How social interaction and isolation influence our physical and mental health
Dear Friends,

Five years ago, the Salk Board, faculty, staff, and you, our dedicated supporters, welcomed me into the role of Salk president, a position I never aspired to achieve when I began my scientific career, but one I have cherished nonetheless.

This summer, the Institute began the process of identifying my successor as president so that I may return to my lab full time. I want to thank the Salk community at large for the trust and faith you’ve placed in me to lead Salk during a time of transformation that presented both significant opportunities and daunting challenges. It has been both an honor and a privilege.

As I reflect on the journey of serving as Salk’s president, the path has not always been straight, easy, or clear. But the one constant has been a sense of continual evolution and growth of the leadership team, the community, and the faculty—growth propelled by a commitment to our mission of serving humanity by conducting the most impactful science in a supportive environment.

Until we identify a successor (which you can read more about from Board Chair Marna Whittington on page 3), I remain committed to leading the Institute even as I return some of my focus to my lab.

In this issue of *Inside Salk*, we take a look at an exciting new avenue in neuroscience research that has been emerging from several of our research labs over the past few years: how our social health influences our mental and physical health. Additionally, Gerald Joyce, senior vice president and chief science officer, shares his motivations, research on the origins of life, and vision for the future of Salk science. We also have discussions with Mallory Zaslav, vice president of Diversity, Equity & Inclusion, about her team’s work and plans for the future; and Postdoctoral Fellow Katia Troha about her studies on how diet influences an organism’s response to infection.

We also pay special tribute to two influential Salk community members who died earlier this year: Professor Emeritus Walter Eckhart, who led Salk’s Cancer Center and Molecular and Cell Biology Laboratory for more than 30 years, and Georg Heinrich “Heini” Thyssen, a former trustee and generous supporter of Salk and chairman of the NOMIS Foundation. The next issue of *Inside Salk* will feature Distinguished Professor Emeritus Charles “Chuck” Stevens, who passed away in October. We are deeply saddened by the passing of these colleagues and friends. They will be missed.

As we approach the holiday season, I would like to extend my sincere thanks and appreciation for all you have done this past year to support Salk’s science. Your dedication and loyalty have allowed our scientists to pursue our dreams of creating a healthier world.

The Institute’s future is bright because of our talented and forward-thinking faculty and staff, and the incredible generosity of supporters like you.

Sincerely,

Fred H. Gage
President

*“The one constant has been a sense of continual evolution and growth of the leadership team, the community, and the faculty—growth propelled by a commitment to our mission of serving humanity by conducting the most impactful science in a supportive environment.”*
Dear Salk Supporters,

We often refer to Salk scientists as bold in their pursuit of answers to the world’s biggest challenges. This is very true, and one part of what makes the Institute such a special place. Our scientists prove that no challenge is beyond solving if given enough hard work and dedication. It’s an example I find particularly inspiring.

Therefore, my fellow leaders and I are not daunted by the work required by two significant opportunities ahead of us right now. The first one, which I am very excited about, is helping to raise the funds needed to allow the Institute to recruit new faculty and trainees, invest in emerging computational technologies, and build the space necessary to ensure 60 more years of life-changing scientific discovery.

The second, and more immediate, need is to find a worthy successor to Rusty Gage, who has served the Salk Institute as president for the past five years. His leadership in the face of tremendous challenges, including a disruptive, ever-shifting global pandemic, has been something none of us have taken for granted. Rusty has been a visionary leader in guiding the future of Salk’s science. We are grateful for his commitment to stay on as president to ensure continuity and a smooth transition.

The first step in finding Rusty’s successor was to form a search committee this past summer, comprising Salk Board members and faculty, with support from Salk administrative leaders. Since then, we have engaged a leading executive search firm to facilitate a nationwide search process and held extensive conversations with the broader Salk community.

While we doubt this search will be a quick one due to the high bar set by Rusty during his tenure, we promise it will be thorough. I look forward to announcing Rusty’s successor when the decision is made.

My many thanks for your support and dedication. Together, we will improve the health of the world.

Sincerely,

Marna C. Whittington
Chair, Board of Trustees
IN THE NEWS

Salk scientists lead $126 million effort to map the aging human brain

The largest grant in Institute history has established the new Center for Multomic Human Brain Cell Atlas to detail the many individual cells that make up the human brain—their molecular features, where they are found, and how they change with age.

With a five-year, $126 million grant from the National Institutes of Health (NIH), a team led by Salk Institute scientists has launched the new Center for Multomic Human Brain Cell Atlas. Part of the NIH’s Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative, the project aims to describe the cells that make up the human brain in unprecedented molecular detail, classify human brain cells into more precise subtypes, and pinpoint the location of each cell in the brain. What’s more, the team will track how these features change from early to late life.

The goal is to better understand how neurotypical human brains work and age. The project will also establish a baseline against which scientists will be able to compare brains with neurological or psychiatric conditions, such as Alzheimer’s disease, autism, depression, and traumatic brain injury.

“The brain map we develop could help point disease researchers in the right direction...this information might help us design gene therapies that target only the cell populations where the treatment is needed—delivering the right genes to the right place at the right time.”

JOSEPH ECKER

From left: Margarita Behrens and Joseph Ecker.

Event goes awry to cause that disease,” says center leader Professor Joseph Ecker, director of the Genomic Analysis Laboratory at Salk and Howard Hughes Medical Institute investigator. “And ultimately, this information might help us design gene therapies that target only the cell populations where the treatment is needed—delivering the right genes to the right place at the right time.”

In addition to Ecker, the Center for Multomic Human Brain Cell Atlas includes Research Professor Margarita Behrens and collaborators at UC San Diego, UC Irvine, and Washington University in St. Louis.

Salk will be awarded approximately $77 million of the center’s funding, making it the largest single grant the Institute has received in its 62-year history.

The Center for Multomic Human Brain Cell Atlas, part of the NIH’s new BRAIN Initiative Cell Atlas Network, builds upon a five-year effort to map the mouse brain, a project that was known as the BRAIN Initiative Cell Census Network. A special issue of Nature published in October 2021 described the results of that effort, including how different cell types are organized and connected throughout the mouse brain.

“Similar to the way we learned about space travel from short trips to the moon, the mouse brain mapping project taught us a lot about how to approach a much bigger brain and the types of genomic information we would need to be able to truly map the human brain,” Behrens says. “This project is an example of how fruitful teamwork can be in science—these types of projects cannot be accomplished in a single lab.”

In the Center for Multomic Human Brain Cell Atlas, researchers will examine 1,500 brain samples (30 human brains ranging in age, 50 regions each). The center is concerned mostly with epigenetics—the molecular events that influence whether genes are turned “on” or “off” in a given cell type or at a particular time—rather than genetic sequences of each cell. The center will also take into account which cells live where. Location is important because cells talk to each other, Ecker says.

“Essentially, we want to take millions, even hundreds of millions of brain cells, learn everything we can about their epigenetics and how their chromatin is arranged, and project them in a spatial context so we can see where these cells live and understand how all of the cells in any brain region are organized, and at any age,” says Ecker, who also holds the Salk International Council Chair in Genetics.
MAKING A MEMORY POSITIVE OR NEGATIVE

Professor Kay Tye, co-first author Hao Li, and team have discovered a molecule in the brain responsible for associating good or bad feelings with a memory. Their finding paves the way for a better understanding of why some people are more likely to retain negative emotions than positive ones—as can occur with anxiety, depression, or post-traumatic stress disorder (PTSD).

Neurons often get most of the credit for keeping our brains sharp and functioning—as well as most of the blame when it comes to brain diseases. But star-shaped cells called astrocytes, another abundant cell in the human brain, may bear the brunt of the responsibility for exacerbating the symptoms of some neurodevelopmental disorders. Associate Professor Nicola Allen and colleagues have now identified a molecule produced by astrocytes that interferes with normal neuron development in Rett, fragile X, and Down syndromes.

Salk scientists discovered a gene and a group of cells that prevent escalated aggression in the brains of fruit flies. The findings have implications for disorders such as Parkinson’s disease, which can sometimes cause behavioral changes like increased aggression and combativeness.

HOW THE BRAIN GATHERS THREAT CUES AND TURNS THEM INTO FEAR

Assistant Professor Sung Han, co-first authors Sukjae Joshua Kang and Shijia Liu, and colleagues have uncovered a molecular pathway that distills threatening sights, sounds, and smells into a single message: Be afraid. A molecule called CGRP enables neurons in two separate areas of the brain to bundle threatening sensory cues into a unified signal, tag it as negative, and convey it to the amygdala, which translates the signal into fear. The research may lead to new therapies for fear-related disorders such as PTSD or hypersensitivity disorders such as autism, migraines, and fibromyalgia.

