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ON THE COVER:

The Salk Institute is shifting its focus from studying just the causes of disease to understanding the mechanisms nature uses to resist disease and protect health. This issue's feature unveils Salk's five-year scientific and philanthropic initiative, "Campaign for the Future: Building a More Resilient World."

PRESIDENT'S LETTER

Dear Friends,

When the Salk Institute was founded more than 60 years ago, Jonas Salk had a vision to attract the world's top scientists to the cliffs of La Jolla where, working collaboratively, they could pursue answers to the most difficult health challenges facing humanity. Salk understood that an intimate physical environment could facilitate science across disciplines. He hired famed architect Louis Kahn to realize that vision in stunning buildings that are now considered masterpieces of midcentury architecture. The beauty of the Southern California coast, the opportunity to collaborate with scientists pursuing bold ideas to better humanity, and the architectural design of the buildings that overlook the Pacific Ocean would establish the Institute as one of the top scientific research organizations in the world.

In this issue of *Inside Salk*, we share our vision for the future of science at Salk. As stewards of Jonas Salk's vision for the Institute, we are launching a five-year scientific and philanthropic initiative called the "Campaign for the Future: Building a More Resilient World." Our focus on resilience is a shift from studying just the causes of disease to a more holistic approach that focuses on understanding the mechanisms animal and plant biology use to resist disease and protect health.

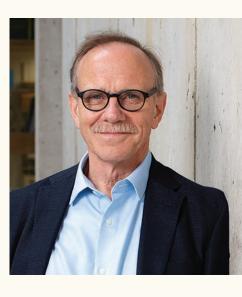
In particular, we are able to take this approach due to the rapid evolution in technology—including deep learning and computational biology—that has opened new avenues for pursuing answers to the biggest challenges of our time. However, to gather and make sense of the massive amounts of new biological data requires new types of science.

Our capacity to accelerate discoveries is limited in part by the lack of lab and research space to pursue new areas of science. Building more labs and space for discovery is an essential part of the Campaign for the Future, which features a new \$250 million-dollar state-of-the-art Science and Technology Center. Thoughtfully designed in tribute to the original, midcentury aesthetic of Louis Kahn's iconic structures, the new building will be constructed on the east end of the campus. It will be home to four Centers of Excellence in plant biology, cancer, healthy aging, and biological computation/engineering. This ambitious effort will allow us to reimagine the campus, expand the use of computational biology to advance discoveries across the Institute's disciplines and realize the critical new space we need to pursue important science for decades to come. I look forward to sharing more about this ambitious campaign with you in the months ahead.

This issue profiles Salk Professor Susan Kaech and explains how she is leading the Institute's research on infectious disease and immune biology as director of the NOMIS Center for Immunobiology and Microbial Pathogenesis. We share how Postdoctoral Scholar Nuttida Rungratsameetaweemana uses computational methods to look at brain states that lead to seizures and details of Staff Scientist Carl Procko's journey to Salk from Australia and how his study of Venus flytraps informs the larger field of plant genetics.

As we embark on the Campaign for the Future, I want to take the opportunity to thank each of you for your support and steadfast dedication. Together, we will turn dreams into reality and help shape the pursuit of scientific discovery at Salk for a new generation.



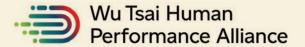


"Our focus on resilience is a shift from studying just the causes of disease to a more holistic approach that focuses on understanding the mechanisms animal and plant biology use to resist disease and protect health."

IN THE NEWS

Joe & Clara Tsai Foundation Launch Human Performance Alliance Enlisting Salk Scientists in Transformative Research on Peak Athletic Performance

A Salk team led by Professor Satchin Panda, along with teams from UC San Diego, Stanford University, Kansas University, University of Oregon and Boston Children's Hospital have been awarded a total of \$220 million by the Joe and Clara Tsai Foundation to establish the Human Performance Alliance (HPA). The six organizations will pursue research around four scientific "moonshots" designed at transforming human health on a global scale through the discovery and translation of the biological principles underlying peak athletic performance.



By understanding how athletes achieve peak physical performance, injury prevention and recovery, the HPA seeks to improve the health and fitness of all people.

Panda, who holds the Rita and Richard Atkinson chair at Salk, is a world expert in how biological clocks (AKA circadian rhythms) contribute to health or disease. He and the Salk team will map the molecules and gene activity of human performance as part of the alliance's Molecular Athlete Moonshot.

The Salk moonshot will systematically collect data on the molecular and cellular composition of human and animal body tissues to help understand how various cellular components and systems interact. The point is to build a foundational map that can be used to predict

how intrinsic factors (sex, age, menstrual cycle, etc.) interact with extrinsic factors (diet, exercise, sleep, etc.) to determine physiological performance, injury potential, healing, and recovery. This work is expected to fuel innovations in functional nutrition, personalized training, biomarker discovery and diagnostics, therapeutics, regenerative repair and surgery, and recovery regimens.

In true Salk spirit, multiple Institute faculty will collaborate to integrate laboratory cell cultures and organoids, human samples, animal models, and human data with computational models to identify biological principles governing human physical performance, injury risk and recovery.

These faculty include Professor and Howard Hughes Medical Institute Investigator Joseph Ecker; Assistant Professor Dannielle Engle; and Professors Susan Kaech, Joseph Noel and Alan Saghatelian.



The Ecker lab will work to characterize the epigenetics of tissues and biological samples. Epigenetics are the chemical tags on DNA that turn genes on or off, and help our bodies adapt to changing conditions without altering our fundamental DNA.

The Saghatelian lab will focus on the metabolites produced or consumed by tissues during metabolism, which can change significantly in response to exercise, rest and injury.

The Kaech lab will analyze tissueresident and circulating immune cells,
since immune health is essential for peak
performance. Well-coordinated immune
cell function is critical for scarless
healing, while chronic inflammation
or insufficient immune cell activation
exacerbates injury.

The Noel lab, which has expertise in biochemistry, will investigate natural compounds that can promote healing and tissue regeneration.

The Engle lab will develop organoid models of muscles, ligaments and tendons.

The Salk team will collaborate with teams at UC San Diego, Stanford University, Kansas University, University of Oregon, and Boston Children's Hospital to translate scientific findings into practice.

DISCOVERIES

INERER GY BOUATION

SCIENCE ADVANCES 04/2021

Parkinson's, cancer, type 2 diabetes share a key element that drives disease

When cells are stressed, chemical alarms go off, setting in motion a flurry of activity that protects the cell's most important players. During the rush, a protein called Parkin hurries to protect the mitochondria, the power stations that generate energy for the cell. Now, Salk Professor Reuben Shaw and colleagues have discovered a direct link between a master sensor of cell stress and Parkin itself. The same pathway is also tied to type 2 diabetes and cancer, which could open a new avenue for treating all three diseases.

Imbalances in cells' energy can open the door to disease



Salk researchers are tackling deadly tumors by targeting cancer's metabolism." www.salk.edu/cancer202109





Research advances one step closer to stem cell therapy for type 1 diabetes

Type 1 diabetes, which arises when the pancreas doesn't create enough insulin to control levels of glucose in the blood, is a disease that currently has no cure and is difficult for most patients to manage. Now, research led by Juan Carlos Izpisua Belmonte, and including co-first authors Postdoctoral Fellow Ronghui Li, Staff Researcher Hsin-Kai Liao and former Research Associate Haisong Liu, has led to a new way to create insulin-producing pancreatic beta cells from stem cells that is much more efficient than previous methods. When tested in a mouse model, these beta cells brought blood sugar levels under control within about two weeks and could someday lead to better treatments for people with type 1 diabetes.



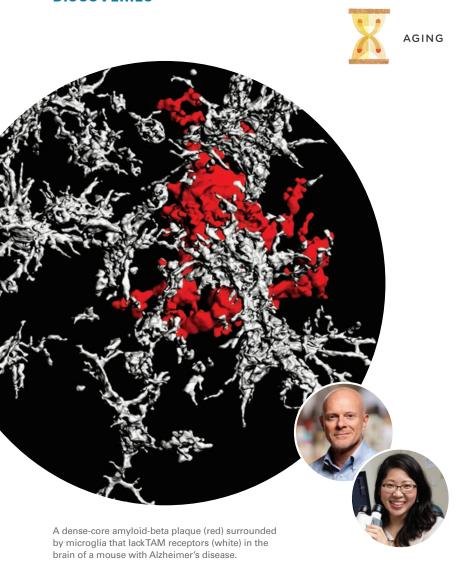
"Bad fat" suppresses killer T cells from attacking cancer

In order for cancer to grow and spread, it has to evade detection by our immune cells, particularly specialized "killer" T cells. Professor Susan Kaech, Postdoctoral Fellow and first author Shihao Xu and colleagues have found that the environment inside tumors (the tumor microenvironment) contains an abundance of oxidized fat molecules. which, when ingested by the killer T cells, suppresses their ability to kill cancer cells. The discovery suggests new pathways for safeguarding the immune system's ability to fight cancer by reducing the oxidative lipid damage in killer T cells, such as blocking a cellular fat transporter called CD36.

READ

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

DISCOVERIES



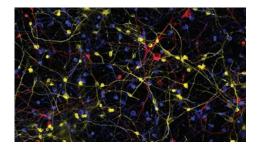
IN A SURPRISING TWIST, SOME ALZHEIMER'S PLAQUES MAY BE PROTECTIVE, NOT DESTRUCTIVE



One of the characteristic hallmarks of Alzheimer's disease (AD) is the buildup of amyloid-beta plaques in the brain. Most therapies designed to treat AD target these plaques, but they've largely failed in clinical trials. New research by Professor Greg Lemke and Youtong Huang, a postdoctoral researcher and first author of the study, upends conventional views of the origin of one prevalent type of plaque, indicating a reason why treatments have been unsuccessful. The research suggests that dense-core plaques play a protective role, so treatments to destroy them may do more harm than good.

