up molecular interactions in pulses without bleaching them. Charting never-before-seen interactions on the T cell's surface is the first step in designing small molecules that can turn on or off T cells at will, providing a new defense against a host of diseases. 



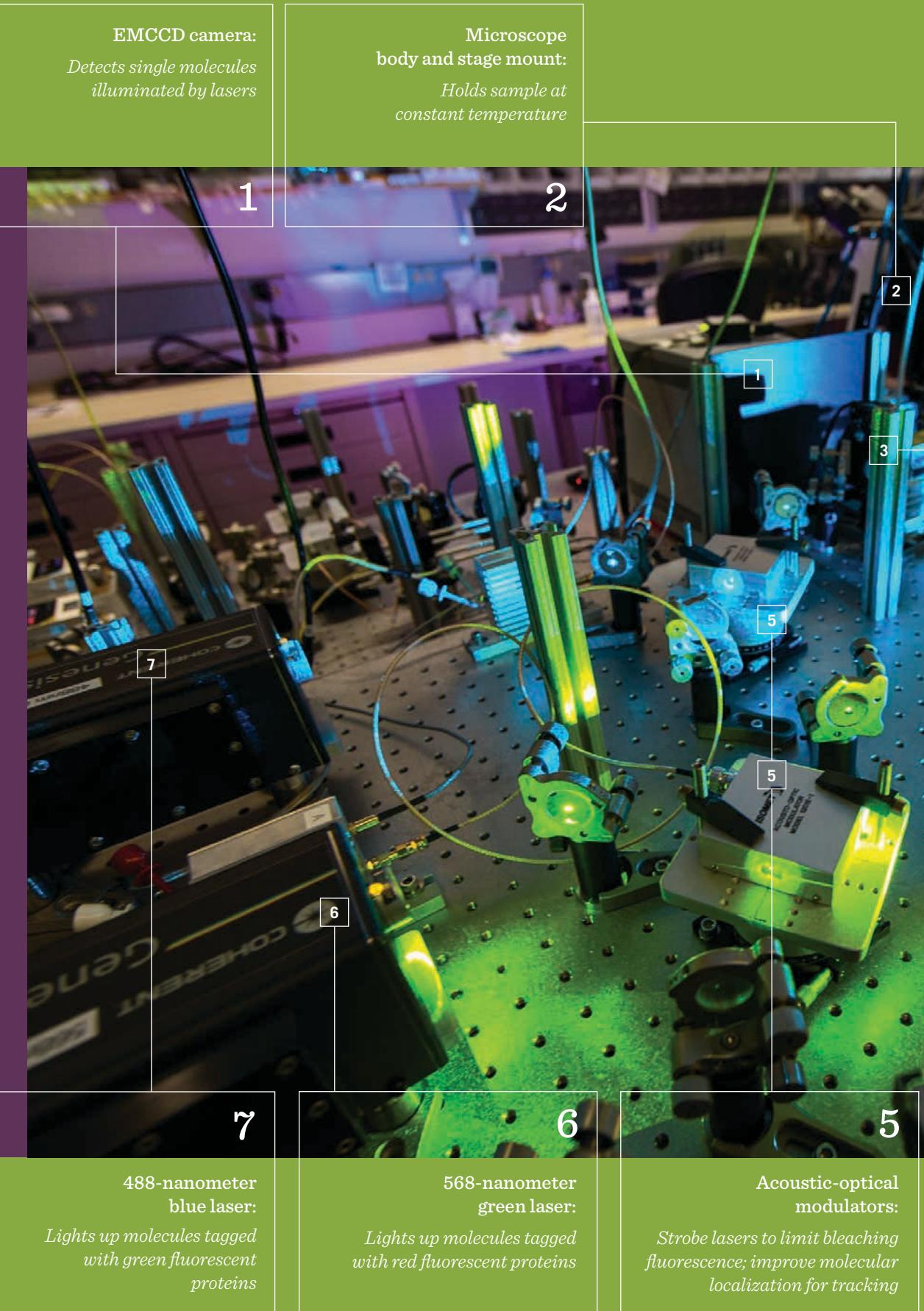
ANALYSIS →

Visit the next page to learn more about the custom microscope.

