# WINTER | 2018 WHERE CURES BEGIN. inside Salk IN THE FOOTSTEPS OF GIANTS,

AN INNOVATIVE GENERATION EMERGES



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#### ON THE COVER:

Salk's junior faculty follow in the footsteps of past scientific giants by asking big, bold questions in biological research. This new generation of explorers is tackling pressing problems related to cancer, the brain, plant biology, the immune system and more.

From left: Renato Dulbecco, Francis Crick, Edwin Lennox, Jacques Monod, Jonas Salk, Leslie Orgel, Jacob Bronowski and Melvin Cohn

#### **PRESIDENT'S LETTER**

#### Dear Friends,

I was reminded recently of the magnificent power science has to transform our world for the good of all humankind. I received a hand-addressed envelope in my office, something that has become increasingly rare since the advent of email. The author, a longtime supporter of Salk, wrote a deeply personal letter explaining his profound gratitude for Jonas Salk and his establishment of the Institute.

The writer told me about how, in the early 1980s, he sent a letter to Jonas Salk wishing him a happy birthday and expressing gratitude for the impact Salk's vaccine had on the author's life. Despite Salk's fame, not to mention the demands of his research and role leading the Institute, he found time to reply and express his gratitude for the birthday wishes. While Salk was appreciative that his work helped protect the writer's children from polio, he wrote that he remained hopeful that children across the world would also benefit from his discovery. Today, the World Health Organization reports that 85 percent of infants worldwide receive vaccination against polio. Only Afghanistan, Pakistan and Nigeria still harbor the disease; sadly, war and extreme poverty continue to create barriers to polio's complete eradication.

As with so many in the writer's generation, the polio vaccine Jonas Salk developed and gifted to humankind transformed the writer's life. He and countless others stand witness to a world where polio killed and maimed indiscriminately. They remember when the only treatment was quarantine or an iron lung. And they still treasure the announcement, in April 1955, that Salk's vaccine was safe and effective, news that was greeted as a miracle and trumpeted in headlines worldwide.

Much has changed since that historic day when Salk announced his discovery, including how we receive correspondence. The exchange of letters between two men whose lives were changed forever by scientific discovery is heartwarming, but it also serves as a reminder of the power of science to make the world a healthier, happier place.

This edition of *Inside Salk* explores new breakthroughs in our understanding of the human circadian rhythm, spearheaded by Professor Satchin Panda; his findings have significant implications for overall health and wellbeing. We also profile a new generation of scientists who are pursuing their research with passion, curiosity and boldness. Like the renowned Salk researchers in whose footsteps they follow, this generation is seeking scientific discoveries that have the potential to transform their fields and the world. Moreover, their work is receiving well-deserved awards and accolades from prestigious scientific institutions and foundations.

While we celebrate the successes of our young scientists, we are also reminded that life is fleeting and we should strive to make the most of it. Within this issue, we mourn the loss but celebrate the lives of two of Salk's founding fellows: Melvin Cohn, PhD, and Edwin Lennox, PhD.

As 2018 comes to an end, I speak for all of us at Salk in offering our gratitude to you for your unfailing partnership. May the new year bring you health, happiness and a continued curiosity for scientific discovery.

Sincerely,

Fred H. Gage President



"As 2018 comes to an end, I speak for all of us at Salk in offering our gratitude to you for your unfailing partnership. May the new year bring you health, happiness and a continued curiosity for scientific discovery." In the last few months, Salk scientists have had groundbreaking work published in top journals and covered in notable media outlets. Read on to learn more.

C READ

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

### **RESEARCH** AT SALK



#### NEUROSCIENCE

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



#### GENETICS

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



#### COMPUTATIONAL BIOLOGY

Modern scientific research has yielded massive amounts of data—but few good ways to understand the information. We are developing mathematical and analytical frameworks to uncover new connections in biological systems.

# X

#### AGING

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

#### METABOLISM

At Salk, we seek to understand human metabolism and what happens when this biological system breaks down. The problem is important as diabetes becomes more prevalent and more of a burden on an already-taxed healthcare system.

#### PLANT BIOLOGY

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



#### CANCER

We are rapidly demystifying cancers and leading the search for the next generation of targeted cancer therapies. We see a future where transformational treatments destroy tumors before they develop drug resistance.



#### REGENERATIVE MEDICINE

Many disorders and life-threatening diseases could be cured by replacing or fixing dysfunctional cells. We aim to uncover novel ways to transplant new cells, tissues and even organs while minimizing their rejection.



#### IMMUNE SYSTEM BIOLOGY

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



#### **PROTEIN INTERACTIONS**

Proteins—large, complex molecules catalyze virtually all of the chemical reactions that take place in the body. We study their interactions to discover how they heal or how they harm.

#### **DISCOVERIES**

# THE NOSE KNOWS:

New ways to understand odor



NEUROSCIENCE



#### Widespread connections among neurons help the brain distinguish smells

Distinguished Professor Emeritus Charles Stevens and coauthor Shyam Srinivasan illuminated how, in a brain area responsible for processing information about smells (called the piriform cortex), what looks like a messy jumble of connections between neurons is actually critical to how the brain distinguishes between similar odors. Aside from better describing how smells are processed, the research could also lead to greater insight into how some parts of the brain organize information.



COMPUTATIONAL BIOLOGY

#### SCIENCE SIGNALING 08/2018

NATURE PLANTS

08/2018

#### A mathematical model reveals a map for odors from the natural environment

Associate Professor Tatyana Sharpee, first author Yuansheng Zhou and collaborators have discovered a new way to organize odor molecules based on how often they occur together in nature. They mapped this data to discover regions of odor combinations humans find most pleasurable. The findings open new avenues for engineering smells and tastes.



#### PLANT BIOLOGY

#### A switch to turn fragrances on and off

Professor Joseph Noel, co-first author Suzanne Thomas and collaborators at Purdue University discovered the switch in plants that turns off the production of terpenoids carbon-rich compounds that play roles in plant physiology and are used by humans in everything from fragrances and flavorings to biofuels and pharmaceuticals. Plants often make terpenoids in such low quantities that extracting them for commercial use is difficult. The discovery could lead to more-efficient ways to obtain sufficient amounts of these products to the benefit of humans.

#### DISCOVERIES



CELL REPORTS 08/2018



CANCER

CELL

Top panel: Significant numbers of invasive cancer cells with Sox10 (red) in them can be found outside the tumor (green cells, outlined). The bottom panel shows the invasive cells' proximity to blood vessels (white). Credit: Salk Institute/ Sanford Consortium for Regenerative Medicine

#### SALK SCIENTISTS SHED LIGHT ON BREAST CANCER

Professor Geoffrey Wahl, first author Raj Giraddi and collaborators used cutting-edge techniques to generate an atlas of the genes expressed in each breast cell from very early in development until adulthood. They used this "single-cell-transcriptome atlas" to compare genes expressed in human breast cancers, which led to an understanding of how the stem cells of the breast arise in early development as well as provided insight into the reprogramming of adult cells into states associated with cancer.

In addition, Wahl, first author Christopher Dravis and colleagues identified a master switch that appears to control the dynamic behavior of tumor cells that makes some aggressive cancers so difficult to treat. The gene Sox10 directly controls the growth and invasion of a significant fraction of hard-to-treat triplenegative breast cancers. MOLECULAR CELL 06/2018

#### WHAT THE SATELLITES IN YOUR BODY DO

Copies of repetitive DNA sequences called satellite RNAs are high in certain types of cancer, such as breast and ovarian. But whether they cause cancer or merely coincide with it has been unclear. First author and former Salk postdoctoral researcher Quan Zhu, Professor Tony Hunter and colleagues discovered that a specific type of satellite RNA, called hSATa, induces breast cancer by directly interfering with DNA copying and repair. The research suggests that targeting satellite RNAs could provide another approach for treating multiple types of cancer, including breast, ovarian, prostate and pancreatic.

NATURE GENETICS 09/2018

#### NEW METHOD OF PINPOINTING CANCER MUTATIONS COULD LEAD TO MORE-TARGETED TREATMENTS

Cancer cells often have DNA mutations that can give scientists clues about how the cancer started or which treatment may be most effective. Finding these mutations can be difficult, but a new method may offer more complete, comprehensive results. Helmsley-Salk Fellow Jesse Dixon and collaborators have developed a new framework that can combine three existing methods of finding these large mutations—called structural variants—into a single, more complete picture. The new method could help researchers find structural variations within cancer cells' DNA and learn more about how those cancers begin.

NEUROSCIENCE

eLIFE 09/2018

#### RESEARCH INTO YEAST LEADS TO SERENDIPITOUS FINDING ABOUT A CENTRAL NERVOUS SYSTEM DISORDER

Professor Tony Hunter, first author Zheng Wang, colleagues and collaborators found that an important cellular quality-control mechanism in baker's yeast is closely connected to hypomyelinating leukodystrophy, a debilitating neurodegenerative disease that occurs in children. The findings could indicate a therapeutic approach for this rare disease, as well as for multiple sclerosis and other neurodegenerative diseases.



An artist's rendering of yeast cells, dividing by budding.



Credit: Phil Richardson, Woods Hole Oceanographic Institution.

#### NATURE 09/2018

#### PHYSICISTS TRAIN ROBOTIC GLIDERS TO SOAR LIKE BIRDS

Professor Terrence Sejnowski and UC San Diego collaborators used reinforcement learning to train gliders to autonomously navigate atmospheric thermals, soaring to heights of nearly 2,300 feet. The results highlight the role of vertical wind accelerations and roll-wise torques as viable biological cues for soaring birds. The findings also provide a navigational strategy that directly applies to the development of autonomous soaring vehicles or unmanned aerial vehicles.