SALK SCIENTISTS REVEAL HOW BRAIN CELLS IN ALZHEIMER'S GO AWRY, LOSE THEIR IDENTITY

Despite the prevalence of Alzheimer's, there are still no treatments, in part because it has been challenging to study how the disease develops. Now, Salk President and Professor Rusty Gage and Jerome Mertens, assistant adjunct professor and first author of a new paper, have uncovered new insights into what goes awry during Alzheimer's by growing neurons that resemble—more accurately than ever before—brain cells in older patients. And like patients themselves, the afflicted neurons appear to lose their cellular identity. The findings showed that these brain cells are characterized by markers of stress as well as changes in which the cells become less specialized. Interestingly, many of the alterations seen in these cells are similar to what's been observed in the cells of cancer-another disease linked to aging.



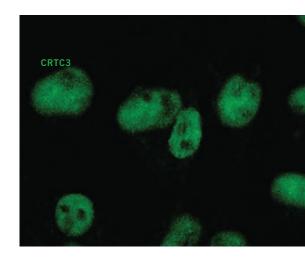
This image is a composite of induced neurons (brain cells) from different individuals with Alzheimer's disease.



SALK SCIENTISTS REVEAL ROLE OF GENETIC SWITCH IN PIGMENTATION AND MELANOMA



Despite only accounting for about 1 percent of skin cancers, melanoma causes the majority of skin cancer-related deaths. While treatments for this serious disease do exist, these drugs can vary in effectiveness depending on the individual. A study by Professor Marc Montminy and Staff Scientist Jelena Ostojić reveals new insights about a protein called CRTC3, a genetic switch that could potentially be targeted to develop new treatments for melanoma by keeping the switch turned off.

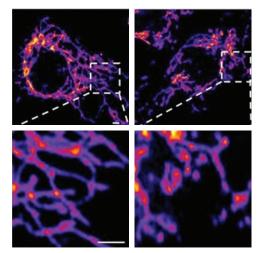


A microscopic view showing that the CRTC3 protein is located in the nucleus of melanoma cells.



CONTROL

SPIKE PROTEIN



Representative images of vascular endothelial control cells (left) and cells treated with the SARS-CoV-2 spike protein (right) show that the spike protein causes increased mitochondrial fragmentation in vascular cells.

THE NOVEL CORONAVIRUS' SPIKE PROTEIN PLAYS ADDITIONAL ROLE IN ILLNESS

CIRCULATION RESEARCH 04/2021

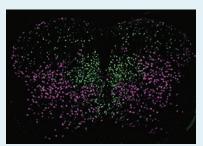
Scientists have known for a while that SARS-CoV-2's distinctive "spike" proteins help the virus infect its host by latching on to healthy cells. A new study by Assistant Research Professor Uri Manor shows that the virus spike proteins (which behave very differently than those safely encoded by vaccines) also play a role in the disease itself. The paper also demonstrates exactly how the SARS-CoV-2 virus damages and attacks the vascular system on a cellular level, and suggests that vaccine-generated antibodies are protective against COVID-19 infection and spike protein damage.





RESEARCHERS TRACE SPINAL NEURON FAMILY TREE

Spinal cord nerve cells branching through the body resemble trees with limbs fanning out in every direction. But this image can also be used to tell the story of how these neurons—their jobs becoming more specialized over time—arose through developmental and evolutionary history. Professor Samuel Pfaff and graduate student Peter Osseward, co-first author of the study, have, for the first time, traced the development of spinal cord neurons using genetic signatures and revealed how different subtypes of the cells may have evolved and ultimately function to regulate our body movements. The findings offer researchers new ways of classifying and tagging subsets of spinal cord cells for further study, using genetic markers that differentiate branches of the cells' family tree.



Researchers discovered a genetic marker that differed between spinal cord neurons that only had short connections (green) and those that had more longrange connections (purple).

INHIBITORY NEURONS TARGET THE WEAKEST-RESPONDING NEURONS IN THE BRAIN TO FACILITATE TRANSMISSION OF SIGNALS

A new study by Professor Tatyana Sharpee and first author and postdoctoral researcher Wei-Mien Hsu shows that inhibitory neurons do more than just inhibit neuron activity like an off-switch; they actually increase the amount of information transmitted through the nervous system when it needs to be flexible. The work could help scientists better understand and treat conditions such as anxiety and attention deficit disorders.



TATYANA SHARPEE

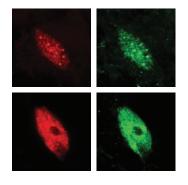




HOW PLANTS QUICKLY ADAPT TO SHIFTING ENVIRONMENTAL CONDITIONS



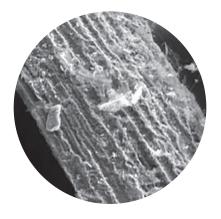
Professors and Howard Hughes Medical Institute (HHMI) Investigators Joanne Chory and Joseph Ecker, along with HHMI/ Chory lab Research Specialist Björn Willige and colleagues, offer a new understanding of how gene activity directs plant growth, and how quickly plants respond to their environment—with shifting light conditions triggering molecular changes in as little as five minutes. The findings may help farmers increase yield and safeguard world food production as climate change shrinks the planet's arable land.



Nuclei of plant cells are seen before and after the plant was exposed to shade. In the top images (before), the transcription factor PIF7 (red) is confined in speckles that contain the plant's light sensors (green). In the lower images (after), in the shaded plant, PIF7 is released, which is then free to bind to DNA and initiate gene activity.

TRANSFORMING ATMOSPHERIC CARBON INTO INDUSTRIALLY USEFUL MATERIALS

Plants are unparalleled in their ability to capture CO2 from the air, but this benefit is temporary, as leftover crops release carbon back into the atmosphere. A more permanent, and even useful, fate for this captured carbon could be turning plants into a valuable industrial material called silicon carbide (SiC). Professor Joseph Noel, Visiting Scientist James La Clair, and Staff Researcher and first author Suzanne Thomas transformed tobacco and corn husks into SiC and quantified the process with more detail than ever before. The findings are crucial to helping researchers evaluate and quantify carbonsequestration strategies to potentially mitigate climate change as CO2 levels continue to rise to unprecedented levels.

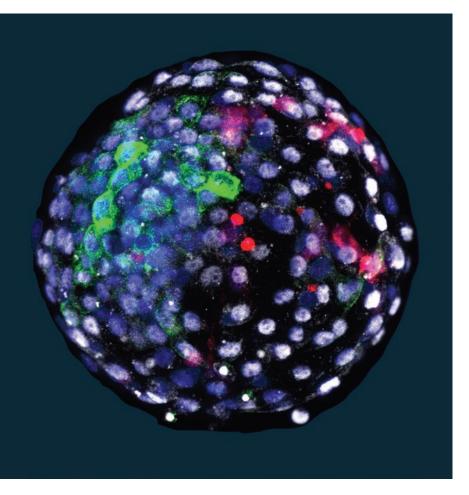


Scanning electron microscopy image of SiC petrified corn husks.

DISCOVERIES

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Using fluorescent stains, researchers are able to visualize cells of different species origins in an early stage embryo.



CHIMERIC TOOL ADVANCED FOR WIDE RANGE OF REGENERATIVE MEDICINE, BIOMEDICAL RESEARCH APPLICATIONS

CELL 04/2021

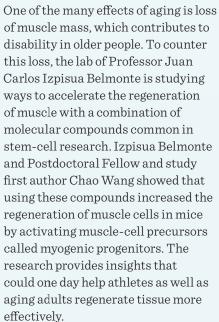
The ability to grow the cells of one species within an organism of a different species offers scientists a powerful tool for research and medicine. It's an approach that could advance our understanding of early human development, disease onset and progression and aging; provide innovative platforms for drug evaluation; and address the critical need for transplantable organs. Yet developing such capabilities has been a formidable challenge. Researchers led by Professor Juan Carlos Izpisua Belmonte have now come one step closer toward this goal by demonstrating a new integration of human cells into animal tissue.

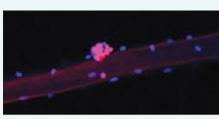


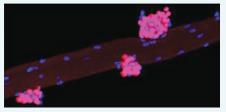
NEW STUDY SHOWS HOW TO BOOST MUSCLE REGENERATION AND REBUILD TISSUE

"Our laboratory has recently developed novel gene-editing technologies that could be used to accelerate muscle recovery after injury and improve muscle function."

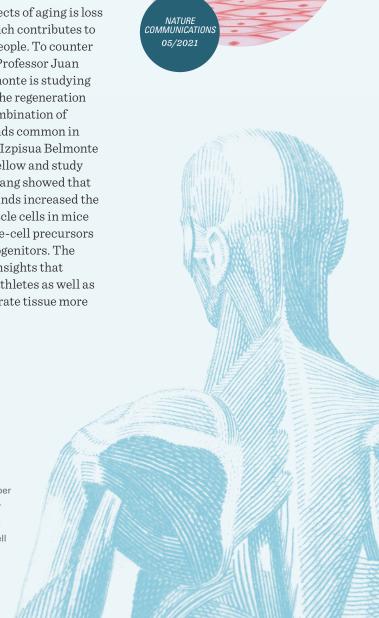
JUAN CARLOS IZPISUA BELMONTE







Using specific molecular compounds in muscle fibers increases the number of muscle precursor cells. Top, control; bottom, treatment. Red-pink color is Pax7, a muscle stem-cell marker. Blue indicates muscle nuclei.







The second pillar is thoughtful growth. The only way to fully meet these challenges is to expand Salk's faculty, both in size and expertise, recruiting a new generation of biologists, engineers and information theorists to discover new insights and facilitate dynamic collaborations that evolve with the research goals.

The third pillar is expanding the place where it all happens. Before Salk can recruit new scientists, expand current faculty's research or add cutting-edge tools and technologies, the Institute must grow its current facilities, creating additional space to catalyze discovery.