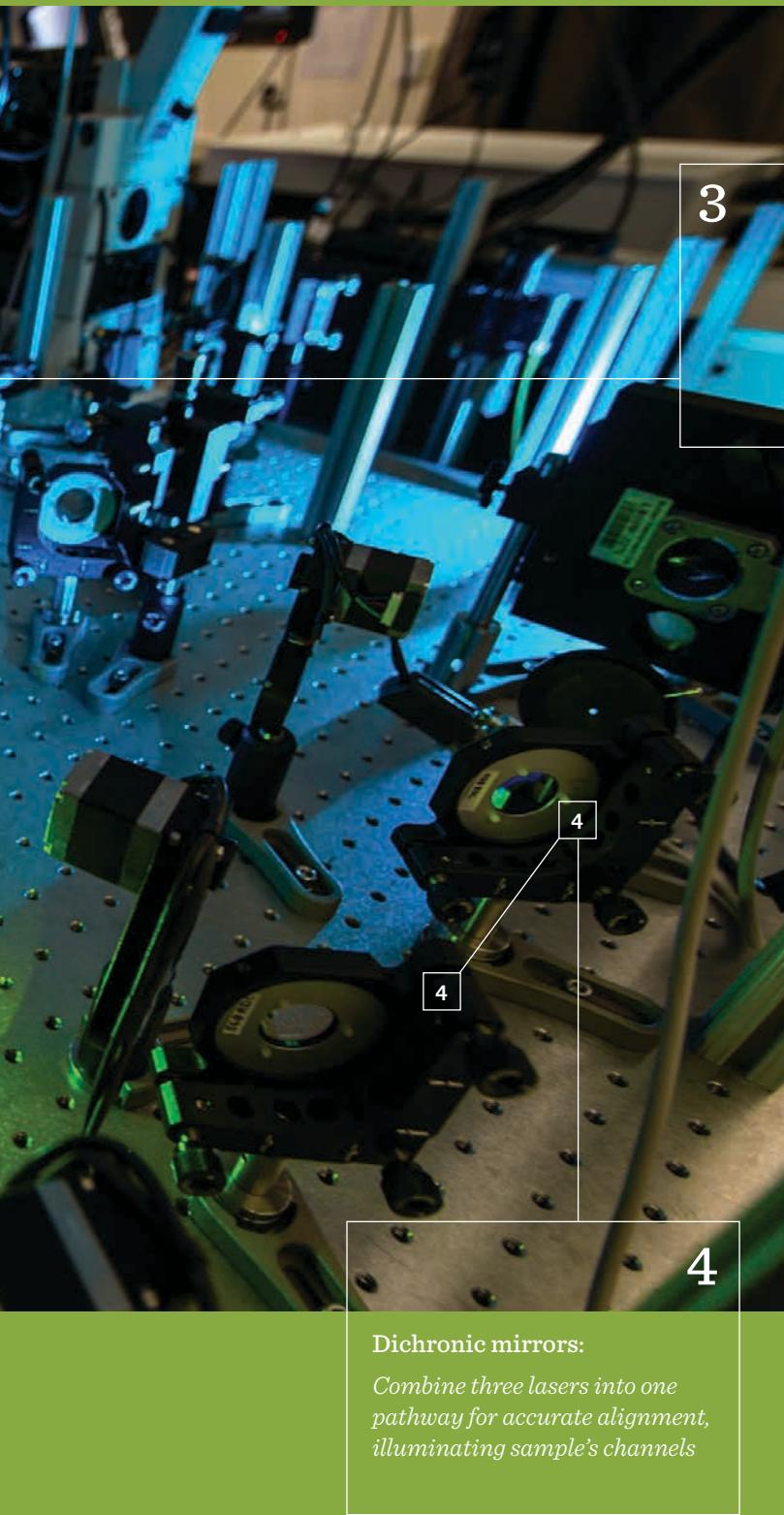


WWW.SALK.EDU/INSIDESALK/0416/KATZ

ANALYSIS

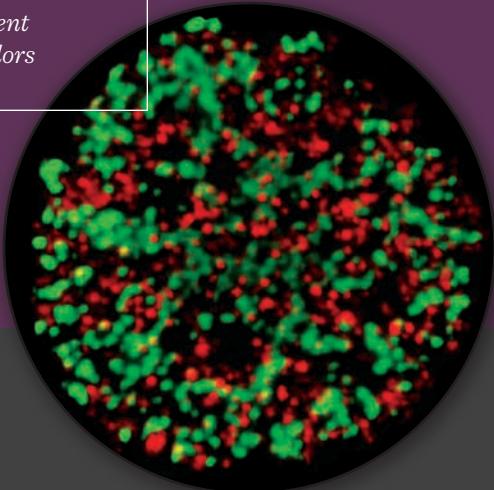


ILLUMINATING INVISIBLE MOLECULES TO BETTER UNDERSTAND THE IMMUNE SYSTEM



405-nanometer UV laser:

Ultraviolet energy alters molecular conformations; makes invisible molecules appear or fluorescent proteins switch colors



This image, generated by the custom microscope, shows the surface of a T cell as it recognizes an infection. The T cell receptors (green) recognize the infection and relay signals to the next molecule in the pathway (red).

In the Nomis Foundation Laboratories for Immunobiology and Microbial Pathogenesis, Björn Lillemeier's team uses a custom-built, high-speed microscope to record the fast interactions of molecules involved in the immune response. The microscope's high-power lasers, mirrors and other optical elements take snapshots of single molecules in live cells at the nanometer scale. Using this set-up, the lab discovered a new mechanism by which signaling molecules help immune cells called T cells recognize an infection after a few seconds. **IS**

The Salk Institute Board of Trustees welcomes three new trustees



MARKUS REINHARD

Reinhard is the managing director of the Nomis Foundation, which promotes and funds highly innovative basic research in the natural sciences, social sciences and the humanities.

Prior to Nomis, Reinhard held several senior executive positions at Baxter International in Chicago.

Known as an innovative global thought leader, Reinhard brings a wealth of business acumen to the Institute.



HAEYOUNG KONG TANG

Tang is a local philanthropist with a PhD in pharmacology and holds patents related to biology, genetics and neurology.

She has been a strong supporter of Salk for the past 10 years and most recently became a member of the Salk Institute Council.