#### DISCOVERIES



METABOLISM

CELL SCIENCE METABOLISM SIGNALING 08/2018 07/2018

#### CELLS AGREE: WHAT DOESN'T KILL YOU MAKES YOU STRONGER



Research led by Professor Gerald Shadel suggests why, at a cellular level, the expression "What doesn't kill you makes you stronger" might be true. His team reported that brief exposures to stressors can be beneficial by prompting the cell to trigger sustained production of antioxidants, molecules that help get rid of toxic cellular buildup related to normal cell metabolism.

In addition, Shadel, along with collaborators from Yale, Appalachian State University and other institutions, found that a protein called ATM (short for ataxia-telangiectasia mutated) can sense in normal cells the presence of harmful products called reactive oxygen species and responds by sounding the alarm to trigger the production of antioxidants. The work could have implications for a disease in which ATM is dysfunctional—and could also help reveal ways to boost cellular health overall.

Mitochondria (purple) surrounding cell nuclei (blue) visualized by fluorescence microscopy.



#### PERIODS OF FASTING MAY PROTECT AGAINST OBESITY AND DIABETES

Professor Satchin Panda, first author Amandine Chaix and colleagues found that mice lacking the biological clocks thought to be necessary for healthy metabolism could still be protected against obesity and metabolic diseases by having their daily access to food restricted to a 10-hour window. The work suggests that the health problems associated with disruptions to animals' 24-hour rhythms of activity and rest can be corrected by eating all calories within a 10-hour window.

#### **CLOCKLESS GROUP**



Health issues associated with disruptions to the circadian rhythm (represented by mice without biological clocks) can be alleviated by a time-restricted diet.

NATURE COMMUNICATIONS 07/2018

#### DEPLETING MICROBIOME WITH ANTIBIOTICS CAN AFFECT GLUCOSE METABOLISM

Panda, along with Salk Professor Alan Saghatelian and collaborators from UC San Diego, found that mice with microbiomes depleted by antibiotics had decreased levels of glucose in their blood and better insulin sensitivity. The research has implications for understanding the role of the microbiome in diabetes. It also may lead to better insight into the side effects of being treated with high levels of antibiotics.

#### DISCOVERIES



GENETICS

#### NATURE 09/2018

#### REPROGRAMMING WOUND CELLS HEALS LARGE ULCERS AND REGENERATES SKIN

The image represents the first proof of principle for the successful regeneration of a functional organ (the skin) inside a mammal, by a technique known as AAV-based *in vivo* reprogramming. Epithelial (skin) tissues were generated by converting one cell type (red: mesenchymal cells) to another (green: basal keratinocytes) within a large ulcer in a laboratory mouse model.



Professor Juan Carlos Izpisua Belmonte and first author Masakazu Kurita, along with collaborators, have developed a technique to directly convert the cells in an open wound into new skin cells. The approach relies on reprogramming the cells to a stem-celllike state and may be useful for healing skin damage, countering the effects of aging and helping to better understand skin cancer.



Tweaking cells' gatekeepers could lead to a new way to fight cancer.

GENES & DEVELOPMENT 09/2018

#### SALK SCIENTISTS DEVELOP METHOD TO MANIPULATE NUMBERS OF NUCLEAR PORES

VP, Chief Scientific Officer Martin Hetzer and first author Asako McCloskey have devised a method to manipulate numerous individual nuclear pores, which are essential elements of cells that provide controlled ways to move material into and out of a nucleus. The breakthrough may lead to insights into how to stop cancerous cells from proliferating out of control. NATURE COMMUNICATIONS 08/2018

CELL 09/2018

#### MOLECULAR STRUCTURES OF GENETIC-ENGINEERING TOOL, THERAPEUTIC VIRUS REVEALED





Assistant Professor Dmitry Lyumkis, first author Sriram Aiyer and collaborators used cryo-electron microscopy (cryo-EM)—a cutting-edge technology that enables researchers to capture the structure of complex molecules in unprecedented detail to show the structure of AAV2, a version of a virus, advancing the technique's capabilities and the virus' potential as a delivery vehicle for gene therapies.

In addition, Lyumkis, together with co-corresponding author and Helmsley-Salk Fellow Patrick Hsu, first author Cheng Zhang and colleagues, used cryo-EM to report the detailed molecular structure of CRISPR-Cas13d, a promising enzyme for emerging RNA-editing technology.

Electron microscopy provides a new view of a virus with therapeutic potential. Inset shows the cryo-EMderived structure of an AAV2. Full image shows the experimentally determined density (gray) and the fitted atomic model based on that density. For almost every atom in the amino acids (the building blocks of proteins) in the reconstruction, we can begin to see the full atomic structure, including oxygens (red), nitrogens (blue), carbons (yellow) and sulfurs (green).



IMMUNE SYSTEM BIOLOGY

CELL 08/2018

COMMON DIETARY ELEMENTS CURE LETHAL INFECTIONS, ELIMINATING THE NEED FOR ANTIBIOTICS

Associate Professor Janelle Ayres found that giving mice dietary iron supplements enabled them to survive a normally lethal bacterial infection and resulted in later generations of those bacteria being less virulent. The approach demonstrated in preclinical studies that non-antibioticbased strategies—such as nutritional interventions—can shift the relationship between the patient and the pathogens away from antagonism and toward cooperation.

# **OBSERVATIONS**



# SALK'S NEW EXPLORERS

### A close-up of some of Salk's junior faculty

Like people, institutions move forward generation by generation. The Salk Institute's first group of scientists included founder Jonas Salk, famous for developing the first effective and safe polio vaccine; and Renato Dulbecco, who demonstrated how viruses can cause cancer and who was awarded the Nobel Prize in Physiology or Medicine in 1975.

This group imbued the Institute with a spirit of self-sufficiency. There were no departments, and faculty were expected to ask difficult questions and develop innovative ways to find the answers. But they were also part of a greater whole. An immunologist might have a lab next to a chemist who was, in turn, next to a cancer biologist. Like the cells they studied, these researchers were independent but interrelated.

Later, a new generation arose at the Salk Institute. To name just a few, Professor Ronald Evans identified the roles hormones play in cancer, diabetes and other conditions. Tony Hunter, American Cancer Society Professor, helped illuminate cancer-signaling molecules called tyrosine kinases, paving the way for targeted tumor therapies, such as Gleevec. Professor Joanne Chory pioneered efforts to understand how plants sense light and produce growth hormones, knowledge that could help increase food supplies by growing plants adapted to harsh environments and a changing climate. And Ursula Bellugi, distinguished professor emerita, illuminated how the brain processes American Sign Language and other human interactions, shedding new light on neural function.

And now, another generation of Salk researchers is just as brilliant and driven as its predecessors. These scientists are asking bold questions about cancer, neurons, plant biology and the immune system. They look for support and inspiration from their peers in other disciplines, and they're not afraid to take risks to figure things out. *Inside Salk* sat down with several junior faculty across a sampling of fields to see how they are tackling pressing biological problems and what inspires them.

#### Why did you choose Salk?

I'm a neuroscientist, so my other choice would have been to go into a neuroscience department, which would also have been fantastic, but then you're interacting with people who think about the same questions as you all the time.

Here, I have to explain what I'm doing to people who work in plant biology or cancer biology, and they can come back with novel insights. I like being in a place where people have broad research backgrounds because it helps me think about my science in a different way. That back-and-forth really expands the research.

#### What big questions are you trying to answer?

The big question for us is: How does the brain actually form? The human brain has billions of neurons, and they have to find the right partner during development and connect at a place called a synapse, and there are trillions of these.

We want to understand how this happens and how it goes wrong. There are a lot of neurodevelopmental disorders, such as autism spectrum disorders and schizophrenia, where there's some level of disconnection. We want to understand if we can fix it when it gets damaged.

#### Compared with others in your field, how is your approach different?

A lot of neuroscientists are interested in these questions. The way we approach it is to think, okay, we know the brain has lots of neurons, but we also know they're surrounded by other cells, called glia. We've been working to understand how these glial cells, specifically astrocytes, talk to neurons and regulate their function. They are the cells telling neurons when to make connections and how to change those connections with experience. We believe we can use this information to repair these connections when they've been damaged.

#### How have technological advances impacted your work?

We're not driving technology, but we're always on the lookout for technological advances, like improvements in sequencing. Also, massive data sets are being generated by other researchers who are looking at these glial cells. So now we can use that data to look at our favorite genes, which we know could be involved in different disorders, dig into it and see what's going on.

MOLECULAR NEUROBIOLOGY LABORATORY HEARST FOUNDATION DEVELOPMENT CHAIR **NICOLA ALLEN** ASSISTANT PROFESSOR What are the big questions you're trying to answer?

The traditional perspective for treating infectious diseases is to kill the pathogen, and that view has really shaped how immunological research is done. We have an excellent understanding of how the immune system kills infectious disease microbes. I felt that view was too simplistic: there must be other things that ensure people survive infections.

For example, sepsis is caused by microbes entering parts of the body that are otherwise sterile. When our immune systems recognize these microbes, they mount an inflammatory response that is so powerful it can lead to multi-organ failure and death.

The traditional way to treat sepsis is to give patients broad-spectrum antibiotics or antivirals, but it's the patient's own response that's doing more damage than the microbe itself. We have to find ways to fix that damage to ensure the patient is going to survive.

