SUMMER | 2020

WHERE CURES BEGIN.

InsideSalk

APART & TOGETHER

RESPONDING TO THE PANDEMIC

CONTENTS

ON THE COVER:

As COVID-19 spreads across the world, organizations like the Salk Institute are mobilizing to respond.

PRESIDENT'S LETTER

Dear Friends,

Jonas Salk notably said, "our greatest responsibility is to be good ancestors." Living now, in these extraordinary times, we as individuals and an Institute recognize that we must respond with clarity and morality.

At the time of this magazine's printing in late June, it remains hard to overstate the impact of the novel coronavirus infection, COVID-19. The pandemic has impeded world economies and education, and halted personal freedoms often taken for granted, including the simplicity of an in-person interaction. As the effort to slow the spread of COVID-19 continues, the world is reminded of how crucial basic scientific research is to human health.

It is also impossible to ignore the parallels between the fear and anxiety we are experiencing today with the fears of a prior generation who faced the polio virus. At its height, polio paralyzed or killed half a million people globally each year. Today, polio is 99 percent eradicated globally, thanks to the effective polio vaccine.

While the world works on treating and defeating COVID-19, it is an unprecedented period for global scientific collaborations. Indeed, the Salk Institute has tapped its experts in virology, immunology and infectious disease on potential approaches and put together a committee to identify and review COVID-19 research proposals. Already, 11 new research proposals have received preliminary approval to proceed.

The Institute, like organizations across the world, is being impacted financially. Most of our revenue streams have dropped, and safety measures implemented to prevent transmission of the virus have required the cancellation of events, including our 25th anniversary Symphony at Salk fundraiser in August. One of the bright spots is that many of our Symphony at Salk sponsors continued their contributions to this event despite the cancellation. Because Symphony at Salk proceeds support our unrestricted annual operations, their generosity provides essential funding to help us navigate this period.

In the midst of the COVID-19 pandemic, the killing of George Floyd in Minnesota in May sparked protests across the world. The abhorrent racial discrimination and violence against Black people are devastating reminders of the vital importance of how our mission to better humanity must extend beyond science. Just as "every cure has a starting point" is championed as our mantra in research toward eliminating disease and other issues threatening human health, it so too must be our mindset in doing our part to eradicate systemic racism and injustice. For each, the essential starting point is an absolute commitment to being constructive forces for progress and agents of meaningful change. We stand with our Black community, and our commitment is unwavering.

In this issue, you will learn more about how the Institute improves global well-being on multiple fronts and continues to be a faithful steward of Jonas Salk's vision. I trust the updates contained in these pages—ranging from new coronavirus research to profiles of our innovative scientists—inspire your hope in our shared future. Know that all of us at the Salk Institute look forward to the day when we can safely come together again. Until then, please stay safe and healthy.

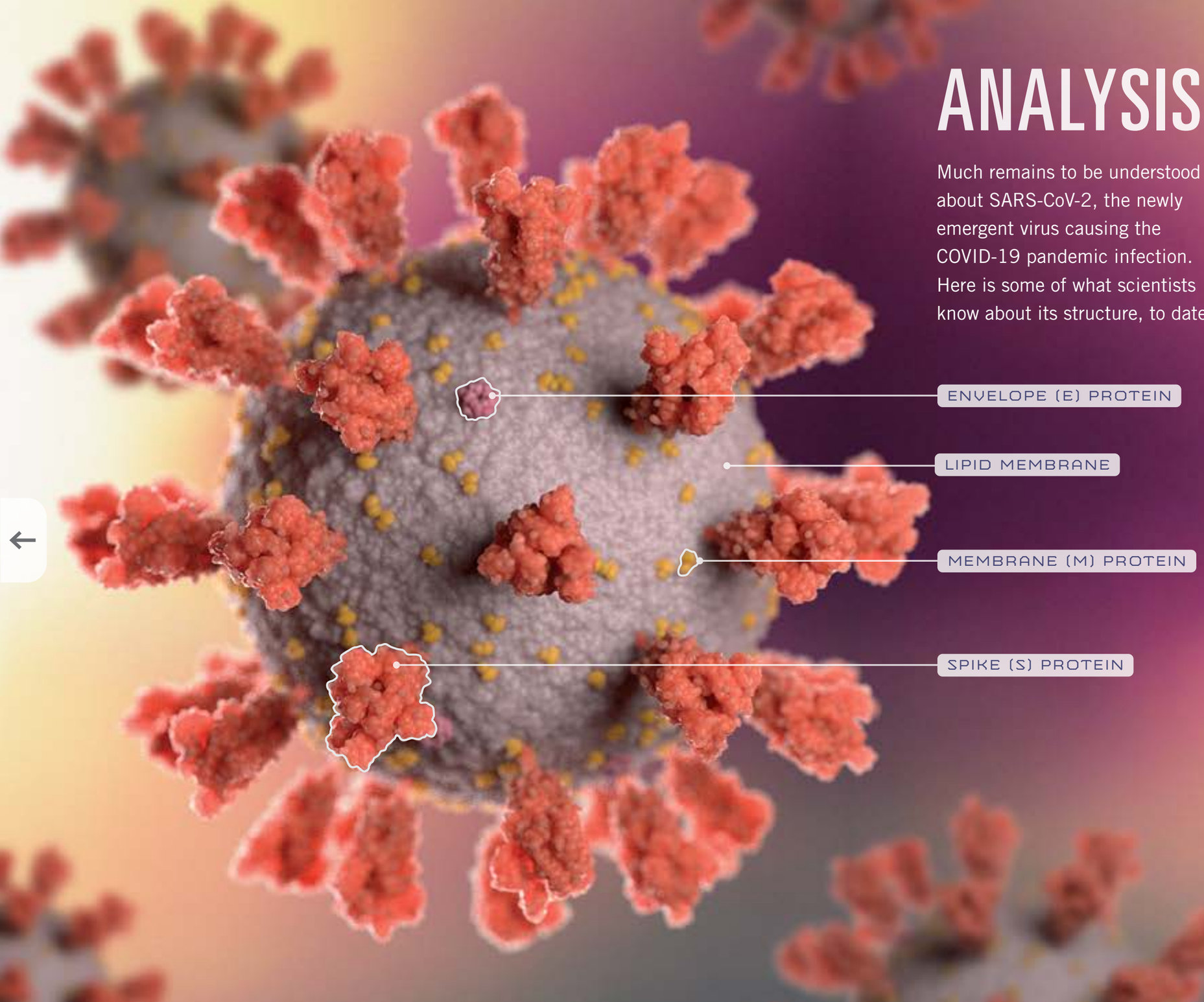
Sincerely,

Fred H. Gage
President

"The Salk Institute has tapped its experts in virology, immunology and infectious disease on potential approaches and put together a committee to identify and review COVID-19 research proposals."

ANALYSIS

Much remains to be understood about SARS-CoV-2, the newly emergent virus causing the COVID-19 pandemic infection. Here is some of what scientists know about its structure, to date.



ENVELOPE (E) PROTEIN
This small structural protein (purple) is involved with the virus' life cycle, including the assembly of other proteins and development of the COVID-19 disease.

LIPID MEMBRANE
This membrane (gray) is composed of a double layer of polarized fat molecules. Similar to how dish soap washes away oily grease, soap breaks down this fat membrane, destroying the virus. This is why handwashing is recommended to prevent the spread of coronavirus.

MEMBRANE (M) PROTEIN
This is the most abundant structural protein (yellow) in the virus. It defines the shape of the lipid membrane, which surrounds the virus, and may help it evade the immune system.

SPIKE (S) PROTEIN
This structural protein (red) is what gives the coronavirus its name, as the proteins, seen through an electron microscope, cause the virus to appear to have a corona or crown of spikes. These spikey proteins hook onto human cells and pull the virus inside, where the virus can co-opt cellular machinery and begin churning out copies of itself. Because of its essential role in transmission, the S protein is now a key target for vaccines and therapeutic antibodies.

Learn more about Salk research and COVID-19	
WATCH	www.salk.edu/video202005

Pandemics, past and present

In 1960, when Jonas Salk founded his eponymous Institute, he was arguably the most famous scientist in the world for having developed the first safe and effective vaccine for a terrifyingly contagious viral disease called polio. At its peak, polio paralyzed or killed hundreds of thousands of people (primarily children) annually worldwide.

In 2020, humanity is facing another highly infectious viral disease, COVID-19, whose long- term effects are not yet known. Although polio and COVID-19 are caused by different viral species that affect different systems in the body, there is a chilling superficial similarity in the way both diseases can cause difficulty breathing. Indeed, it is easy to think of today's ventilator as yesterday's iron lung.

Polio, which is transmitted via fecal-oral routes, is, paradoxically, thought to have become a public health threat due to improvements in public sanitation in the early 20th century. Before sanitation improved, and polio was more widespread, most people encountered polio as babies, while they still had their mothers' immune antibodies as protection against the virus. Once public sanitation cleaned up water and waste, children didn't encounter the virus until they were older and no longer had their mothers' protective antibodies. Older children (and some adults) whose immune systems had never previously encountered polio were immunologically vulnerable.

Like polio, COVID-19 exploits a vulnerability in the immune system's armor: because the SARS-CoV-2 virus—the novel coronavirus that causes COVID-19—appeared in humans recently, our immune systems have no experience with the virus—and sometimes have difficulty fighting it.

"Long-term immunity, also called 'immune memory,' is a process by which we develop the ability to have protective immune responses later on that are targeted to pathogens that we have encountered before," says Professor Susan Kaech,

NOMIS Chair and director of Salk's NOMIS Center for Immunobiology and Microbial Pathogenesis. "So our immune system learns from the first exposure, and the memory of the pathogen is then imprinted in our immune system in specialized cells, aptly named memory T and B cells. Those memory cells can persist for many years, sometimes an entire lifetime, and allow us to respond swiftly and robustly to clear out that same pathogen if encountered later on."

Because SARS-CoV-2 is thought to be more infectious, and deadlier, than seasonal influenza, many people around the world are becoming critically ill and straining medical systems, which are not designed to handle so many additional patients simultaneously.

Thus, COVID-19 represents a perfect storm of threats, one that requires an unprecedented response. Immunologists are focused on several areas related to COVID-19, such as developing a protective vaccine or anti-viral drugs; understanding the difference in immune response between those who have severe illness versus mild illness; determining what is driving lung damage and death seen in some patients; and figuring out which types of memory cells generated against the virus are the most protective. This latter information could help generate immuno-therapies for severely infected patients until there is a vaccine, and will also help teach researchers which vaccines may be the most protective. Scientists around the globe have been racing to find solutions in a monumentally collaborative effort, while also maintaining social/physical distancing—a challenge for work that often needs to be conducted in close quarters in a lab.

During this public health crisis, the Salk Institute's leadership and scientists have faced a conundrum: how to rapidly shut down all non-essential research as effectively as possible while minimizing loss of data and doing everything possible to assist with the unfolding public health crisis.

"We realized early on we needed to take swift action to minimize opportunities for viral transmission through the community, help that community stay connected, and safeguard valuable research materials and projects for the future," says Professor Martin Hetzer, Salk's VP/CSO. "Thanks to the flexibility and innovation of the entire Institute, staff and scientists alike, we were able to move quickly to protect the Salk community in the face of this growing pandemic."

An iconic campus goes into "maintenance mode"

Enacting a partial shutdown of a research institution is different from shutting down many other kinds of organizations. Many experiments that involve biological samples or plant and animal studies cannot simply be paused. The Institute's 52 labs and approximately 1,200 scientists, students and staff sustain research projects that result in the publication of upwards of 300 papers per year in leading academic journals. Salk has critical cell lines, plants and animals that need a physical human presence to ensure their survival.

On Monday, March 2, 2020, Hetzer began meetings with the Institute's Crisis Management Team (CMT)—a combination of faculty and administrators—to evaluate the emerging public health crisis and to make plans for how the Institute would respond.

"While some things like writing manuscripts and analyzing data can be achieved remotely," says Professor Gerald Shadel, the Audrey Geisel Chair in Biomedical Science and a member of the CMT, "most science requires hands-on experiments and collaborations that cannot be achieved remotely. Secondly, there are many moving parts to a world-class scientific institute like Salk, in addition to the labs: scientific core facilities, animal resources, development, communications, safety, human resources, IT, security, facilities—the list goes on and on. Each decision has a butterfly effect on most, if not all, operations, making the task of reducing operations at the Institute as a whole very challenging."