For the past six years, Tang served on the board of directors for Voices for Children.



TERRY ROSEN

Rosen is a chemist and co-founder and CEO of South San Francisco-based Arcus Biosciences, a drug discovery company focused on the treatment of cancer by blocking tumor induced immunosuppression.

Prior to founding Arcus, he was co-founder and CEO of Flexus Biosciences, acquired by Bristol-Myers Squibb in February 2015.

He is also the former vice president of Therapeutic Discovery at Amgen and site head for Amgen South San Francisco.

HELMESLEY-SALK FELLOWS RECEIVE NIH DIRECTOR'S EARLY INDEPENDENCE AWARD

Helmsley-Salk Fellows Dmitry Lyumkis and Patrick Hsu are among 16 scientists nationwide to receive the National Institutes of Health (NIH) Director's Early Independence Award. The award supports junior scientists in their efforts to pursue innovative approaches to major contemporary challenges in biomedical research.

Lyumkis will receive \$1.25 million in direct funding over five years and has made groundbreaking innovations in biological imaging using a cutting-edge technology called single-particle cryo-electron microscopy (cryoEM). CryoEM enables the visualization of large proteins and protein complexes under near-native conditions, allowing scientists to build three-dimensional models of the imaged objects.

Hsu will receive \$1 million in direct funding over the next four years to conduct his research. Hsu has played a key role in developing the CRISPR-Cas9 genome engineering technologies for efficient and precise application in human cells. Genome editing enables rapid manipulation of the genetic building blocks and architecture of biological systems, breakthroughs that are transforming biomedical research and gene therapy.