My lab discovered that our bodies encode mechanisms we call the cooperative defense system, which protects us from infectious diseases by alleviating physiological damage without killing pathogens. We're trying to understand the underlying mechanisms of the cooperative defense system so we can promote patient survival without killing microbes.

#### How do you, as a foundational scientist, see the impact of your work?

The problem is, society has been focusing entirely on new ways to kill microbes—it's our sole approach against infectious diseases. But antibiotics drive microbial resistance, and we haven't developed vaccines for many infections. We want to develop evolution-proof drugs to treat infectious diseases that won't drive drug resistance.

We're on the right track with that. We can boost the cooperative defense system, and we can treat infections without microbes developing resistance. Also, by promoting the cooperative defense system, we can make pathogens evolve into benign microbes that no longer cause disease. We've shown that can happen.

#### Which Salk scientists have inspired you?

I think a lot of people, after they've had their labs for 30 or 40 years, slow down a bit. But some scientists, like Ronald Evans, show no signs of slowing down. He's not scared to go in new directions. He will look at a field, see there's a problem, find a way to approach that problem, and go for it. That is inspiring.

#### What job would you have in an alternate universe?

If I had another job, it would involve rescuing animals. I am always saddened by the number of stray dogs I see when I visit other countries, particularly in Central and South America. I want to somehow help those animals and don't want to wait to be in an alternative universe to do it. JANELLE AYRES NOMIS CENTER FOR IMMUNOBIOLOGY AND MICROBIAL PATHOGENESIS HELEN MCLORAINE DEVELOPMENTAL CHAIR ASSOCIATE PROFESSOR



#### Why did you choose Salk?

I thought, and I still think, that Salk is the best place for me because it creates an environment where I can do absolutely crazy science, in the sense that I can take the science in directions I could not even dream of at other places. I came in knowing that, within walking distance, there's an expert in protein chemistry, in mathematics, and in bioinformatics, for example.

#### What big questions are you trying to answer?

Experience is called different things in different contexts. Sometimes it's called learning. But if a prior experience was stressful, it might cause fear and generate an anxiety response later in life.

We're trying to understand the fundamentals of how the nervous system extracts information from the environment and integrates current information with past experience to generate an appropriate response. Understanding these basics could help us to better treat conditions such as post-traumatic stress disorder, anxiety disorder and autism.

There are 86 billion neurons and 150 billion nonneuronal cells in the human brain. That's more connections than there are stars we can see. It's overwhelming, so we use simple systems to solve these complex problems. In particular, we study worms called *C. elegans*, which have just 300 neurons and 9,000 connections. *C. elegans* can learn and remember, and show fear and anxiety in circuits that have similarities to mammals. They are powerful tools to understand how the brain works.

#### How do you, as a foundational scientist, see the impact of your work?

The most common thing people have observed in children with an autism spectrum disorder is reduced social interaction. By sequencing these children's DNA, researchers have identified changes in about 800 genes, compared to children with typical development. If I take one of those genes and mutate it in *C. elegans*, that worm will not join a social aggregate; it just hangs out by itself.

I'm not saying the *C. elegans* has autism, just that nature uses the same mechanisms to solve the same problems across the plant and animal world. That's why simple systems can work so well to help us understand larger, more complex systems like the human brain.

#### What do you hope to accomplish in the next 10 years?

For questions as complex as those my team and I are working on, we needed to develop new technology. We use ultrasound to manipulate cells noninvasively in a new area I coined "sonogenetics." This interdisciplinary program is unique to Salk.

We believe our technology can replace many surgical interventions. For example, we want to embrace deep brain stimulation, which is used to treat Parkinson's disease. We want to build a biological pacemaker that could replace an electronic pacemaker. We want to replace an electronic insulin pump with a biological pump. And we are optimistic we can get there.



#### Why did you choose Salk?

I knew about the science at Salk and how expansive it is. When visiting, I was explicitly told by Tony Hunter that they expected me to be doing something different in five years, to be collaborating, to draw from my neighboring labs and allow them to push me to venture into areas I normally would not go.

The Institute's structure facilitates these interactions. There's a community spirit, a sense we are here to cross interdisciplinary boundaries. It's not just talk. I can see it happening in the research.

#### What big questions are you trying to answer?

We are interested in epigenetic regulators. These are proteins that largely tell a cell which genes to turn on and which ones to turn off. They are highly mutated in cancer. Our goal is to understand how these mutations disrupt cellular function and ultimately give rise to disease.

#### Compared with others in your field, how is your approach different?

We started in a relatively straightforward way, just looking at the mutations. But our data led us to start thinking about non-epigenetic processes. We're getting interested in interactions with mitochondria and other organelles that, normally, I would not be studying at all. It's the collaborations here that allow us to do that.

For example, we've started collaborating with Salk Professor Gerald Shadel. Some of the findings in our data were similar to findings his team had, from manipulating mitochondria. We looked at each other and he asked, "Do you think mitochondria are affecting the nucleus, or do you think genes in the nucleus are affecting mitochondria?"

Maybe we can look at his signature in my cells, and my signature in his cells, and get down to how these two organelles are communicating. It's a nice example of this collaborative spirit.

#### How do you, as a foundational scientist, see the impact of your work?

The impact is fairly direct. We know these mutations are highly prevalent in cancer. What we don't understand is why. We have evidence in the human population that they are definitely cancer drivers. We just don't have a sense, mechanistically, of how that is happening.

We're talking about common cancers: colorectal, lung, ovarian. That resonates with family and friends because many people actually have cancer or know someone who has cancer.

#### What inspires you?

My lab inspires me. The data inspires me. I really enjoy being at Salk. I find it incredibly inspirational looking at my colleagues and what they're coming up with.

ASSISTANT PROFESSOR | MOLECULAR AND CELL BIOLOGY LABORATORY | RICHARD HEYMAN AND ANNE DAIGLE ENDOWED DEVELOPMENTAL CHAIR DIANA HARGREAVES



#### Why did you come to Salk?

It was definitely not part of the plan. My background is in computer science. I spent pretty much all of my undergraduate, graduate and postdoc years in computer science or machine learning. That was home for a long time.

My interest in biology started during my postdoc. It connects to the theme of my lab now, which studies algorithms in nature this idea that biological systems have to solve problems to survive. These are basic computational problems that arise and, over millions of years of evolution, some of these systems have evolved really ingenious strategies to solve them. It's amazing what millions of years of randomness and selection can do. We want to learn the strategies these systems have evolved in order to enhance computer science and machine learning, as well as present a new perspective on how biological systems process information.

As I started applying to organizations, I was much more excited talking to someone who was doing immunology or plant biology or cancer biology than I was talking to computer science people studying computer graphics. The idea of having colleagues who have in-depth knowledge of many different biological mechanisms, that's exciting for me.

#### What big questions are you trying to answer?

One area I've been studying is the interface between machine learning and neuroscience. The brain is one of the most efficient computational devices in the world. It's doing things that no computer can do, and it's doing it with approximately 20 watts of power, which is like a standard light bulb. So the dream is to understand the basic principles of how the brain works in such a way that we can use these strategies to enhance machine learning.

We're in a time now when we can really map out circuits and connectivity, electrophysiology and anatomy, in ways that get into the details of how the brain actually works.

#### What job would you have in an alternate universe?

When I was growing up, I thought I'd be playing in the NBA. I thought I'd be the first Indian playing for the Miami Heat. I'd be draining threes from the corner, and the crowd would be going wild. I believe in the multiverse. In some other universe, that's what I'm doing.



#### How do you, as a foundational scientist, see the impact of your work?

The key question in genetics asks how an organism's characteristics (its phenotype) are encoded into the genome. Which parts of the genome, and which mechanisms, make us different from animals or animals different from plants? To study this, I use root systems.

Trees take a long time to grow. We want to use the genome sequence, when it's a seedling or even a seed, to determine what a tree would look like and whether it would withstand certain environmental conditions, such as stress and disease.

Roots search the soil for nutrients and water, but not all nutrients are distributed equally. If we understood which genes help roots find nutrients, we could tailor crops for specific soils or environmental conditions.

This is even more important now with climate change. If I knew which genes were important, I could tell farmers they need to plant this varietal to get the maximum output from this soil in these conditions. We could tell breeders to cross certain varietals or we could introduce gene editing to make a new subtype that is well-adapted and maximizes output.

#### How have technological advances impacted your work?

We measure many different strains and identify the genes responsible for root development. We use a method called genome-wide association mapping, based on having the sequence information of many varieties. That has only become possible over the past 10 years thanks to the sequencing revolution.

We can also measure a lot of phenotypes, such as root length or thickness. Image-processing software is essential for that, and we are using deep learning to increase our abilities. We do a lot of measurement, so advances in the ability to compute complex statistics have really driven our work forward.

We pioneered tools to grow a lot of roots, take pictures and measure the roots from these images. Initially, we measured around three million to four million roots. Since coming to Salk, we have built a robot that allows us to screen millions of plants each year.

#### Which scientists inspire you?

There's a long list, but Charles Darwin and Gregor Mendel are the giants. Darwin even experimented with roots, and postulated that root tips act as a kind of brain for the plant.

At Salk, it's Joanne Chory and Joe Ecker. Even when I was still a student, I knew of Salk because the first reverse-mutant collection [mutated genes that are further altered to enhance study] was made here by Joe Ecker. Joanne Chory did fundamental work on how plants sense the environment and respond to it, and she investigated the mechanisms that are responsible. Salk was always on my radar.