In addition to the gravitational pull of Salk's research and daily operations, the Institute's historically significant architecture typically draws 150 visitors to campus every day, many of them international tourists who come to witness one of the finest examples of modernist architecture in the world. But, as early indications of COVID-19's rapid spread suggested that the public health crisis was likely to get much worse, the Institute closed the campus to visitors on March 4.

Next, the team started to plan for what would happen if the Institute had to close down. Time was of the essence; as each day passed, news of COVID-19 became grimmer and the possibility of shutting down the campus—and its experiments—looked more and more likely, even before official state shutdown orders.

By the time California Governor Gavin Newsom issued a stay-at-home order to residents on Thursday, March 19—the first state in the nation to do so in response to the COVID-19 pandemic—Salk, for several weeks, had already been preparing its temporary closure. The week of March 9, the Institute finalized processes for working from home; determined which staff would be considered essential for continued work on campus; and decided how to wind down laboratory research for the campus-wide "maintenance mode" of limited activity until more information around the threat of the pandemic—and how best to mitigate risk—became available.

"Even though it was a difficult decision [to potentially lose many hours of experimental research], helping to 'flatten the curve' of infections and hospitalizations was of the utmost importance."

MARTIN HETZER
VP/CSO

"I'm grateful that we were ahead of the curve and responded fairly quickly," Hetzer says. "At the time our taskforce convened, the situation was still evolving very rapidly, but we felt it was important to act with an abundance of caution to protect both visitors to Salk as well as the Salk community. Even though it was a difficult decision, helping to 'flatten the curve' of infections and hospitalizations was of the utmost importance."

One of the greatest challenges in shutting down was evaluating which experiments could continue and which would have to be paused or terminated. Salk's maintenance mode entailed operating at a minimal level to conserve resources, both in terms of personnel and of materials that could be affected by supply-chain disruptions. In some cases, cells can be frozen and later thawed to resume work, but in other cases, projects that are too costly in terms of resources must be discontinued. Due to a rigorous one-week evaluation process, the Institute was able to establish how resources could be channeled toward

experiments that could not be paused without losing months or even years of work.

"Labs and administrative departments moved very quickly, within the short span of a few days, to completely reconfigure their labs and experiments," says Salk President and Professor Rusty Gage. "And not only that, but many people at Salk wanted to donate blood to the San Diego Blood Bank and extra personal protective equipment to local hospitals. The way the Salk community pulled together was extraordinary."

Mark Bouchard, director of Environmental Health & Safety (EH&S), worked quickly to ensure new safety measures for the Institute as well as manage fear around contagion. "Due to the COVID-19 epidemic, we had to rapidly instill enhanced infection control procedures such as maintaining a social distance of 6 feet, wearing additional personal protective equipment (PPE), and performing decontamination procedures at an increased frequency," he says. "Something as simple as a cough in the lab can cause anxiety, so we also aim to provide a quick response and good communications around safety processes to not only minimize any real risks but also alleviate fears."

A vital part of ensuring safety is providing sufficient personal protective equipment to staff, despite shortages. Nicole Lack, senior director of Procurement Services, feels this issue keenly: "This situation has definitely had an impact on our supply chain for essential components like personal protective equipment and CO_2, an element needed for many lab functions. We've had to respond quickly to uncertain supplies—looking for new suppliers or finding ways to ration items, for example—to help the Institute maximize safety while continuing critical experiments."

In addition to adapting to the new reality on campus, the Institute established tools and protocols for remote work using collaboration platforms, such as Slack, and videoconferencing technologies, like GoToMeeting and Zoom.

"Obviously, working from home is a completely different experience than working in an office or lab," says Rebecca Newman, VP of External Relations. "It presents a number of challenges that can take some adjustment. While everyone misses the physical energy of being on the campus, I am amazed at how quickly the Salk community has adapted to the use of all the technologies that can keep us connected and highly productive. There is a new appreciation and understanding of colleagues' roles across the Institute and a positive attitude that we are moving through this crisis together."

"Many Salk scientists were already conducting research that is highly relevant to COVID-19."

JANELLE AYRES
PROFESSOR AND CHAIR OF THE COVID-19 RESEARCH COMMITTEE

"While some things like writing manuscripts and analyzing data can be achieved remotely, most science requires hands-on experiments and collaborations that cannot be achieved remotely."

GERALD SHADEL
AUDREY GEISEL CHAIR IN BIOMEDICAL SCIENCE AND A MEMBER OF THE SALK'S CRISIS MANAGEMENT TEAM

Above: The Wahl Lab collaborates virtually through a Zoom meeting work space during the COVID-19 pandemic.

Science continued

Finding ways to transition from working at a lab bench to working remotely is a significant challenge for many researchers. But Salk scientists have risen to the occasion with creativity and resolve.

Just as a few examples, Professor Geoffrey Wahl's lab used time away from the lab to revise and submit paper revisions, write grants and hold virtual happy hours as well as a journal club to stay connected. Assistant Professor Dmitry Lyumkis' lab implemented a "back-to-school" virtual program consisting of biweekly presentations on a research topic, journal club meetings, and a guest lecture on Fridays. Many labs have also focused on computational projects that can be done remotely, carrying out bioinformatics, image processing and algorithm design.

Professor Jan Karlseder, the Donald and Darlene Shiley Chair, says that many lab members continue to feel anxious about how the change in work space will impact their careers and their futures. "We're trying to solve that by staying on top of everyone's experiments. We're talking about them; we're discussing many papers as journal clubs, and we're trying to plan out what we will do when research fully resumes," he says.

To help early career researchers navigate the challenges of having their work disrupted, often while needing to take care of young children all day at home, Salk formed a Career Development Committee, led by Associate Professor Sreekanth (Shrek) Chalasani and Vice President for Equity and Inclusion Mallory Zaslav, to identify professional opportunities that can be conducted remotely. (See sidebar on the postdoc experience on page 11.)

During maintenance mode, the Institute planned for stages of ramp up in accordance with federal, state and local guidelines and in consultation with local and peer institutes across the country. In late May, Salk published a guidebook detailing operations for phased returns and in June, the Institute shifted from its maintenance mode to Phase 1 in conjunction with an ease of the statewide shutdown. Phase 1 entailed adding

temperature checks to the Institute's entry points; reconfiguring work spaces; and implementing shift work so that more research could safely continue, while still requiring staff to work remotely whenever possible.

Despite a gradual resumption of activities on campus, there is no return to "normal" anytime soon. All tasks that can be done off-site—such as writing papers or providing administrative support—will continue to be remote for the immediate future. Large gatherings and events have been moved to virtual platforms or postponed. Day-to-day lives, and research, have fundamentally changed for the time being, but Salk's scientists continue to adapt and rise to the challenge.

Tackling the novel coronavirus

Like scientists all over the world, Salk researchers are eager to contribute to efforts to put an end to this pandemic and prevent future ones. On March 24, the faculty COVID-19 Research Committee was created, chaired by Professor Janelle Ayres and composed of experts in immunology, infectious disease and virology, to identify and shape Salk's research approach to COVID-19.

"Many Salk scientists were already conducting research that is highly relevant to COVID-19," says Ayres, who holds the Helen McLoraine Developmental Chair.

Salk faculty whose research has direct relevance to COVID-19 include Ayres, who was already studying pneumonia and acute respiratory distress syndrome (ARDS, which occurs in COVID-19 patients); Kaech, who studies immunity to infections, including via vaccines; Greg Lemke, who studies receptors that regulate the immune response and prevent the "cytokine storms" that develop in COVID-19; Satchin Panda, who is studying long-term gene activity in COVID-19 patients; Marga Behrens, who is studying the effects of virus-induced maternal immune activity on brain development of offspring; Tony Hunter, whose discovery of molecular switches called tyrosine kinases led to anti-cancer drugs called tyrosine kinase inhibitors, several of which are in clinical trials for their ability to block activation of immune cells and potentially reduce ARDS; Dmitry Lyumkis, who investigates protein molecules made by viruses and how the insights inform the design of novel vaccines and antivirals; and others.

"I hope this will remind us even more how important vaccines really are, and the essential role they play in public health. We have to look at vaccines at the population level, not the individual level, and realize they save lives."

SUSAN KAECH
NOMIS CHAIR AND DIRECTOR OF SALK'S NOMIS CENTER FOR IMMUNOBIOLOGY AND MICROBIAL PATHOGENESIS

Ayres says the committee is especially looking for innovative proposals for science to address the pandemic that isn't necessarily going to be done someplace else. "Researchers within the Salk Institute became really ignited by the pandemic; they want to make a difference, they want to contribute to the response, so they are developing diagnostics and performing fundamental research that is necessary for identifying candidate therapeutic targets," she says. For details about new research projects approved by Salk's COVID-19 Research Committee, see pages 14-15.

A vaccine against the virus that causes COVID-19 is likely many months away, but the disease is a powerful reminder of the importance of fundamental biological research, which seeks to understand at a basic level how living things function.

The research that goes on at Salk every day—bringing about new understandings in infectious disease, cancer, aging, metabolism, neuroscience, plant biology and more—is a kind of insurance policy against future health threats, both known and unknown. Jonas Salk did not develop the polio vaccine out of the blue in 1955; for many years before he developed his vaccine, Salk had been studying the influenza virus. It was the critical insights he gained by developing a vaccine for influenza that later allowed him to conquer polio: by 1979, polio had been eradicated in the United States.

"Vaccines have proven to be one of the very best approaches to save lives and improve human health. They have been so effective that the threats they prevent no longer feel like threats," says Assistant Professor Edward Stites, who in addition to being a cancer researcher is also a physician.

"Polio is a great and highly relevant example. Once there is a COVID-19 vaccine, it will be a phenomenal tool to control this new threat, and hopefully that will re-instill a widespread commitment to vaccination compliance."

Kaech adds, "I hope this will remind us even more how important vaccines really are, and the essential role they play in public health. We have to look at vaccines at the population level, not the individual level, and realize they save lives. Sadly, I think some people have forgotten this because we haven't had anything threaten our society globally, quite like this, in the past 40 or so years, like polio and smallpox once did."

Despite the challenges of the pandemic, everyone at Salk has expressed appreciation for the way people have pulled together to continue groundbreaking research as well as pursue ways to tackle the coronavirus. Once it is safe to do so, the Institute will also bring back its highly anticipated scientific and public events, including the annual Symphony at Salk.

"We look forward to the day when scientists, staff and visitors can all return to our iconic campus," says Gage. "We are confident that scientific endeavors across the world will help mitigate this public health crisis and prevent further tragedies."

LISTEN | www.salk.edu/podcast/COVID19

PERSPECTIVE FROM A POSTDOC: CORINNE LEE-KUBLI

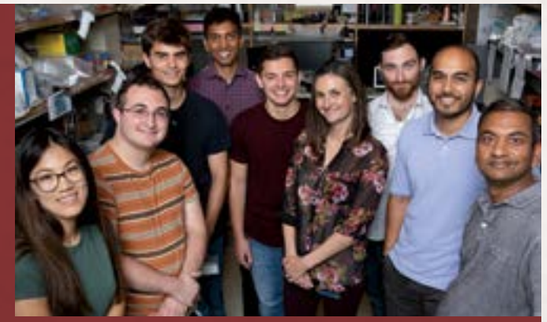
Salk has roughly 200 postdoctoral fellows whose science is being impacted by the COVID-19-induced maintenance mode. While some scientific models, such as the tiny worm *C. elegans*, can be easily frozen for months at a time, experiments involving other model systems, such as organoids—tiny three-dimensional organs in a dish—cannot be so easily paused.

Thus, some essential experiments have continued in order to not disrupt critical projects. Corinne Lee-Kubli, a postdoctoral researcher in the Chalasani lab, just finished the last part of her project testing a new technology, called sonogenetics, which activates neurons non-invasively using ultrasound. She is thankful that she was almost finished with her project when the maintenance mode went into effect. Now, she is looking forward to reviewing the scientific literature, writing up her results and submitting her manuscript to an academic journal.

"Reviewers may suddenly have a lot more time to read new research articles, and I imagine they'll be more conscientious about what they request in terms of follow-up experiments, since most labs are closed," says Lee-Kubli. "Theoretically, we could see a surge in scientific publications, which would be very exciting!"

In addition to her research project, Lee-Kubli plans to use her time away from the lab to start writing a draft of a research grant and prepare her applications for her first faculty position. "I think one of the most helpful things I've found for maintaining productivity is sticking to a schedule."