To achieve that goal, the Institute is launching a five-year philanthropic and scientific campaign. The Campaign for the Future: Building a More Resilient World is an ambitious effort to raise philanthropic support, recruit the best minds in science, advance Salk's scientific initiatives on climate change, lifelong health, cancer and neurogenerative diseases and build a 100,000-square-foot Center for Science and Technology—the campaign's focal point.

The new center will house biologists, computer scientists and engineers, along with advanced technologies. This custom-crafted scientific ecosystem is designed to accelerate exploration and transport Jonas Salk's vision into the next century.

"The Campaign for the Future embodies Salk's dreams for the Institute and his charge to us to turn those dreams into reality."

MARTIN HETZER

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"The Campaign for the Future embodies Salk's dreams for the Institute and his charge to us to turn those dreams into reality," says Martin Hetzer, senior vice president and chief science officer. "His quest to improve the lives of humanity, as he did with the polio vaccine, remains at the forefront of our critical mission."

The Institute has a long history of achieving ambitious goals that advance science worldwide, and this will be no exception. The work has already begun. In fiscal year 2021, Salk donors contributed a record \$100 million toward the \$500 million campaign goal to expand campus facilities and advance the Institute's research agenda.

"Jonas Salk was a visionary, and the model he created has served us well: address the most prominent problems; understand the biology at the deepest levels; and bring people together who will work across disciplines," says Gage. "Our job is to expand on that vision by adding new talent and technologies—ones that Salk could barely have dreamed of in his day—to tackle our most pressing problems."



The Road Less Taken

Medical science has made great progress against disease, but for many patients, the clinical reality looks like a game of whack-amole: as each new condition crops up, another therapy is added.

Resilience is a more strategic approach. Precisely targeting the right biological pathways, such as aging, inflammation and immunity, can make people less vulnerable. Rather than solely focusing on individual conditions, instilling increased resilience can reduce the overall disease burden.

"We're collaborating across fields like computational science, neuroscience, cellular biology and more to understand aging and Alzheimer's so that people can live healthier, longer lives," says Satchin Panda, professor in the Regulatory Biology Laboratory and Rita and Richard Atkinson Chair. "In one recent collaboration, funded by the Joe and Clara Tsai Foundation's Human Performance Alliance, we are uncovering how the biological workings of elite athletic performance could inform strategies to boost all people's resilience and help them live healthier lives."

Evidence of resilience is all around. Many who contracted COVID-19 were completely asymptomatic. Others have brains full of amyloid plaques, the biological anomalies linked to Alzheimer's, but never lose cognitive function. This happens over and over—some people are vulnerable to disease, others resilient.

These are not random occurrences. There are biological mechanisms at work that are protecting people. The Institute's mission is to investigate and understand these systems, identifying the molecular targets that will help instill resilience.

"We are constantly being bombarded with viruses, toxic bacteria and cancerous cells, but we're usually fine," says Hetzer. "Our immune system offers a perfect example of how our bodies maintain resilience and what can happen when that resilience is lost. We want to understand the biological changes that create the distinction between robustness and vulnerability."

Salk's Plan to Build Resilience

Plants Cooling a Warming Planet

Global climate change may be the greatest challenge humanity faces. A warming planet is degrading the environment day by day: rising sea levels, catastrophic storms and droughts, waves of extinctions and the migration of novel diseases, such as malaria, dengue fever and West Nile virus. In other words, climate resilience is health resilience.

Climate change is essentially a physics problem. Too much carbon dioxide (CO₂) in the atmosphere is warming the globe. People must reduce the CO₂ being released and remove what has already accumulated.

Salk is focusing on the second piece. The Harnessing Plants Initiative (HPI) is developing a new generation of crop and wetland plants that capture atmospheric CO_2 and hold it underground for decades. The key is molecules like suberin, a carbon-rich polymer found in cork, avocado skins and plant roots. Because suberin is mostly carbon, and resists decomposition, it has tremendous potential to capture and contain CO_2 .

"Our goal is to have plants do what they do naturally to help solve the world's climate change, by storing excess carbon from the atmosphere," says Joanne Chory, HPI co-director, Howard H. and Maryam R. Newman Chair in Plant Biology and Howard Hughes Medical Institute Investigator.





The Push to Increase Healthy Aging

Aging is hardwired into human biology. And while it is not optional, Salk researchers believe there are ways to mitigate some of its harsher aspects, such as cancer, neurodegenerative conditions, diabetes and infectious diseases. The goal is to increase lifelong health: the number of years people are free from age-related disease.

"What makes a 40-, 50- or 60-year-old successfully maintain health while someone else the same age has a predisposition to some form of disease?" asks Hetzer. "We need to gain a granular understanding of what health really means at different stages in life. And also, we need to understand environmental factors—social interactions, exercise, diet. What role do all these external inputs play in our biological age?"

Through a \$19.2 million grant from the American Heart Association-Allen Initiative, Salk scientists are investigating the mechanisms that drive aging and how these can be adjusted to help people maintain resilience. In addition, as referenced above, Panda, and teams from five other organizations, recently received \$220 million from the Joe and Clara Tsai Foundation's Human Performance Alliance to explore healthy aging. For more on aging, read "The Aging Puzzle Comes Together" (see "Frontiers" in Spring 2021 issue).



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The Secrets to Strong Immunity

As the COVID-19 pandemic unfolded, Salk scientists, and many others, noted the important role our immune system played. Some people were infected but completely asymptomatic. In others, the immune response was more dangerous than the pathogen.

Like aging, immunity is a biological switch researchers can toggle to engage resilience. Scientists at the NOMIS Center for Immunobiology and Microbial Pathogenesis are working to understand the mechanisms that keep some people completely asymptomatic—in response to COVID and other conditions—while others end up on respirators.

"If there's anything the COVID-19 pandemic has taught us, it's how important basic research is to immunology," says Susan Kaech, NOMIS Chair and director of the NOMIS Center. "By understanding infectious disease and the immune system, we are aiming to prevent pandemics of the future."



Cutting Off Cancer's Escape Routes

Cancer and aging are part of a shared process. Something happens to the body as it ages that allows tumors to take root. Salk scientists seek to identify and counteract some of the age-associated changes that make it easier for cancers to thrive.

Researchers know that specific gene mutations drive cancer cells' aberrant growth, but that only tells part of the story. Salk researchers are investigating the mechanisms that help one tumor remain benign for twenty years, while another grows rapidly. Identifying the factors that give some people a resilient tumor response could provide new tools to control that response.

Nearly all tumor cells rewire their metabolisms to change how they take up and use nutrients. Understanding the molecular switches that control metabolic shifts in different cancers has helped Salk researchers develop therapies that cut the fuel lines that help feed malignant cells.

Tumors can also reprogram immune cells to see them as normal tissue and hijack immunity to support their growth and metabolic needs. Immunotherapies, which restore immune cells' anti-cancer capabilities, have already revolutionized cancer treatment, but they can be quite toxic and don't serve all patients. Salk investigators are trying to understand the complex relationships between immune cells and tumors to better harness this powerful system.

Salk's Conquering Cancer Initiative is exploring other strategies: decoding cancer epigenomics to reprogram some cancers back to normal; extinguishing the inflammatory signals that promote tumors; and using computational methods and integrative biology to design novel therapeutic strategies.

"There are hundreds of different cancers and many factors that contribute to each one," says Salk Cancer Center Director and Professor Reuben Shaw. "That's why at Salk we bring in so many different disciplines. It's a complex problem, and we need to level up to meet that complexity. Tumors find ways to escape treatment, and we are going to cut off those escape routes with teams of diverse researchers working together. Salk has become a hotbed for innovative approaches to treat cancers based on what we learn from other disciplines, including aging, metabolic diseases and neurodegenerative diseases."





Finding the Big Picture on Neurodegenerative Diseases

"There are disorders, like Alzheimer's, Parkinson's and ALS, in which people may have had a genetic predisposition their entire lives. Something changes with age that creates an environment that allows the disease to progress."

NICOLA ALLEN

Alzheimer's research has largely focused on eliminating amyloid plaques and tau tangles, which are thought to drive disease progression. Unfortunately, dozens of drugs have failed in clinical trials.

Focusing on plaques and tangles may miss the bigger picture—the environment within the brain. Again, some people accumulate plaques but never experience neurological decline. Something in their neural environment is keeping them safe.

Salk researchers are working to understand the safeguards that keep people healthy. Specific biological changes are happening that allow Alzheimer's, Parkinson's, ALS, multiple sclerosis and other neurodegenerative diseases to take hold. However, there must be ways to reverse those changes and strengthen the neural environment to prevent disease.

"There are disorders, like Alzheimer's, Parkinson's and ALS, in which people may have had a genetic predisposition their entire lives," says Nicola Allen, associate professor in the Molecular Neurobiology Laboratory. "Something changes with age that creates an environment that allows the disease to progress."



Using Research Data to Create Solutions

Advances in technology and artificial intelligence is providing new opportunities to approach some of biology's most challenging problems in new ways.

Deciphering answers from vast amounts of biologic data is shaping the future of discovery. New, high-resolution instruments, such as genomic sequencers and mass spectrometers (which are used to analyze proteins and other molecules), produce overwhelming amounts of data, often measured in terabytes or even petabytes.

To find useful nuggets of information in seas of data, Salk is growing its computational capabilities. Machine learning, and other artificial intelligence techniques, can sort through massive data sets, decipher biological complexity and separate signal from noise. Algorithms are the new microscopy.

"We need people with different skills and from different scientific backgrounds," says Hetzer. "To understand how plants work, we need chemists, physicists and soil scientists. To understand the human brain, we need computer theorists, geneticists and mathematicians. It's the only way we're going to unwind all that complexity and make the information actionable."



Information theory is the universal language that will help researchers identify the convergence between aging, neurodegenerative diseases, cancer and other conditions and understand the mechanisms that drive cellular health and resilience.

That means recruiting researchers who are thoroughly grounded in computational methods and engineering. These experts will do more than interpret the data; they will help identify, and ultimately harness, the biological mechanisms that drive resilience.