INTEGRATIVE BIOLOGY LABORATORY SSOCIATE PROFESSOR | PLANT MOLECULAR AND CELLULAR BIOLOGY LABORATORY **NOLFGANG BUSCI** 



The Helmsley-Salk Fellows Program brings impressive young scientists to the Institute to drive innovation. Having recently earned their doctorates, these investigators embrace original ideas and novel approaches. In other words, they fit right in.









Many researchers study how different molecules (proteins, RNAs, etc.) control gene expression. Dixon is looking at the forest rather than the trees. He wants to understand how genomes are organized in three-dimensional space, how that packaging regulates gene expression and how it might go awry in disease.



Patrick Hsu earned his PhD at Harvard and was an early contributor to CRISPR-Cas9 gene-editing technology. He wants to refine this technology to improve patient care. Hsu combines synthetic biology, genomics and neuroscience to address neurodegenerative diseases and complex genetic disorders.

He uses gene editing to examine cell processes and understand how small genomic adjustments can generate big changes in an organism. In addition, Hsu's lab has developed a new CRISPR system to edit RNA, which will help him and others gain even more insight into how the genome mediates health and disease.



**Dmitry Lyumkis** was recently promoted to assistant professor. He was one of the first Helmsley-Salk Fellows, coming to the Institute in 2014. The following year, he was honored with a prestigious NIH Director's Early Independence Award.

Lyumkis is trying to solve one of the most difficult problems in biology-how to image a protein to discern its structure. This is critically important work because, with proteins, structure equals function.

To get there, Lyumkis uses an emerging electron microscopy technology called cryo-EM, which allows him to visualize proteins in near-native conditions and build three-dimensional models.

Lyumkis is particularly focused on illuminating the atomic machinery that helps HIV insert its DNA into human genomes. This structural information could lead to new therapeutic targets and antiviral drugs. His lab is also refining the technology to achieve higher resolutions and image other biological machines, such as ribosomes, which read RNA and build proteins.

Salk Professor Satchidananda (Satchin) Panda runs his life like clockwork. Most mornings, if he's not traveling, he wakes up around 6 a.m. without an alarm. One of the first things he does is go out to his backyard to check on his provisions for wild birds. Their feeder is on an automatic timer that opens at 6:15 a.m., which is no surprise given that Panda's research is on biological timing in animals and humans, and how disruptions to this timing can result in obesity, stress, metabolic disorder and possibly even cancer.

## Living in circadian rhythm ANAATAGE OFTINE

LOSE WEIGHT. Supercharge Your Rearry. and Transform Your Realth from Morning to Midnight THE CIRCADIAN CODE SATCHIN PANDA, PHO

The Circadian Code by Satchin Panda, published in 2018 by Penguin Random House, provides an in-depth look at what the circadian clock is, why it's important, how it works and how to readjust when it's not working. Based on his decades of research, Panda's book explores the genes, molecules and cells that keep our bodies on schedule and offers tips for adjusting this clock to improve overall health. Having spent more than two decades unwinding the mysteries of biological clocks, Panda doesn't just conduct circadian research—he lives it. An hour after Panda wakes and gets his daughter ready for school—which is enough time for his "sleepiness" hormone (melatonin) to wind down and his "wakefulness" hormone (cortisol) to begin ramping up—he has breakfast with his wife. (He looks forward to his daughter's school district moving to a later start time, which will allow her to live in better alignment with her circadian rhythm.) His breakfast of homemade cottage cheese or yogurt, oatmeal and fruit yields enough complex carbohydrates and protein to keep his rising digestive enzymes busy and keep him fueled for much of the day.

At 8:00 a.m., Panda arrives at his lab, which is on the first floor of the Salk Institute, two levels below ground. Thanks to the ingenious "light wells" designed by architect Louis Kahn, the subterranean space gets plenty of natural illumination, which, according to Panda, is critical for helping to synchronize the cellular master clock in the brain and keep all the other body clocks on time.

These body clocks, or circadian rhythms, are 24-hour cycles that govern the behavior of living things, all of which evolved in the context of the planet's alternating day/night pattern. Panda often refers to the "discipline of the clock," an idea that biological activity—such as the production of proteins that help process food—rises during an animal's waking period and slows during its resting period.

"The circadian clock is the body's internal timing system, which interacts with the timing of light and food to produce our daily rhythms," says Panda. "The best way to achieve optimal health is to live in accordance with the clock rather than fight it."

While the body's activities shift according to molecular timekeepers in almost every cell or organ, environmental influences, such as artificial lighting and constant access to food, can throw these circadian rhythms out of whack. Panda believes that understanding more about circadian rhythms—and how to manipulate them—could be the key to dramatically improving health.

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#### **Circadian Clock**

Because our early ancestors evolved to forage or hunt during the day and sleep at night, human biology is designed to support eating and physical activity during the day and cellular repair and cleanup at night, according to Panda. But refrigeration and other modern conveniences mean that many of us are eating during a window of 15 or 16 hours each day, giving our cells much more digestive work to do and not enough time for recovery and restoration.

#### **Circadian Lifestyle**

#### **Erratic Lifestyle**



#### **Food Timing**

Right: Using tools such as smart watches and customized apps, the Panda lab charts participants' exposure to light and food throughout the day.

For improved health, Panda recommends avoiding food for at least one hour after waking up as well as two to three hours before bedtime.



And he has the data to back his thinking. As a researcher at the Genomics Institute of the Novartis Research Foundation in 2002, Panda was one of the discoverers of light-sensitive cells in the mammalian eye that function to set the master clock. That breakthrough earned his group and two others a place on *Science* magazine's list of "Top 10 Discoveries of 2002." And more recently, in a paper published in *Science* in February 2018, Panda and colleagues found that nearly 80 percent of genes in many tissue types and brain regions follow a day/night rhythm, with activity spiking in the morning and late afternoon and quieting down in the evening, around bedtime.

"The body cannot accomplish all its tasks at once, so functions such as digestion, growth and repair occur at certain times determined by the circadian rhythm," Panda says. "This suggests that eating, exercising and sleeping during those times is more efficient and therefore better for our bodies and our health."

The field of circadian science has only been gaining prominence as, increasingly, studies are finding links between circadian rhythm disruption and a wide range of health problems, from digestive ailments such as acid reflux to chronic diseases such as diabetes and dementia. Panda (who wears a specialized watch to monitor his own exposure to light and carefully tracks his eating, heart rate and motion) has seen firsthand the impact that changes in environment can have on one's mood, productivity and health.

#### Food timing: a simple change with drastic results

Unfortunately, many of the conveniences we enjoy in modern life seem to be at odds with our natural rhythms—in particular, exposure to artificial light and access to food around the clock.

The retinal cells that Panda and others discovered are sensitive to blue light—the kind emitted by many electronic devices and energy-efficient light bulbs—which means nighttime exposure tricks our brains into thinking it's daytime, suppressing melatonin and making it hard to fall or stay asleep. One way to address this is to use the recent "nighttime" options in electronics that reduce blue light from screens. (Panda turns on his filter around 8 p.m. and avoids any harsh lighting at home.)

Another, perhaps more significant, factor disrupting our clocks is 24-hour access to food. Because our early ancestors evolved to forage or hunt during the day and sleep at night, human biology is designed to support eating and physical activity during the day and cellular repair and cleanup at night, according to Panda. But refrigeration and other modern conveniences mean that many of us are eating over the course of 15 or 16 hours of every day, giving our cells much more digestive work to do and not enough time for recovery and restoration.

In 2012, Panda, his then-postdoctoral researcher Megumi Hatori (now a researcher at Keio University) and colleagues published a trailblazing study in *Cell Metabolism*, in which they fed two genetically identical groups of mice the same amount of high-calorie food. The critical difference was that one group had 24-hour access to the food; the other was restricted to eating during an 8-hour window. The group with 24-hour access became obese and began developing signs of disease such as high cholesterol and insulin resistance. The time-restricted group, however, was lean and healthy—despite eating the same number of calories as the obese group.

Then, in 2014, Amandine Chaix, another postdoc in the lab (now a staff scientist), conducted a follow-up study with mice, in which she again observed an 8-hour time-restricted group, but also had groups restricted to 9, 10 and 12 hours. She got the same results: the mice with round-the-clock access to food gained weight and became unhealthy, while mice in the food-restricted groups stayed lean and healthy.

"We knew that the clock had an influence on metabolism, but we were really surprised to find that just restricting the timing of food could protect animals against weight gain and type 2 diabetes," Chaix says.

More significantly, when she put the obese mice back on a timerestricted diet, they lost weight and regained their health, reversing course on high cholesterol, elevated blood sugar, high blood pressure and other markers of ill-health that lead to disease.

The groundbreaking studies have launched a whole new approach to improve human health with a relatively simple adjustment: restricting one's calorie intake to an 8- to 10-hour window, which could confer a host of health benefits, including weight loss. On this regimen, one may occasionally go up to 12 hours of eating or may extend eating beyond 12 hours for a day or two in a week.

To find out whether humans can benefit in the same way, Panda's team has been collecting data since 2015 about the eating habits of people all over the world via a mobile phone app called "MyCircadianClock," in which people upload photos of everything they eat. Timestamps on the hundreds of thousands of photos submitted through MyCircadianClock reveal when the food was consumed. Aside from interesting tidbits about people's eating habits (for instance, many people start with coffee and milk at 6 a.m. and end with a glass of wine or a bowl of ice cream at 9 or 10 p.m.), Panda's team is seeing preliminary findings that indicate restricting food to within an 8- to 10-hour window benefits humans as well.

Even though the research in humans is early, Panda's preliminary positive results have generated interest from fellow scientists, the media and the public across the globe. After a recent TV interview, media employees working behind the scenes swarmed Panda to learn more tips for doing the "circadian diet."