A dedicated schedule has also helped Lee-Kubli and her husband juggle two young children at home. Every day the parents take turns, with one working while the other watches the children. "My husband built the kids a playhouse in the backyard, so that's helped our family spend more time outside." Soaking up some San Diego sun helps her family stay positive, despite challenging times.



Lee-Kubli in center (fourth from right) with Chalasani lab (July 2019).

"I am also grateful to have a supportive and flexible mentor," says Lee-Kubli. "Dr. Chalasani has kept our weekly lab meetings as well as our individual meetings, to help us develop obtainable goals during the closure."

The Career Development Committee is also working on initiating a virtual seminar series, where postdocs can present their work and practice job talks. Other faculty members, such as Associate Professor Julie Law, are hosting virtual happy hours for trainees to socialize and release stress. The committee is also suggesting that faculty members discuss individual development plans with each trainee to set career goals and next steps.

"I appreciate how the coronavirus and the associated risks were taken seriously by Salk," says Lee-Kubli. "Knowing that I could trust the decisions of Salk's coronavirus Task Force helped alleviate stress and take pressure off the situation. Now, I can focus on my work."

A Conversation with MARTIN HETZER

Salk Vice President and Chief Science Officer

In the last few months, Salk Vice President and Chief Science Officer Martin Hetzer spearheaded the Institute's efforts to respond to the pandemic from both an administrative as well as a scientific perspective. *Inside Salk* spoke with Hetzer on how he led the charge to shift research in the face of continuing uncertainty, as well as what makes him hopeful about Salk's—and the world's—future.

Very early on in the face of the COVID-19 pandemic, you set up a COVID-19 Task Force and other committees to handle the rapidly changing day-to-day circumstances for the thousand-plus employees at the Institute. At the same time, you and other faculty began evaluating ways that Salk's unique research strengths could help tackle COVID-19. What did it take to so swiftly change course for such a prolific and productive Institute?

MH: We took several big steps early on when the pandemic was first coming to light. At that time, in early March, it was still a very rapidly evolving situation, and we chose to act with an abundance of caution. In that sense, we were able to stay ahead of the curve and respond to events fairly quickly, well before California Governor Newsom's stay-at-home order. This approach helped us to not only pause or quickly end experiments where we could, but also, unfortunately, terminate other experiments, as efficiently as possible.

Together with our Crisis Management Team, the faculty leadership as well as each lab worked hard to figure out how to bring activity—and therefore lab population density—down to a minimum so that anyone who had to go to work to carry out essential functions (caring for animals, for example) could do so in a safe manner, following CDC guidelines. These were not easy decisions. Many research projects unfold over not just days or weeks but over months or even years, so we wanted to avoid an undue burden in terms of loss of valuable experimental material and insights. The labs, including my own, had to grapple with these difficult questions over a very few days. Remarkably, based on an impressive level of cooperation, researchers were able to wind down activities significantly in that short period of time, while also thinking of ways to bring unique scientific approaches to better understanding the novel coronavirus.

"The Institute's approach since its founding has been to understand fundamental biological processes, in order to make discoveries that can inform treatments and cures."

MARTIN HETZER
VP/CSO

Q: Could you talk a bit more about that, and Salk's efforts to help stem COVID-19?

MH: The Institute's approach since its founding has been to understand fundamental biological processes, in order to make discoveries that can inform treatments and cures. So we wanted to take a similar approach to the novel coronavirus and ask where we could make the biggest impact. Salk scientists are highly collaborative and have expertise in a broad range of research areas, many of which are highly relevant for infectious diseases such as COVID-19. Several of our faculty are world experts in using viruses to fight diseases or in understanding resistance and tolerance strategies that allow organisms to survive infections. Others work on understanding the body's immune response from various angles, which includes using metabolism to slow infections; understanding how various immune cells help or hinder immunity; and finding which cellular targets may be best for therapies or vaccines. Some of the labs are recalibrating their already-relevant research to focus on the novel coronavirus, while others are beginning exciting new lines of work.

Q: In the beginning of June, you developed a plan to move the Institute to a phase of limited shift work for researchers, with plans for additional phases following local and federal guidance. What do you see as the next steps for resuming scientific research at the Institute?

MH: For now, we are adapting to new guidelines as they are released by public health authorities, which entail moving the Institute to new phases in a very thoughtful, staggered process to maintain the social distancing requirements needed to keep everyone safe. Each individual lab has developed plans for how they can safely expand research activities as well as move quickly on the new COVID-19 areas of research. We have also determined appropriate steps as to how we can bring back the different administrative units who support reopening, in an effective way.

In addition, we are continuing to recruit new faculty, because we are not merely focused on getting through the next few months under the pandemic, but are also looking ahead to the best ways to tackle other major health problems that the world faces, such as climate change, Alzheimer's, cancer and diabetes to name a few.

Q: Any parting thoughts?

MH: Very much in the spirit of Jonas Salk, I believe that foundational basic research plays a central role in mitigating the impact of a crisis such as COVID-19, and also to prevent such crises in the future. So, if anything, this pandemic has only strengthened my conviction of the power and importance of basic research to meet the greatest challenges of our time. As for Salk specifically, our strength lies in our people: the dedicated researchers and staff who, day in and day out, strive to make the Institute a place "Where cures begin." I cannot predict when we will all be back on our beautiful campus again, doing critical research, holding public events and enjoying one another's company, but I am greatly looking forward to it.

NEW COVID-19 RESEARCH

In addition to Salk's ongoing research areas relevant to COVID-19, several new coronavirus-specific projects have recently launched. These innovative projects range from understanding the structure of the virus to mobilizing the body's immune reaction.

TONY HUNTER GERALD PAO

01 In severe COVID-19 cases, immune cells in the infected windpipe and lungs can release high levels of damaging inflammatory proteins called cytokines, colloquially known as a "cytokine storm." American Cancer Society Professor Tony Hunter previously showed that the cytokine LIF (leukemia inhibitory factor) plays a role in pancreatic cancer. He will test whether cytokines, like LIF, play a role in the immune overreaction seen in some COVID-19 patients.

02 Gerald Pao, a staff scientist in the Hunter lab, will work with the Sanford Burnham Prebys Medical Discovery Institute to generate a virus system that expresses a spike protein that mimics the ones on the coronavirus. The team will then examine the immune response to these spike proteins.

03 In collaboration with UC San Diego, USC and Sanford Burnham Prebys Medical Discovery Institute, Pao will develop a test to detect the presence of COVID-19 genomes in human nose and throat samples. He has designed this test, which will combine CRISPR with an imaging technology, so that it will only take a few minutes.

04 Pao will also engineer CAR-T cells, cells that can target specific proteins, to aid in the development of a coronavirus vaccine. These cells are repurposed from cancer immunotherapy to provide immune surveillance and kill coronavirus-infected lung cells that have a spike protein on their surface, early in the infection.

CLODAGH O'SHEA ALAN SAGHATELIAN JOSEPH NOEL

It will take a virus to kill a virus. Professors Clodagh O'Shea, Alan Saghatelian and Joseph Noel are exploiting the atomic structures of the SARS-CoV-2 virus, together with proprietary synthetic virology and chemical biology platforms, to create transformative vaccines and gene therapies. Their pipeline will target i) SARS-CoV-2 prevention by creating synthetic live viral vaccines that induce broad and long-lasting immunity and ii) SARS-CoV-2 treatment through viral gene therapies that express synthetic nanoparticles that seek, neutralize and destroy SARS-CoV-2 and prevent pathology. This research will uncover underlying principles and overcome intractable clinical challenges, not just of SARS-CoV-2 today, but of SARS-CoV-3 tomorrow.

SUSAN KAECH

01 Professor Susan Kaech, who studies how we develop immunity to severe viral infections, such as influenza and now COVID-19, will collaborate with The Scripps Research Institute and La Jolla Institute to study the types of memory T and B cells that form in the lung following SARS-CoV-2 infection as a way to understand if and how long-term immunity can be established. This work will be critical to understanding the types of memory T cells that COVID-19 vaccines will need to re-create in vaccinated individuals to establish benchmarks for generating protective immunity.

02 Creating a protective coronavirus vaccine is currently one of the world's greatest challenges. Kaech believes that immune cells called memory B and T cells are likely critical for controlling the infection, and could therefore be excellent targets for vaccines to enable long-term immunity. Her lab, in collaboration with The Scripps Research Institute, will examine the role of memory T cells inside the lungs during a COVID-19 infection.

03 In a separate study, in collaboration with pulmonary physicians at UC San Diego and the VA hospital, Kaech will examine changes in the levels and composition of surfactant in COVID-19 patients. Surfactant is a substance in the lungs that allows us to breathe. The study will compare surfactant levels with the health outcomes of COVID-19 patients to determine if a drop in surfactants is associated with more severe disease. Her lab will also test if genetic alterations in pathways that control surfactant levels in the lungs alter the course of the disease.

DMITRY LYUMKIS

01 Assistant Professor Dmitry Lyumkis will examine the molecular mechanisms by which the non-structural protein NSP1 halts host protein production. This process ultimately helps the virus in promoting the production of its own viral proteins and the development of COVID-19.

02 The Lyumkis lab will also explore how the non-structural protein NSP2 affects host cells during the development of COVID-19.

JUAN CARLOS IZPISUA BELMONTE

Professor Juan Carlos Izpisua Belmonte is collaborating with a San Diego biotechnology company to develop COVID-19 treatments using nanoparticles. The researchers will use RNA-targeting CRISPR-Cas technology to destroy the SARS-CoV-2 virus' RNA. This treatment will prevent the virus from replicating in the body, thereby reducing the severity of an individual's COVID-19 infection and limiting the virus' chances of spreading. If successful, this approach could be extended to treat other RNA viruses in the future.

THANK YOU

Symphony at Salk

a concert under the stars

SAVE THE DATE
AUGUST 21, 2021

While Symphony at Salk, our annual concert under the stars, will not take place this summer, the singular event will return August 21, 2021. It is guaranteed to be a celebration of the power of Salk science with our many valued supporters.

Here is a list of 2020 Symphony at Salk sponsors and donors whom we would especially like to thank for their generosity and support of Salk. The individuals and organizations recognized here have chosen to continue with their donations despite this year's cancellation.

The Institute extends a special note of gratitude to Board Chair Dan Lewis for his inspirational challenge to fellow sponsors to maintain their sponsorship of Symphony at Salk despite its cancellation.

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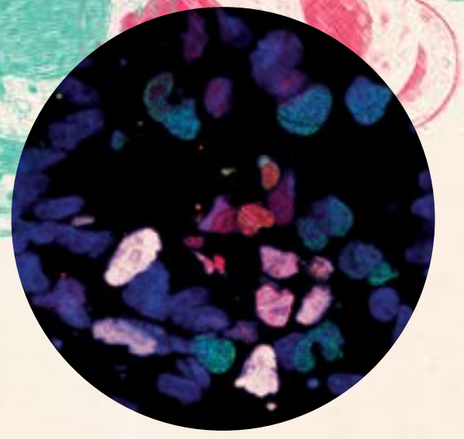
Science Continued

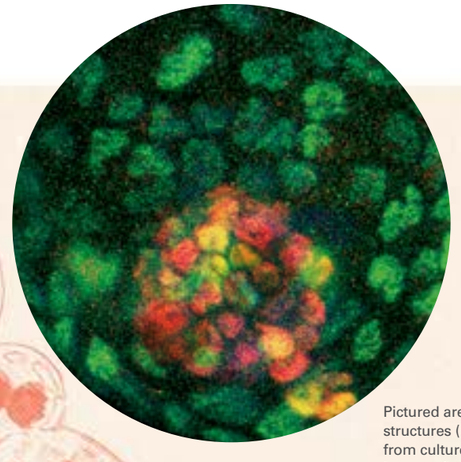
Even as the Salk Institute shifts to tackling COVID-19 both institutionally and scientifically, it continues its groundbreaking research on other global problems facing humanity. In the following pages you will read about breakthrough discoveries that happened before and during the COVID-19 pandemic, and learn more about scientists who are pushing the boundaries in aging, cancer, plant science, neuroscience and many other areas.

UNLOCKING THE BLACK BOX OF EMBRYONIC DEVELOPMENT

Little is known about the molecular and cellular events that occur during early development of organs such as the uterus, ovary and brain. Now, research published by Salk labs illuminates significant developmental processes for the first time, and provides new methods to inform issues around pregnancy, infertility, and developmental disorders such as autism spectrum disorder (ASD).