Dmitry Lyumkis



Patrick Hsu

TERRENCE SEJNOWSKI RECEIVES COVETED NEUROSCIENCE PRIZE

Terrence Sejnowski, professor and head of the Computational Neurobiology Laboratory and holder of the Francis Crick Chair, received the coveted Swartz Prize for Theoretical and Computational Neuroscience. Sejnowski, who is also a Howard Hughes Medical Institute investigator, earned the recognition for his role in founding and growing the field of computational neuroscience as well as his efforts to understand the computational resources of the brain. Sejnowski recently uncovered how the loss of a critical receptor in a class of inhibitory neurons may be responsible for neurodevelopmental disorders and generated a new estimate for memory capacity in the brain (see page 6).



Terrence Sejnowski

BEVERLY EMERSON NAMED AAAS FELLOW

Beverly Emerson, a professor in the Regulatory Biology Laboratory and holder of the Edwin K. Hunter Chair, was named a 2015 Fellow of the American Association for the Advancement of Science (AAAS), the world's largest general scientific society. Emerson earned the recognition for her distinguished contributions to the understanding of the mechanisms by which genes are transcriptionally regulated and how these processes can malfunction to cause disease. She studies how different genes are turned on and off through the course of cancer—from the time cells become precancerous until the time they develop into a mature cancer and spread to new organs.



Beverly Emerson

REUBEN SHAW NAMED NEW DIRECTOR OF SALK CANCER CENTER



The Salk Institute has named Reuben Shaw as the new director of its National Cancer Institute-designated Cancer Center. Shaw is a member of the Molecular and Cell Biology Laboratory and holder of the William R. Brody Chair.

The Salk Cancer Center was established in 1970 to uncover the fundamental aspects of cancer biology and is just one of seven NCI-designated Basic Research Cancer Centers in the country. Shaw succeeds Tony Hunter, who led the center for the past eight years and made the seminal discovery of a new type of enzyme called tyrosine kinases, which are altered in many cancers and targeted by a number of cancer drugs.

Shaw's research focuses on cancer metabolism: how metabolic pathways are altered in cancer and play a role in the origins and progression of the disease. 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. This energy-sensing pathway had been previously studied as the target of the most widely prescribed type 2 diabetes medication worldwide (metformin), suggesting an unexpected and direct link between metabolic pathways and cancer.

SHAW NAMED RECIPIENT OF THE WILLIAM R. BRODY CHAIR IN DECEMBER 2015

The chair was dedicated to former Salk President William Brody on behalf of the Salk Board of Trustees in appreciation of his six years of leadership at the Institute. Joan and Irwin Jacobs, along with Ralph O'Connor, his wife Becky, and 13 other trustees, contributed to the establishment of the William R. Brody Chair.

ONE to WATCH

Corina Antal, a Salk research associate in Ronald Evans' lab, has garnered attention for her leading work on proteins that suppress tumor growth. The 29-year-old landed a spot on *Forbes'* 2016 "30 under 30" list that is comprised of "bright entrepreneurs, breakout talents and change agents" in 20 sectors. Antal was also named a Damon Runyon Fellow in November 2015 by the Damon Runyon Cancer Research Foundation for her efforts to increase the efficacy of pancreatic cancer therapies.



Corina Antal



EVANS CO-LEADS FIRST PANCREATIC CANCER RESEARCH 'DREAM TEAM'

Salk scientist Ronald Evans is co-leading the pancreatic cancer dream team, made up of researchers from the United States and United Kingdom. Stand Up To Cancer (SU2C), Cancer Research UK and the Lustgarten Foundation selected Evans, director of Salk's Gene Expression Laboratory, to help head the team of nearly two dozen scientists. The \$12 million project focuses on launching a fresh attack on pancreatic cancer by reprogramming the biology of both cancerous cells and noncancerous cells that surround a tumor.