"It is an appealing idea to lose weight and feel healthier not by cutting calories but just by timing your eating habits a little differently," he says. "Everyone wants to learn more."

Panda has written a book to share the health insights based on his own research and that of other circadian scientists with the public—*The Circadian Code: Lose Weight, Supercharge Your*  *Energy, and Transform Your Health from Morning to Midnight.* In it, Panda recommends a window of 8-12 hours for eating. He favors an 11-hour window, which includes breakfast and dinner. He doesn't eat lunch, because it makes him sleepy and less productive, which he, as the head of a lab of 40 people who travels frequently, can't afford.

#### Benefits beyond weight loss

Restricting one's calories and using other methods to match our circadian clock to a more natural rhythm has benefits beyond weight loss.

In January 2018, Panda and first author Gabriele Sulli published a paper in the journal *Nature*, describing how targeting the circadian clock in cancer cells could work as a therapy. Normal cells are used to producing and consuming nutrients only during specific windows of time determined by their circadian clocks. But cancers disrupt their cellular clocks so they can get nutrients all the time to support their unchecked growth. The team found that when drugs are used to reactivate the clock in tumors, cancer cells can't survive. Healthy cells, however, are unharmed because they are already accustomed to the discipline of the clock, pointing to a new possible target for cancer therapy.

Additionally, the Panda lab's research has implications that could help shift workers—such as healthcare employees, members of the media and first responders—who often suffer much higher rates of chronic diseases due to disrupted sleep schedules. To explore this angle, the team received a \$1.5 million grant from the Department of Homeland Security for a three-year study in collaboration with UC San Diego and the San Diego Fire Department to see whether restricting food intake to a 10-hour window can improve the health of firefighters, who—like many shift workers—have disrupted day/ night schedules.

There is no shortage of projects involving circadian rhythms. Panda is collaborating with an MD/PhD scientist in training on a study of how circadian disruption in intensive care units affects patient health. Panda is also working with a visiting architect on developing guidelines to incorporate circadian-friendly lighting into building design.

After a packed day tackling his many projects, Panda usually leaves the lab between 4:30 p.m. and 6:30 p.m. to have dinner and time with his family. After some exercise and more work, he goes to bed by 11:00 p.m. at the latest. He has an eye mask to ensure complete darkness and keeps earplugs handy in case the coyotes from a nearby canyon get raucous.

Seven hours later, typically rested and refreshed from his disciplined routine, the circadian researcher begins the cycle again.

#### Tips to Lessen Jet Lag

With collaborations in Europe, Africa and Asia, Satchin Panda spends a lot of time traveling. In a recent twomonth period, he jetted from his home base in San Diego to Chicago; Dallas; Nairobi, Kenya; Seoul, South Korea; Nashville; Denver; and Nagoya, Japan. Yet he rarely has jet lag.

Jet lag occurs when you travel across two or more time zones in a day. Most people's circadian clocks take a day to adjust to each time shift so if you travel from one US coast to the other, for example, it may take you three days to fully adapt to your destination, says Panda. He recommends paying attention to your exposure to food and light to help adjust more comfortably to a new time zone. His tips (based more on personal experience than direct experimental data) include the following:

- **Cut your calories by half on travel days**, when your physical activity will be significantly restricted.
- **Proposed Section 2** For morning flights, don't eat between the time you wake up and the time the plane takes off. Use your flight time to catch up on sleep. Many flights leave before 8:00 a.m., which means you are already sleep-deprived from getting up early or not sleeping well the night before your trip.
- When sleeping on flights, **wear earplugs and a sleep mask to get deeper sleep**. Consider using a nasal breathing aid—getting more oxygen will help you sleep.
- For afternoon flights, you will likely arrive at your destination at night. **Don't sleep on the flight, but do eat dinner if you are hungry.** Once you arrive, wait until the following morning to eat.
- If you arrive at your destination at night, avoid
  brightly lit places like grocery stores or drug stores that may affect your ability to fall asleep.
- On very long international flights, try to sleep much
  of the time. This will help you avoid more than one
  meal and allow you to feel more rested.

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# Driven to Succeed

As the son of a farmer and a homemaker from a village in southwest India, Raj Giraddi could not have imagined the path his life would take, far from the family's fields of chilies, peanuts, sunflowers, lentils and onions. rom once being a schoolboy sitting on the floor of a rural classroom with no electricity, to now being a breast cancer researcher in the laboratory of Geoffrey Wahl, Raj Giraddi's deep and abiding interest in biological research has always driven him forward.

You could say it was onions that started him down that path.

In a general biology course at Bangalore University, Giraddi did a simple lab assignment that required him to grind up the roots of an onion to view the stages of cell division through a microscope—he was transfixed.

"When I started looking at the cells and saw the chromosomes, I was stunned," he recalls. "Those pictures were fascinating and, for some reason, even though I was studying math, chemistry and physics at the same time, those images stuck in my head."

Bangalore, a metropolis of millions, is also India's research capital. While Giraddi was getting his bachelor's and master's degrees, he would ride his bicycle around the campuses of various biotech institutes, sneaking into departments to read notice boards with posters describing how research was done. He wanted to be involved in scientific research, but it wasn't an option at his university. For that, he figured he would have to be at the elite Indian Institute of Science (IISc), nearby. But every ambitious student in the country wanted to be accepted to IISc. For someone with no formal research training, it was challenging to get in.

Instead, Giraddi began working at a local hospital that was developing a new research program in triplenegative breast cancer. Although his mother had been diagnosed with an aggressive brain cancer a decade earlier, Giraddi didn't consciously notice the cancer coincidence. Over time, his team got excellent data from their breast cancer project; so when his supervisor transferred the project to IISc, she convinced the new lab to take Giraddi, too. Giraddi hit the ground running as a project assistant. During this early research, he won his first award, for a conference poster presentation in which he described his research with stem cells. The judge was a woman named Connie Eaves, one of the world's foremost authorities on breast cancer.

The following year, Giraddi, who was deeply interested in different cell types and the relationship between normal breast tissue and tumor tissue, decided he wanted to get his doctorate. He applied to a competitive program at Cancer Research UK making it through the first two rounds against stiff competition from people with Ivy League educations. For the third round of 120 applicants. Giraddi had a personal interview with the prospective investigator, John Stingl, who, it turned out, had just completed his postdoctoral training with none other than Connie Eaves.

The shared connection helped Giraddi land the position in Stingl's lab at the University of Cambridge.

"It was a very challenging experience to begin with because I was so overwhelmed," he says. "You're surrounded by brilliant scientists, and everyone wants to do something important, so it's a competitive environment. But those interactions helped me understand what scientists' work means for society. It was really motivating."

He recalls walking in Cambridge on a bike path that had been painted with the actual DNA sequence of the BRCA2 gene. It occurred to him that it was the discovery of the BRCA1/2 genes that had transformed breast cancer biology and helped to prevent aggressive breast cancer in millions of women. For the first time, he realized that research interests must go beyond personal curiosity, to productive science that contributes to our understanding of diseases and enables successful therapies.

Giraddi next decided on a lab in Belgium for his postdoctoral training, but that was a more difficult experience. Although he had been contributing to an ongoing project to identify the cell of origin in breast cancer, the project Giraddi had chosen for himself was a very risky, ambitious experiment, which failed after three years. He decided to return to India and take stock of his next research project. During the hiatus, Giraddi read a paper by the Wahl lab.

"It was one of the milestone papers published in our field," he says. "The comparison of embryonic cells versus malignant breast cancer cells fascinated me."

He contacted Wahl about working in the lab, proposing a project to follow the development of a cell from its earliest embryonic state through its entire life, and expressed interest in improving our understanding of static cell types and cell states. Wahl laughed, saying, "We're already working on it." A series of conversations led Wahl to believe he and Giraddi were very much on the same page scientifically, so, even though they hadn't yet met in person, Wahl offered Giraddi a research associate position.

Giraddi has thrived at Salk, working to push cancer research to the next level. He was the first author on a recent landmark paper in *Cell Reports* detailing the lab's cutting-edge techniques to generate an atlas of the genes expressed in each breast cell from very early in development until adulthood, which the team compared with genes expressed in human breast cancers, identifying similarities that could be used for new diagnostic tests or treatments.

Giraddi's mother, who survived for 25 years after her cancer diagnosis, is now in a hospice and hasn't been aware of his recent successes. But Giraddi is keenly aware of the potential impact of his work for people with cancer, and it drives him onward.

As for onions? Giraddi now just cooks with them. §

## A HISTORY OF Scientific Breakthroughs

	Jonas Sall founder, un first safe, e vaccine	Jonas Salk, founder, unveils the first safe, effective polio vaccine		Suzanne Bourgeois joins the Salk Institute and goes on to establish the Regulatory Biology Laboratory and conduct pioneering work on the regulation of gene expression		Catherine Rivier joins the Salk Institute, where she identified a large number of hormonal functions and new endocrine pathways throughout the body		illemin obel Prize for s concerning e-hormone of the brain
	1955	1962	1966	1968	1970	1975	1977	1979
		Francis Cr Salk foundir wins the No for the disco structure of its role in in transfer in I		ck, fellow, Prize ery of the NA and wrmation ing material Robert W. Holley wins the Nobel Prize for the interpretation of the genetic code and its function in protein synthesis		Renato Dulbecco wins the Nobel Prize for discoveries concerning the interaction between tumor viruses and the genetic material of the cell		Tony Hunter and Bart Sefton discover tyrosine phosphorylation, which leads to the creation of a class of cancer drugs known as tyrosine kinase inhibitors (e.g., Gleevec, Iressa, Tarceva)
A	T			-	1	=	1	

For more than 50 years, the Salk Institute has been at the forefront of biological research. Whether in neurobiology, cancer, metabolism, plant biology or myriad other fields, Salk leads the way, transforming how humanity understands the world in which we live. Salk's leadership in foundational biological research includes:



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Mel Cohn ca. 1970.