Day 17 of a cultured primate embryo; the various colors indicate markers of cellular differentiation (specialization).



Pictured are blastocyst-like structures (blastoids) from cultured cells immunofluorescently stained for the trophectoderm marker CDX2 (green) and the inner cell mass marker SOX2 (red). The trophoectoderm makes up the outer cells of the blastoid.

CELL 10/2019

SCIENCE 10/2019

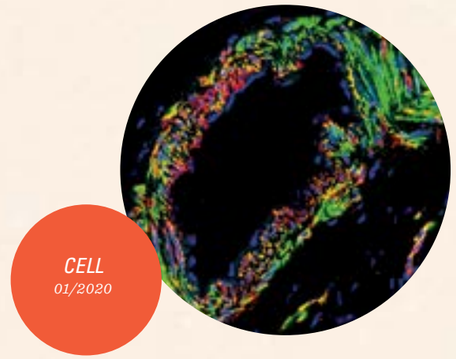
Understanding early cell development

After an egg is fertilized, cells begin to divide and form a blastocyst, a two-layered cluster of cells. The way a blastocyst develops has implications for whether a pregnancy is successful, how organs form, and potentially even for diseases later in life, but studying blastocysts has been a challenge. Professor Juan Carlos Izpisua Belmonte and colleagues created mouse blastocyst-like structures, dubbed "blastoids," that had the same structure as natural blastocysts, and offering a powerful new tool to advance research by circumventing the need for natural embryos.

The Izpisua Belmonte lab also wanted to study a critical milestone in development after the formation of the blastocyst: gastrulation. This stage occurs when an embryo transforms into a three-layered structure, from which all future tissues and organs will be derived. Izpisua Belmonte led an international team to uncover new insights into gastrulation by creating a method enabling primate embryos to grow in the laboratory longer than ever before. The research, while done in nonhuman primate cells, could potentially inform approaches to regenerative medicines.

A road map for ovarian health and aging

Izpisua Belmonte's lab published additional work uncovering how ovaries age in nonhuman primates in unprecedented detail. This road map reveals several genes that could be used as biomarkers and could point to therapeutic targets for diagnosing and treating female infertility and age-associated ovarian diseases, such as ovarian cancer, in humans.



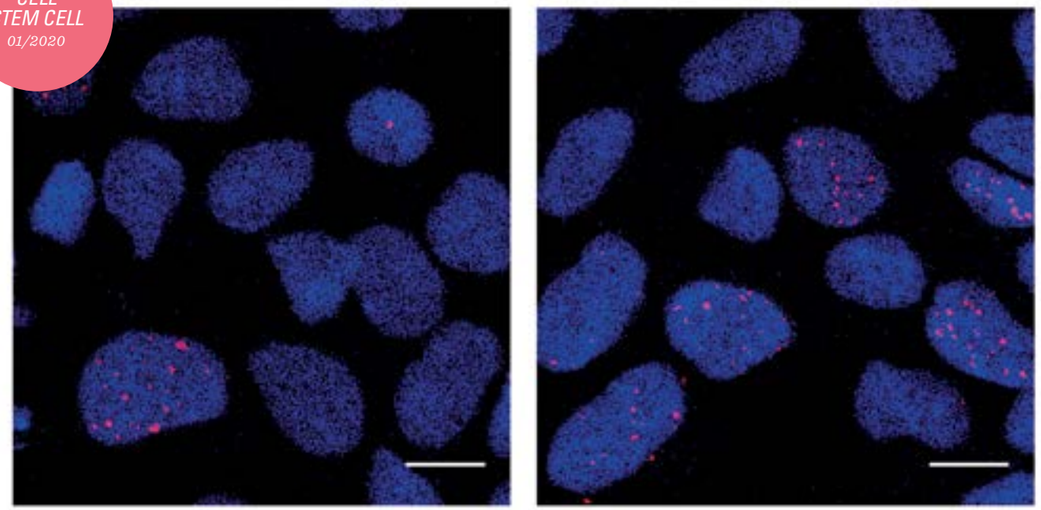
CELL 01/2020

Immunofluorescence analysis of classic markers for smooth muscle cells in the ovary, including muscle filaments (green), smooth muscle proteins (red) and nuclear DNA (blue).

READ

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

CELL
STEM CELL
01/2020



Cells that will eventually become neurons (neural progenitor cells) derived from individuals with autism spectrum disorder (right panel) exhibit increased DNA damage (indicated by the red stain) compared to those derived from healthy individuals (left panel).

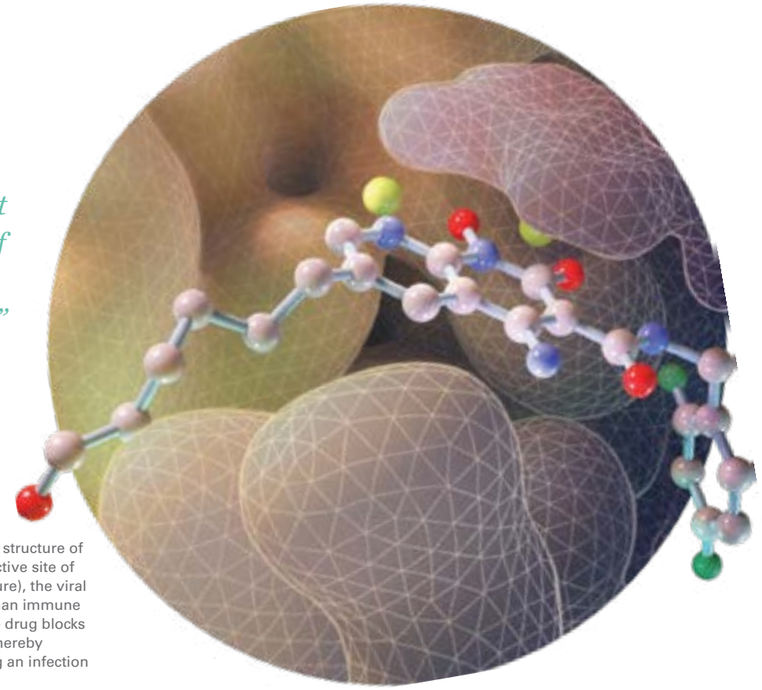
Team links rapid brain growth in autism to DNA damage

Research into the developing brain, led by Professor and Salk President Rusty Gage, first author Meiyan Wang and colleagues, revealed a unique pattern of DNA damage that arises in brain cells derived from individuals with a macrocephalic form of autism spectrum disorder (ASD). They found that cells from people with this type of ASD not only proliferate more, but also naturally experience more replication stress, spurring DNA damage. The observation helps explain what might go awry in the brain during cell division and development to cause the disorder.

INFECTIOUS DISEASE

"In previous structures, we learned about intasome biology, but here, we've really started to gain insight into the therapeutic angle of how drugs can target these important viral assemblies."

DMITRY LYUMKIS



This illustration depicts the molecular structure of an HIV drug (at center) bound to an active site of the HIV intasome (surrounding structure), the viral machine that allows HIV to infect human immune cells. By filling the binding pocket, the drug blocks the normal function of the machine, thereby preventing the virus from establishing an infection in the target cell.

ADVANCES IN IMAGING TECHNIQUE AND NEW INSIGHT INTO HOW HIV DRUGS WORK AT ATOMIC LEVEL

SCIENCE
01/2020

PROGRESS IN BIOPHYSICS AND MOLECULAR BIOLOGY
09/2019

Assistant Professor Dmitry Lyumkis' team uses and optimizes an advanced imaging technique called cryo-electron microscopy (cryo-EM) to visualize large protein complexes within cells and to uncover how these structures work. In the fall, Lyumkis and Philip Baldwin co-authored a study that provides a foundation for quantitatively determining how differences in viewing angles affect the resulting 3D structures of proteins. Then, in January, Lyumkis, Salk co-first author Dario Passos and colleagues reported on how a powerful class of HIV drugs binds to a key piece of HIV machinery. By resolving this complex in 3D for the first time while different drugs were attached, the researchers discovered structural reasons for why these therapies are so potent.

From left: Dario Oliveira Passos, Dmitry Lyumkis and Ilona K. Jóźwik

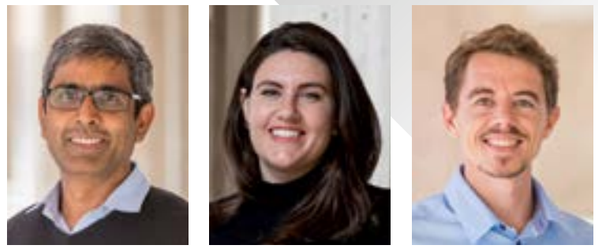
NEUROSCIENCE + METABOLISM

CIRCADIAN CYCLES CAN BENEFIT OUR HEALTH

Professor Satchin Panda studies circadian clocks, the internal programs that mediate our daily biological rhythms and affect our health. In two recent papers, Panda and his team examined how the body sets these clocks, while a third paper reveals what these rhythms can mean for our well-being.

In the first paper, Panda and colleagues reported a novel technique for determining how neurons communicate, which was employed in mice to uncover details about how the brain responds to light signals received by the retina. In the second study, Panda, Salk first author Ludovic Mure and colleagues reported the discovery of three cell types in the eye that detect light and align the brain's circadian rhythm to ambient light.

In the third paper, Panda, Salk first author Emily Manoogian and colleagues described their clinical study of eating schedules based on circadian rhythms. They found that a 10-hour time-restricted eating intervention, when combined with traditional medications, resulted in a variety of health benefits for participants with metabolic syndrome, including weight loss, reduced abdominal fat, lower blood pressure and cholesterol, and more stable blood sugar and insulin levels. This pilot study could lead to a new treatment option for patients who are at risk for developing life-altering and costly medical conditions such as diabetes.



From left: Satchin Panda, Emily Manoogian and Ludovic Mure.

CELL REPORTS 10/2019

CELL METABOLISM 12/2019

SCIENCE 12/2019

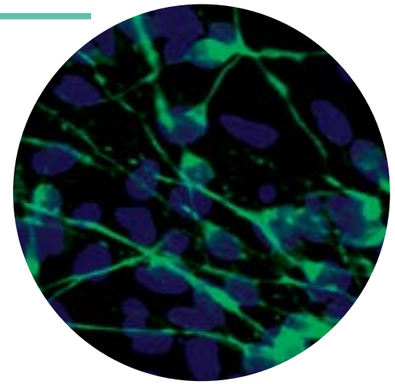
WATCH www.salk.edu/panda202005

NEUROSCIENCE

ALTERED POTASSIUM LEVELS IN NEURONS MAY CAUSE MOOD SWINGS IN BIPOLAR DISORDER

BIOLOGICAL PSYCHIATRY 10/2019 & 02/2020

People with bipolar disorder experience dramatic shifts in mood, oscillating between often debilitating periods of mania and depression. Now, a sweeping new set of findings by Professor and Salk President Rusty Gage, first author Shani Stern and colleagues has revealed previously unknown details about why some neurons in bipolar patients swing between being over- or underexcited. In two recent papers, the team used experimental and computational techniques to describe variations in potassium and sodium levels in brain cells derived from people with bipolar disorder, which may help to further explain why one-third of patients respond to lithium and the rest do not.



Healthy CA3 pyramidal neurons stained to show the cell body (blue) and axons (green).

NEW INSIGHTS INTO HOW GENES CONTROL COURTSHIP AND AGGRESSION

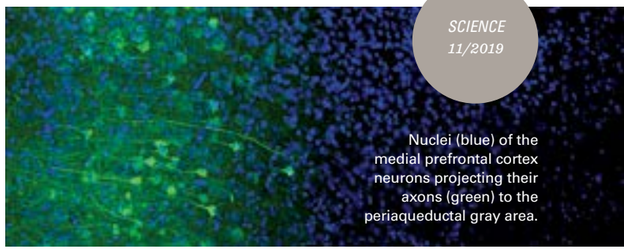
ELIFE 04/2020

Fruit flies, like many animals, engage in a variety of courtship and fighting behaviors. Assistant Professor Kenta Asahina and co-first authors Kenichi Ishii and Margot Wohl have uncovered the molecular mechanisms by which two sex-determining genes affect fruit fly behavior. The male flies' courtship and aggression behaviors, they showed, are mediated by two distinct genetic programs. The findings, both published in *eLife*, demonstrate the complexity of the link between sex and behavior.

Researchers studied how sex-determining genes affect neurons known to control courtship (shown in orange on the left) and aggression (shown in blue on the right) in fly brains.