THOMSON REUTERS

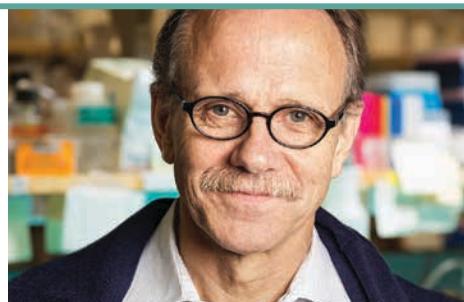
INFLUENTIAL FACULTY

Congratulations to three Salk faculty named Highly Cited Researchers in 2015 by Thomson Reuters: Joanne Chory, Joseph Ecker and Rusty Gage.

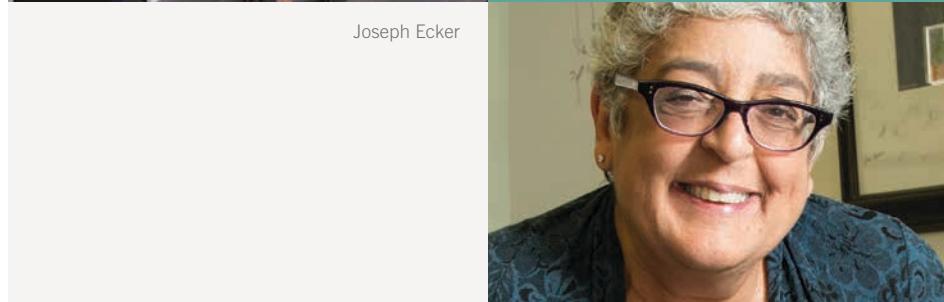
The report identifies the world's most influential scientific researchers across 21 fields. About 3,000 researchers earned the distinction by writing the greatest number of reports officially designated as highly cited papers, which rank among the top 1 percent most cited for their subject field and year of publication. Read more at <http://highlycited.com>.



Joseph Ecker



Rusty Gage



Joanne Chory

EVENTS



CAMPAIGN SUCCESS CELEBRATED

Nearly 200 Salk donors, faculty and trustees celebrated the Campaign for Salk on November 11, 2015 with an evening of music, memories and talks on the Institute's future as a global research leader. The six-year campaign, the Institute's first major fundraising effort since opening its doors in the early 1960s, surpassed its \$300 million objective of raising private resources to address the decline in federal funding for science and the rising cost of new technologies. The celebratory event included exhibits and videos depicting campaign successes and archival footage of faculty who helped establish the Institute.

▶ WWW.SALK.EDU/INSIDESALK/0416/CAMPAGN



SALK'S EDUCATION OUTREACH PARTNERS WITH STEAM LEADERSHIP SERIES

Salk's Education Outreach program welcomed 300 high school girls from the San Diego Unified School district for a Women in Biotech lecture on November 17, 2015. The event was part of the STEAM (Science, Technology, Engineering, Arts and Math) Leadership series, which focuses on career opportunities within those fields and connects business leaders to local students. The keynote speakers were Tina Nova, president and CEO of Molecular Stethoscope, and Salk's Janelle Ayres, assistant professor in the Nomis Foundation Laboratories for Immunobiology and Microbial Pathogenesis. Carol Marchetto, a Salk senior staff scientist, and two researchers from the San Diego Zoo Institute for Conservation Research concluded the presentation with a panel discussion.



Sreekanth Chalasani



From left: pianist Helen Sung, jazz musician Victor Goines, bassist Emma Dayhuff and drummer Greg Artry, Jr.



Diana Hargreaves presenting her cancer research at Women & Science.



SOLD-OUT CROWD AT SCIENCE & MUSIC SERIES

Jazz legend Victor Goines and his quartet played to a sold-out crowd on January 24, 2016 for the third concert in the Salk Science & Music series. Sreekanth Chalasani, assistant professor, gave a riveting talk about his latest developments on brain research in Salk's Molecular Neurobiology Laboratory. The final concert of the season takes place April 24 with a duo piano concert by Sean Chen and Karen Joy Davis. For information, visit www.salk.edu/music.