"It helps us become more efficient in using experimental data," says Tatyana Sharpee, professor in the Computational Neurobiology Laboratory and Edwin K. Hunter Chair. "We can extract more information and answer a lot more questions. If the methods are better, we can pick up weaker signals that we were never able to pick up before and get more answers."

But this vision goes beyond analyzing data. Cells are constantly making the right decisions: performing their intrinsic functions and responding to environmental changes. There are cellular algorithms driving this precision. Learning how these function could inform better computer systems, which could in turn help answer complex biological questions.

These approaches are parts of a much larger picture. Salk is recruiting computer scientists to better understand how biological systems interact with each other and their surrounding environments, as well as engineers who will collaborate with life scientists and develop new types of instruments that improve how they measure and analyze data. Salk researchers often ask questions that have never been asked before—they need new tools to find those answers.

"We have amazing life scientists here, but most of us were not trained as engineers," says Eiman Azim, assistant professor in the Molecular Neurobiology Laboratory and William Scandling Developmental Chair. "We frequently need to develop specialized and automated tools for our experiments to advance alongside our rapidly evolving questions and these solutions are often not commercially available. Working alongside talented mechanical and electrical engineers allows us to make prototypes much faster and maintain the pace of our work."

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"Hope lies in dreams, in imagination and in the courage of those who dare to make dreams into reality."

JONAS SALK

TRUE TO OUR ROOTS

Adding a cutting-edge research facility to the Salk Institute must enhance Salk science and respect the current campus. Louis Kahn's original architecture is beautiful, functional and iconic. Preserving that breathtaking vista and historic vision is critically important.

As a result, designing the Center for Science and Technology was a thoughtful and iterative process, creating a structure that would meet the Institute's scientific vision and fit seamlessly into the existing campus. The new facility will replace a parking lot on the eastern corner of the campus and serve as a new main entry for visitors.

The center will mirror Salk and Kahn's efforts, using teak, travertine, concrete and other materials found in the original structures. The building will offer an expansive and uninterrupted view of the original Courtyard and complement the overall aesthetic.

Built around a large, central courtyard, the center's spacious and open structure will provide unique opportunities. The Courtyard will offer a meeting place where scientists can discuss new projects and hold scientific meetings, exhibitions, receptions, concerts and other events. Skylights will provide the natural light so essential to health and creativity.

The design, materials and architecture will replicate Salk's existing look and feel. In addition, the building will house historical exhibits about the Institute. The center will help advance Salk science into the next century and serve as an innovation hub, welcoming others to support the life-changing work being conducted on Torrey Pines Mesa.

Building a Center for Innovation to Drive New Discoveries

When Jonas Salk and Louis Kahn designed the Salk Institute in the early 1960s, they created a new model for the modern laboratory. There are few barriers between labs, and no departments, eliminating silos that isolate both people and ideas. Laboratories were designed to grow as the science dictated.

The Institute has applied this design ethos to the new building. Located on the east side of campus near Torrey Pines Road, this flexible space will provide much-needed growing room to expand Salk's research capabilities.

Like the original buildings, Salk's newest facility will be built for versatility, allowing labs to reconfigure quickly and inexpensively, moving walls and lab benches as needed. Research spaces will be designed, and redesigned, to meet each lab's unique needs and change when the science dictates, just as Salk and Kahn envisioned.

It will provide ample opportunities to add faculty from multiple disciplines and expand interactions between biologists, bioengineers, information theorists and others. The ripple effect will be huge, providing more room for existing labs to expand and bringing off-campus capabilities back to Torrey Pines Mesa.

As has been the case for 60 years, donor support is critical to achieve Salk's scientific goals. The additional lab space will support recruitment, create greater opportunities for collaboration and help augment critical technologies, such as genomics, bioinformatics and many others.

Most importantly, the new building, and the many changes it will help drive around the Salk campus, will create an even more creative and collaborative environment.

"We're taking what Jonas Salk taught us and building on that," says Gage. "Uniting cell biologists, immunologists, geneticists and epigeneticists, neurobiologists, information theorists, engineers and others on nimble teams will multiply the Institute's capacity to help solve some of the world's most dire problems."







SUSAN KAL

How T cells remember

Your brain isn't the only part of your body that has a long-term memory. Long after your immune system has fought off an infection, memory T cells stick around in organs throughout your body, ready to quickly target returning pathogens.

Salk Professor Susan Kaech, director of the NOMIS Center for Immunobiology and Microbial Pathogenesis, has made it her mission to gain a better understanding of how these T cells form, how they exchange molecular signals with the surrounding tissue, and how we can use this knowledge to prevent or treat infections.

Inside Salk spoke with Kaech, who also holds the NOMIS Chair, about her career path and how the COVID-19 pandemic has affected her research.

Did you always want to be a scientist?

SK: In high school, my favorite classes were physics, chemistry and math (yes, I actually liked doing trigonometry homework), but I was pretty naïve about scientific careers. In fact, the only science career I really knew much about was engineering, so I started college with a major in chemical engineering. However, my freshman year I signed up for biology as an elective course and it ended up being a complete life-changer. It was the first time I'd learned about cells and genetics and physiology—it was very different from my rudimentary high school biology class, which had focused mainly on taxonomy.

At the same time, as part of my financial aid package to attend college, I was given access to work-study jobs and I selected a really cool job to work in a lab that studied viruses that cause cancer. I worked on a project using anti-sense RNA technology to block viral gene expression, which was nearly 15 years before the Nobel Prize was given for RNA inhibition (RNAi) in 2006! So it was really interesting for me, then as a very young scientist, to watch and later realize that things that you were actually working on could, over time, have a huge impact in biology.

How did you begin studying T cells?

SK: My PhD was in developmental biology, which I loved, but as I was getting closer to the end of my PhD I wanted to take some time to consider other areas of research. I'd been exposed a little to host-defense and immunology and understood the basics of how your immune system protects you from pathogens, but I started sitting in on immunology lectures and realized how exciting the field was and how inflammation and immunity are central to nearly every disease. In particular, I became fascinated with this concept of long-term immunity and saw a lot of unanswered questions about how this forms in our bodies.

What big questions about T cells are you trying to answer?

SK: When I started my lab, using my background in developmental biology, my team and I were really focused on uncovering genetic pathways that control the formation of long-lived memory T cells. What happens in T cells when they're exposed to a virus that gives them the ability to remember that virus? What signals dictate which T cells live to develop into memory T cells that remember the virus versus those that die after an immune response? Now, my lab has started to zoom out and look at how T cells crosstalk with the tissues around them. How do the immune cells change if the tissue is stressed? What if the tissue is affected by metabolic disease or cancer? We already know that lots of different proteins can alter T cells but we're only beginning to understand how other types of molecules—like metabolites produced within tissues—can change T cell metabolism and activity.

This line of research can aid our understanding of chronic diseases and how the immune system adapts to disease over time. T cells stick around for years and years, so there's bound to be adaptation in how they're interacting with organs over that time frame.

At an even broader level, the questions we're asking revolve around what inflammation is, in the first place. Why are some types of inflammation beneficial for the body and other types pathological, and what differentiates those at a molecular level?

How has the COVID-19 pandemic affected the trajectory of your work?

SK: It's certainly been an exciting year for the field and my lab, especially as the public has become so much more aware of the importance of immunology, vaccines and particularly, long-term immunity. We have been able to contribute to research on COVID-19 because we were already studying how memory T cells infiltrate the lungs in people with influenza and provide protection against reinfection. So we saw an

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opportunity to carry out similar studies in people with SARS-CoV-2. We've been looking at how memory T cells form in the lungs after COVID-19 or after immunization for COVID-19, and how long they stick around in each case. Understanding T cells in this context will help researchers develop better vaccines for not only COVID-19, but other pathogens or future pandemics.

I love that the general public's appreciation for developing long-term immunity to pathogens is growing as well as their awareness and interest in understanding our immune system. I sincerely hope this interest lasts after the pandemic is over!

What are some of your favorite things to do outside of work?

SK: I hang out with my family as much as I can. My husband Gerry Shadel [also a Salk Professor] and I have two teenage daughters and know we have a short period of time with them at home before they head out into the world. I also like to hike and cook, and I've recently started doing hot yoga! My happy places are hiking in the Cascades [of Washington State], snorkeling in coral reefs or just hanging out with friends and enjoying some wine in our backyard.

What do you wish the public better understood about the immune system?

SK: I wish for the public in general to have a better understanding of what vaccines are doing at a cellular level. I think if more people understood the fundamental concepts about the immune system and how vaccines generate long-term immunity, it could help quell some fears about vaccines and mitigate some vaccine hesitancy. Many non-scientists don't realize that what a vaccine is doing is helping your body generate these specialized memory T and B cells that have the ability to live in your body for decades. The vaccine itself doesn't stick around, but these long-lived populations of cells do. And that is what gives you long-lasting immunity!

$Where is your \, research \, heading \, next?$

SK: We are very excited about our work uncovering how T cells are controlled by locally available nutrients within tissues and how this is affected by diet, especially in the context of cancer, where we know diet and obesity play important roles. We are also starting to explore the interplay between T cells and the brain and neurons. Just like T cells can infiltrate the lungs, they can also infiltrate the brain—but we know almost nothing about what they do in the brain. We are eager to examine the long-term impact that these brain-resident T cells can have on brain health as we age and, conversely, how neurons can impact the function of T cells. Salk is such a world-class place to do neuroscience that I think it lends itself to being a place where we can study the 'nervous' immune system in new ways. §

Salk Education Outreach

Hands-On Science Education



Jonas Salk founded the Salk Institute with the philosophy that it should both drive scientific breakthroughs and inspire the next generation of elite scientists. Out of Jonas Salk's vision, the Institute's Education Outreach program was born. Its mission is threefold:

To teach

students, teachers and the community about scientific literacy in addition to the role of basic biological research in our world.