BRAIN BIOMARKER PREDICTS COMPULSIVE DRINKING

SCIENCE 11/2019



Nuclei (blue) of the medial prefrontal cortex neurons projecting their axons (green) to the periaqueductal gray area.

Although alcohol use is ubiquitous in modern society, only a portion of individuals develop alcohol use disorders or addiction. Yet, scientists have not understood why some individuals are prone to developing drinking problems, while others are not. Professor Kay Tye and colleagues have discovered a brain circuit that controls alcohol drinking behavior in mice. The findings suggest a biomarker for predicting the development of compulsive drinking and may pave the way for a better understanding of human binge drinking and addiction.

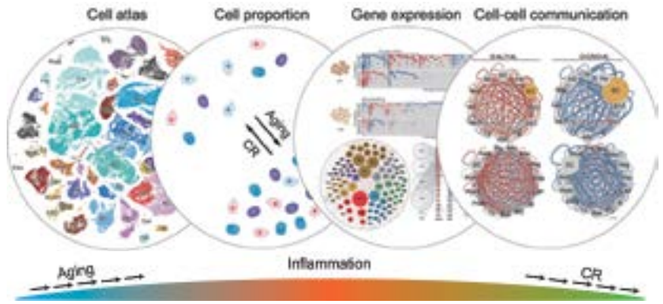
WATCH www.salk.edu/tye202005

METABOLISM

EAT LESS, LIVE LONGER

CELL 02/2020

If you want to reduce levels of inflammation throughout your body, delay the onset of age-related diseases and live longer—eat less food. That's the conclusion of a new study led by a collaborative group of scientists, including Salk Professor Juan Carlos Izpisua Belmonte, that provides the most detailed report to date of the cellular effects of a calorie-restricted diet in rats. While the benefits of caloric restriction have long been known, the new results show how this restriction can protect against aging in cellular pathways.



The illustration represents the ways in which caloric restriction affects various aspects of cellular function, with the overall result of reducing inflammation and the activity of many aging-related genes.

WATCH | www.salk.edu/belmonte202005

PROTEIN INTERACTIONS

MICROPROTEINS HAVE MAJOR IMPLICATIONS FOR HUMAN DISEASE

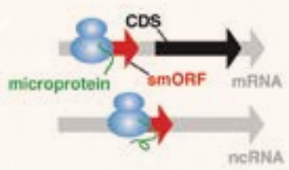
NATURE COMMUNICATIONS 10/2019

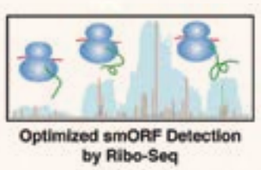
NATURE CHEMICAL BIOLOGY 12/2019

Roughly 25,000 genes code for biologically relevant proteins, most of which are large chains of 300 or more linked amino acids. But, increasingly, "microproteins," with fewer than 100 amino acids, are being found to have important roles in health and disease.

In a study published in October, Professor Alan Saghatelian, co-corresponding author Uri Manor, first author Qian Chu and colleagues showed that the microprotein PIGBOS contributes to mitigating cell stress. In the second study, published in December, Saghatelian and first author Thomas Martinez identified over 2,000 new, small genes that may encode for microproteins—expanding the number of human genes by 10 percent. Both publications provide a better understanding of human biology that may eventually have implications for diseases ranging from cancer to diabetes.

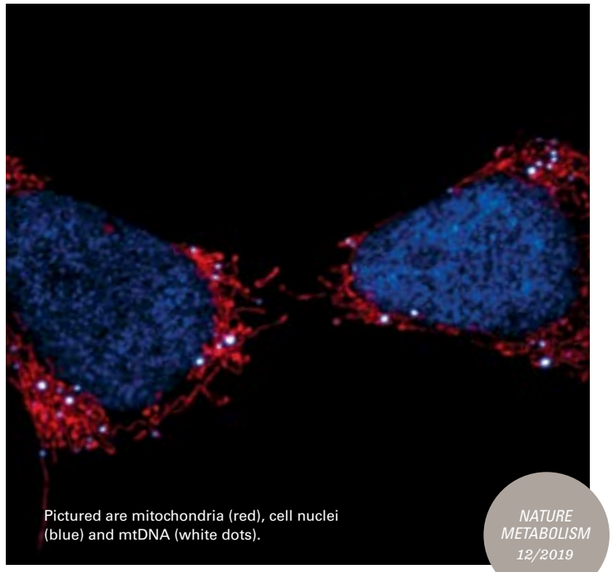
WATCH | www.salk.edu/saghatelian202005





The "microproteins" encoded by smORFs have been linked to immune function, cell stress and many other cellular processes, which suggests that detecting smORFs could lead scientists to new biomarkers and drug targets for human diseases.

CANCER



NATURE METABOLISM 12/2019

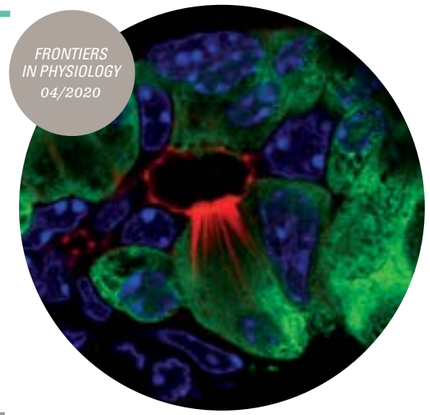
MITOCHONDRIA ARE THE "CANARY IN THE COAL MINE" FOR CELLULAR STRESS

Mitochondria, tiny structures present in most cells, are known for their energy-generating machinery. Professor Gerald Shadel, first author Zheng Wu and colleagues have discovered a new function of mitochondria: they set off molecular alarms when cells are exposed to stress or to chemicals that can damage DNA, such as chemotherapy. The results could lead to new cancer treatments that prevent tumors from becoming resistant to chemotherapy.

MYSTERIOUS TUFT CELLS FOUND TO PLAY ROLE IN PANCREATITIS

FRONTIERS IN PHYSIOLOGY 04/2020

The function of tuft cells—cells sensitive to chemical changes—in the pancreas has largely remained a mystery. Now, Professor Geoffrey Wahl, co-first authors Kathleen DelGiorno and Razia Naeem, and colleagues have uncovered how tuft cells form during pancreatic inflammation as well as their surprising role in immunity, using mouse models of pancreatitis. The findings could lead to the development of new biomarkers to test for pancreatitis and pancreatic cancer.



Pancreatitis tuft cells (red, microvilli and actin rootlets) in the injured pancreas (green); nuclei (blue)

From left: Geoffrey Wahl, Kathleen DelGiorno and Razia Naeem

PLANT BIOLOGY

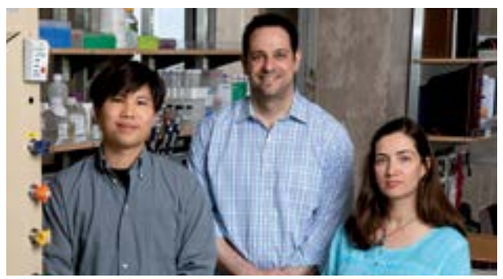
HOW PLANTS SOUND THE ALARM ABOUT DANGER

NATURE PLANTS 03/2020

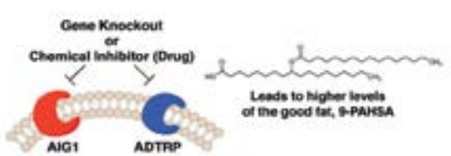
One role of plant hormones is to perceive trouble—whether an insect attack, drought or intense heat or cold—and then signal to the rest of the plant to respond. Now, Professor Joseph Ecker, Salk co-first author Mark Zander and collaborators report new details about how plants respond to a hormone called jasmonic acid, or jasmonate. The findings reveal a complex communication network and could help members of Salk's Harnessing Plants Initiative develop crops that are hardier and more able to withstand rapid climate change.

Arabidopsis thaliana, a small flowering plant in the mustard family.

GENETICS



From left: Justin Wang, Alan Saghatelian and Meriç Erikci Ertunc.



EXPERIMENTAL DRUG BOOSTS LEVELS OF GOOD FATS

JOURNAL OF BIOLOGICAL CHEMISTRY 05/2020

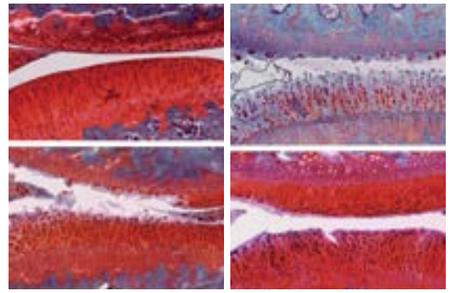
Professor Alan Saghatelian, first author Meriç Erikci Ertunc and a collaborative team of scientists have identified two genes that can regulate levels of healthy fats called FAHFAs, in mice. Because FAHFAs decrease inflammation and increase insulin sensitivity, a better understanding of the activity of their regulatory genes may eventually lead to therapies for people with diabetes and inflammation. They found that the loss of the genes led to higher-than-normal levels of the beneficial FAHFAs, while blocking the genes' activity with an experimental drug also increased FAHFA levels.

AGING

ALZHEIMER'S DRUG CANDIDATES REVERSE BROADER AGING, STUDY SHOWS

eLIFE 12/2019

Scientists from the lab of Professor David Schubert, including first author Antonio Currais and co-corresponding author Pamela Maher, have shown how the Alzheimer's drug candidates CMS121 and J147 can slow aging in healthy older mice, blocking the damage to brain cells that normally occurs during aging and restoring the levels of specific molecules to those seen in younger brains. The research points out a new pathway that links normal aging to Alzheimer's disease.

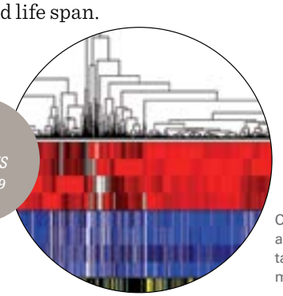


The top left image shows a knee joint in a healthy rat. (Red [surrounding white] indicates cartilage.) Bottom left image shows a joint with grade 2 untreated osteoarthritis. Top right image shows a joint with osteoarthritis that has worsened from grade 2 to grade 4 after six weeks of placebo therapy. The bottom right image shows a joint with osteoarthritis that improved from grade 2 to grade 1 (mild) after six weeks of combination therapy with alphaKlotho and sTGFbR2.

DIABETES DRUG HAS UNEXPECTED, BROAD IMPLICATIONS FOR HEALTHY AGING

Metformin is the most commonly prescribed type 2 diabetes drug, yet scientists still do not fully know how it works to control blood sugar levels. Professor Reuben Shaw, director of Salk's NCI-designated Cancer Center, and collaborators have used a novel technology to investigate why it functions so well. The findings, which identified a surprising number of biochemical "switches" for various cellular processes, could also explain why metformin has been shown in recent studies to extend health span and life span.

CELL REPORTS 12/2019



Computational analysis revealing targets of metformin.

From left: Juan Carlos Izpisua Belmonte, Paloma Martinez-Redondo, Isabel Guillen-Guillen and Pradeep Reddy.

DRUG COMBO REVERSES ARTHRITIS IN RATS

PROTEIN & CELL 01/2020

People with osteoarthritis, or "wear and tear" arthritis, have limited treatment options: pain relievers or joint replacement surgery. Research co-led by Professor Juan Carlos Izpisua Belmonte and Salk co-first authors Paloma Martinez-Redondo and Isabel Guillen-Guillen, has discovered that a powerful combination of two experimental drugs reverses the cellular and molecular signs of osteoarthritis in rats as well as in isolated human cartilage cells.

UPDATE ON INITIATIVES TO SUPPORT

DIVERSITY *AND* BIPOC

The COVID-19 pandemic is affecting every dimension of American life, and laying bare many of the deep, structural inequities of our society. These include who has access to healthcare; whose work is considered essential; which communities have greater air pollution (thus putting their residents at greater risk for poor outcomes from infections); and much more.

Adding to the collective trauma is the racism and racial injustice being experienced by communities of Black, Indigenous and other people of color (BIPoC).

Salk's mission to better humanity extends beyond science. The Institute stands with BIPoC at Salk and everywhere, not only in the spirit of solidarity, but also with actions that will continue to contribute to the betterment of humanity and lead to meaningful change. Repugnant racial discrimination and violence against Black people are devastating reminders that individuals, institutions and communities must urgently and continually assess and enhance efforts to change.