BEYOND NEURONS: HOW CELLS CALLED ASTROCYTES CONTRIBUTE TO BRAIN DISORDERS

The brain mechanisms that cause aggressive behavior have been well studied. Far less understood are the processes that tell the body when it’s time to stop fighting. Associate Professor Kenta Asahina and colleagues have now identified a gene and a group of cells in the brain that play a critical role in suppressing aggression in fruit flies. The findings have implications for disorders such as Parkinson’s disease, which can sometimes cause behavioral changes like increased aggression and combativeness.

“We can actually manipulate this switch to turn on positive or negative learning. Ultimately, we’d like to try to identify novel therapeutic targets for this pathway.”

HAO LI

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“Making a memory positive or negative”

Professor Kay Tye, co-first author Hao Li, and team have discovered a molecule in the brain responsible for associating good or bad feelings with a memory. Their finding paves the way for a better understanding of why some people are more likely to retain negative emotions than positive ones—as can occur with anxiety, depression, or post-traumatic stress disorder (PTSD).

Sung Han

Sukjae Joshua Kang

Shijia Liu
Insect-eating plants have fascinated biologists for more than a century, but how plants evolved the ability to capture and consume live prey has largely remained a mystery. Professor Joanne Chory, Staff Scientist Carl Procko, and colleagues from Washington University in St. Louis have found evidence that plant carnivory evolved from mechanisms plants use to defend themselves. The findings broaden scientists’ understanding of how plants interact with their environments.

Plants lengthen and bend to secure access to sunlight, yet scientists do not fully understand this process. Professor Joanne Chory, first author Yogev Burko, and colleagues have discovered that two plant factors—the protein PIF7 and the growth hormone auxin—are the triggers that accelerate growth when plants are shaded by canopy and exposed to warm temperatures at the same time. The findings will help scientists increase crop productivity despite the yield-harming global temperature rise.

**THE BEST OFFENSE IS A GREAT DEFENSE FOR SOME CARNIVOROUS PLANTS**

Assistant Professor Dmitry Lyumkis, co-first author Dario Passos, and colleagues from Rutgers University have determined the molecular structure of HIV Pol, a protein that plays a key role in the late stages of HIV replication—the process through which the virus propagates itself and spreads through the body. The molecule’s structure helps answer long-standing questions about how the protein breaks itself apart to advance the replication process. The discovery reveals a new vulnerability in the virus that could be targeted with drugs.

**LIGHT AND TEMPERATURE WORK TOGETHER TO AFFECT PLANT GROWTH**

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**IMAGING SOLVES MYSTERY OF HOW LARGE HIV PROTEIN FUNCTIONS TO FORM INFECTIOUS VIRUS**

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**HAIR-RAISING RESEARCH: THE FASCINATING LINK BETWEEN THE IMMUNE SYSTEM AND HAIR GROWTH**

Associate Professor Ye Zheng, first author Zhi Liu, and colleagues have uncovered an unexpected molecular target of a common treatment for alopecia, a condition in which a person’s immune system attacks their own hair follicles, causing hair loss. Their findings describe how immune cells interact with skin cells using a hormone as a messenger to generate new hair follicles and hair growth.

From left: Zhi Liu and Ye Zheng.

**RNA PROCESSING GOES AWRY IN RARE IMMUNE DISEASE**

Professor Juan Carlos Izpisua Belmonte and colleagues from King Abdullah University of Science and Technology (KAUST) in Saudi Arabia have discovered a new underlying cause of Wiskott-Aldrich syndrome, a rare genetic disease that leads to bleeding and immune deficiencies in babies. Their findings involve the way cells cut and paste strands of RNA in a process called RNA splicing. The genetic mutations associated with Wiskott-Aldrich syndrome, they found, disrupt this process, ultimately preventing numerous immune and anti-inflammatory proteins from being made correctly.

Left: Hutchinson-Gilford progeria syndrome cell with signs of premature aging. This cell shows less histone protein (green), which normally helps maintain the cell’s DNA integrity and function. Right: The cell shows fewer signs of aging when LINE-1 RNA is reduced, and there is more histone protein present.

**NEW TARGET IDENTIFIED FOR TREATMENT OF PREMATURE AGING DISEASE**

Professor Juan Carlos Izpisua Belmonte, co-first author Pradeep Reddy, and colleagues from KAUST in Saudi Arabia have discovered that a stretch of DNA that hops around the human genome plays a role in premature aging disorders. In people with early aging, or progeria, RNA encoded by this mobile DNA builds up inside cells. What’s more, the scientists found that blocking this RNA reverses the disease in mice.

“Targeting LINE-1 RNA may be an effective way to treat progeroid syndromes, as well as other age-related diseases that have been connected to LINE-1, including neuropsychiatric, eye, metabolic disorders, and cancers. Eventually, we think that this approach may lead to treatments to help extend human health span.”

JUAN CARLOS IZPISUA BELMONTE

From left: Juan Carlos Izpisua Belmonte and Pradeep Reddy.
DISCOVERY ADVANCES THE POTENTIAL OF GENE THERAPY TO RESTORE HEARING LOSS

Sensory hair cells in the inner ear use long, hair-like structures called stereocilia to transduce sound. In the absence of the protein EPS8, stereocilia are too short to function, leading to deafness. Assistant Research Professor Uri Manor and colleagues from the University of Sheffield found that delivery of EPS8 can rescue stereocilia elongation and function in mice affected by the loss of EPS8. Their study shows promise for the development of gene therapies to repair hearing loss.

“I was born with severe to profound hearing loss and feel it would be a wonderful gift to be able to provide people with the option to have hearing.”

URI MANOR

SURPRISING LINK BETWEEN MITOCHONDRIAL DNA AND INCREASED ATHEROSCLEROSIS RISK

Mitochondria are known as cells’ powerhouses, but mounting evidence suggests they also play a role in inflammation. Professor Gerald Shadel and colleagues from UC San Diego examined human blood cells and discovered a surprising link between mitochondria, inflammation, and DNMT3A and TET2—two genes that normally help regulate blood cell growth but, when mutated, are associated with an increased risk of atherosclerosis.

Make a tax-free gift with an IRA

You can give any amount up to $100,000 per year from your IRA directly to the Salk Institute without paying income taxes on the revenue if you are 70 1/2 years of age or older. You can also name Salk as a beneficiary of your retirement plan simply by filling out a form with your plan’s administrator. When left to Salk, retirement plan assets pass tax-free, allowing us to put 100 percent of your gift toward new discoveries in healthy aging, neurodegenerative disease prevention, climate change mitigation, and other major global challenges.

People who make a planned gift to Salk in their estate plans become members of our legacy society, Partners in Research, a visionary group that invests in the future of science.

Drive new discoveries where cures begin.
How social interaction and isolation influence our physical and mental health

If there’s one thing the COVID-19 pandemic made abundantly clear, it’s that staying healthy involved more than merely avoiding the coronavirus itself. For many people, the social disruption and isolation wrought by the pandemic was emotionally challenging. According to a March 2022 scientific brief from the World Health Organization (WHO), anxiety and depression increased by 25 percent worldwide during the pandemic’s first year.

As a social species, humans need connection and interaction to thrive. Studies are increasingly linking social isolation and loneliness to a variety of negative health outcomes. These include physical conditions like heart disease and strokes, psychiatric issues like anxiety and depression, and cognitive problems like dementia.

Salk neuroscientists study how our brains allow us to experience, interpret, and interact with the world around us. They explore how individual brain cells and chemicals help us pursue rewards and avoid harm. Many of these researchers are now studying not only the brain alone, but the brain in a social context.
Even before the pandemic, Salk Professor Kay Tye, a Howard Hughes Medical Institute investigator and the Wylie Vale Chair, was investigating the neural circuitry of social behavior and the emotions behind it.

In 2016, her lab (then at MIT) identified a cluster of neurons in mice that were associated with a drive to socialize after being isolated from other mice. The team thought these neurons—part of a group of neurons called the DRN in the brainstem—might respond to what humans refer to as loneliness.

In mice housed together, DRN neurons were not very active.

“But after a mouse was separated from the group and reintroduced after time alone, its DRN neurons went wild,” Tye says. “In fact, the reintroduced mouse was even more social than the others, went wild, “Tye says. “In fact, the reintroduced after time alone, its DRN neurons responded to what humans refer to as loneliness.”

Mice whose DRN neuron activity was purposely suppressed didn’t experience this surge in sociability after isolation, supporting the idea that the DRN “loneliness” neurons were driving the urge to interact.

In 2020, Tye (by then at Salk) and her MIT colleagues published the results of a follow-up study in humans. This study focused on a small brain region called the substantia nigra, which has been implicated in people’s cravings for drugs. It is thought to be evolutionarily related to the DRN neurons in mice.

Healthy volunteers were required to have one session in which they fasted for 10 hours at home, and another in which they were socially isolated in a windowless room for 10 hours. Every two hours, the subjects completed questionnaires about how they were feeling, physically and emotionally.

In the social-isolation session, subjects were allowed to read preapproved documents, work on puzzles, or play solitary games (such as Tetris), but they were not allowed any social contact, including on their phones. Meals were dropped off outside the door to the room.

