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InsideSalk

SEEDS OF CHANGE

The Harnessing Plants Initiative is scaling a new kind of crop that could save the future of farming–and the planet.

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With spin-out company Cquesta, Salk's Harnessing Plants Initiative is scaling up—bringing Salk Ideal Plants® to fields around the world. These crops are optimized to draw down excess carbon dioxide from the atmosphere and store it underground for a longer time.

PRESIDENT'S LETTER

Dear Friends of Salk,

As we step into a new season of discovery and innovation, I am happy to share with you the latest issue of *Inside Salk*. This edition highlights some of the most exciting research happening at our Institute—work that has the potential to reshape our understanding of science and create lasting global impact.

The cover story features our Harnessing Plants Initiative, a bold effort to clean our air and improve crop resiliency by enhancing the natural ability of plants to capture and store carbon deep in the soil. This pioneering work leverages genetic advancements to develop crops with deeper, more extensive root systems—an approach that has the potential to significantly reduce atmospheric carbon levels. With the world facing an escalating climate crisis, Salk's nature-based solutions offer a hopeful and powerful means of intervention.

In parallel with our work in environmental sustainability, 2025 marks Salk's Year of Alzheimer's Disease Research. As one of the defining medical challenges of our time, Alzheimer's disease affects millions of individuals and their families, placing an immense emotional and economic burden on society. Despite decades of research, effective treatments remain elusive. But here at Salk, we are taking a bold new approach.

Our researchers are exploring the links between Alzheimer's and chronic inflammation—driven by genomic instability and dysregulated energy metabolism which may hold the key to unlocking new preventive strategies and therapeutic interventions. Unlike traditional research that has largely focused on amyloid plaques and tau tangles, Salk's scientists are widening the scope, examining the fundamental cellular and molecular processes that drive neurodegeneration. This shift is already yielding new insights that could one day lead to treatments that slow, halt, or even prevent the disease. On page 34, postdoctoral researcher Irene López Gutiérrez shares what it's like to be a part of this shift, as she and her colleagues use Salk's new research models to better understand inflammation in the aging brain.

Science at Salk thrives because of you, our generous donors and supporters who believe in the power of discovery. Your investment in our work enables us to push the boundaries of knowledge, take risks, and accelerate breakthroughs that will benefit humanity for generations to come. Whether it is through our efforts to combat climate change or our quest to defeat Alzheimer's, your partnership is making an impact where it matters most.

As we continue our mission to advance science for the betterment of society, I invite you to engage with us—through philanthropy, advocacy, or simply by sharing our vision with others who believe in the power of research. Together, we can harness the power of biological discovery to build a healthier, more sustainable world.

With gratitude,

Gerald Joyce Salk Institute President



"As one of the defining medical challenges of our time, Alzheimer's disease affects millions of individuals and their families, placing an immense emotional and economic burden on society. Despite decades of research, effective treatments remain elusive. But here at Salk, we are taking a bold new approach."

IN THE NEWS



MICHELLE CHAMBERLAIN

Michelle Chamberlain named Salk's new Vice President of External Relations

Michelle Chamberlain assumed the role of Salk's Vice President of External Relations on April 2.

In this role, Chamberlain serves on the Institute's Executive Leadership Team and oversees all fundraising efforts, communications, community engagement, education outreach programs, foundation relations, and stewardship activities. "Michelle brings a wealth of experience, energy, and vision to this role," says Salk President Gerald Joyce. "She is well-known for her ability to inspire confidence and build strong, lasting donor relationships. Her unique approach and passion for our mission mark the beginning of an exciting new era in our fundraising efforts, one that will enhance our capacity to do what we do best: high-impact science. I'm also grateful to members of Salk's Board of Trustees Executive Committee, Executive Leadership Team, Academic Council, and Office of Community & Engagement for providing valuable input throughout this recruitment process."

Since 2008, Chamberlain served in various leadership roles at Claremont McKenna College in Claremont, California, where she was most recently Vice President for Advancement and Student Opportunities and Dean of the Robert Day Scholars Program. In her VP role, she led a fundraising campaign that surpassed the original goal of \$800 million, ultimately raising more than \$1 billion in eight years—a national record among liberal arts colleges.

"I am honored to join the Salk Institute and contribute to its world-renowned mission of groundbreaking scientific discovery," Chamberlain says. "I am incredibly grateful for my years at Claremont McKenna College, where I had the privilege of working alongside dedicated colleagues and inspiring students. The experiences and relationships I built there have profoundly shaped my approach to leadership and philanthropy. I look forward to bringing that same spirit of collaboration and innovation to Salk as we advance its vital work."

Prior to Claremont McKenna College, Chamberlain was an attorney at O'Melveny & Myers, LLP in Los Angeles. She earned a Bachelor of Arts from the University of Southern California, a Master of Arts in education from Claremont Graduate University, and a Juris Doctor from Southwestern Law School.

Trustee Richard A. Heyman donates \$4.5 million to enable early-stage innovative research

Richard A. Heyman, a member of the Salk Institute's Board of Trustees, and his wife, Anne Daigle, have donated \$4.5 million to establish the new Richard A. Heyman Collaborative Innovation Fund to support Institute faculty on collaborative, early-stage studies aimed at big, bold questions.