Below: Suzanne Bourgeois-Cohn and Mel Cohn at the Chihuly at the Salk event in 2010.

Below, right: Fellows and President Joe Slater in 1969. From left to right: Jonas Salk, Francis Crick, Joe Slater, Bob Holley, Warren Weaver, Steve Kuffler, Jacques Monod, Mel Cohn, Ed Lennox, Salva Luria, Danny Lehrman, Jacob Bronowski, Renato Dulbecco and Leslie Orgel.





### Remembering immunology titan and Salk founding fellow Melvin Cohn

On October 23, 2018, Salk was saddened to learn of the passing of Professor Melvin Cohn, titan of immune system biology and a pioneering researcher in the field of gene regulation. He was 96. Cohn leaves an indelible legacy at Salk.

"Mel Cohn has been a mainstay of the Institute since its very first days," says Salk President Rusty Gage. "He stood with Salk through its entire history and all of us will miss his presence and his wisdom. His work in the field of immunology and his impact on Salk are both profound and influential. Throughout his career, Mel showed an incredible ability to adapt to the dynamic needs of the field of science. We are fortunate to have his innovative example to follow as we continue seeking new ways to understand ourselves and the world we call home."

Cohn joined Salk in 1961 as a founding and resident fellow, with his wife and fellow researcher Suzanne Bourgeois-Cohn, at the personal request of Jonas Salk, discoverer of the first effective polio vaccine. Cohn held a faculty appointment with neighboring UC San Diego for more than 30 years. Prior to joining Salk, Cohn was a National Science Foundation fellow at the Pasteur Institute in Paris and was previously a professor at Stanford University and Washington University in St. Louis. He was named a professor emeritus of Salk in 2011 and maintained an active research group until shortly before his passing.

"Mel was a dedicated, active scientist until the day he died," says Bourgeois-Cohn. "Mel helped to make Salk what it is today. He was a giant in the field of biology and a wonderful person. I and his many friends will miss him terribly."

In the field of gene regulation, Cohn worked with Nobel Laureate Jacques Monod on seminal research describing the *E. coli* lac operon, a set of genes that encode proteins to break down lactose (sugar). This research laid the foundations for better understanding how genes are turned on and off, work that would go on to be recognized with Monod's 1965 Nobel Prize.

Recently, Cohn and his wife established the Suzanne Bourgeois and Mel Cohn Research Resource Fund, providing approximately \$15,000 in total awards each year to Salk researchers. Cohn was able to see the award's very first recipient receive their prize at a Women & Science showcase event shortly before his passing.

At Salk, Cohn studied the body's immune response, which protects us from the lethal effects of pathogens. After nearly a decade of working in the field of enzyme regulation, he turned to the problem of antibody synthesis. While the immune system cannot predict which of the diverse array of pathogens it will encounter, it nevertheless must respond promptly to defend the host organism from invaders. Cohn's investigations were largely theoretical and dealt with the evolutionary selection pressures that shape the immune system, contributing to an understanding of humans' evolution and defense mechanisms.

To this end, Cohn established a mouse myeloma (cancer) library that contained lines of cells that could be manipulated in tissue culture. With this library, Cohn and his team were able to prove the somatic hypermutation model of antibody synthesis—the idea that immune cells/antibodies mutate in direct response to infection and exposure to pathogens in order to fight disease. A byproduct of Cohn's work was a number of antigen-presenting cell lines, macrophages and reticular cells for a wide number of diseases. These important lines are still being maintained. S



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#### **EDWIN LENNOX** 1920 - 2018



Edwin Lennox, PhD, Salk founding fellow as well as an expert in physics and cellular and molecular immunology, passed away on June 9, 2018, following a sudden illness.

Lennox had a long career in science, spanning several fields of research, with more than 100 research papers to his name. Following time as a graduate student at the University of Rochester, Lennox received a letter from famed theoretical physicist Victor Weisskopf inviting him to work at an "undisclosed location on an unidentified project."\* He soon arrived at Los Alamos National Laboratory in New Mexico to take part in the Manhattan Project. There, he worked alongside future Nobel laureates Richard Feynman and Leo Szilard.

Following the war, Lennox pivoted away from physics. He completed his PhD in theoretical physics at Cornell University but later, while attending a seminar put on by Melvin Cohn at Cold Spring Harbor Laboratory, became intrigued by the specificities that underlie the various immunoglobulins that contribute to the human immune system. The following summer, Lennox joined Cohn's lab at Washington University in St. Louis. Lennox spent much of his career focusing on cellular and molecular immunology. The pair, Lennox and Cohn, would go on to host several Antibody Workshops supported by the National Science Foundation, where researchers shared findings and ideas to accelerate the pace of discovery in the field of immunology.

In 1961, Lennox and Cohn arrived at the Pasteur Institute to work with another future Nobel laureate, Jacques Monod. It was at this time that Lennox was personally asked by Jonas Salk to join the Salk Institute, with a formal offer from Salk the next year. Lennox was one of the first four fellows to join the Salk Institute alongside Cohn, Jacob Bronowski and Renato Dulbecco.

Lennox was born in 1920 in Savannah, Georgia. He pursued his undergraduate degree at Vanderbilt University where he studied under Max Delbrück, a future Nobel Prize winner and influencer on many of Salk's early faculty. His work as a biotechnology pioneer would lead him to become the director of research at Celltech synthesizing drugs engineered using recombinant DNA methods. **S** 

\*Bourgeois, Suzanne. *Genesis of the Salk Institute: the Epic of its Founders*. Berkeley: University of California Press, 2013.

# SPOTLIGHT

#### DISTINGUISHED SCIENTISTS TO JOIN SALK INSTITUTE, FOCUSED ON BRAIN CIRCUITRY, PANCREATIC CANCER

The Salk Institute announced that globally renowned neuroscientist Kay Tye will join its faculty in January 2019 as a full professor. She is currently an associate professor in the department of brain and cognitive sciences, part of the Picower Institute for Learning and Memory at the Massachusetts Institute of Technology (MIT).

Tye focuses on a wide variety of cutting-edge technologies and approaches to better understand the brain circuitry underlying emotion and motivation. Her discoveries are helping pave the way for more targeted and efficient treatments for brain disorders, such as addiction-related behaviors, attention deficit disorder, anxiety and depression. For example, she has examined how emotional states such as increased anxiety may increase the propensity for substance abuse by facilitating long-term changes associated with reward-related learning.

Tye is the recipient of numerous accolades and grants, including a Presidential Early Career Award for Scientists and Engineers; an NIH Director's Pioneer Award; an NIH Director's New Innovator Award; a Society for Neuroscience Young Investigator Award; the Daniel X. Freedman Prize; a McKnight Fellowship; and many others. She received her BS degree from MIT and her PhD from UC San Francisco, before working as a postdoctoral fellow at Stanford University and the Ernest Gallo Clinic and Research Center.

In addition, the Salk Institute is honored to welcome Dannielle Engle back to Salk as an assistant professor in the Salk Cancer Center. She is currently a senior fellow at Cold Spring Harbor Laboratory, in New York, where she focuses on the early detection and treatment of pancreatic cancer. Engle conducted research in the lab of Salk Professor Geoffrey Wahl for six years as part of her doctoral program at UC San Diego.

Pancreatic cancer is one of the deadliest cancers because it is difficult to detect and is especially resistant to treatment. As part of her postdoctoral training with David A. Tuveson at Cambridge Research Institute (UK) and Cold Spring Harbor Laboratory, Engle developed miniature pancreas organ cultures ("organoids") using both human and mouse cells to identify biomarkers and treatments for pancreatic cancer.

Engle holds a bachelor's degree in biological sciences and Asian studies from Northwestern University and a doctorate in biological sciences from UC San Diego. She is the recipient of a California Breast Cancer Research Program Fellowship, a UC San Diego Chancellor's Fellowship and a National Institutes of Health/National Cancer Institute Career Transition Award, among other honors. She begins her appointment in January 2019.



Kay Tye



**Dannielle Engle** 

#### **SPOTLIGHT**

#### TATYANA SHARPEE NAMED AMERICAN PHYSICAL SOCIETY FELLOW

Associate Professor Tatyana Sharpee, a member of the Computational Neurobiology Laboratory, has been elected a 2018 Fellow of the American Physical Society (APS) for her outstanding contribution to physics. Sharpee aims to develop a unifying theory of how biological systems process information. This honor recognizes her efforts to "advance our understanding of how neurons represent sensory signals and make decisions by pioneering new methods for analyzing neural responses to natural stimuli and uncovered organizing principles for closed loop behaviors," according to the organization.



Tatyana Sharpee

#### MARTINA AND DAN LEWIS GIVE \$2 MILLION FOR CANCER RESEARCH

The Salk Institute recently announced a \$2 million gift in support of its Conquering Cancer Initiative from Board of Trustees Chair Dan Lewis and his wife, Martina. The funds will be used to advance the Salk Cancer Center's highest research priorities, including new investigations into five of the deadliest cancers: lung, pancreatic, brain (glioblastoma), ovarian and triple-negative breast. The gift made possible the recruitment of incoming Salk Assistant Professor Dannielle Engle, whose unique work on pancreatic cancer may lead to new treatments.