After each type of session, subjects had their brain activity measured by functional MRI (fMRI) while viewing stock photos—either of yummy-looking food (after the fasting session) or of people enjoying social interactions (after the isolation session). A baseline fMRI of each person was done at the beginning of the study.

The post-session fMRIs showed similar brain activity in the substantia nigra following both fasting and social isolation.

“This suggested to us that we crave social contact when we are lonely the way we crave food when we are hungry,” Tye says.

What’s more, the level of brain activity was correlated with people’s questionnaire ratings of how strongly they craved either food or social activity. So people who felt hungrier or lonelier had stronger brain activity when viewing images of food or socializing than people who felt less hungry or lonely.

Together, these studies point to specific brain circuits that drive mice and humans to seek social interaction, a process that can be impaired in anxiety disorders, depression, and addiction, among other neuropsychiatric conditions.

“Alcohol sales went up something like 20 percent in 2020,“Tye says. “It’s not how everyone coped with stress and loneliness, but certainly epidemiological data suggests a significant number of people did.”

(In fact, Tye lab postdoctoral researcher Reesha Patel—soon joining the faculty at Northwestern University—is nearing publication of a study of how social isolation affects alcohol consumption.)

Social animals naturally form hierarchies, with varying degrees of status among the members.

Tye speculates that if you’re used to being top dog (or top mouse), you might feel lonely sooner than a mouse who’s getting bullied by other mice every day. Indeed, her graduate student Christopher Lee—while investigating how social isolation affects animals over time—is finding that dominant animals make distress calls sooner after being isolated than subordinate animals do.

To tackle not only a deficit in the quantity of social contact but also in the quality, the team wanted to explore social exclusion. Tye and graduate student Caroline Jia are studying social exclusion via more clever experiments with mice. In one study, a mouse is given treats but separated from its cage-mates by glass. While neural activity is recorded, the mouse can see the others also getting treats, but can’t join them. Mice that are excluded show increased sensitivity to physical pain, suggesting there is a common neurological basis for physical and social pain.

The results are not in for Lee’s and Jia’s experiments yet, but for all Tye’s research, the point is to illuminate the neural circuitry of social behavior, both to reduce stigma about mental illness and to find better treatments for it.

“When we think about the deficits of social contact, there’s quantity, and then there’s quality,” says Tye. “The pandemic showed us the effects of both. Maybe you had almost no social contact at all, and that was terrible. Or you got COVID and had to isolate temporarily and so you had Thanksgiving dinner by Zoom, while the rest of the family was all together. And that was rough, too. The pandemic really brought it all to the forefront.”

“This suggested to us that we crave social contact when we are lonely the way we crave food when we are hungry.”

SUNG HAN
This made Asahina wonder whether social isolation impacts life span differently in male and female flies. In most species, females live longer than males, but the versatility of flies as genetic models allowed Asahina to examine the question in a unique way: Because fly neurons are determined by sex, it’s possible to genetically engineer flies with female brains and male bodies, or female bodies and male brains. The lab tested the effects of social isolation on both types of engineered flies as well as fully female and fully male flies.

As expected, fully female flies (female body, female brain) lived the longest. But in the other groups, “things got more interesting,” Asahina says.

Flies with male brains didn’t live as long. Something about the male brain appears to shorten life span. Social isolation, however, did not seem to significantly impact life span in either sex. “Male-specific motivations or behaviors, such as fighting, may be more costly,” says Asahina.

In work that is currently underway, Donovan Ventimiglia, a postdoctoral researcher in Asahina’s lab, has found that male flies that are beaten up repeatedly by other males lose their motivation to fight back and begin trying to get away.

In both flies and humans, the neurochemical dopamine plays an important role in behavior related to motivation and reward-seeking.

But when Ventimiglia blocked the dopamine-responding neurons, the flies continued to fight.

This work suggests that the dopamine neurons are signaling something akin to what humans experience as fear, and shutting the neurons down prevents the flies from getting the message to avoid potentially dangerous situations.

“I don’t know whether we should be calling this behavior ‘fear,’” says Asahina cautiously. “But there are clear behavioral changes after this social-defeat experience, and maybe what’s happening in the fly brain has some similarity to what people call a fear response.”

FEAR FACTOR

Assistant Professor Sung Han, who holds the Pioneer Fund Developmental Chair, is an expert on the fear response. Using mouse models, he studies small chemicals known as neuropeptides and how they influence the brain’s built-in alarm system.

This system first recognizes environmental threats detected by the senses, and then issues commands to change physiology, metabolism, behaviors, and emotions to avoid these threats.

“For example, if you smell smoke, then see flames and feel heat, you understand that there’s a fire and you need to get away,” Han says.

Earlier this year, Han, postdoctoral researcher Sukjae Joshua Kang, and graduate student Shijia Liu uncovered a molecular pathway that distills such threatening smells, sights, and sensations into a single warning. The team discovered that a molecule called CGRP enables neurons in two separate areas of the brain (the thalamus and brainstem) to bundle threatening sensory cues into a unified signal. Tag it as negative, and convey it to the amygdala—which translates the threat signal into the feeling of fear.

“But, just as with house or car security technology, the biological alarm system can malfunction and generate false alarms,” Han says.

This hypersensitivity to otherwise normal sensory stimuli is linked to PTSD, panic disorders, anxiety disorder, chronic pain disorder, schizophrenia, and autism spectrum disorders.

The same brain regions that express CGRP in mice also do so in humans. Han’s team is now eager to study how the molecule might be involved in hypersensitivity disorders, and whether a drug that blocks the molecule could be helpful in relieving symptoms.
Hypersensitivity disorders often involve our sense of touch—people with autism may not like certain textures, while people with neuropathic pain may find light touch painful. Touch sense is a focus for Associate Professor Eiman Azim, who aims to piece together the neural underpinnings of movement, especially skilled motions like reaching, grasping, and manipulating objects.

Recently, Azim, who holds the William Scandinling Developmental Chair, and graduate student Jacqueline Mosko became interested in how our internal states—including emotions—might influence touch sensitivity. “For example, fear can be associated with greater sensitivity to touch, which can be beneficial, in the short term, in scenarios where one needs to be exquisitely aware of details about the environment,” Azim says.

This change in touch sensitivity, however, can be problematic when it becomes chronic. Preliminary work suggests that the stress of prolonged social isolation, in addition to affecting our mental health, can lead to aberrant sensitivity to touch.

The team’s preliminary experiments in mice suggest that regulation of touch processing in an evolutionarily ancient structure in the brainstem, the cuneate nucleus, might be key.

Azim and staff researcher James Conner recently published a study about the cuneate nucleus showing that this structure—previously thought to be only a relay station for sensory information coming from the body—actually helps filter the information before routing it to other brain areas. This filtering is important for preventing distracting sensations from interfering with relevant ones. (When your fingers are typing an email, for example, you don’t need to be aware of your sleeve brushing your arm.)

Azim, Mosko, and Conner wonder if this filtering is disrupted by the stress of social isolation, leading to hypersensitivity to touch. In this scenario, typically innocuous sensations, like the feel of clothes touching skin, could become distracting or unpleasant and could even evoke abnormal behaviors such as avoidance of touch. The team is currently conducting experiments to test their hypothesis and exploring any implications their work might have for remedies.

Social isolation in and of itself is not necessarily a bad thing. Salk Professor and President Rusty Gage points out. “Short-term isolation that’s by choice can be refreshing—a meditation retreat, for example, or a backpacking trip;” he says. “The problem is when isolation becomes chronic and isn’t by choice that the brain can begin rewiring itself in harmful ways.”

Gage, a neuroscientist, is perhaps best known for discovering that the brain continues to make new neurons in adulthood, a process called neurogenesis. “New neurons help with familiarity—knowing if you’ve met someone before—and familiarity is very helpful in social situations,” Gage says.

But, he says, chronic stress decreases the brain’s ability to generate neurons, especially in a region of the brain known as the hippocampus, which recognizes and makes distinctions between events, emotions, objects, and people.

Fortunately, there is a way to promote neurogenesis to improve health and well-being, and perhaps even help alleviate health issues caused by social isolation and chronic stress.

“One of the best things people can do for neurological health is exercise, because it gets blood flowing,” says Gage, who holds the Vi and John Adler Chair for Research on Age-Related Neurodegenerative Disease. “Physical exercise is therapeutic for depression, for anxiety, for traumatic brain injury. It reduces the risk of dementia.”

This also applies for people with autism, who have a decreased capacity for social interaction, which Gage says is itself isolating. “Some of the best behavioral therapy for autism is finding the right vehicle of communication with the autistic individual so that they can do things that help them get authentically reinforcing rewards. What does a person with autism find enjoyable? A lot of times it’s repetitive movements. There are repetitive computer activities they can do that are actively stimulating. And then if you can build physical exercise into an enriched environment, that’s even better.”