To inspire

enthusiasm and interest in advanced levels of science instruction, and particularly in science as a career.

To promote

public awareness of Salk and the value of basic research as it relates to career readiness, critical thinking skills and the development of an informed citizenry.



Salk Education Outreach serves San Diego County students, teachers and other community members through its programs: Mobile Science Lab, Heithoff-Brody High School Summer Scholars, March of Dimes High School Science Day, SciChats@Salk and the Ellen Potter Research Connections for Teachers Symposium. These programs are offered at no cost to students, teachers and schools, thereby reducing economic barriers to high quality STEM education. Over the past 40 years, Salk Education Outreach has delivered innovative, engaging STEM learning experiences to thousands of students—a majority of whom come from underrepresented and underserved communities.

To learn more about Education Outreach, please email education@salk.edu.

Lessons from carnivorous plants

One minute a fly is delicately exploring the interior surface of a crimson clamshell-like leaf, and the next minute—SNAP!—the clamshell closes and the unsuspecting insect becomes dinner for a Venus flytrap plant. As someone who studies carnivorous plants, that's the type of high-stakes drama Staff Scientist Carl Procko sees every day.

By studying Venus flytraps and their close relatives, Sundew plants, Procko gains insight into the ultra-fast biochemistry of plants and how they can sense touch. It doesn't hurt that these bug-eating plants are a great way to get kids—and adults—interested in science, Procko says. "A lot of people tend to not be very intrigued by plants in general, but it's easy to get them hooked by bizarre plants that do incredible things."

INSIGHTS

Carl Procko

Staff Scientist



PATH TO SALK

Procko didn't always want to be a plant biologist. He grew up in southern Australia and went to college to study law. But classes in science—and then work in a biology lab studying embryonic stem cells—sidetracked him. He flew halfway around the world for graduate school at Rockefeller University in New York, where his research focused on how the nervous system of *C. elegans* worms develops. It was there that he learned the fundamentals of genetics.

"The nice thing about genetics is that the principles are translatable to just about any system," says Procko. "Whether you're studying worms or plants, you're using similar technology to make genetic changes and test their effect on the traits of that organism."

So, after graduate school, when Procko started looking for a change of pace, he knew he'd be able to apply that knowledge of genetics to a totally different type of organism—like plants.

DAY-TO-DAY

Like everyone else in the lab of Professor and Howard Hughes Medical Investigator Joanne Chory, Procko wants to know how plants respond to their environments. He is especially interested in leaves—the site of most photosynthesis in a plant.

To understand how different leaves have evolved, Procko compares the genetics and the gene activity of different plants and plant cells. He tests the roles of individual genes by mutating them and watching how a plant grows and responds.

In one recent study, Procko homed in on which genes are active in the trigger hairs of Venus flytrap leaves, which snap shut in response to prey. He discovered a new gene that he and his colleagues named *FLYCATCHER1*, or *FLYC1* for short.

SPREADING SCIENCE

Procko is not only passionate about his own research projects, but also about hooking other people on science. Carnivorous plants make great ambassadors—even his three-year-old daughter becomes engrossed with his Venus flytraps, poking their at-home collection with grass and toothpicks to see what will happen. To help pique other people's interest, Procko has taken his plants to events at the Fleet Science Center, and shown them off at Explore Salk days in the past.

"I think there's a responsibility that comes with being an academic scientist to also do outreach," he says. "It improves your own ability to communicate about your science at the same time as making the public more science literate."

He is also an instructor at the University of San Diego and has developed a project for undergraduate students to analyze the collections of bacteria—or microbiomes—that live on and in carnivorous plants. "It's a simple way for students to learn the basics of next-generation sequencing while also getting excited about plants," Procko says.

FUN FACT

Procko is a twin, and his brother is also a researcher in the United States. The pair grew up exploring the beaches in Australia, watching David Attenborough, and making their own amateur documentaries about mangroves and the seashore.

"When you grow up as a twin, you grow up in the same environment and interact all the time, so it's not too surprising that we ended up following similar paths," says Procko.

His brother, Erik, studies protein structures and computational protein design at the University of Illinois and the two have had a few chances to collaborate—Erik was a co-author on the latest Venus flytrap paper, for instance, after helping Procko characterize the protein corresponding to the new *FLYC1* gene.

LONG VIEW

While most plants don't snap at flies, they do respond to touch—a tree's trunk thickens in response to wind, for instance—so Procko's research on carnivorous plants might help inform a better understanding of other plant systems.

More broadly, understanding how plants adapt to their environments and how they have evolved over time has implications for altering plants to yield better crops, adjust to global warming, or help combat climate change by drawing down excess carbon from the atmosphere.

"This is really important as environments are changing at the moment, and as we grow crops in areas that we typically haven't before," says Procko.

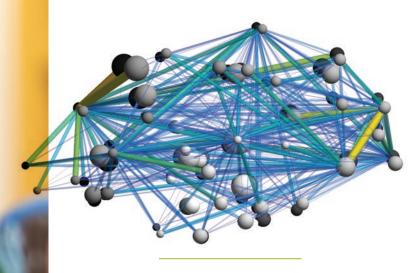
To that end, Procko is part of Salk's Harnessing Plants Initiative, which aims to develop plants that can store more carbon in the ground, within their roots—this not only decreases carbon levels in the atmosphere, but also improves soil health. Since Procko's current focus is on the leaves of plants, he's especially curious how changing photosynthesis in the leaves might affect root growth.

Procko's work could eventually have implications for human biology as well. One of his collaborators at Salk, Associate Professor Sreekanth Chalasani, is studying how the touch-sensitive proteins found in Venus flytraps might be genetically inserted into mammalian cells to make them sensitive to ultrasound simulation. This could make human cells that respond to ultrasound with any number of desired behaviors—increasing the production of a particular protein or medicine, perhaps.

"There are very cool potential applications for this work," says Procko. "But there's also just the joy of the basic science. At the end of the day, I do this research because it's fun. It's nice to go to work and be energized by what you're doing."



Nuttida Rungratsameetaweemana, a Salk postdoctoral researcher who studies neuroscience, was introduced to the perplexities of the brain at age 14 during a chance encounter in a hospital waiting room. Rungratsameetaweemana had nearly been swept away by floodwaters that destroyed her home on a river in northern Thailand. Her father was injured while saving her. In a hospital in Lampang, an hour's drive from their village, she waited anxiously while he underwent spinal cord surgery.



"Knowing the timing and severity
of a seizure several minutes
beforehand may help researchers to
develop better kinds of treatments
to help patients."

A woman in the waiting room, perhaps in her late 60s or early 70s, struck up a conversation with her. She asked the teenager where her middle school was and about her favorite subject. They discussed Rungratsameetaweemana's love of drawing before the woman returned to reading her magazine. A few moments later, she turned back to Rungratsameetaweemana. Which middle school did she attend? What was her favorite subject?

Rungratsameetaweemana was stunned. It was like the previous few minutes had never happened.

Her father recovered and, within two years, Rungratsameetaweemana earned a scholarship to a high school in Bangkok. She never saw the woman from the waiting room again, but the puzzling encounter had launched Rungratsameetaweemana's academic interest in the brain.

After high school, Rungratsameetaweemana headed to the United States to attend Middlebury College, though she spoke so little English when she first got to campus that she recalls watching professors' lips move with no comprehension of what they were saying.

After graduating in 2014, she was thrilled to be accepted to the University of California San Diego (UC San Diego) neuroscience graduate program. While there, Rungratsameetaweemana collaborated with John Serences, professor of neuroscience and psychology, and Larry Squire, a professor of psychiatry, neurosciences and psychology who is affiliated with the Veterans Affairs (VA) Medical Center in San Diego, on work that involved brain-injured patients. She completed her PhD degree in 2020.

Rungratsameetaweemana seeks to understand how the brain transforms raw sensory information into a form useful for goal-directed behavior, such as solving a jigsaw puzzle based on visual cues. Her work has implications for treating diseases such as schizophrenia and Alzheimer's, which affect thought and memory. Working with Terrence Sejnowski,

Salk professor and head of the Computational Neurobiology Laboratory, Rungratsameetaweemana looks at how the brain processes information to make decisions when confronted by uncertainty, such as deciding how to react to an unfamiliar sound or encountering an unknown object in a familiar setting. To this end, they're building a computational model based on the actual properties and types of neurons in the human brain.

"In addition to working with healthy populations or clinical populations, we're now also working with an artificial human brain," she says. "We're asking, 'What kind of behavior would this model generate?' Our model predicts the type of neural computation important for the brain to process probabilistic information."

The results from the artificial brain model will be compared to the intracranial recordings from human participants—as well as to behavioral and non-invasive data from healthy individuals and memory-impaired patients she collected in graduate school.

She also uses computational methods to look at brain states that lead to seizures. In work partially funded by the US Army Research Laboratory, Rungratsameetaweemana and colleagues analyzed data recorded by electrodes placed directly on brain tissue of patients with epilepsy to predict the timing of their next seizures based on oscillations—rhythmic electrical activity—within the brain. "We're trying to see if we can predict not just when a seizure is going to happen, but also how extensive it will be," she says.

Some seizures stay in one hemisphere of the brain while others spread to both hemispheres. "Knowing the timing and severity of a seizure several minutes beforehand may allow researchers to develop better kinds of treatment to help patients," she says.

Rungratsameetaweemana has been recognized as one of the country's most up-and-coming young neuroscientists. She received a 2020/2021 Anuradha Rao Memorial Award, given in honor of a neuroscientist and science editor who died unexpectedly at age 44. The \$1,000 award is given annually to a graduate student or postdoc to cover expenses for travel to the Society for Neuroscience annual meeting.

Even working in a multicultural field like science, Rungratsameetaweemana often gets asked about her last name. When her grandparents emigrated to Thailand from China, they needed to change their short Chinese name to one more akin to multisyllabic Thai names in order to work. Her grandfather came up with Rungratsameetaweemana. "It means perseverance," she says. "In his defense, he had no idea I would someday be taking the SAT and filling out so many bubbles."