CANCER RESEARCHER DIANA HARGREAVES CAPTIVATES SALK'S WOMEN & SCIENCE EVENT

Diana Hargreaves, assistant professor in Salk's Molecular and Cell Biology Laboratory, discussed the latest in cancer research at the Salk Women & Science event in December. In her talk, "Interior Remodeling for Cancer Defense," Hargreaves shared how proteins called epigenetic regulators can make regions of our genome more or less accessible for activation, affecting what kinds of tissues cells become. Similar to remodeling a house, cells must rearrange their packaged DNA—with the help of these epigenetic regulators—to carry out certain functions while making others inaccessible. Hargreaves studies a particular epigenetic regulator whose subunit is mutated in many solid tumors, such as in ovarian, bladder and colorectal cancers. She aims to understand how mutations in this complex contribute to the creation of tumors and potentially find new targets for therapy.

About 100 business and community members attended the event. Salk's Women & Science program offers three lectures a year given by the Institute's esteemed female faculty as well as staff scientists and up-and-coming researchers. The next Salk Women & Science event will take place on Wednesday, July 20, 2016.

To learn more about the program:

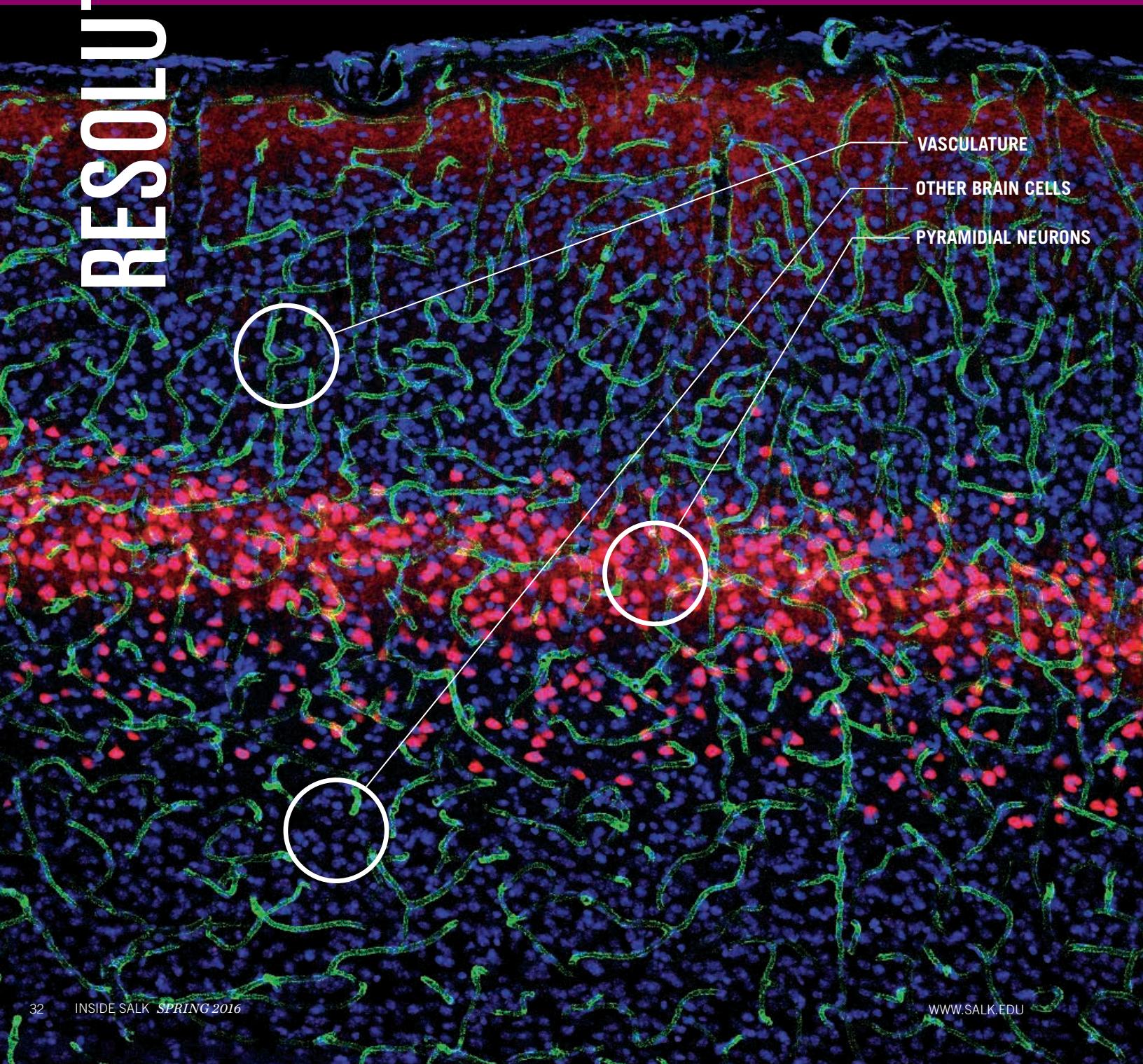
Contact Betsy Collins,
director of Donor Relations
(858) 500-4883
becollins@salk.edu
www.salk.edu/womenandscience