Lewis' story was inextricably tied to Salk following his diagnosis with chronic myeloid leukemia (CML) in 2006. A diagnosis of CML had previously been akin to a terminal illness. But Salk Professor and former Cancer Center director Tony Hunter's discovery of cellular switches called tyrosine kinase inhibitors led to the creation of the cancer drug Gleevec. Gleevec is used to manage CML as a chronic disease, preventing it from becoming fatal.

Martina and Dan Lewis



#### SALK SCIENTISTS AWARDED TRANSLATIONAL GRANT FOR STEM-CELL-BASED THERAPY

The lab of Ronald Evans has received a \$1.6 million grant from the California Institute for Regenerative Medicine (CIRM) to develop a new diabetes therapy called immune tolerant human islet-like organoids (HILOs). These transplantable, insulinproducing human pancreatic islet cells, created from pluripotent stem cells, could help dramatically improve quality of life for people with type 1 diabetes. The award is part of CIRM's Discovery Quest program, which invests in research that can be rapidly translated into treatments.



#### SALK AWARDED KEEPING IT MODERN GRANT BY GETTY FOUNDATION

As part of its Keeping It Modern initiative, the Getty Foundation has awarded the Salk Institute a \$200,000 grant to support the conservation of Salk's celebrated concrete façades. The grant project will take place over the next five years. The announcement is part of more than \$1.7 million in architectural conservation grants announced by the foundation in 2018 for 11 significant 20th century buildings.

The new award will allow Salk to implement concrete conservation and set a new model for this prevalent and challenging modern building material. The repair program incorporates methods and materials that are similar to the existing materials in character and appearance while offering enhanced durability. A benefit to many more places besides Salk, the project will inform concrete conservation practices that can be used in buildings around the world.

#### PADRES PEDAL THE CAUSE KEEPS ON ROLLING



The 2017 Padres Pedal the Cause cycling event raised more than \$2.4 million for cancer research in San Diego. Salk Institute scientists Ronald Evans, Diana Hargreaves, Tony Hunter, Graham McVicker and Geoffrey Wahl were among the first wave of researchers to receive funding through Pedal the Cause's Discovery Grants program.

The 2018 Salk Cancer Center team featured 45 riders/walkers/runners and volunteers who joined together in support of leading-edge cancer research—more than 3,000 people participated overall.

Pedal the Cause awards research grants to cross-institutional teams of physicians and scientists from San Diego's top cancer institutions, including the Salk Institute, Moores Cancer Center at UC San Diego Health, Sanford Burnham Prebys Medical Discovery Institute and Rady Children's Hospital. It is one of the largest standalone cancer fundraising events in San Diego.

From left: Henry Juguilon, Nick Brideau, Sam Pfaff, Tony Hunter, Zac Davis, Corina Antal, Travis Berggren, Mark Schmitt

#### Janelle Ayres garners multiple prestigious awards

Associate Professor Janelle Ayres has been awarded a 2018 Pioneer Award by the National Institutes of Health (NIH) for her innovative research into host-pathogen interactions that promote the health of the host. The highly sought-after grant, which awards \$3.5 million over five years, "supports scientists with outstanding records of creativity pursuing new research directions to develop pioneering approaches to major challenges in biomedical and behavioral research," according to the NIH.

In addition, Ayres is the recipient of a \$1 million grant from the W.M. Keck Foundation to study new ways to treat deadly infections, including sepsis and the flu, both of which require therapies beyond antibiotics and antivirals to be treated effectively.





Left: Janelle Ayres

Above: Salk Professor Ronald Evans and Associate Professor Janelle Ayres at the Blavatnik Awards, which honored Ayres as the 2018 Laureate in Life Sciences (image courtesy of David Schneider).





#### CLODAGH O'SHEA RECEIVES ALLEN DISTINGUISHED INVESTIGATOR AWARD TO STUDY GENOME

Clodagh O'Shea, a professor in Salk's Molecular and Cell Biology Laboratory and a Howard Hughes Medical Institute Faculty Scholar, has been selected as a recipient of The Paul G. Allen Frontiers Group's Allen Distinguished Investigator (ADI) program. She will be awarded \$1.5 million over three years to conduct research into how DNA and its associated proteins (known collectively as chromatin) are packaged in the nucleus of cells. The work has implications for better understanding not only a range of diseases but also the fundamentals of human biology.

Clodagh O'Shea

JUAN CARLOS IZPISUA BELMONTE ONE OF TIME MAGAZINE'S "50 MOST INFLUENTIAL PEOPLE IN HEALTH CARE" FOR 2018

Juan Carlos Izpisua Belmonte, a professor in Salk's Gene Expression Laboratory, has been named one of *Time* magazine's 50 Most Influential People in Health Care for his scientific innovations in addressing the shortage of human organs for transplant. The list, which is curated by *Time*'s health reporters and editors, recognizes people who changed the state of healthcare in America this year and bear watching for what they do next.

Izpisua Belmonte, who holds the Roger Guillemin Chair at Salk, is globally recognized for his expertise in stem cell biology. Notably, in 2017, Izpisua Belmonte published a proof-of-concept study showing that functional organs from one species can be grown in another, an important early step toward addressing the critical shortage of human donor organs available for transplant.

INSIDE SALK WINTER 2018

#### **SPOTLIGHT**

#### SALK AWARDED \$19.2 MILLION BY THE AMERICAN HEART ASSOCIATION-ALLEN INITIATIVE TO STUDY ALZHEIMER'S AND AGING IN THE BRAIN

A team of Salk Institute researchers led by President Rusty Gage has been awarded \$19.2 million over eight years by the American Heart Association-Allen Initiative in Brain Health and Cognitive Impairment to investigate mechanisms underlying Alzheimer's disease and aging-related cognitive decline and uncover new therapies. This bold venture will comprehensively analyze interactions between five areas key to brain health: proteins, genes, metabolism, inflammation and epigenetics.

"At the Salk Institute, we have devised a completely new way of approaching Alzheimer's and aging research," says Gage, a world-renowned researcher in neuroscience and genetics who holds the Vi and John Adler Chair for Research on Age-Related Neurodegenerative Disease. "With the generous support of The Paul G. Allen Frontiers Group, the American Heart Association and other philanthropic donors to this initiative, we believe we can make significant progress in the diagnosis and treatment of Alzheimer's and other age-related cognitive diseases."

An aging-related disorder that results in severe memory loss, Alzheimer's disease represents a global health crisis with estimates suggesting that 130 million people will be affected by 2050. To date, there are no therapies to effectively treat the disease.

To respond to this critical need, Gage will be leading a multidisciplinary team of 10 Salk scientists, all luminaries in their respective fields across metabolism, immunology and inflammation, genetics and epigenetics, and protein analysis. The all-star interdisciplinary group believes that Alzheimer's and other age-related brain disorders are triggered not by a single event, but by a failure of complex,



interdependent biological systems in our body that start to break down as we age. Failure in any one of these systems can cause a domino-like crash that results in devastating brain disorders like Alzheimer's. By studying the networks that keep our brains healthy, the team aims to reveal new targets for therapeutic research and biomarkers of early stage cognitive decline.

"We are grateful for this support, which will help us learn more about the role of inflammation in Alzheimer's and how it affects other cellular processes associated with this disease," says Professor Susan Kaech, director of Salk's NOMIS Center for Immunobiology and Pathogenesis, holder of the NOMIS Chair, and a member of the project's leadership team. "We are hopeful this work will lead to the breakthroughs humanity so desperately needs."

To accomplish this, Salk research teams are developing cutting-edge methods to study aging and diseased neurons and other brain cells through cell cultures, brain organoids and a new primate model of cognitive aging.

"Since the effects of aging are themselves comprehensive, taking a systems approach seems promising," says Professor Jan Karlseder, a member of the project's leadership team who directs the Glenn Center for Biology of Aging Research and holds the Donald and Darlene Shiley Chair. "We very much appreciate the generosity of The Paul G. Allen Frontiers Group and American Heart Association in supporting this research to advance our understanding of aging."

The other Salk investigators on the grant are: Assistant Professor Nicola Allen; Professor Joseph Ecker; Vice President, Chief Science Officer Martin Hetzer; Assistant Professor Saket Navlakha; Professor John Reynolds; Professor Gerald Shadel; and Professor Reuben Shaw.

### Salk Education Outreach

Tomorrow's breakthroughs depend on today's students and teachers



the community about scientific literacy

enthusiasm and interest in science

nspire

public awareness about research at Salk

Jonas Salk firmly believed that the Salk Institute had a duty to mentor the next generation of scientists. Salk's Education Outreach Department fulfills that vision and aims to meet two critical challenges: improve science literacy and stimulate students' interest in STEM careers.

Salk Education Outreach serves all of San Diego County through the program's core handson curricula. While its programs serve San Diego school children of all ages, the majority of students are from economically disadvantaged communities and are underrepresented in the STEM education and career pipeline. Over the past 40 years, the Salk Institute has worked with thousands of students, sparking their interest in science and inspiring them to pursue careers in the field.

#### For more information or to donate, please contact:

Lisa Farnan | Associate Director of Foundation Relations (858) 453-4100 x2062 | Lfarnan@salk.edu | www.salk.edu/education





#### SYMPHONY, LESLIE ODOM, JR. LIGHT IT UP AT CONCERT UNDER THE STARS

#### On August 25, 2018, the Salk Institute once again transformed into a stunning musical venue for the 23rd annual Symphony at Salk.