In her spare time, in addition to running and cooking, Rungratsameetaweemana still draws plants, animals and people, but says her work is more cartoonish now than the realistic depictions of plants she once did in the riverside house that was destroyed by the flood and rebuilt.

Rungratsameetaweemana still thinks about the woman in the waiting room. She hopes to one day unravel the intricacies of human memory in a way that makes a difference in people's lives.

SPOTLIGH

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Talmo Pereira

Institute appoints new Salk Fellow

The Salk Institute recently appointed neuroscientist Talmo Pereira to the Salk Fellows Program. Pereira, who begins at Salk this fall, comes from Princeton University, where he developed computational methods for quantifying animal behavior through motion tracking technology that leverages artificial intelligence (AI). Pereira is interested in building and using computational tools that leverage AI to solve biological problems that would not be tractable otherwise.

At Salk, he plans to develop new computational methods to quantify and model biological dynamics across a diverse set of application areas, including social behavior, motor control, plant morphology, and single cell states throughout development and disease.

"I am so grateful for the united efforts of the Salk community to identify and recruit a rising star as bright as Talmo Pereira," says Salk Professor Kay Tye, who chaired the Salk Fellows Search Committee. "A true genius, Talmo is already forming collaborations in areas ranging from plant growth to social hierarchies, and adds profoundly to the diversity, depth, and dimension of our scientific community at Salk in terms of who he is as a person, who he is as a theoretician, who he is as a scientist, and the way his mind works."

The Salk Fellows Program brings scientists from broad disciplines to the Institute to trigger innovation and perpetuate the collaborative spirit of the Institute. Most fellows come directly from a PhD or MD program and have expertise in a wide range of innovative technologies. The Institute welcomed its inaugural class of fellows from 2014 to 2016, and all three are now in tenure-track faculty positions at Salk or UC Berkeley.

SALK PROMOTES DIANA HARGREAVES



Diana Hargreaves

Diana Hargreaves was promoted to the rank of associate professor after the latest round of faculty reviews determined she is a scientific leader who has made original, innovative and notable contributions to biological research.

The promotion was based on recommendations by Salk faculty and nonresident fellows, and approved by President Rusty Gage and the Institute's Board of Trustees in April.

Hargreaves, who is a member of Salk's Molecular and Cell Laboratory, and holder of the Richard Heyman and Anne Daigle Endowed Developmental Chair, studies how the diversity of cell types in our body is controlled by proteins, called epigenetic regulators, that selectively activate genes particular to each cell type, whether it be skin, liver, brain or others. She applies her knowledge of biochemistry and epigenomics to investigate epigenetic regulation in models of cancer, embryonic-stem-cell pluripotency, and immune cell function.

Among other honors, she was awarded the Pew-Stewart Scholar for Cancer Research in 2019 and the American Cancer Society Research Scholar Award in 2020 to support her work on a better understanding of the causes, diagnosis and treatment of cancer.

SALK PROFESSOR KAY TYE WINS BLAVATNIK NATIONAL AWARD FOR YOUNG SCIENTISTS

Salk Professor and neuroscientist Kay Tye has been named one of three winners of the prestigious Blavatnik National Awards for Young Scientists. Tye, the laureate in the Life Sciences category, will receive \$250,000 for her trailblazing work in studying the neural circuits and behaviors related to anxiety and social interaction.

Tye, who is a professor in Salk's Systems Neurobiology Laboratory and holds the Wylie Vale Chair, seeks to understand the neural circuit basis of emotion that leads to motivated behaviors such as social interaction, reward-seeking and avoidance. Her lab's findings may help to inform treatments for conditions such as anxiety, depression, addiction and impairments in social behavior.

The 2020 and 2021
Blavatnik National
Laureates and Finalists will
be honored at an awards
ceremony on September
28, 2021, at the American
Museum of Natural History
in New York City. Tye is the
second Salk Blavatnik Life
Sciences Laureate, the first
being Salk Professor Janelle
Ayres, who won the award
in 2018.



Kay Tye

The Blavatnik Family Foundation founded The Blavatnik Awards in 2007, and since that time has awarded more than \$11.9 million and recognized 359 young scientists and engineers from 47 countries, working in 36 scientific and engineering disciplines.

Institute receives Charity Navigator's highest rating for TENTH CONSECUTIVE TIME



For the tenth consecutive time, the Salk Institute has earned the highest ranking—4 out of 4 stars—from Charity Navigator,

America's largest independent charity and nonprofit evaluator. Only three percent of the roughly 10,000 nonprofits evaluated have achieved this recognition ten consecutive times. The coveted ranking indicates the Salk Institute has demonstrated strong financial health and commitment to accountability and transparency, outperforming most other charities in America in regard to executing best fiscal practices and carrying out its mission in a financially efficient way.

"This recognition by Charity Navigator of Salk's continued success achieving the highest level of fiscal accountability and transparency among our peers is exciting and something we are proud to receive once again," says Salk Institute President Rusty Gage.

Charity Navigator's data-driven analysis of the 1.5 million American charities has been covered by *Forbes, Business Week* and others for providing donors with a way to recognize nonprofits that provide greater accountability, transparency and concrete results.

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"Our donors showed their faithful support of Salk science through an uncertain year, as our scientists and the world worked through the many challenges presented by a global pandemic," says Rebecca Newman, Salk's vice president of External Relations. "We are deeply gratified that the Charity Navigator rankings reflect our donors' confidence in the Institute's stewardship and trustworthiness."

Since receiving its previous rating from Charity Navigator in 2019, the Salk Institute has made bold progress in pursuing ambitious solutions to the difficult challenges facing humanity, including climate change, aging and cancer.

Support for these initiatives included gifts of \$30 million from the Bezos Earth Fund and \$12.5 million from Hess Corporation, both in support of Salk's Harnessing Plants Initiative. This scalable approach to help humanity deal with a warming planet aims to optimize plants to store more carbon and adapt to diverse climate conditions.

In addition, the NOMIS Foundation gave \$9.5 million to Salk's NOMIS Center for Immunobiology and Microbial Pathogenesis to grow and expand, while the center continues to be a leader in health and immunity research.

The Institute continues to make bold progress through its Conquering Cancer Initiative, which seeks to tackle six deadly cancers: colon, pancreatic, ovarian, lung, glioblastoma and triple-negative breast.

"I wish to congratulate Salk Institute for Biological Studies on attaining the coveted 4-star rating ten consecutive times. This designation sets Salk apart from its peers and demonstrates to the public its trustworthiness," says Michael Thatcher, president and CEO of Charity Navigator.

Since 2002, Charity Navigator has used objective analysis to award only the most fiscally responsible organizations a 4-star rating: only a quarter of charities rated receive this distinction. In 2011, Charity Navigator added 17 metrics, focused on governance and ethical practices as well as measures of openness, to its ratings methodology. These Accountability and Transparency metrics, which account for 50 percent of a charity's overall rating, reveal which charities operate in accordance with industry best practices and whether they are open with their donors and stakeholders.

SALK SCIENTISTS AWARDED \$10,000 TO \$100,000 BY KAVLI SMALL EQUIPMENT GRANT PROGRAM IN 2021

The Kavli Foundation champions scientific research through its Small Equipment Grant program that provides scientists with unconstrained opportunities to drive greater discovery. The funding will support Salk faculty and research professors working in neuroscience and related fields to purchase or build equipment needed to further their research, ranging from \$10,000 to \$100,000.



Individual awardees include Salk faculty John Reynolds, Kenta Asahina, Sreekanth Chalasani and Xin Jin.
Collaborative awardees include Eiman Azim and Martyn Goulding; as well a group effort led by Dannielle Engle, which includes Dmitry Lyumkis, Graham McVicker, Pallav Kosuri and Satchidananda Panda.

SALK PROFESSOR ON NATIONAL COMMITTEE TO STUDY IMPLICIT BIAS



Implicit bias, defined as "an unconscious favoritism towards or prejudice against people of a particular race, gender, or group that influences one's actions or perceptions," is garnering a good deal of societal interest lately, but it's also the subject of a growing body of scientific research.

Salk Professor and neuroscientist Thomas Albright says everyone's perceptions are framed by unconscious inferences, or biases. They are part of the way the human brain deals with the uncertainty of new information: Is that person running towards me shouting to warn me of danger, or to threaten me? Our brain tries to reduce uncertainty by relating the new experience to other experiences we've had: what social scientists call "priors."

Often, our "priors" are based on incomplete or faulty information, which is what can lead us to behave in ways that may harm others. We're usually not even aware of the unconscious beliefs we hold, which are based on countless previous experiences or societal influences.

One way we see this play out is in the legal system. Many people are wrongly accused of crimes based on unreliable eyewitness testimony, which can stem from eyewitness' unconscious ideas about which kinds of people are more likely to commit crimes—people of a certain age, race or gender, for example. Albright says understanding that we all make unconscious inferences is the first step toward not acting on them in ways that cause harm. In 2020, the Albright lab published a paper in *Nature Communications* proposing a new method of doing police lineups that would help eliminate unconscious biases that shape people's decisions without their awareness (see "Discoveries" in Winter 2020 issue).

More recently, Albright served on a committee of the National Academies of Sciences (NAS) to study implicit bias in detail. The NAS' mission is to provide "independent, objective advice to the nation on matters related to science and technology." As a member of the committee, Albright helped organize a two-day workshop on implicit bias in March 2021.

The workshop presentation and videos are available to the public on the National Academies' website, **www.nationalacademies.org/events**

The Salk Institute regularly offers implicit bias training for staff through the Office of Equity and Inclusion (OFI). Learn more about OFI at:

www.salk.edu/about/equity-inclusion

LEARNING ABOUT SCIENCE, VIRTUAL EDITION: EDUCATION OUTREACH CONTINUES SUCCESSFUL SUMMER PROGRAMS

Starting the summer of 2020, Salk's Education Outreach programs went virtual in response to the COVID-19 pandemic. This year, the team continued its mission of teaching and inspiring students to pursue careers in science, remaining flexible through uncertain times by offering virtual and hybrid versions of its two summer 2021 programs.