RESOLUTION

seeing connections

The microscope image below, from the laboratory of Salk Professor Edward Callaway, shows the architecture of part of the mouse visual cortex. His lab discovered a new subtype of nerve cells called pyramidal neurons (red), helping to explain how the brain processes visual information. In the image, blood vessels are shown in green and other brain cells in blue.

Credit: Euiseok Kim





Support a legacy where cures begin.

The power of charitable gift annuities

Did you know a gift to the Salk Institute of \$20,000 or more can provide fixed payments for you and your loved ones? Charitable gift annuities provide tax savings and an income for you, while benefitting research and discovery at the Salk Institute. You can feel confident knowing you've made smart decisions about your financial and philanthropic priorities.

Sample Rates

YOUR AGE (S)	RATE
70	5.1%
76/73	5.0%
80	6.8%
83/80	6.0%
90	9.0%

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

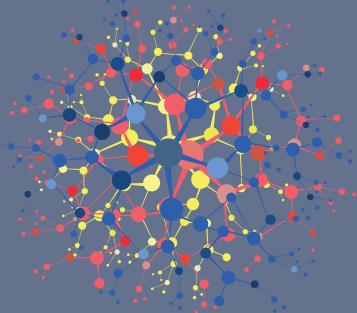
Your age(s) and current interest rates determine the rate Salk can offer.

salk
Where cures begin.®

DISCOVER SALK

EVERY CURE BEGINS WITH YOU.

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



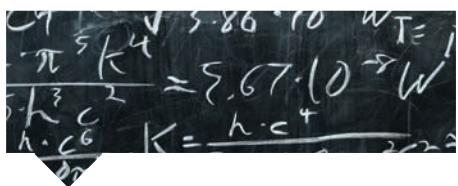
Learn more about the many options for joining the Salk community by visiting www.salk.edu/support or calling (858) 453-4100 x1201.

Salk giving programs offer a range of ways to get involved.

Learn about Salk science and support vital research:

GIVING PROGRAMS

EDUCATION OUTREACH



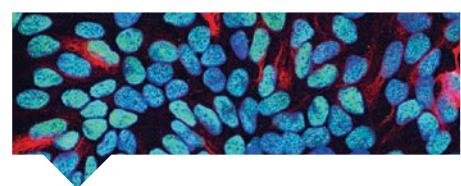
Offering nearly half a century of programs to inspire—and launch—the next generation of scientists, Salk's Education Outreach includes a Mobile Science Lab, High School Scholars curriculum and SciChats@Salk.

SALK WOMEN & SCIENCE



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

SALKEXCELLERATORS



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

PARTNERS IN RESEARCH



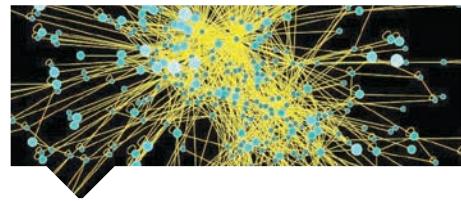
Invest in the future of cancer, aging, Alzheimer's disease and diabetes research by incorporating philanthropic support for Salk into your estate plans.

PRESIDENT'S CLUB



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