Gage says the pandemic has made society acutely aware of the negative consequences of social isolation on mental health, and of the importance of research into the molecular mechanisms that result from it. “At Salk, the important part is getting people from different perspectives coming together and discussing the issue. Coming up with animal models, coming up with mathematical models, ways in which we can generate a hypothesis about what’s happening and test it—in a way that’s translatable to humans—so we know how to best modify our environments or reset ourselves to build resilience and cope better in our ever-changing world.”
Gerald Joyce was appointed Salk’s senior vice president and chief science officer earlier this year. But long before then, he referred to himself as “a Salkie deep in the veins.”

Inside Salk sat down with Joyce to learn about the evolution of RNA, as well as the evolution of his career, science, and Salk.
Joyce was born in Kansas and grew up in Chicago. He went to college at the University of Chicago and then earned both his MD and PhD at UC San Diego. When it came time to do his PhD thesis research, Joyce walked across the street to Salk—or what his glossy UC San Diego recruiting brochure had called “The Castle”—and joined the lab of one of the Institute’s original Resident Fellows, Professor Leslie Orgel.

After finishing his medical degree and clinical internship, Joyce returned to the Institute for his postdoctoral training, during which time he and his wife were married in the Salk Courtyard.

Joyce went on to serve as dean of the faculty at the Scripps Research and institute director of the Geomics Institute of the Novartis Research Foundation (GNF) before returning to Salk yet again in 2017, this time as a professor.

Joyce’s research has long focused on the chemistry and biochemistry of RNA, or ribonucleic acid. At Salk, his lab is interested in two key questions: How did life begin? And how do we know? These questions are at the heart of the origin of biological structures, it’s thought that life was based on RNA, just as proteins (the functional material). Over their lunches, Crick and Orgel came to the conclusion that it all very likely started from random molecules. That fascinated me, and it still does.

Why did you decide to pursue both a medical degree and PhD?

GJ: I love science, but it was the late 1970s when I was finishing college, and there was a lot of instability in the world, to say the least—the oil embargo, runaway inflation, a hostage crisis. I just felt like the whole world as we knew it might collapse. Maybe young people have that same fear now. But it made me second-guess my decision to become a Darwinian engineer in such a world. I figured I needed a skill, and no matter how bad things get, we always need doctors.

While research is my focus, to this day I do keep my medical license active. I spent seven years running a drug discovery team at Novartis, and it turned out that being a licensed physician and having that medical training enables you to engage in drug discovery beyond the basic science, to understand what’s going to happen if and when that therapeutic compound gets to the clinic.

What’s so special about RNA?

GJ: These days everybody talks about RNA because we are fortunate to have RNA-based vaccines to protect us against COVID-19, but my take on RNA is more ancient than that. Before there were cells or other complex biological structures, it’s thought that life was based on replicating RNA molecules. That idea was born here at the Salk Institute. In 1968, then Salk Fellows Francis Crick and Leslie Orgel were good friends and frequently enjoyed lunches together out on the patio. The pair were founding members of the discipline now known as molecular biology. They were at the forefront of figuring out, at a molecular level, how biology works—from DNA (our genetic material) to RNA (the messenger material) to proteins (the functional material). Over their lunches, Crick and Orgel came to the conclusion that it all very likely started with just RNA. RNA was once the only show in town: a molecule that both contained genetic information and had function. They laid out the concept of what is now called “the RNA World,” the idea that biology in the ancient world, roughly 4 billion years ago at the dawn of life, was based on RNA.

What is “test-tube evolution,” the focus of your research today?

GJ: If we can understand what life is and how it began, then maybe we can restart it ourselves in the lab. We’re not talking about Frankenstein’s monster—not an organism or even a cell. We’re simply talking about biological structures, it’s thought that life was based on replicating RNA molecules. That idea was born here at the Salk Institute. In 1968, then Salk Fellows Francis Crick and Leslie Orgel were good friends and frequently enjoyed lunches together out on the patio. The pair were founding members of the discipline now known as molecular biology. They were at the forefront of figuring out, at a molecular level, how biology works—from DNA (our genetic material) to RNA (the messenger material) to proteins (the functional material). Over their lunches, Crick and Orgel came to the conclusion that it all very likely started with just RNA. RNA was once the only show in town: a molecule that both contained genetic information and had function. They laid out the concept of what is now called “the RNA World,” the idea that biology in the ancient world, roughly 4 billion years ago at the dawn of life, was based on RNA.

Just like with my work on RNA and the origins of life, I like being at the very beginning of the process.

GERALD JOYCE

How did you become interested in studying the origins of life and evolution?

GJ: The summer after my sophomore year, I drove an industrial laundry truck to factories around Chicago to help pay my way through college. It was hard labor, but at lunch I was always reading. A turning point for me was Thomas Pynchon’s book Gravity’s Rainbow. It starts out quite depressing—it’s about how the universe is inevitably moving toward a state of chaos and nothingness. But then the novel pivots to the organizing force, or “Titans of the Earth,” which opposes the destructive force. It’s a natural process that takes us away from physical randomness and toward biological invention and organization. And, of course, that process is Darwinian evolution.

So that was my new motivation—I wanted to summon the Titans of the Earth by engineering the organizing force. When I came back for my junior year, I turned to biochemistry and molecular genetics so I could understand how one can evolve complex living systems starting from random molecules. That fascinated me, and it still does.

How do you think science itself has evolved over your career?

GJ: Science has definitely changed—for the better. When I was a student and a postdoc in the 1980s, every laboratory was sort of its own little world. They would collaborate, of course, especially at Salk, but it was still mostly an individual effort. Now science is done differently, for two main reasons: constraints evolving technology platforms, the necessity of forming interdisciplinary teams before you even begin to address a research question, and “big data.” Thanks to all this technology and collaboration, we now harvest and analyze far more data than we could have even stored back then.

As chief science officer, what’s your vision for the future of Salk?

GJ: Our prime objective has always been to produce high-impact science—that’s why we’re here. But we need to evolve as science evolves. To ensure that Salk will always lead the world in fundamental discovery research, we now have an exciting, comprehensive fundraising campaign underway that is focused on six critical research areas: cancer, healthy aging, plant biology, immunobiology, neuroscience, and computational biology. We are recruiting the best people and building the technology and research space that we need to create new opportunities in these areas. The investments we make today will launch a thousand ships tomorrow. I can’t wait to see what we will achieve together.

How might your work relate to life beyond Earth?

GJ: When you start thinking about the origins of life, you also start thinking about what is and isn’t “life.” How do you define it? Everyone has their favorite notion, but there is no agreed-upon scientific definition of what life is. And yet it’s a problem we’re all interested in, particularly when we start exploring other planets. If we’re looking for signs of life, what exactly are we looking for? And how will we know when we’ve found it? Over the years I’ve helped advise on these concepts for groups like NASA, their Jet Propulsion Laboratory, and the US National Academy of Sciences.
IN MEMORIAM

Walter Eckhart

exemplified generosity and kindness

Considered one of the forces that contributed to Salk’s unique DNA, Walter Eckhart elevated the Institute’s cancer research to unprecedented heights of success, while showering those around him with generosity and kindness over a lifetime.

Early last summer, the world lost a revolutionary scientist and generous man.

May 22, 1938

June 21, 2022

“Walter possessed this unique capacity to reduce the stress in any situation, sometimes just by listening, or offering a warm smile, or saying a few constructive words.”

GEOFFREY WAHL
Eckhart, professor emeritus and director of the Salk Institute’s National Cancer Institute-designated Cancer Center and head of the Molecular and Cell Biology Laboratory for more than 30 years, died on June 21, 2022, at his home in La Jolla, California, at the age of 84.

He is survived by his wife, Karen Lane; her daughter and son-in-law, Jasmine Penick and David Penick; and their children, Shane and Emma; Eckhart’s sister, Elizabeth Nagle; and his wife’s husband, Jack Nagle; nephew Rob Nagle and his wife, Heather Allyn; nephew David Nagle, his wife, Siana Nagle, and their daughters, Imogen and Sally; and by his first wife, Karen Eckhart.

“Walter was a brilliant scientist, a wonderful person, and a terrific member of the Salk community. His career spanned from the origins of Salk as a bright and creative researcher through to current times, where he gave generously of his time and resources to support the Institute in many ways,” says Salk President Rusty Gage. “We miss him a great deal.”

The Institute hosted a celebration of life for Eckhart on its campus on September 2, during which time members of the Salk community shared fond memories of Eckhart—their colleague, mentor, and friend.

“I interviewed with Walter for a position as a laboratory technician in 1974. He took a risk on me then, a very young and inexperienced technician. He gave me a chance to learn, make mistakes, and mature under his kind and fair guidance,” said Suzanne Simon at the service. She worked alongside Eckhart for many years and had lunch with him daily. “Walter’s gentle manner and his willingness to take a risk on a young recruit is a theme you will hear repeated by the alumni of our lab.”

Eckhart joined Salk in 1965 as a postdoctoral scholar in the lab of Nobel Laureate and cancer researcher Renato Dulbecco. He went on to become one of the first assistant professors at the Institute in 1969.