HEITHOFF-BRODY HIGH SCHOOL SUMMER SCHOLARS

This summer's hybrid class was comprised of six scholars, including one who returned to the Stem Cell Core for a second summer after previously attending in 2019. The eight-week internship, generously made possible through an endowment established by the Heithoff Family Foundation, provides high school students the opportunity to gain experiences in scientific research and develop crucial skills needed to pursue a career in STEM (science, technology, engineering and mathematics).

Founded more than 40 years ago, the program fulfills Jonas Salk's vision of introducing high school students to laboratory life and the possibility of a career in science

This summer's scholars dedicated 25 to 30 hours a week to the hybrid program. Up to 10 hours was spent performing research with their assigned mentors in Salk labs. Scholars spent their remaining time participating in virtual lab meetings and virtual seminars and completing independent projects.



SALK INTRODUCTION TO RESEARCH SCIENCE & COMMUNICATION

Created last summer in response to the need to provide students a virtual alternative to the Heithoff-Brody High School Summer Scholars, Salk Introduction to Research Science & Communication was such a success that this summer it was increased from a four-week to a five-week program.

Fifty students were selected from a pool of over 500 applicants from all over the country. The class consisted of two cohorts of students. The first group was comprised of exclusively San Diego Unified School District students who were funded by Level Up SD, an initiative of the San Diego Foundation. The second group was comprised of students from all across the country, including three students from North Carolina who were selected by the Burroughs Wellcome Fund in appreciation of their three-year gift to the Heithoff-Brody High School Summer Scholars program.

Over the five weeks, students took part in scientific readings and data analysis, completed virtual lab simulations, learned about laboratory practices and participated in professional development opportunities.

To learn more about Education Outreach visit **www.salk.edu/education**.

DANNIELLE ENGLE AWARDED PRESTIGIOUS PANCREATIC CANCER RESEARCH GRANT HONORING RUTH BADER GINSBURG



Dannielle Engle

Salk Assistant Professor
Dannielle Engle was selected
as the first recipient of the
Lustgarten FoundationAACR Career Development
Award for Pancreatic Cancer
Research in Honor of Ruth
Bader Ginsburg, the late
Supreme Court Justice and
women's rights pioneer.

Engle will receive \$300,000 to fund her pancreatic cancer research, which is focused on understanding how we

can intercept the signals causing pancreatic cancer to metastasize and become so deadly.

Each year, more than 45,000 Americans lose their lives to pancreatic cancer—now the third-leading cause of cancer-related deaths, with a five-year relative survival rate of 10 percent. Through these awards, the Lustgarten Foundation and the AACR seek to help close the gap in the number of early-career women and under-represented scientists applying for and receiving funding to conduct research leading to a better understanding and treatment of pancreatic cancer.

SALK RECEIVES INSIGHT INTO DIVERSITY MAGAZINE'S 2021 INSPIRING PROGRAMS IN STEM AWARD

Salk's Education Outreach program received the 2021 Inspiring Programs in STEM Award from *INSIGHT Into Diversity* magazine, the largest and oldest diversity and inclusion publication in higher education. The Inspiring Programs in STEM Award honors colleges and universities that encourage and assist students from underrepresented groups to enter the fields of science, technology, engineering and mathematics (STEM). Salk will be featured, along with 78 other recipients, in the September 2021 issue of *INSIGHT Into Diversity* magazine.

INSIGHT Into Diversity selected Salk's Education Outreach program for its continued efforts in delivering innovative, engaging STEM learning experiences to thousands of San Diego students of all ages, the majority of whom come from underrepresented and underserved communities.

Education Outreach serves San Diego County students of all ages through its core programs: Mobile Science Lab, Heithoff-Brody High School Summer Scholars, March of Dimes High School Science Day and the Ellen Potter Research Connections for Teachers Symposium. These programs are offered at no cost to students, teachers and schools, thereby reducing economic barriers to high-quality STEM education.

In Memoriam

LOSS OF SALK COLLEAGUE INSPIRES ACTION, CHANGE

The Salk Institute lost one of its brightest colleagues, Swati Tyagi, 34, a postdoctoral researcher in the Hetzer lab, when she was tragically killed on June 23 when a person driving a car struck her from behind while she was riding her bike. In the days following, Tyagi's colleagues and friends established an emergency fund to help her family during the difficult time.

Tyagi's death was one of a dozen bicyclevehicle fatalities in San Diego in 2021. The deaths prompted fervent advocacy by bicyclist groups who urged government officials to improve the city's infrastructure and make streets safer for bicyclists in order to prevent future tragedies.

In August, San Diego Mayor Todd Gloria announced his administration would take several measures to improve bike safety, including: creating bike lanes more quickly, joining the National Association of City Transportation Officials to learn and adopt best practices, and working to reduce the time it takes to process a bike infrastructure permit.



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Mentoring the Next Generation at Salk

Mentoring is incredibly valuable to anyone wanting to succeed in a new career, but is even more crucial for those entering or just getting started in science, technology, engineering and mathematics (STEM). Mentoring opens doors to achievement and career enrichment; studies have shown that those who have mentors thrive in nearly all STEM settings.

Enabling innovative science that can solve the world's challenges starts with actively training tomorrow's mentors. That's why Salk is committed to offering valuable mentoring resources to its early-career scientists to ensure they can succeed now, and in the future. Whether it's training mentors or providing young scientists the tools and mentorship they need to succeed, Salk is dedicated to mentoring in several ways:

LEARNING

Salk's Office of Equity and Inclusion (OEI) facilitates "Entering Mentoring," a six-week series based on curricula from the Center for the Improvement of Mentored Experiences in Research. The series is offered to various cohorts including recently appointed junior faculty, postdoctoral researchers, graduate students and other scientific staff. It provides a safe group learning space to share and ponder challenging scenarios with colleagues, aimed at accelerating and supporting individuals in their journey toward independence and becoming an effective research mentor.

"Both formal and informal mentoring relationships are invaluable in the working, learning and training environment," says Mallory Zaslav, vice president of Salk's Office of Equity & Inclusion. "Effective mentoring relationships can expand the horizons of both the mentee and mentor by introducing new perspectives, advancing underrepresented populations, transferring knowledge and creating connections that may introduce opportunities for personal and professional growth."



CONNECTING

Launched in February, the Institute's
Postdoctoral Mentoring Program works in
partnership with Salk alumni and Salk Women
& Science to provide a forum for postdoctoral
trainees to engage directly with Salk supporters
and alumni through professional development
and networking opportunities. This program
reflects and expands upon Salk's culture of
collaborative and continuous learning.



LEADING

Salk actively encourages and enables faculty in their efforts to serve as effective mentors. The life experiences, thoughts and opinions of Salk's diverse faculty of varied backgrounds are of great value to others. For example, in a recent article in *Nature Portfolio*, Assistant Professor Christina Towers shared her experiences as a mentee and mentor; challenged early-career scientists to find their mentors; and encouraged scientists no matter the stage of their career to consider becoming a mentor for the benefit of future scientists.







SALK'S SREEKANTH CHALASANI WINS 2021 NPA GALLAGHER MENTOR AWARD

Salk Associate Professor Sreekanth Chalasani has won the 2021 National Postdoctoral Association (NPA) Gallagher Mentor Award. The announcement was made at the 2021 NPA Annual Conference, which took place April 15 and 16. Chalasani was one of eight finalists for the prestigious award.

According to the NPA, the award recognizes those who advocate for postdoctoral scholars; exhibit outstanding communication skills; embed diversity, equity and inclusion values in mentoring; demonstrate respect for the work and career paths of postdoctoral scholars; create productive working environments to enhance the postdoctoral experience; and show resilience and creativity as mentors during the pandemic.

At Salk, Chalasani has made a host of discoveries around the brain, and developed a technique called sonogenetics, which manipulates neurons using ultrasound and has vast implications for therapeutics.

"STEM careers often require one to navigate multiple stages successfully. Each of these stages are also very competitive, thus making mentorship critical to the entire journey," says Chalasani, a member of Salk's Molecular Neurobiology Laboratory.

He advises potential mentors to trust their instincts and be flexible, consistent, and true to their own values.



www.salk.edu/chalasani202109

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NOMIS CENTER FOR IMMUNOBIOLOGY AND MICROBIAL PATHOGENESIS ANNOUNCES ITS 2021 NOMIS FELLOWS



Launched in 2008, the NOMIS Center for Immunobiology and Microbial Pathogenesis aims to shed light on the molecular mechanisms that cause infectious diseases, define key molecules involved in the body's response to injury and infection, elucidate the rules of engagement between the body's microbiome and immune system, and understand why inflammatory processes spin out of control under some circumstances.

Recently, NOMIS announced its 2021 NOMIS Fellows:



DAN CHEN
Postdoctoral Fellow,
Kaech Lab

Chen will direct her expertise in cancer research toward understanding the anti-tumor immune response to one of the deadliest forms of cancer: glioblastoma. Glioblastoma affects cells in the brain and nervous system, which makes it extremely difficult to treat with typical approaches such as chemotherapy.



36

ANDRE MUPostdoctoral Fellow,
Ayres Lab

Mu's project will address why some patients develop severe illness while others seem to have no symptoms of disease despite the pathogens' ability to infect, replicate and transmit. He aims to determine the compositional structure of gut microbiomes before and during infectious diseases in order to identify signature microbiome markers that may predispose a person to acquiring infections.



LIDIA JIMÉNEZ
Postdoctoral Fellow,
Lemke Lab

Jiménez will be studying TAM receptors on macrophages in the thymus and the spleen. Both tissues have a high ratio of cell death due to normal physiological processes occurring within the tissue itself, and TAM receptors are known to play a crucial role in clearing dead cells and controlling immune homeostasis.