Salk's leadership and the Institute's Office of Equity and Inclusion have been working on several initiatives to this end:

- **DIVERSITY & INCLUSION TASK FORCE**
  When the Campus Culture Advisory Committee was formed in 2019, the Institute committed to creating a Diversity and Inclusion Task Force, which has now been formally established. It is being co-chaired by Assistant Professor Dannielle Engle and Professor Kay Tye, both of whom have been active throughout their careers in promoting diversity and parity in science. Working in concert with faculty and staff, the Task Force will focus on increasing the diversity and inclusion of BIPoC at Salk, with an immediate charge of identifying ways in which the Institute can fight systemic racism and injustice.

- **MANDATORY EDUCATION AND TRAINING**
  In late 2019, the Institute began developing mandatory training that will roll out in July 2020, focusing on explicit and implicit bias, privilege, and bystander-to-upstander guidance. The training also provides tools to help people be proactive and empowered to assist others in need.

- **MISSION STATEMENT AND CORE VALUES**
  Salk's mission statement will be refined and a set of clearly articulated core values will be documented. As stewards of the inspiring legacy of founder Jonas Salk, the Institute is adamant in its opposition to racism and stalwart in its support of diversity and inclusion. For those values to endure and to guide our progress, they must be embodied in everything Salk does.

- **CAMPUS CLIMATE SURVEY**
  At the recommendation of the Campus Culture Advisory Committee, the Institute is developing a campus-wide survey that will assess the extent to which Salk provides an environment that welcomes and enables participation by all members of the Institute; seeks diversity in individual backgrounds and perspectives; provides access and resources for all; and determines whether the campus is experiencing the values we espouse when articulating campus culture. The results will help inform measures that can be implemented to further Salk's commitment to promote a diverse and inclusive environment.

- **DISCUSSION SESSIONS**
  OEI launched a quarterly discussion club about issues pertaining to equity and inclusion as well discussion sessions, called "Collective Voices for Community Healing," for the Salk community. These efforts aim to amplify diverse voices and offer the opportunity to engage in constructive dialogue.

- **INCREASED COMMUNICATIONS**
  The Institute will provide expanded and enhanced communications to help bolster education and raise awareness on issues of equity and inclusion on multiple fronts.

Jonas Salk notably said, "our greatest responsibility is to be good ancestors."He sought to found an institution that would be concerned not merely with nature, but with the human side of nature—what he referred to as "the human dimension." Particularly in these challenging times, this means we must be vigilant in helping to end racism and injustice, continue to actively support diversity in our people, ideas and research, and ensure that everyone has a voice, at Salk and beyond.

EIMAN AZIM

DECODING DEXTERITY

Humans can move their bodies to do incredible things. Some can play concertos or hit home runs, but for the rest of us, even everyday movements such as buttoning a shirt or typing an email are acts of astonishing complexity. We need to coordinate the contraction of dozens of muscles with precision to accomplish these dexterous tasks, yet scientists still do not have a clear understanding of how the nervous system is able to orchestrate such complex behaviors.

Eiman Azim, assistant professor in the Molecular Neurobiology Laboratory and the William Scandling Developmental Chair, seeks to uncover how the brain and spinal cord control dexterous movement of the arms, hands and fingers. By using sophisticated molecular genetic tools, his lab is uncovering how circuits in the nervous system work together to create movement, and how the function of these pathways is affected by neurodegenerative disease and injury.

Inside Salk chatted with Azim to learn about his thoughts on what's next in neuroscience, how all scientists are philosophers and what he learned about movement from observing his newborn.

What big questions are you trying to answer in science?

EA: We're trying to understand how the brain controls behavior. Asking these types of questions is like trying to solve a large puzzle where we have to figure out how all the pieces fit together, often without even knowing what all the pieces are. And not just how they fit together in a static picture, but how they dynamically change with time as well. For example, as you reach down to tie your shoe, how does the communication of different neural circuits change to coordinate behaviors? If you stumble, how do the circuits respond so you don't fall?

My lab tries to gain insight on how the brain processes signals to produce a desired outcome, and what goes wrong in conditions that affect movement, such as Parkinson's disease and amyotrophic lateral sclerosis (ALS). I believe that if we want to develop better approaches to diagnose and treat disease and injury, we need a much better understanding of how the normal system fundamentally operates.

Neuroscience is an established field. Why do scientists still know so little about how the brain controls movement?

EA: The human brain contains nearly 100 billion neurons with a huge variety of cell subtypes, all intermingled in incredibly complex networks. Trying to disentangle these networks to decipher the function of each type of neuron is difficult. Over the past few decades, there's been a molecular genetic revolution in neuroscience. What this means is that we can now take advantage of the fact that different types of cells, including neurons, express different genes. These diverse gene expression patterns allow us to differentiate between different types of neurons, and to use their genetic identities to access them selectively in our experiments. So, if we can decipher these molecular codes, then we can look at how these neurons connect to each other to form circuits. We can also remove specific neurons from the circuit, or turn them on or off at will, to investigate their function. Molecular genetics gives us the tools to access the brain with precision, so we can ask targeted questions about each type of neuron's contribution to movement.

Do you have any exciting projects in your lab right now?

EA: I find them all exciting! Big picture, we're interested in learning more about how two major types of pathways interact to control movement. The first is the chain of events that sends commands from your brain down to your spinal cord, and ultimately out to your muscles to move. The second pathway involves all of the feedback from your body (such as your skin and your muscles) that gets sent back into your spinal cord and brain to report the consequences of the movement. These command and sensory pathways are constantly interacting in a dynamic way, and we are trying to define how these interactions take place and why they are needed for dexterity.

One of the specific projects in my lab right now is examining how to control the strength of the sensory feedback transmitted to the brain. Our bodies are bombarded with stimuli that activate sensory receptors. Much of this sensory information is distracting or noisy, suggesting that we need a way to "turn down" some of these signals, while allowing the important signals to make it into the brain. We've been identifying circuits in the brain that can adjust the strength of tactile signals that come from our skin, a process that appears to be critical for effectively grasping and manipulating objects to interact with the world.

Growing up, did you always know you wanted to become a neuroscientist?

EA: I have always loved science, but it really wasn't until college that I fell in love with neuroscience. When I was at Stanford University as an undergraduate, I was passionate about philosophy, specifically philosophy of mind. As I dove deeper into the subject, I became fascinated with the questions, which were grand, but a bit frustrated with our inability to come up with definitive answers.

And so that's when I decided to enter laboratory science to perform experiments and collect data on accessible problems in the brain that could eventually shine some light on these larger questions about the human condition.

Do you think your background in philosophy informed your current career in research?

EA: I do. I think philosophy teaches us how to think about a problem. We're all philosophers; scientists gain their training by earning a doctorate in philosophy. The life sciences have long been a branch of philosophy, where we look at the world, are curious about a problem, and try to come up with rational and intelligent ways to address that problem.

"Molecular genetics allows us to disentangle the brain with surgical precision, so we can now finally uncover each type of neuron's role and function in movement."

EIMAN AZIM

What brought you to Salk and what keeps you here?

EA: The Salk Institute is different than any other institution I was considering. It's small by design and incredibly collaborative. There are no departments and very few barriers or boundaries between disciplines. When you're walking through the beautiful campus, you run into some of the best scientists in the world. For example, I might have coffee with a plant biologist one day and a cancer scientist the next. That doesn't happen quite as easily at big universities.

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

EA: I play the guitar. I really enjoyed playing in a band in college, and I recorded an album while I was doing my postdoctoral fellowship in New York. I have yet to find the time or the bandmates here in San Diego, so it's on the back burner for now. One of the reasons time is scarce is that my wife and I recently had our first child, which has been pretty incredible.

What is it like having a baby while being a full-time research scientist?

EA: I'm still figuring that out, but it's a balancing act. Before having my son, my friend gave me the following advice: "You basically have to get the same amount done in a lot less time." And he was not wrong. So, I've tried to cut out a lot of the extraneous stuff in my life to better focus on the science when I'm at work, and my son while I'm at home.

Is sleep considered extraneous?

EA: Often.

Since you study how the nervous system controls movement, are you excited to watch your son reach developmental milestones such as crawling and walking?

EA: Oh, absolutely. It's been fascinating. When he rolled for the first time, it was just amazing to watch. Babies are experimentalists; they try something and then it works or produces an outcome, and they do it again and again to confirm that it's true. And if something fails, they'll go and try something new. These are good lessons for the lab.

What do you think the future holds for understanding the neural basis of movement?

EA: We're at a fascinating and fast-changing moment in neuroscience. The field of movement research is already gaining insights that are telling us how our nervous system might be working, and also showing us what might go wrong in disease and injury. For example, the development of prosthetics that receive signals from and send signals to the brain is moving at an incredible pace, helping people that have lost motor function. The way we can continue to develop advanced technologies like these is by using the lessons we've learned in basic science laboratories, and for scientists to continue to learn lessons from the patients who can benefit. This two-way communication between experiments in the lab and patients in the clinic inspires me every day.

LISTEN | www.salk.edu/podcast/eiman-azim

RESOLUTION

A scanning electron microscope image of sensory tissue in the cochlea, the spiral cavity of the inner ear, including the outer (green) and inner (yellow) hair cells, named for their hair-like structures that vibrate back and forth in response to sound.

LISTEN | www.salk.edu/podcast/uri-manor

Credit: Leo Andrade and Uri Manor, Salk Institute for Biological Studies

"Our greatest responsibility is to be good ancestors."

JONAS SALK

INSIGHTS

From bacteria to humans, every living organism has a unique genetic code in the form of DNA, a sequence of four letters that spell out instructions for the organism's genes to follow. Using a technology called next-generation DNA sequencing, scientists can get a readout of those instructions, allowing them to answer important biological questions about gene function in health and disease.

Staff Scientist Nasun Hah can vividly remember using this technology for the first time, during graduate school, to examine gene expression. It was expensive and took more than a week to receive the results, but she was elated—and hooked. Hah is now the director of the Next Generation Sequencing (NGS) Core at Salk, where an entire genome containing over 20,000 protein-coding genes can be sequenced in a single day. "The amount of data and knowledge we can receive from sequencing technology is immense," says Hah, then laughs. "And this technology keeps getting better and better, so I can never leave the field!"

Nasun Hah

Director of the Next Generation Sequencing Core

DAY-TO-DAY

Salk's NGS Core houses state-of-the-art equipment to allow scientists to examine genetic codes. As the director of the NGS Core, Hah collaborates with everyone from plant biologists to neuroscientists to provide support and information about sequencing genes and entire genomes. On any given day, she may explain differences in techniques, provide hands-on training and review experimental design.

PATH TO SALK

Hah was studying the humanities in high school when she first read about the Human Genome Project, a $2.7 billion venture that represented the first complete catalog of the human genome, the DNA sequences that make up our 23 pairs of chromosomes. The project armed scientists with a genetic map that enabled them to start exploring related questions about topics such as the function of each gene. Blown away by the subtle biological differences that helped explain human complexity, Hah immediately signed up for her first biology class. "I was always so intimidated by science until I learned that it was logical and filled with patterns that I could decipher," says Hah.

Hah studied biochemistry at Yonsei University, in South Korea, and later attended graduate school at Cornell University, where she examined how estrogen could directly and immediately alter gene expression, and how genetic errors could result in breast cancer. She also investigated transcription regulation, the process of creating an RNA copy from a DNA template, as well as nuclear receptors, which drew her to the work of Professor Ronald Evans at Salk. Evans' lab discovered nuclear receptors, a large family of molecules that respond to various steroid hormones such as estrogen, which are now primary targets in the treatment of cancers, osteoporosis and asthma.

"Evans' work came up a lot as I wrote my dissertation; he was my scientific hero," says Hah. "So, by the time I was finishing my PhD, I knew I wanted to work with him."

During her postdoctoral fellowship in Evans' lab, Hah researched how potent anti-inflammatory drugs suppressed inflammatory messengers sent by genes. She was fascinated by a still unresolved scientific paradox: how can certain receptors activate some genes yet repress others? She also examined the role of gene expression in acute inflammation and used a variety of genomic approaches to dissect the inflammatory signaling.

Near the end of her fellowship, Hah decided she wanted to focus on cutting-edge, next-generation sequencing and took on the role of NGS Core director. Now, Hah's main goal is to make the NGS Core accessible to the entire Salk community.