Special guest artist Leslie Odom, Jr., a Tony Award winner for his role as Aaron Burr in the Broadway smash hit *Hamilton*, wowed 750 guests and 100 volunteers with his charm and dazzling vocal skills during the concert under the stars. Spectacular lighting in the courtyard highlighted the art of Salk's biophotonics imagery, the paintings of Françoise Gilot and the live shots of the performance by Odom and the San Diego Symphony.

As the sun slowly dipped toward the Pacific horizon behind the stage, guests enjoyed camaraderie, a champagne reception and a gourmet dinner before the concert. "Symphony at Salk is a very special event that inspires and uplifts the spirits of all who attend while typically raising more than \$1 million for Salk's Education Outreach program and scientific discovery," says Salk President Rusty Gage.

Symphony at Salk depends on its many generous sponsors, who this year included Zenith sponsors Joan and Irwin Jacobs, and Debra Turner; Golden Sun sponsor Tina Simner; and Supernova sponsors Martina and Dan Lewis, Tori and Terry Rosen, and Audrey Geisel/Dr. Seuss Fund. Philanthropy funds more than 50 percent of Salk scientists' high-risk, high-reward research.

#### **BIRTHDAY WISHES FOR TONY HUNTER**

Family, friends and colleagues joined Salk American Cancer Society Professor Tony Hunter on August 25 at the Sanford Consortium for Regenerative Medicine to celebrate his 75th birthday. Hunter, holder of the Renato Dulbecco Chair in the Molecular and Cell Biology Laboratory, came to Salk in 1971 as a postdoctoral fellow and joined the faculty just a few years later.



#### HIGH SCHOOL SCHOLARS IMMERSE THEMSELVES IN SCIENCE AT SALK



This past summer, high school students spent eight weeks at the Salk Institute, thanks to Education Outreach's Heithoff-Brody Scholars Program. The students conducted hands-on work in a Salk research lab, supervised by a Salk faculty member. Students learned how to formulate and test hypotheses, prepare experiments, and draw conclusions from their results. At the end of the program, students presented their research projects to their mentors, lab members and families.



SALKEXCELLERATORS AREN'T STRESSING AFTER HEARING ABOUT MITOCHONDRIA

On October 3, 2018, Salk Professor Gerald Shadel, holder of the Audrey Geisel Chair in Biomedical Science, spoke to the Salkexcellerators group about his work on mitochondria in aging, disease and the immune system. Shadel's team reports that for mitochondria—the energy factories in your cells—brief exposures to stressors can be beneficial, by prompting the cell to trigger the sustained production of antioxidants. Salkexcellerators are the next generation of community members who commit to supporting scientific discoveries and engage with Salk science through a year-round calendar of special events.

Gerald Shadel

# EVENTS



#### SALK INSTITUTE OPENS ITS DOORS TO SAN DIEGO WITH EXPLORE SALK

The Salk Institute opened its doors to more than 2,000 members of the community who attended Explore Salk on October 27. The free open house featured science booths, hands-on experiments for kids, self-guided architecture tours and poster sessions by high school students. The event also celebrated the history of the Institute and its founder, Jonas Salk, with a screening of *The Shot Felt 'Round the World, a* documentary about the development of the first safe and effective polio vaccine. Featured throughout the day were talks about Salk's Harnessing Plants and Conquering Cancer Initiatives, the science of architecture, and the use of circadian rhythms to improve human health and help us age well. About 100 volunteers helped make this a fun and educational day for our visitors.









#### **30 YEARS OF CREB SIGNALING**

Coinciding with Salk Institute Professor Marc Montminy's 62nd birthday, colleagues past and present gathered from around the globe to honor him at an August 31 symposium. The event highlighted the progress of his lab and its research on understanding signaling molecules that help keep all the cells in the body on the same page when it comes to metabolism.

Salk President Rusty Gage (left) presented Marc Montminy with a photo of the Institute, signed by many who have worked alongside him.

# Back to Basics

#### PANDA GOES BACK TO BASICS

On September 12, 2018, Professor Satchin Panda presented his research on how the circadian clock relates to weight, the immune system and overall health to a packed house. The twice-yearly Back to Basics lectures introduce the Institute's science to the general public.



#### **SCIENCE & MUSIC SERIES OPENS CURTAIN**

The sixth season of the Salk Science & Music Series got off to a rousing start with a performance by pianist Wei Luo on October 21, 2018, in the Conrad T. Prebys Auditorium. The series consists of four remarkable Sunday afternoons that bring together virtuosos from the worlds of science and music. Salk Professor Susan Kaech shared her scientific research for the opener and delivered fascinating insights into immunology. The series continues on February 24, 2019, with cellist Amit Peled, pianist Karen Joy Davis and Salk Professor Jan Karlseder.

Pictured from left: Susan Kaech and Wei Luo





#### ART OF SCIENCE ON DISPLAY AT WOMEN & SCIENCE SHOWCASE

One way the Salk Institute continues the legacy of founder Jonas Salk is by celebrating the connection of the worlds of science and art. Salk Women & Science showed how those disciplines are often intertwined, with a unique event on October 10.

The annual Design and Discovery Showcase displayed 11 incredible microscopy images submitted by Salk scientists and selected as the top entries by a panel of judges. More than beautiful, these images illustrate scientific concepts explored by Salk researchers—concepts that may lead to cures. The winning image was submitted by Tong Zhang, a light-microscopy specialist in the Waitt Advanced Biophotonics Core (see the image on page 49).

The Design & Discovery Showcase event featured art and science presentations, a reception and an auction of the 11 stunning images.

Salk Women & Science is an ongoing program that connects women in the community with leaders in biological science and technology. The program provides a dynamic and vibrant forum in which community and business leaders and Salk's women of science have an opportunity to gather as friends, entrepreneurs and researchers to discuss the latest discoveries in science and technology while inspiring more women to embrace scientific research as a focus of personal and philanthropic interest.

Left: Professor Clodagh O'Shea awes the Women & Science audience with new research breakthroughs.



The Women & Science program also hosted an event on July 11 featuring Salk Professor Susan Kaech and Associate Professor Janelle Ayres, who shared the fascinating work of the NOMIS Center for Immunobiology and Microbial Pathogenesis.

From left: Kim Witmer, Susan Kaech and Janelle Ayres

# RESOLUTION

#### **BEAUTY IN IMAGERY**

This image shows a 1-millimeter-thick section of mouse brain neurons engineered to express tdTomato, a bright red fluorescent protein derived from Anthozoa (sea coral). Using the Zeiss Z1 Lightsheet microscope—which boasts unprecedented speed and resolution for imaging in 3D—scientists were able to image all of the neurons in the tissue. The multiple colors represent different depths, with warmer colors (red) closer and cooler colors (blue) farther away from the microscope objective. Images such as these help scientists better understand the relationships between different types of brain cells and map the connections between neurons.

This image won the Women & Science Design and Discovery Showcase competition.

Credit: Tong Zhang, PhD, and Uri Manor, PhD Waitt Advanced Biophotonics Core Facility/Salk Institute

# Every cure begins with you.

#### **Education Outreach**

For nearly half a century, Salk has offered programs to inspire and launch—the next generation of scientists, Salk's Education Outreach program includes a Mobile Science Lab, Heithoff-Brody 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. Salk giving programs offer a range of ways to get involved. Learn about Salk science and support vital research.

> discover SALK

#### President's Club

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

#### **Chairman's Circle**

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

#### Architecture

**Conservation Program** Ensuring the Modernist buildings envisioned by Jonas Salk and brought to life by Louis Kahn are preserved for generations to come.

#### Cancer Center Director's Fund

Dedicated to spearheading the ambitious new research directions Salk cancer researchers are pursuing in their continued quest for novel avenues into cancer therapies.

#### Alumni/Faculty Fellowship Fund

Training the next generation of scientists is central to Salk's mission. Contributions to the Salk Alumni program support the hundreds of research associates at the Institute.

#### Get involved.

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



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#### INSIDE SALK SHOWS WELL AT 2018 AWARDS

The Salk Institute's triannual publication, *Inside Salk*, collected a number of wins and several honorable mentions in the nonprofit consumer category for the annual Folio awards. Considered one of the most prestigious awards programs in the publishing community, the Folio Awards saw more than 2,000 entries across 200 categories in editorial and design excellence for print and online publishing.

#### 2018 FOLIO EDDIE AWARDS: EDITORIAL EXCELLENCE

WINNER Best Full Issue Inside Salk, Summer 2017: "Untangling the Mysteries of the Spinal Cord"

WINNER Best Newsletter Inside Salk Newsletter

#### 2018 FOLIO OZZIE AWARDS: DESIGN EXCELLENCE

WINNER Overall Design Excellence Inside Salk

WINNER Site Design Inside Salk (inside.salk.edu)



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#### CALENDAR

#### FEBRUARY

- 6 Salkexcellerators Lecture
- 11 Partners in Research Luncheon
- 24 Salk Science & Music Series featuring Amit Peled, Karen Joy Davis and Professor Jan Karlseder

#### MARCH

27 Back to Basics

#### APRIL

- 10 NOMIS Immunology Symposium
- 28 Salk Science & Music Series featuring Brubeck Brothers Quartet and Assistant Professor Sung Han

#### THERE ARE MANY WAYS TO SUPPORT SALK.

For detailed information on opportunities, please email giving@salk.edu or call (858) 453-4100 x1201 or visit www.salk.edu/support

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Salk Institute has received the highest rating 8 consecutive times from Charity Navigator, the nation's foremost charity evaluator.





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