JAN PENCIK
Postdoctoral Fellow,
Shaw Lab

Pencik is focusing on non-small cell lung cancer, the most common type of lung cancer. His work will serve to identify some of the most critical proteins linked to a gene called STK11 (also known as LKB1) that regulate a loss of therapeutic efficacy, providing valuable insights for designing optimal therapeutic strategies tailored toward hard-to-treat non-small cell lung tumors.

Learn more about each of the 2021 NOMIS Fellows by visiting www.salk.edu/nomis-center.

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POSTDOC RECEIVES PATHWAY TO INDEPENDENCE AWARD



Laura Newman

Congratulations to Laura Newman, a postdoctoral researcher in the Shadel lab, for being awarded an NIH Pathway to Independence award for a 5-year study of the role of mitochondrial/ER contacts in the regulation of mtDNA release from mitochondria, innate immune signaling, and responses to viral infection.

Congratulations to Professor Susan

Kaech on being the recipient of

a \$300,000 grant in memory of

The CART Fund founder Roger Ackerman. The CART Fund is a

SUSAN KAECH AWARDED \$300,000 GRANT IN HONOR OF THE CART FUND FOUNDER ROGER ACKERMAN



grassroots nonprofit that supports cutting-edge research and created by Rotarians dedicated to finding a cure for Alzheimer's disease.

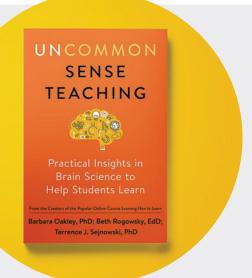
Susan Kaech

SAN DIEGO NATHAN SHOCK CENTER ANNOUNCES FIRST GRANT AWARDEES

The San Diego Nathan Shock Center (SD-NSC) of Excellence in the Basic Biology of Aging, a consortium between the Salk Institute, Sanford Burnham Prebys (SBP) and UC San Diego, recently announced the first class of pilot grant awardees. Six recipients from different institutions will receive up to \$15,000 to pursue research that advances our understanding of how humans age, with the ultimate goal of extending the number of years of potentially healthy, disease-free life.

The six pilot grant awardees are: Ana Chucair-Elliot, staff scientist at Oklahoma Medical Research Foundation; Vanessa Delcroix, postdoctoral researcher at The Scripps Research Institute; Maria Clara Guida, staff scientist at SBP; Adam Konopka, assistant professor at the University of Wisconsin-Madison; Lara Labarta Bajo, postdoctoral fellow at the Salk Institute; and Maria Mihaylova, assistant professor at The Ohio State University.

The awardees were named at SD-NSC's first training workshop, held on March 26, 2021.



UNCOMMON SENSE TEACHING: PRACTICAL INSIGHTS IN BRAIN SCIENCE TO HELP STUDENTS LEARN

Professor Terrence Sejnowski, head of Salk's Computational Neurobiology Laboratory, director of the Crick-Jacobs Center and holder of the Francis Crick chair, has published a new book to improve teaching based on the latest research in neuroscience about how students learn. The book, called *Uncommon Sense Teaching: Practical Insights in Brain Science to Help Students Learn*, is accompanied by a Coursera massive open online course (MOOC) called "Uncommon Sense Teaching," as a follow-up to Sejnowski's popular MOOC "Learning How to Learn."

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A MILESTONE EVENING TO REMEMBER— SYMPHONY AT SALK

On August 21, the Salk Institute celebrated the 25th anniversary of Symphony at Salk, welcoming donors and guests back to the campus for the first time since the COVID-19 pandemic began. The event included the official launch of Salk's Campaign for the Future (see this issue's "Frontiers" for details).

Grammy Award-nominated singer, songwriter and actor Josh Groban, presented by Joan and Irwin Jacobs, was accompanied by the San Diego Symphony, conducted by Sean O'Loughlin and presented by Dan and Martina Lewis. Together, they provided a spectacular evening of music for all in attendance and helped the Institute celebrate the 25th anniversary of Symphony at Salk.

The concert under the stars also featured a remarkable light and video show cast on the iconic study towers in the Courtyard.

The 25th Symphony at Salk was made possible by many generous sponsors, including Zenith sponsors Dan and Martina Lewis and Joan and Irwin Jacobs; Golden Sun sponsors Karen and Don Cohn; and Supernova sponsors Anonymous, Rita and Brian Kaspar, Liz Keadle, Victoria and Terry Rosen, and Ann Tsukamoto-Weissman and Irv Weissman.

This year's event raised a record-breaking amount of \$1.5 million for the Institute's unrestricted fund, which is used to respond to unforeseen research and technology needs, recruit talented scientists and more.







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fundraising event

25th Annual SYMPHONY at SALK

a concert under the stars

Because of your generosity, Symphony at Salk's 25th anniversary celebration on Saturday, August 21, 2021 raised more than \$1.5M, an alltime record.

Your dedicated support enables Salk to accelerate its pace of scientific discovery on the path to improving human health in the areas of aging, cancer, immunology, neuroscience, climate change and more.



For more information, visit: www.salk.edu/symphony or call (858) 597-0657

ZENITH

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GOLDEN SUN

Karen and Don Cohn

SUPERNOVA

Anonymous Rita and Brian Kaspar Liz Keadle Victoria and Terry Rosen Ann Tsukamoto-Weissman and Irv Weissman

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SALK ALUMNI PROGRAM HOSTS VIRTUAL WEBINAR

In June, the Salk Alumni Program presented a live virtual panel, featuring four Salk alumni who shared their experiences on pursuing academic and industry careers with current Salk scientists. The panelists included Nikoosh Carlo, CEO of CNC North Consulting LLC; Mirella Dottori, associate professor at Illawarra Health and Medical Research Institute, University of Wollongong; Pablo Hollstein, an oncology research scientist at Amgen, Thousand Oaks, California; and Christopher Howard, assistant professor of neuroscience at Oberlin College, Oberlin, Ohio.

In addition to events such as this, the Salk Alumni Program, supported by the Alumni-Faculty Fellowship Fund, has awarded the prestigious Alumni-Faculty Fellowship to a talented postdoctoral scholar at Salk the last nine years.





Dannielle Engle



Pallav Kosuri

INSTITUTE COUNCIL VIRTUAL EVENT

On May 20, Salk conducted its sixth annual Institute Council meeting, which highlighted key campus plans and discussed where science is headed in the next 60 years. The meeting featured presentations by Assistant Professors Dannielle Engle and Pallav Kosuri on their labs' cutting-edge technology and how those technologies will impact the future of scientific research. The meeting also introduced the Council's new co-chairs and recognized the past chair for exceptional leadership.

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CROWDFUNDING INITIATIVE LAUNCHED AT SALK CANCER SUMMIT



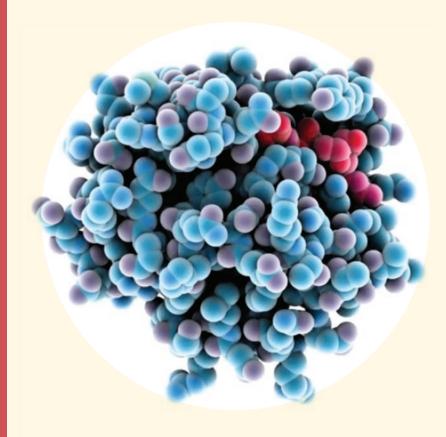
Tim Schoen

On September 1, Conquering Cancer Initiative Chair and Salk Trustee
Tim Shoen announced the start of a crowdfunding campaign to raise
\$100,000 to fund the acquisition of a new, state-of-the-art live-imaging microscope for Salk's Cancer Center.
The announcement came at the Salk Cancer Summit which focused on cancer and metabolism. Learn more about how you can make a difference by visiting salk.edu/crowdfunding.



1 LEARN MORE

www.salk.edu/crowdfunding



POWER OF SCIENCE: DETERMINING HOW CANCER PATIENTS RESPOND TO TREATMENT

On May 5, Assistant Professor Edward Stites spoke as a physician-scientist in a public talk titled "Mutants, Bad Influences, Loners and Cancer." Stites presented his computational approaches for determining why cancer patients respond differently to cancer treatment, and the unexpected ways in which mutations in our cells caused by cancer can determine whether or not a cancer patient responds to treatment.



Edward Stites

1 LEARN MORE

www.salk.edu/powerofscience202109

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Discover your legacy at the Salk Institute

 $\emph{Jonas Salk changed the world.}$ You, too, can have a transformative impact on the future of humanity.

Leaving a gift to the Salk Institute in your will or by beneficiary designation will support foundational research that could help manage cancer, fight climate change, treat Alzheimer's and more.

Making a lasting impact through a planned gift can be simple. Gifts of any size can help accelerate innovation, support the next generation of scientists and enable life-changing discoveries.

Whether you would like to put your donation to work today or benefit us after your lifetime, you can find a charitable plan that lets you provide for your family and support the Salk Institute.

Plan your future. We can help you get started.



Contact Cheryl H. Dean, Esq., at cdean@salk.edu or 858.500.4884 for help finding the right gift plan.



For 60 years, the Salk Institute has pursued Jonas Salk's vision of fearless, interdisciplinary science tackling some of the biggest challenges facing humankind. With a legacy of six decades of life-changing discoveries, the Salk Institute has launched the Campaign for the Future:

Building a More Resilient World.

The Campaign, like Salk science, is a bold, collaborative five-year, \$500M vision to expand and accelerate Salk's critical research.

Included in the Campaign is a new 100,000 square foot state-ofthe-art Science and Technology Center housing four Centers of Excellence focused on plant biology, cancer, healthy aging and computational biology/engineering. Without your support, Salk scientists could not pursue the bold, audacious research needed to understand the biology behind our body's resilience to disease, to stem climate change and to transform the health of the world for the better.

We Invite You to Join Us

Sign up to learn more about how you can accelerate scientific discoveries and you will receive the latest updates, giving opportunities, event invitations and more

www.salk.edu/resilient





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