LEISURE TIME

Hah loves spending time outdoors and recently went skydiving for the first time. "It was amazing to jump from a plane and feel gravity pull me back towards the earth," she says. "The sun was setting over the ocean, and it was just so beautiful. I was uncontrollably laughing with happiness the entire time."

She also has a passion for orchids and last year trekked along the Inca Trail, in Peru, searching for exotic blooms. She counted nearly 25 different species during her trip, including the mountain-growing *Brachtia andina*, with its vibrant, long-lasting, yellow-orange flowers. She looks forward to exploring the renowned Orchid House at the San Diego Zoo in the near future.

INSPIRATION

"So much of biology is hard to prove. It's complicated and intricate, yet it somehow comes together in the most sophisticated way," says Hah. "Uncovering these connections is fascinating and reminds me of the importance of basic science." Hah also finds inspiration in discussing ideas with other scientists; even casual conversations at Salk's coffee cart can be a catalyst for an innovative research project.

FUN FACT

Although Hah is originally from South Korea, she has spent large portions of her life living in the Netherlands, Japan and the United States. Her father worked as an executive for an airline company, so his role required the family to relocate to countries with entirely different languages and cultures. Due to her diverse upbringing, Hah values being open-minded and enjoys working with people from all backgrounds.

LONG VIEW

Sequencing technologies have evolved over time, zooming in from the entire genome and homing in on other categories of information, such as variations of gene expression in each cell. "Sequencing technologies are improving all the time," says Hah. "In the future, I think we will see a shift towards single-cell sequencing and capturing spatial information such as where genes are located in a given organ or tissue. This spatial information could aid scientists in defining detailed molecular maps for each cell type in diverse tissues. Genomic sequencing is going to get more complicated, but it's also going to be more exciting."

LISTEN | www.salk.edu/podcast/molly-matty

A spotlight illuminates a young woman, positioned center stage, wearing red-framed glasses. She grips the microphone, readying herself for the next cue. The judge declares that the subject is…SCIENCE.

"Whenever I see my worms wiggle across the plate, I know I should study their movement—it's a 'sine'!" says the performer, Molly Matty. The audience laughs, appreciative of her pun alluding to the serpentine motion of worms as sine waves.

Pun competitions draw sold-out crowds. The rules are simple: following the given theme, make a pun within 10 seconds or you're out. Only one person will remain to become the Pun Master.

Outside of punning, Matty spends her time as a postdoctoral researcher, studying the nematode *Caenorhabditis elegans* in the lab of Associate Professor Shrek Chalasani. Punsters may appreciate that the name is pronounced "see elegance." Indeed, although these tiny worms are only half an eyelash in length, their transparent bodies allow scientists to view the worms' inner workings, making them an elegant model organism for research. In fact, Matty's research involves observing the worms as they consume their favorite food: bacteria.

Similar to the human gut, the *C. elegans* gut is in regular communication with the rest of its body, including its nervous system. Matty wants to know how ingested bacteria integrate into the worm's gut microbiome to affect this communication.

"If different bacteria can alter the gut microbiome, then could they also affect behavior through this chain of signaling to the brain?" Matty asks.

Understanding how bacteria affect the brain and behavior could provide insights into human conditions such as anxiety and depression. These disorders may be affected, and possibly improved, by ingesting certain bacteria. In fact, the gut-behavior field is growing as more and more studies suggest a connection between food and mood.

Matty shares that *C. elegans* makes an ideal model for studying this connection for a few reasons: the environment (a petri dish) can be perfectly replicated, the worms self-fertilize to produce genetically similar offspring, and the microbes that they ingest are closely monitored. These factors allow for exceptionally controlled experiments that would be impossible in most other species.

Matty not only brings her humor and passion for science to the public through being punny but also by volunteering with Salk's Education Outreach Program.

"Science outreach is the thing that keeps me going," Matty says. "When I can break science findings down into analogies and fun vignettes for people to understand, that's when I get inspired to go back into the lab and do the work."

Recently, Matty visited a kindergarten class at a local elementary school, where she guided the students through the examination of worms under a microscope. She asked the students what they thought they had in common with a worm. Many students pointed out that "both worms and people poop." Amused, Matty explained that another similarity is that nematodes have neurons that make up a series of connections similar to those of a human brain. That makes them ideal models in the study of neural circuitry related to emotion and other factors.

"Every kid should know that being a scientist is a career they can have. Scientists can look, talk and be like them," Matty says. "Many of us deal with imposter syndrome as adults. I like to remind people: just remember, you belong here.'"

She also likes to share science through what she calls "Uber outreach." Every time she takes a ride-hailing service, such as Uber, she incorporates science into the conversation. On one trip, she shared with her driver that she studies how the microbiome affects behavior. He happened to be studying nutrition at a local college and was immediately intrigued. The car ride turned into an open forum of questions.

"Science outreach is the thing that keeps me going."

"I enjoy doing 'Uber outreach' because it breaks down barriers. It allows members of my community to feel empowered to ask a question that they've always been afraid to ask," Matty says. "And it gives me a chance to practice explaining things that I've maybe never had to explain before."

Outside of her science and outreach efforts, Matty enjoys running. Every year, she runs her age in kilometers to celebrate her birthday. Since moving to San Diego, Matty has embraced the Southern California lifestyle; she has learned to surf and regularly practices yoga at one of the local studios. She also practices her puns for competition.

"I hope talking about my microbiome project didn't 'bug' you too much," Matty says, laughing.

SPOTLIGHT

WOLFGANG BUSCH PROMOTED TO PROFESSOR

The Salk Institute has promoted Wolfgang Busch to the rank of professor for his notable contributions to plant biology. 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.

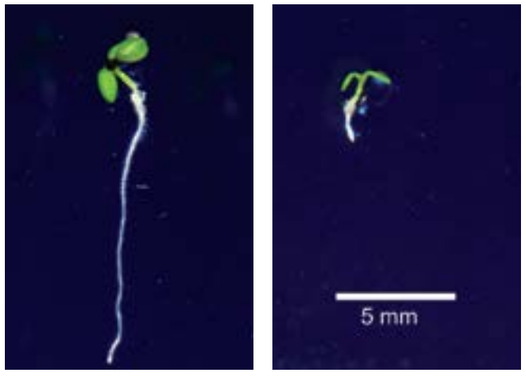
Busch, a member of the Plant Molecular and Cellular Biology Laboratory and the Integrative Biology Laboratory, studies plants' roots, which are critical for obtaining water and nutrients from the soil. His research seeks to understand which genes and molecular mechanisms determine how a plant's genetic information interacts with the environment and is translated by molecular, cellular and physiological networks to shape plant root growth.

"Wolfgang's keen insights into the functions and genetics of plant roots are an invaluable asset to the Institute's effort to address climate change using plants. In addition to his contributions to plant biology research, his general leadership and computational skills are having a broad and positive impact at Salk."

RUSTY GAGE
SALK PRESIDENT

Recently, Busch uncovered a gene responsible for helping plants thrive in stressful environments. Prior to that, he discovered a gene that determines whether a root grows deep or shallow in the soil.

Wolfgang Busch



Busch recently discovered the GSNOR gene. The gene is required for high iron tolerance in plants. Iron toxicity leads to impaired leaf and root growth. Plants (*Arabidopsis thaliana*) with the functional gene (left) grow better with high iron levels than plants without the functioning GSNOR gene (right).

PLANT GENETICIST TODD MICHAEL JOINS SALK FACULTY AS A RESEARCH PROFESSOR

Todd Michael will return to Salk as a research professor in the Plant Molecular and Cellular Biology Laboratory, where he will oversee his own research group as well as provide key expertise in genomics to the Harnessing Plants Initiative (HPI). Michael completed his postdoctoral research at Salk in 2007 under the direction of Professor Joanne Chory. The non-tenured research professor track was created by Salk in 2018 to attract and retain top talent to the faculty.

"We are elated that we could recruit Todd, who is a creative scientist of the highest integrity. His unique skill set in genomes of plants will contribute enormously to the success of HPI programs to fight climate change," says Chory.

Todd Michael

As part of the HPI leadership team, Michael will help efforts to optimize a plant's natural ability to store carbon in order to mitigate the disastrous effects of climate change while providing more food, fuel and fiber for a growing population. His research group will provide genome sequencing support to create Salk Ideal Plants™, plants with deep, robust root systems capable of storing excess amounts of atmospheric carbon deep in the ground. In particular, his team will be investigating the genetic architecture controlling specific traits, such as deeper rooting.

Michael previously published the first near-complete plant genome of *Oropetium thomaeum*, a type of grass that can survive extreme drought, by pioneering the use of new sequencing technologies and genome analysis tools. His group also used the model plant *Arabidopsis thaliana* to provide molecular evidence that the circadian clock enables plants to anticipate changes in their environment such as daily light-dark cycles as well as seasonal changes. They found that the time-of-day gene-expression networks were conserved by evolution across higher plants, which enables advanced breeding for next-generation crops.

Michael received his PhD in molecular and cellular biology from Dartmouth College and his BA in biology from the University of Virginia. He previously served as professor and director of Informatics at the J. Craig Venter Institute, fewer than two miles from Salk. Prior to that, he held positions including director of Genomics at Abbott Laboratories; head of the Genome Analysis Center at Monsanto; and assistant professor at the Waksman Institute of Rutgers University.

SALK BOARD WELCOMES NEW TRUSTEES LARRY JENNINGS, JR., AND TIMOTHY SCHOEN

In January, the Salk Board of Trustees welcomed two new trustees, Larry Jennings, Jr., a private equity and municipal finance expert, and Timothy Schoen, a real estate and corporate finance executive.


Larry Jennings, Jr.

Jennings is co-founder and senior managing director of ValStone Partners, where for 20 years he has co-led the company's strategic direction, investment decisions and investor relations. From 1987 to 1994, Jennings was co-head of the Legg Mason public finance investment banking department. He also founded and served as CEO of Carnegie Morgan Partners from 1995 to 2001. He is a member of the board of trustees of Carnegie Mellon University; chairman of the Morgan State University Foundation Investment Committee; and board chair of the Baltimore Municipal Golf Corporation. He earned a BS in mathematics and economics and an MS in industrial administration (MBA), both from Carnegie Mellon University.


Timothy Schoen

Schoen has served as president and CEO of BioMed Realty since 2016. Prior to his current role, he held various executive management positions at Healthpeak from 2006 to 2011 and was executive vice president and CFO from 2011 to 2016. Schoen served as vice president of corporate finance at Kilroy Realty Corporation for nine years prior to his time at Healthpeak. He is also the chair of Salk's Conquering Cancer Initiative Advisory Committee. He received a BS in finance and international business from Minnesota State University and earned his MBA from the University of California, Irvine, graduate school of management, where he was a Dean's Scholar.

INSTITUTE RECEIVES CHARITY NAVIGATOR'S HIGHEST RATING FOR NINTH CONSECUTIVE TIME

Salk executes consistent best financial practices

For the ninth 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 nine consecutive times. The coveted ranking indicates the Salk Institute outperforms most other charities in America in regard to executing best fiscal practices and carrying out its mission in a financially responsible way.

"We are grateful for the faithful generosity of our donors and this recognition as we continue to pursue answers to challenging questions in cancer, neuroscience, genetics, immunology, aging, plant biology and more," says Salk Institute President Rusty Gage. "We simply could not make the life-changing discoveries Salk is known for without our supporters."

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.

"Our donors supported Salk science in record fashion the past fiscal year, and I believe one of the significant reasons for that is the confidence they have in the Institute's stewardship," says Rebecca Newman, Salk's vice president of External Relations. "We are honored to be included in such elite company."

The Institute continues to make bold progress in pursuing ambitious solutions to the difficult challenges facing humanity, including climate change, aging and cancer.

"I wish to congratulate the Salk Institute for Biological Studies on attaining the coveted 4-star rating nine consecutive times, demonstrating strong financial health and commitment to accountability and transparency," 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.

There are many deserving causes worthy of support. That's why the Salk Institute takes great pride in carrying out its mission in a financially responsible manner. Thanks to Salk's best fiscal practices, those who support Salk can be confident their generosity will impact their designated field of research and, in turn, accelerate the pace of scientific discovery at the Institute.