“I was attracted by the world-class research being done at the Institute,” Eckhart said in an interview in the Fall 2022 edition of Inside Salk magazine. “The collaborative, interactive environment was exceptional.”

Eckhart was a leader in understanding the basic biology underpinning cancer. He studied regulation of cell growth, including the effects of cancer-causing genes (oncogenes), growth factors, and communication between adjacent cells (gap junctional intercellular communication).

“Walter played a key role in the early days of the Institute, being tasked to recruit the first cohort of assistant professors at the Institute in 1969,” says Professor Tony Hunter, who followed Eckhart as Salk Cancer Center director from 2008 to 2016. “Walter was my postdoctoral adviser at the Institute and recruited me as an assistant professor in 1974, and without his mentorship and support, I could never have been so successful.”

Eckhart was born in 1938 in Yonkers, New York, where he grew up. He attended Gorton High School in Yonkers and was the school’s newspaper editor and class valedictorian.

Eckhart took a ship to England, and once on the Cambridge campus, he roamed around for two days, too nervous to meet his hero. He finally worked up the courage and went on to work in Crick’s lab for a year.

Following his stint at Cambridge, Eckhart worked at the Woods Hole Oceanographic Institution in Massachusetts in 1961. He then attended the University of California, Berkeley, where he earned his PhD in molecular biology in 1965.

Eckhart looked up to Crick, who shared the 1962 Nobel Prize in Physiology or Medicine for discovering the molecular structure of DNA. But it was a famed cancer researcher who drew him to the Salk Institute.

“When I thought about who I wanted to work with, one name came to mind—Dulbecco,” said Eckhart in a 2014 article in the San Diego Union-Tribune. (Crick, too, later joined the Salk faculty.)
A WELCOMING LISTENER AND FRIEND

Colleagues describe Eckhart as someone who was generous with his time and always willing to talk about whatever was on your mind, be it science or life.

“He seemed to always have time for people,” Gage said at Eckhart’s memorial service. “If you wanted to talk to him, he would just take the time and sit down with you. If he thought you needed it, he’d give you advice, and if not, he’d just nod and reassure you that you were on the right thing. You’d move on, always feeling better having spent some time with him.”

“You didn’t have to make an appointment to see Walter,” added Gerald Joyce, Salk senior vice president and chief science officer. “You could just talk to him. Now, he did hold regular office hours—in the Courtyard, at the middle bench on the south side with his sandwich—but I knew I could always catch him there at noon, and he was happy to talk about anything.”

At the memorial service, former Salk chief science officer Martin Hetzer shared that Eckhart put him at ease from the moment they met in 2003.

“He was genuine, unassuming, unpretentious, and very calming,” Hetzer said.

“He was that quiet presence who could be counted on for thoughtful, sensible advice,” said Professor Geoffrey Wahl, who was hired by Eckhart to join Salk in 1980 and spoke at the memorial. “More than that, Walter possessed this unique capacity to reduce the stress in any situation, sometimes just by listening, or offering a warm smile, or saying a few constructive words. He had this Zen-like ability to cut through tension.”

GENEROUS TO THE END

After his retirement from Salk in 2009, Eckhart and his wife Karen Lane, also a Salk alum, made it their mission to financially support scientific progress at the Institute. To date, Eckhart and Lane have given more than $1 million to the Institute, primarily to Salk’s unrestricted fund, meaning their contributions are given without restrictions to allow the Institute to put their contributions toward the greatest needs.

In the Winter 2020 issue of Inside Salk, Eckhart explained why, after decades of hard work and scientific excellence as a faculty member at the Institute, he felt he could do more to further Salk’s mission.

“I go back to a famous Jonas Salk quote: ‘The reward for a job well done is the opportunity to do more.’ I think about that often when it comes to giving,” Eckhart said. “I’ve worked in basic research my entire career, so I can tell you the impact basic research has on society is far-reaching. I also think it’s important to know that Salk is training the next generation of scientists.”

In October 2022, the Institute lost another treasured faculty member: Distinguished Professor Emeritus Charles “Chuck” Stevens, an influential neuroscientist who served on Salk’s faculty for 28 years. A tribute to Stevens will appear in the Spring 2023 issue of Inside Salk.

In October 2022, the Institute lost another treasured faculty member: Distinguished Professor Emeritus Charles “Chuck” Stevens, an influential neuroscientist who served on Salk’s faculty for 28 years. A tribute to Stevens will appear in the Spring 2023 issue of Inside Salk.

A team led by Assistant Professor Sung Han recently revealed how the amygdala, the brain’s emotion center, receives threat cues from different brain areas—including the brainstem (red) and thalamus (green)—and translates the signal into fear. Read more on page 19.
IN MEMORIAM

Salk Institute mourns loss of influential former Board member

The Salk Institute lost a dear friend and former Trustee when Georg Heinrich “Heini” Thyssen-Bornemisza died on September 30, 2022.

The chairman of the NOMIS Foundation, Thyssen studied mathematics at the University of Munich (Germany) and received a law degree from the University of Zurich (Switzerland). In 2008, he established the NOMIS Foundation, whose vision is to “create a spark” in the world of science by enabling and supporting pioneering research in the natural sciences, social sciences, and the humanities that benefit humankind and our planet. The foundation executes its mission through awards, fellowships, research grants, alliances and partnerships, and network development.

Also a former Salk Trustee, Thyssen’s leadership and generosity helped accelerate scientific efforts at the Institute over the years, always with a focus on allowing Salk scientists to continue their pursuit of high-risk, high-impact research.

“Salk will be forever indebted to the generosity and kindness Heini showed the Institute over the years,” says Professor Susan Kaech, director of Salk’s NOMIS Center for Immunobiology and Microbial Pathogenesis and NOMIS Chair. “He loved Salk because our scientists ask bold and innovative questions, often at the intersection between fields where the greatest discoveries can arise. His legacy will reverberate in Salk labs for decades to come. We will miss him greatly.”

Thyssen’s financial support led to the launch of Salk’s NOMIS Center for Immunobiology and Microbial Pathogenesis in 2008. The center aims to shed light on new mechanisms that control immunity to infection and cancer, define key molecules involved in the body’s response to injury and infection, elucidate the rules of engagement between the body’s microbiome and immune system, and understand why inflammatory processes spin out of control under some circumstances.

In 2021, the NOMIS Foundation provided additional funds to endow a NOMIS Center postdoctoral fellowship fund and for faculty recruitment to sustain and expand the impact of Salk’s research in immunity and inflammation. Additionally, the foundation awarded a NOMIS Distinguished Scientist and Scholar Award to Professor Ronald Evans in 2020, and awarded Professor and Laboratory Head Janelle Ayres with a special grant in 2018 for the novel study of mechanisms to promote health.

The Salk Institute extends its deepest condolences to the Thyssen family and the NOMIS Foundation.

1950 – 2022

GEORG HEINRICH
“HEINI”
THYSSEN-BORNEMISZA

Hands-On Science Education

Salk Education Outreach

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

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

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

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

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

To learn more about Education Outreach, please email education@salk.edu
Kate Leonard and Richard Forsyth consider the Salk Institute the epitome of a worthy recipient of their support—a local organization making a global impact by pursuing answers to the world’s biggest challenges.

"Salk is a first-rate institution in every respect," Forsyth says.

When the married couple learned about Salk’s campaign, they didn’t hesitate to cast their generous support behind the five-year, $500 million effort to attract the world’s top scientists and artist alike. The center will allow the Institute to recruit new faculty and trainees and invest in new computational technologies such as artificial intelligence and machine learning.

"I like the fact that Salk is always looking to modernize and continue its reputation as a cutting-edge research facility," Forsyth says.

When asked what philanthropy means to them, Forsyth says the easy answer is "giving back." Leonard says they focus on supporting local institutions that enrich the global community.

The couple "sprinkles" support to more than 45 local organizations, including those providing support for the unhoused, domestic violence organizations, nature groups, libraries, groups for health-challenged individuals, and food banks. In addition, they support many local music organizations.

The couple are both from San Jose and met as Sister City exchange students in Japan. Each began their international careers in Japan: Upon Leonard obtaining her California CPA license and an MBA, and Forsyth his law degree, they moved to the Osaka area of Japan, where Leonard was the only American CPA in Japan’s largest audit corporation and Forsyth practiced law with a major Japanese law firm, representing the United States government, among other clients.

In 1985, the couple moved back to San Diego to continue their careers. Valuing their history with Japan led them to support various local Japan-related organizations, including the Japan Society, the Union of Pan Asian Communities, the Japanese Speech Contest, the Japanese American Historical Society, and the Mingei Museum. Additionally, both take great pride in supporting the Kyoto Prize, Japan’s highest private award for lifetime achievement in the arts and sciences.

Leonard and Forsyth believe contributing to the Institute’s campaign is a way they can honor Jonas Salk’s challenge to be good ancestors.