LEARN MORE | www.salk.edu/the-power-of-science

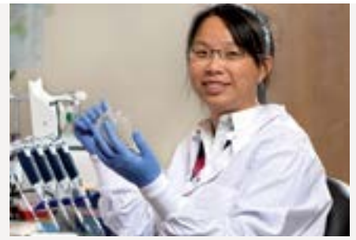
EVENTS

RECIPIENTS OF THE 2020 SALK WOMEN & SCIENCE SPECIAL AWARDS

While a public event lauding the Women & Science recipients was not possible this year, the Institute is proud to share and celebrate their achievements. Every year, the program provides crucial support to graduate students and postdoctoral researchers to pursue high-risk, high-reward research in stages too early to attract traditional funding. The awards are targeted toward supporting future scientific leaders who will also actively foster the increased participation of women and girls in science.

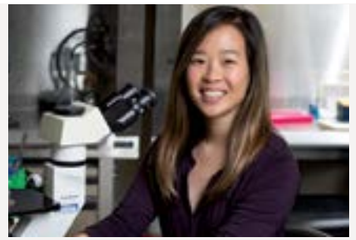
BIANCA BARRIGA | PFAFF LAB
Investigating effects of exercise training on spinal neural networks

Barriga will examine the neurons within the mouse spinal cord that help produce movements—such as walking and running—to better understand what separates the ordinary athlete from runners such as Florence Griffith Joyner, the fastest woman in the world.



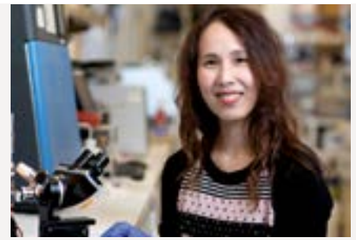
HSIUYI CHEN, PHD | MCVICKER LAB
Generating HIV-resistant human CD4+ T cells by introducing thousands of chimpanzee alleles with massively-parallel genome editing

The chimpanzee and human genomes are extremely similar, yet chimps are more resistant to developing AIDS after HIV infection. Chen will examine the genetic differences between the two species that confer resistance to HIV, to develop HIV-resistant human T cells.



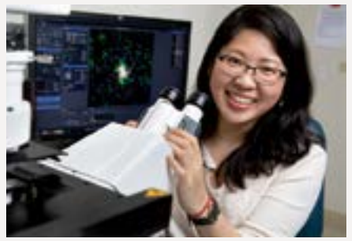
SEJ CHUNG, PHD | ENGLE LAB
Defining the role of CA19-9 in the pancreatic microbiome

Chung will investigate how levels of CA19-9, a sugar molecule associated with one of the deadliest cancers—pancreatic cancer—affects gut bacteria populations. The work could reveal biomarkers for early detection and possible therapeutic targets for pancreatic tumors.



SHARON (HSIANG-HSUAN) HUANG, MD | JIN LAB
Dissecting the role of sensorimotor feedback in action sequencing

Huang will investigate how the brain integrates feedback to control behavior, which will shed light on neurological and psychiatric diseases, such as schizophrenia, that involve difficulty controlling actions.



YOUTONG HUANG, PHD | LEMKE LAB
Microglial TAM receptors as modulators of pathology in amyotrophic lateral sclerosis

Brain and spinal immune cells called microglia are thought to play a crucial role in the development of amyotrophic lateral sclerosis (ALS). Huang will use various techniques to assess the impact of proteins called TAM receptors found on microglia, on ALS disease progression.

ANDREEA MANOLE, PHD | GAGE LAB
Neuroinflammation associated with genetic defects in phospholipase A(2) and glucocerebrosidase

Manole will use induced pluripotent stem cells derived from patients with mutations in two genes involved in fat metabolism (PLA2G6 and GBA) to study metabolism and neuroinflammation in the context of neurodegeneration, which could lead to improved therapeutic strategies for diseases.

HEATHER MCGEE, MD, PHD | KAECH LAB
Investigating the role of radiation-induced innate immune cell activation in unique tumor microenvironments

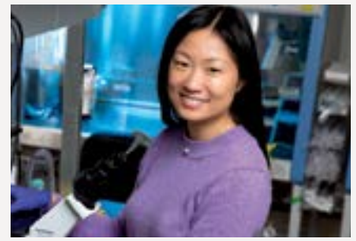
There is limited scientific data characterizing the immune response to radiation therapy for cancer. McGee will investigate radiation-induced cell death to see if it triggers the immune response, leading to anti-tumor immunity and the formation of scar tissue.

JIA NING, PHD | HUNTER LAB
Establishing cell and mouse models to study RNA polymerase III-related neurodegenerative diseases

Mutations in the enzyme RNA polymerase III cause diseases such as hypomyelinating leukodystrophy (HMLD), an early onset neurodegenerative disease. To inform new therapies for this disease, Ning will use genetic models and patient-derived neural stem cells to investigate the mechanism of RNA polymerase III.

ANNELISE SNYDER, PHD | KAECH LAB
Determining the role of microglial metabolic reprogramming in linking infection to Alzheimer's disease

Alzheimer's disease is associated with previous viral infections, although researchers do not understand precisely how. Synder will examine how viral infections may reprogram how brain-resident immune cells, called microglia, use energy sources in a way that promotes the development of disease.



YUAN XUE, PHD | IZPISUA BELMONTE LAB
Creating biocompatible electric organoids for the mammalian system

Xue will draw inspiration from electric rays and eels to create specialized organoids ("mini organs") that can generate their own electrical signal, for biotherapeutic uses—such as generating sufficient power to run a cardiac pacemaker.

JOANNE CHORY RECEIVES TRAILBLAZER AWARD

Professor Joanne Chory was honored with the Trailblazer Award from Salk Women & Science. The award recognizes outstanding achievements made by women in the STEAM (Science, Technology, Engineering, Art and Mathematics) fields. Recipients have pioneered changes within the STEAM fields as innovators, groundbreakers, collaborators and mentors. They have dedicated their lives to making significant advances in both their professional and personal realms. Trailblazers forge their own paths to achieve their vision.

Chory's efforts leading Salk's Plant Molecular and Cellular Biology Laboratory, in addition to her roles as a professor, a Howard Hughes Medical Institute investigator, and the Howard H. and Maryam R. Newman Chair in Plant Biology, have been widely acclaimed. She was awarded the 2018 Breakthrough Prize in Life Sciences and was made a Fellow of the National Academy of Inventors. Her work leading Salk's Harnessing Plants Initiative, which focuses on creating plants that store more carbon in their root networks to help mitigate the effects of climate change, was instrumental in the Institute being chosen in 2019 for funding of more than $35 million through The Audacious Project, a highly competitive program housed at TED.

Salk has a long tradition of offering unique opportunities for the public and supporters to visit its architectural masterwork and engage directly with world-renowned researchers.

While the Institute is currently closed to visitors and has postponed events during the COVID-19 pandemic, supporters can still learn about Salk's cutting-edge discoveries and life-changing science at one of these virtual events:
www.salk.edu/events/public-events

EVENTS

INTRODUCING SALK'S OPTIMAL AGING INITIATIVE

On November 14, the Salk Institute introduced its Optimizing Aging Initiative.

Aging is the biggest risk factor for most diseases, including Alzheimer's, cancer, diabetes and others. The new initiative uses a multidisciplinary approach to understand the fundamentals of aging and how interactions between the major systems of the body contribute to age-related diseases.

The event featured a guest presentation from Mark Collins, president of the Glenn Foundation for Medical Research, an overview of the Initiative by Salk President Rusty Gage, and a panel discussion with Salk scientists Professor and Chief Science Officer/ Vice President Martin Hetzer; Professors Jan Karlseder, Vicki Lundblad and Gerald Shadel; and Associate Professor Nicola Allen.

From left: Jan Karlseder, Martin Hetzer, Nicola Allen, Gerald Shadel and Vicki Lundblad

Clodagh O'Shea

Alan Saghatelian

SALKEXCELLERATORS

On February 26, Salk Professors Clodagh O'Shea and Alan Saghatelian spoke with the Salkexcellerators group about their novel research seeking to unravel the complexities of disease and leverage the knowledge to design biological devices as groundbreaking precision medicines. Salkexcellerators are the next generation of community members who support scientific discovery at Salk and engage with scientists through a full year of activities.

Salk President Rusty Gage

Shadel

SALK SCIENCE & MUSIC SERIES HITS THE RIGHT NOTE

The Salk Science & Music Series played on with two events in the lineup from the current season. The first event on November 3, 2019, delighted guests with the science of Professor Gerald Shadel and music of pianist Fei Fei Dong. Attendees were treated to the beautiful sounds of Alessio Bax and Lucille Chung on piano on January 12, 2020, and an investigation on the ability of plants to help mitigate climate change by Salk Professor Joseph Noel.

SHADEL SHARES THE BASICS OF MITOCHONDRIA

Highlighting one avenue of research as part of the Institute's Optimal Aging Initiative, Salk Professor Gerald Shadel shared details about his work on mitochondria, the powerhouses of cells. On February 12, Shadel, who holds the Audrey Geisel Chair in Biomedical Science, discussed the role mitochondria and mtDNA play in aging and disease to a full auditorium. The Back to Basics lecture series offers the public the opportunity to hear from the Institute's world-renowned scientists throughout the year.

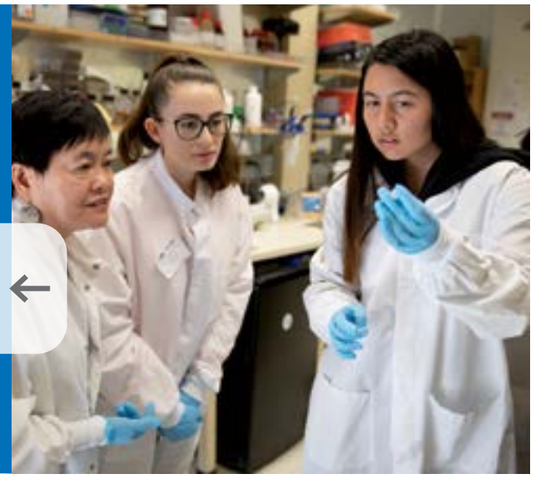
Gerald Shadel

EVENTS

EDUCATION OUTREACH HIGH SCHOOL SCIENCE DAY

On February 29, Salk faculty and staff brought science to life for the next generation of scientists with the 30th March of Dimes High School Science Day. The half-day annual event is designed to encourage high school students to consider an exciting career in science and research. The Institute welcomed about 300 students from all over San Diego who met Salk scientists and received behind-the-scenes, interactive lab tours.

Madison Dodds



DONOR APPRECIATION EVENT

On November 20, Salk supporters were honored for their generous contributions leading to a productive year of science in 2019 at the Institute. Salk scientists shared updates on current research and how donor philanthropy accelerates scientific discovery. The event was attended by Salk leaders, Board members, faculty, staff, volunteers and community donors.

Groundbreaking Salk discoveries *on the go!*

WHERE CURES BEGIN
SALK INSTITUTE PODCAST

Where Cures Begin is the official podcast of the Salk Institute for Biological Studies. In each episode, co-hosts Allie Akmal and Brittany Fair interview Salk researchers about their bold research efforts and learn about the scientists' lives outside of the lab. Join us to hear how Salk researchers are making advances in neuroscience, using plants to fight climate change, developing cures for cancer, mastering our circadian clock and more.

The podcast is available on **iTunes**, **Google Play** and anywhere you listen to podcasts.

To learn more, visit **Salk.edu/podcast**.

SEASON 2 (AVAILABLE NOW):

Marga Behrens *on researching neuropsychiatric disorders*

Wolfgang Busch *on using plant roots to store carbon dioxide*

Martin Hetzer *on understanding aging*

Molly Matty *on examining how bacteria can affect animal behavior*

Uri Manor *on the link between mitochondria and hearing loss*

Joseph Noel *on using coastal ecosystems to fight climate change*

Tatyana Sharpee *on how we perceive our environment via our senses*

Reuben Shaw *on the link between metabolism and cancer*

THE POWER OF SCIENCE

LECTURE SERIES

We are reminded during these sobering times of how critical basic scientific research is to our health, our community and the globe. It was the basic scientific research of the Institute's founder, Jonas Salk, that led to the first safe and effective polio vaccine, saving countless lives. At Salk, world-renowned experts in immunology, infectious diseases, virology and other topics are similarly uncovering the fundamentals of biology and disease. From deadly viruses and cancer, to Alzheimer's and climate change, Salk scientists are on the front lines of discovery. Learn about how these researchers are tackling the biggest challenges facing the world in this timely series.

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Where cures begin.

Please check the link for upcoming virtual lectures where you can hear directly from scientists on their life-changing work.

www.salk.edu/powerofscience

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Salk Institute has received the highest rating 9 consecutive times from Charity Navigator, the nation's foremost charity evaluator.

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