“It's an investment in science," Leonard says. “It’s an investment in your children," adds Forsyth. “Jonas Salk has a famous quote about striving to be good ancestors, and supporting this campaign is something we can all do to meet his challenge to us."

Supporting local institutions making a global impact

DONOR PROFILE

Kate Leonard and Richard Forsyth

Leonard, a retired international tax partner and current Honorary Consul of Japan in San Diego, and Forsyth, a retired international lawyer and business executive, have a strong history of financially supporting Salk.

They first became Salk donors in 2005 while Forsyth was providing outside counsel for Westbridge Research Group, a company that offers innovative, science-based solutions for large agricultural growers. (Coincidentally, Jonas Salk served on the Westbridge board for a time.)

Symphony at Salk was the first event Leonard and Forsyth supported and attended, hosting a contingent from Westbridge. Soon after, they discovered the Salk Women & Science program and have contributed to that effort ever since.

“Keeping women inspired and removing barriers is so important," Forsyth says.

“We have two daughters, so we’re very sensitive about the advancement of women in science," Leonard adds.

“We’ve been fortunate and blessed, and we have the opportunity to give back to the local community and the global community," says Forsyth about their philanthropic efforts.

To join Leonard and Forsyth in helping Salk accelerate life-changing discoveries, visit: salk.edu/campaign.
Mallory Zaslav

Four years ago, Mallory Zaslav created what’s now known as Salk’s Diversity, Equity & Inclusion (DEI) office under the guidance of President Rusty Gage. She conceived it with a clear mission: engage members and supporters of the Institute in initiatives that honor and further the diversity of the Institute’s campus community, reinforce its values, and foster a sense of belonging.

As vice president of Diversity, Equity & Inclusion, Zaslav’s forward thinking and advocacy on this issue have given shape to a range of impact-driven programming and outreach, furthering Salk’s mission of bettering humanity by pushing the boundaries of innovation and discovery.

The DEI team aims to ensure there are structures in place to both attract diverse talent and support them once they have joined.

“Everyone should have agency in their own career path and feel their contributions matter,” Zaslav says.

**ESTABLISHING A FOUNDATION AND SETTING PRIORITIES**

During the unit’s earliest stages, Zaslav understood the importance of joining forces with like-minded organizations. One of her first priorities was for Salk to become a member of an action collaborative formed by the National Academies of Science, Engineering, and Medicine. The collaborative is proactively developing promising practices to prevent sexual harassment in higher education—a critical part of which is recognizing the needs of diverse campus populations. Today, Salk is one of approximately 60 organizations participating in this collective and one of only a few independent research institutions.

Another initial area of focus was conducting Salk’s first campus climate survey. Zaslav championed the effort and ensured a confidential and transparent process to encourage high rates of participation. With survey results in hand, Salk is now embarking on the follow-up process of engaging its community in focus groups to socialize recommended core values and advance other initiatives.

Additionally, Zaslav has spearheaded mentoring programs and supported the formation of affinity groups. Grassroots in nature, the affinity groups aim to bring awareness to individuals with a range of personal identities, while aligning this awareness-raising with Salk’s training and research mission. The mentoring programs are designed to facilitate relationships that open doors through support, advocacy, and sponsorship.

Zaslav maintains that multifaceted DEI programming provides and widens opportunities for outreach and for individuals to come together and share their personal journeys. While this can take the form of offline conversations, it can be further encouraged by programs and offerings, from research fellowships to speakers’ series and more.

**MAKING THE JOURNEY TO SALK**

Early in her career, Zaslav found available job opportunities less than gratifying. She decided to complement her liberal arts education with an MBA in human resources while working full-time recruiting physicians for hospital emergency departments.

“Balancing school and work allowed me to apply what I was learning to understand how companies operate, how people work together, and how that intersection can yield mutual benefit,” she said.

Zaslav went on to earn a law degree from the University of San Diego. She spent several years in business roles within law firms before seizing the opportunity to join Salk’s HR department in 2009.

“Working with people from around the globe, with a broad array of personal identities and myriad life experiences, is enriching, and certainly the case at Salk,” Zaslav says.

“The experiences and roles I had during the early stages of my career infused in me the value of having exposure to different points of view, different ways of thinking, different backgrounds, and different approaches to tackling challenges. In many respects, my role at Salk is a culmination of all those experiences and I’m grateful for the opportunity to have a very tangible impact on the Salk community and the Institute as a whole.”

**LOOKING TO THE FUTURE**

Salk is well-positioned to enter the next phase of its DEI and cultural journey, Zaslav says. The department has added more staff and is excited to support all members of Salk who are embarking on DEI initiatives. The Institute has also been actively developing policies that foster a respectful work environment and recognize the value of remote work.

Zaslav believes the work championed by her and others in her field will, over time, become more widely understood as a critical stand-alone discipline.

“Committed people have been doing this work for decades while wearing many different hats. In recent years, more resources have been allocated to it, which indicates a greater understanding of the criticality of dedicated DEI functions,” Zaslav says. “This is part of the employee value proposition. It is critical that leadership teams listen, learn, and actively participate, acknowledging that people are organizations’ most valuable assets.”

**VALUING THE DIFFERENCES IN BACKGROUNDS AND EXPERIENCES**

Beyond the walls of Salk, Zaslav’s personal interests are equally diverse, as she enjoys live theater, reading, hiking, and traveling, and aims to combine all of them whenever possible. She has two active dogs that serve as excellent companions to her and her husband. Although she enjoys traveling, Zaslav’s trips have been limited since the emergence of COVID-19.

“We went to Asia in December 2019, and I vividly remember reading an article right after we arrived about this perplexing virus and thinking, ‘This definitely does not sound good.’” Zaslav says.

“As vice president of Diversity, Equity & Inclusion, Zaslav’s forward thinking and advocacy on this issue have given shape to a range of impact-driven programming and outreach, furthering Salk’s mission of bettering humanity by pushing the boundaries of innovation and discovery.”

The DEI team aims to ensure there are structures in place to both attract diverse talent and support them once they have joined.

“Everyone should have agency in their own career path and feel their contributions matter,” Zaslav says.
As a child, Katia Troha would mix chemicals from her bathroom to see how they would react. Not all her concoctions worked out, and one day she had to be rushed to the hospital, as her hands had turned dark brown. Despite this setback, her love of experiments continued, and she is now a postdoctoral researcher in the lab of Professor Janelle Ayres, where she studies asymptomatic infections, in which an animal infected with a virus or bacteria doesn’t have any symptoms.

Growing up in Lima, Peru, Troha’s love of science was fueled by watching documentaries where she learned about groundbreaking studies like the first cloned mammal, Dolly the sheep. She was excited to see how this technology would be used for the benefit of human health. Although there were no scientists in her immediate family, Troha knew she wanted to become a scientist to learn all she could about genetics.

When Troha was 14, her family moved to the United States in search of a better life. In college at UC Berkeley, Troha majored in genetics, and during one of her classes she met Sir Ian Wilmut, the English embryologist who led the research group that cloned Dolly. Although nervous, she worked up the courage to ask him something she had always wondered about: Why had he used a mammary gland cell to clone Dolly?

“I was expecting a great scientific explanation, but instead he stated that his funding had come from a milk company. So, the mammary cell was used just because it produced milk,” says Troha. “His response was eye-opening, and I learned a little bit more that day about how science works.”

After college, Troha pivoted her focus when she joined a UC Berkeley lab as a technician, where she studied immunity and infectious microbes, small organisms like bacteria that can cause disease. “There’s this dance between microbes and animals. Sometimes this interaction isn’t good, and people get sick, but other times we gain multiple benefits from these microbes,” she says.

It was in that lab that Troha first met now Salk Professor Janelle Ayres, who was a postdoctoral fellow at the time. Ayres introduced Troha to the study of asymptomatic infections and mentored her on her journey to graduate school.

“During an asymptomatic infection, you can maintain your health, so you don’t feel or look sick,” says Troha. “One of the easiest examples comes from the pandemic.”

While some people who tested positive for COVID-19 were sick with symptomatic infections and had to be hospitalized, other people were asymptomatic and did not have any symptoms at all.”

Troha completed her PhD in immunology and infectious disease at Cornell University in Ithaca, New York, studying how fruit flies respond to infections. But she longed to return to her work with Ayres. After her PhD, Troha reached out to Ayres to see if she could join her lab to continue studying asymptomatic infections at the Salk Institute.

“I had always heard about the Salk Institute, and the amazing science that is conducted there,” says Troha. “To be honest, I was also ready to leave behind the winters in upstate New York. I don’t miss those emails from the administration telling us that it’s unsafe to be outside because it’s so cold.”

In Ayres’ lab at Salk, Troha now examines how different diets can affect the ability of a mouse to survive an infection. She uses an infectious microbe that initially infects the gut and then replicates to spread throughout the whole body. Her goal is to discover dietary interventions that improve health and increase survival during these infections.

Troha has discovered that some diets are able to make the kidneys grow during the infection. Kidneys are typically thought of as a filtration organ, but they also play a role in the response to infection. She believes that the increase in kidney size during infections could help the body tolerate the invader. Although her findings have not yet been published, she is excited about the impact her work could have on the field of infectious diseases and health research.

She was recently named a 2022 Leading Edge Fellow, which is a professional development fellowship aimed at improving the gender diversity of life sciences faculty across the United States. As a fellow, Troha will be able to present her work, meet and connect with other fellows, and receive mentorship and career development training from world leaders in biomedical research. “The fellowship will allow me to learn more about what it takes to become a professor in science and how to develop my research vision,” she says.

Although she now conducts her experiments in a state-of-the-art Salk lab, Troha still reminisces about the days when she mixed chemicals in her home. “Perhaps it’s best that I now wear gloves to pursue my scientific explorations,” she laughs.

“there’s this dance between microbes and animals. sometimes this interaction isn’t good, and people get sick, but other times we gain multiple benefits from these microbes.”

Katia Troha

Discovering diets that boost survival during infection
“Being in a lab every day and being surrounded by scientists gets you in the mindset of a scientist,” says Evelyn Parra, a 2022 program participant and student at Sage Creek High School in San Diego.

Parra’s summer project was focused on understanding how plants respond to our changing climate.

“We saw how plants grow in four different conditions—two dark and two light—and we were able to compare them,” says Parra, who worked in the lab of Professor Joanne Chory, director of the Plant Molecular and Cellular Biology Laboratory and founding director of the Harnessing Plants Initiative at Salk.

Parra was one of 12 applicants selected out of 250 candidates to participate in the eight-week program, which offers paid positions for talented high school students to assist Salk scientists with projects. The program is part of Salk’s Education Outreach department.

“STEM opportunities are so lucrative for students. They help us move the next generation forward,” says Monika Wert-Parkinson, who oversees the Heithoff-Brody High School Summer Scholars program as director of public programs at Salk.

Josh Sohmer was introduced to Salk when he participated in Education Outreach student programs and completed internships in 2013 and 2014. He later became a research assistant in Salk’s stem cell core facility and is now a first-year medical student focused on regenerative medicine.

“The summer internships and student opportunities Salk provides truly solidified my interest in science and gave me the necessary tools to build a career,” Sohmer says. “These programs sparked my interest in stem cells and led me to pursue it professionally and apply it to my future medical practice. I am still involved in the summer student programs now as a mentor, providing guidance on the student presentations.”

The Institute’s Education Outreach programs, including Heithoff-Brody High School Summer Scholars, continue founder Jonas Salk’s vision for the Institute.

“Jonas Salk believed it is our responsibility to be good ancestors. That is really what the program is about—to train the next generation of scientists,” says Wert-Parkinson.

For more than 30 years, the Salk Institute’s Heithoff-Brody High School Summer Scholars program has provided hands-on laboratory experiences for local high school students interested in exploring careers in science, technology, engineering, and math.

“Summer Scholars program paves the way for future scientists.”

For more information, visit salk.edu/education-outreach.

Summer 2023 applications will be available in January.
Innovation and Collaboration Grants announced

Salk’s Innovation Grants program, launched in 2006 from the forward-thinking minds of then Board Chair Irwin Jacobs and his wife, Joan, is designed to fund out-of-the-box ideas that hold significant promise but may not yet have the track record to attract attention from more traditional funding sources.

The Jacobs’ commitment of $8 million since the start of the Innovation Grants Program helped Salk secure additional philanthropic contributions from the Rose Hills Foundation, James Melcher and April Benasich, Fondation Ipsen, and Elizabeth Keadle. Since then, Salk researchers have gone on to leverage early results from Innovation Grant-funded research to access more substantial investments from the National Institutes of Health (NIH) BRAIN Initiative, the Keck Foundation, and other prominent grant-makers.

Awarded semiannually by peer review, Salk’s Innovation Grants program is critical to catalyzing emerging science with the power to redefine the future. At right are this year’s awardees.

From left: Irwin and Joan Jacobs.

Professor Janelle Ayres, Joseph Noel, and Christian Metallo will collaborate to determine if asymptomatic and symptomatic infected animals emit different chemicals—signals that help group mates respond to the infection. The methods they develop may help diagnose community spread of infectious diseases and develop new treatments based on emitted chemicals.

2022 INNOVATION GRANTS

Assistant Professor Sung Han will explore how single neurons orchestrate the release of different transmitters—glutamate versus neuropeptides, for example. With this idea, he and his lab are currently investigating the neuronal coding logic of transmitter co-transmission to encode various types of information. These studies will transform the field’s current understanding of neuronal communication.

The ease with which researchers can track body parts in motion, such as hands and feet, has improved in recent years due to advances in machine learning and computer vision. However, these methods still require researchers to manually label each body part, which is time-consuming and increasingly impractical as the number of labels on the body grows. Associate Professor Eiman Azim is now developing automated approaches to simultaneously track hundreds to thousands of points on the body. These methods will provide better ways to examine how brains control movement and insights into how neurodegenerative disease and injury disrupt behavior.

Professor Joanne Chory, Associate Professor Sreekanth Chalasani, and Staff Scientist Carl Procko will investigate the sensory proteins of plants to see if they are sensitive to high-frequency sound waves. The work could help scientists modify how plants behave in the presence of other plants and contribute to the growing body of research on “sonogenetics,” a method Chalasani developed for noninvasively controlling cells with sound waves. Their findings could also lead to new ways to treat conditions like chronic pain, epilepsy, and PTSD.

Professor Tony Hunter and team generated the first antibodies recognizing phosphorylated histidine (pHiHis), a protein modification that may play a role in cancer. Now, they will engineer the antibodies to bind even better to pHiHis proteins and use them to probe pHiHis function in health and disease.

Assistant Professor Sung Han will collaborate to determine if asymptomatic and symptomatic infected animals emit different chemicals—signals that help group mates respond to the infection. The methods they develop may help diagnose community spread of infectious diseases and develop new treatments based on emitted chemicals.

From left: Irwin and Joan Jacobs.
An international team of researchers, including Professor Janelle Ayres, Salk Institute Legacy Chair, was selected to receive a $25 million Cancer Grand Challenges award to tackle the challenge of cancer cachexia, a debilitating wasting condition that often leads to a poor quality of life for people in the later stages of cancer. Known as the Cancer Cachexia Action Network (CANCAN), the team is co-funded by Cancer Research UK and the US National Cancer Institute, part of the National Institutes of Health. The team hopes to build a deep understanding of what causes cachexia and develop new treatments to intervene.

**Janelle Ayres joins Cancer Grand Challenges team tackling cancer cachexia**

An international team of researchers, including Professor Janelle Ayres, Salk Institute Legacy Chair, was selected to receive a $25 million Cancer Grand Challenges award to tackle the challenge of cancer cachexia, a debilitating wasting condition that often leads to a poor quality of life for people in the later stages of cancer. Known as the Cancer Cachexia Action Network (CANCAN), the team is co-funded by Cancer Research UK and the US National Cancer Institute, part of the National Institutes of Health. The team hopes to build a deep understanding of what causes cachexia and develop new treatments to intervene.

**Cachexia is responsible for up to 30 percent of cancer-related deaths.**

**Todd Michael receives $2 million to build a genome repository for the cassava plant**

Research Professor Todd Michael received nearly $2 million from the Bill & Melinda Gates Foundation to sequence the genomes of multiple lineages of the cassava plant, the large starchy root vegetable also known as yuca root that is consumed in more than 80 countries around the world. A better understanding of cassava genetics will help researchers and plant breeders develop more productive disease- and drought-resistant plants for the future.

**“I have been eager to apply our findings and perspectives from infectious diseases to cancer cachexia for years now. Being able to do so as a member of an exceptional team of clinical and fundamental biologists that have the diverse expertise necessary to address cancer cachexia is an incredibly exciting opportunity.”**

JANELLE AYRES

**“This research will provide scientists and plant breeders with a better understanding of cassava genetics so they can improve crop yields and feed more people, even in an uncertain future.”**

RUSTY GAGE

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RUSTY GAGE

**DANIEL HOLLERN AWARDED SUSAN G. KOMEN GRANT**

With the new three-year, $450,000 Susan G. Komen grant, Assistant Professor Daniel Hollern and team will study immune cells called B cells and how they interact with and recognize metastasized breast cancer cells. They will also test new promising and existing treatments that activate B cell responses against breast cancers to see if they can help patients living with breast cancer metastasis.
Assistant Professor Christina Towers uses a combination of DNA-editing techniques, light-based genetic manipulation (optogenetics), three-dimensional miniature organs (organoids), and detailed imaging to uncover how cancer cells recycle both their own nutrients and the power-generating structures called mitochondria to survive. Her goal is to uncover novel fundamental biology that will lead to new targeted cancer therapies that can block the cancer cell recycling pathways that allow these cells to survive.

For her accomplishments, Towers received several notable awards this year, including a $1.15 million Science Diversity Leadership Award from the Chan Zuckerberg Initiative, in partnership with the National Academies of Sciences, Engineering, and Medicine. The award recognizes outstanding early- to mid-career researchers who have made significant research contributions to the biomedical sciences, show promise for continuing scientific achievement, and promote diversity, equity, and inclusion in their scientific fields.

She was also awarded the $300,000 Young Investigator Award through Black in Cancer, an organization that aims to strengthen the network between Black people in the cancer space while highlighting Black excellence in cancer research and medicine in partnership with the Emerald Foundation, Inc.

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Austin Coley awarded Transition to Independence Fellowship

Austin Coley, a postdoctoral fellow in Professor Kay Tye’s lab, will receive $495,000 over three years from the Simons Collaboration on the Global Brain to help him become an independent investigator. The fellowship facilitates the transition to research independence of outstanding neuroscientists from historically underrepresented backgrounds.

Sara Sameni receives 2022 Berman-Topper Family HD Career Development Fellowship

Sara Sameni, a postdoctoral fellow in Professor Terrence Seyrowksi’s lab, will receive up to $80,000 per year for three years from the Huntington’s Disease Society of America. This prestigious fellowship, made possible in part by the Berman and Topper families, supports young scientists and clinicians who desire to make the study of Huntington’s disease part of their long-term career plan. The fellowship will allow Sameni to create personalized models to predict disease course and treatment response in people with Huntington’s disease.

Nuttida Rungratsameetaweemana awarded Edwards-Yeckel Postdoc Professional Development Award

Nuttida Rungratsameetaweemana, a postdoctoral fellow in Professor Terrence Seyrowksi’s lab, was awarded the inaugural Edwards-Yeckel Postdoc Professional Development Award. Made possible by a generous gift from the Ray Thomas Edwards Foundation, the award is intended to inspire applicants to explore new avenues of investigation and professional growth.

Joseph Swift receives Australia to USA Graduate Education Scholarship

Joseph Swift, a postdoctoral fellow in Professor Joseph Ecker’s lab, received a scholarship from the American Australian Association. As a plant biologist, Swift is driven to conduct research that can help mitigate the effects of climate change. Both Australia and the United States are facing drier futures. To help adapt agriculture, he will study how plants respond to water at the molecular level.

Wen Mai Wong named Damon Runyon Fellow

Wen Mai Wong, a postdoctoral fellow in Associate Professor Sreekanth Chalasani’s lab, was named one of 16 new Damon Runyon Fellows by the Damon Runyon Cancer Research Foundation. The prestigious, four-year fellowship encourages the nation’s most promising young scientists to pursue careers in cancer research by providing them with independent funding. Wong is using ultrasound to examine specific neurons and their impact on animal behavior and disease physiology, including the tumor microenvironment.

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26TH ANNUAL SYMPHONY AT SALK

Salk’s acclaimed annual concert under the stars and largest fundraiser of the year raised more than $1.1 million to support the Institute’s leading-edge research in the fields of aging, cancer, neuroscience, immunology, climate change, and more.

The event was held in the Institute’s iconic Courtyard on August 20 and featured a breathtaking performance by Tony, Grammy, and Emmy Award-winning singer Ben Platt and the San Diego Symphony, conducted by Sean O’Loughlin and presented by Joan and Irwin Jacobs.

The 26th Symphony at Salk was made possible by many generous sponsors, including Zenith sponsors Joan and Irwin Jacobs; Golden Sun sponsors Karen and Don Cohn and Daniel and Martina Lewis; and Supernova sponsors BioMed Realty, Rita and Brian Kaspar, Dr. Frederik Paulsen/Ferring Pharmaceuticals, and Mary Jane Salk.
WOMEN & SCIENCE: A DISCUSSION ON DIVERSITY AND MENTORSHIP

On November 2, the Salk Women & Science program held a special event to announce the 2022 Women & Science Research Award recipients and discuss the importance of diversity and mentorship. The event featured keynote speaker Lola M. Adeyemo, founder and CEO of EQI Mindset LLC, co-founder and COO of Sapient Logic LLC, and author of the book *Thriving in Intersectionality: Immigrants, Belonging, and Corporate America*.

**EVENTS**

**CONGRATULATIONS TO OUR 2022 SALK WOMEN & SCIENCE RESEARCH AWARD RECIPIENTS:**

ANNA GAUTHIER | Joseph Noel’s lab
Discovery of disease tolerance mechanisms for plant and global health

ANNA-MARIA GLOBIG | Susan Kaech’s lab
How the nervous system regulates immune cells called CD8+ T cells in viral infections and cancer

BRITTANY ELLIS JEWELL | Reuben Shaw’s lab
Metabolic regulation in colon cancer, Crohn’s disease, and colitis

CAROLINE JIA | Kay Tye’s lab
How social exclusion changes the way the brain and body respond to physical pain

YUENING LIU | Pallav Kosuri’s lab
How the organization of cells and their interactions affect the outcome of heart disease

MONIKA RAMOS | Daniel Hollern’s lab
Consequences of Lyme disease on cancer risk and behavior

JASMIN REVANNA | Rusty Gage’s lab
How brain cells called microglia contribute to Alzheimer’s disease

KATIA TROHA | Janelle Ayres’ lab
Methionine protects the brain against infection
Salk offers a wide variety of programs to inspire—and launch—the next generation of scientists. The Education Outreach program includes a Mobile Science Lab, Heithoff-Boody Scholars’ curriculum, and teacher training.

This group of highly engaged Visionary donors in the Chairman’s Circle provide the vital resources Salk needs to continue its tradition of excellence in science and support vital research.

Salk programs offer a range of ways to get involved. Learn about Salk science and support vital research.

EDUCATION OUTREACH
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CHAIRMAN’S CIRCLE
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INSTITUTE COUNCIL
This group of highly engaged individuals focuses on advancing Salk’s scientific initiatives and supporting groundbreaking discoveries.

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

PRESIDENT’S CLUB
The President’s Club helps recruit top-tier scientists, acquire cutting-edge technology, and embark on innovative research initiatives.

PARTNERS IN RESEARCH
Partners in Research invest like-minded people in the Institute’s world-renowned research, while connecting with top-tier scientists, acquire cutting-edge technology, and embark on innovative research initiatives.

SYMPHONY AT SALK
This annual concert under the stars features the incredible San Diego Symphony and a guest artist, while supporting the Institute’s world-renowned research and award-winning education outreach programs.

SALK WOMEN & SCIENCE
Showcasing the achievements of Salk’s women of science, this program welcomes community and business leaders interested in inspiring women to embrace scientific research personally and philanthropically.

SALK RECEIVES NUMEROUS COMMUNICATIONS AWARDS

Inside Salk (both print and online) and other Institute collateral garnered numerous accolades across a variety of awards during 2022. The Folio awards are among the most prestigious in the publishing industry, and the San Diego Press Club awards showcase San Diego’s best communicators in media.

Health Care Communicators of Southern California, Finest Awards

• Silver for Best Magazine Inside Salk Spring 2021

FOLIO EDDIE AND OZZIE AWARDS

• Single Article, Association/Nonprofit Medical Journal “How Computational Biology is Making Us Smarter” Inside Salk Winter 2021

• Website Design: Overall Salk.edu

DOT COMM AWARDS

• Gold for Website/Nonprofit Inside Salk.edu

Second Place

• Websites: Overall Use of Design Salk.edu

First Place

• Magazines: Feature Layou Design “Building a More Resilient World,” Inside Salk Fall 2021


• Television/Online Video: Video Editing “How Would You Change the Future?”

HEALTH CARE COMMUNICATORS OF SOUTHERN CALIFORNIA, FINEST AWARDS

• Silver for Best Magazine Inside Salk Spring 2021

PUBLIC RELATIONS SOCIETY OF AMERICA, SAN DIEGO AND IMPERIAL COUNTIES

Chavez Young Scholars’ Curriculum, Mobile Science Lab, Heithoff-Outreach program includes a

SPRING 2023

IMMUNOLOGY

• Silver for Best Magazine Inside Salk Spring 2021

JOURNALISM AWARDS

• Silver for Best Magazine Inside Salk Spring 2021

• Photograph: Still-Portrait “Flying into the Future with Kenta Asahina,” Inside Salk Spring 2022

• PR, PIO, and Trade Publications: Nonprofit Medical Journal “How the Brain Encodes Social Rank, and ‘Winning Mindset’”

• PR, PIO, and Trade Publications: Association/Member Publication Inside Salk Spring 2022

• PR, PIO, and Trade Publications: Newsletter Inside Salk Spring 2022 Newsletter

• PR, PIO, and Trade Publications: Press Release Writing “Serious Subject ‘How the Brain Encodes Social Rank, and ‘Winning Mindset’”

• PR, PIO, and Trade Publications: Special Interest or One-Time Publications “Campaign for the Future”

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VISIT US ONLINE AT: inside.salk.edu

Salk Institute has received the highest rating 11 consecutive times from Charity Navigator, the nation’s foremost charity evaluator.

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