The fund will support research that is often deemed too early, risky, or unconventional for traditional grant funding. Instead, the Collaborative Innovation Fund will enable Salk's researchers to pursue pioneering ideas, foster collaboration, and unearth discoveries that address some of the most pressing challenges in biomedicine, including cancer, Alzheimer's disease, and autoimmune diseases.

"We are honored to receive this generous donation from the Heyman-Daigle Family Foundation," says Salk President Gerald Joyce. "Funds for early-stage studies with the potential to address unmet medical needs are vital to the Salk Institute's mission of advancing transformative science. By supporting innovation at Salk, we can continue to advance scientific discovery for the benefit of all."

> "This Collaborative Innovation Fund combines essential aspects of discovery: fresh scientific perspectives, bold questions, and collaboration amongst the faculty members."

> > **RICHARD HEYMAN**

The new Collaborative Innovation Fund will create opportunities for interdisciplinary collaboration by providing resources that encourage scientists from different fields to work together on complex problems. To be eligible, projects must involve at least two labs working together on novel ideas with the potential for high impact. Grants will be awarded through internal competition, overseen by a Scientific Advisory Board.

Salk has a successful history of using this type of innovation seed funding to spur new discoveries. For example, similar early-stage support made it possible for Salk Professor Sreekanth Chalasani to invent sonogenetics, a technique that uses ultrasound to manipulate neurons, paving the way toward noninvasive deep brain stimulation, cardiac pacemakers, and insulin pumps.

"At Salk, I learned that you have to ask big questions if you want big answers," Heyman says. "This Collaborative Innovation Fund combines essential aspects of discovery: fresh scientific perspectives, bold questions, and collaboration amongst the faculty members. These combinations should allow us to uncover groundbreaking solutions that will improve the world for generations to come."



DISCOVERIES















INSIDE SALK SPRING 20





The lab experiments of today often inspire the therapeutics of tomorrow. But translating a discovery into a new treatment means overcoming the hurdles of drug development, clinical trials, and FDA approvals. At times, the finish line can feel quite far away. But like the initial sprint in a relay, basic science is the crucial first leg in the race to the clinic—without a powerful start, winning just isn't in the cards.

But now and then, our scientists get a chance to burst through the finish line, too.

While searching for new ways to treat diseases like cancer, diabetes, and neurodegeneration, our researchers can sometimes spot a way to speed things up. Rather than designing and testing a whole new drug to target the latest pathway of interest, Salk scientists are keen to explore the possibility that an existing drug may also do the trick. By thinking outside the box and finding new uses for old drugs, our researchers can potentially avoid the biggest obstacles and more quickly aid those in need.

Three recent Salk studies have done just that, each finding an exciting use for an existing drug that could take us straight to the finish line.

ANTIDEPRESSANTS COULD PROTECT AGAINST INFECTIONS AND SEPSIS

SCIENCE ADVANCES 02/2025 Antidepressants like Prozac are commonly prescribed to treat mental health disorders, but new research suggests they could also protect against life-threatening sepsis and

serious infections like COVID-19. Professor Janelle Ayres, postdoctoral researcher Robert Gallant, and colleagues have uncovered how these drugs are able to regulate the immune system and defend against infectious disease. They found that Prozac increased levels of an immune system molecule called interleukin-10 in mice, which led to reduced inflammation and prevented sepsisinduced heart failure. These insights could lead to a new generation of lifesaving medications and enhance global preparedness for future pandemics.



From left: Karina Sanchez, Janelle Ayres, Robert Gallant, Christian Metallo, and Emeline Joulia.

PUTTING A LID ON EXCESS CHOLESTEROL TO HALT BLADDER CANCER CELL GROWTH



Combining simvastatin (Zocor) with a PIN1 inhibitor may help slow or prevent the growth of bladder tumors.

CANCER DISCOVERY 01/2025 Bladder cancer is the fourth most common cancer in men, and, like all cancers, it develops when abnormal cells start to multiply out of control. But what if we could put a lid on their growth? Professor Tony Hunter, postdoctoral

researcher Xue Wang, and colleagues have discovered that PIN1, a protein first discovered in Hunter's lab in 1996, is a major driver of bladder cancer. They revealed that it works by triggering the synthesis of cholesterol—a lipid that cancer cells use as fuel to grow. After mapping out the molecular pathway between PIN1 and cholesterol, the researchers developed an effective treatment regimen that halted tumor growth in mice. The therapy consists of two drugs: sulfopin, an experimental PIN1 inhibitor, and simvastatin, a statin that is already commonly used in humans to lower cholesterol levels and reduce the risk of heart disease.

BILE ACIDS EXACERBATE LIVER CANCER, DIETARY SUPPLEMENT MAY OFFER RELIEF

SCIENCE 01/2025 Immunotherapy has made an incredible impact on treating cancers of the lung, kidney, and skin—but for liver cancer, the treatment has been much less effective. To understand why, Professor Susan Kaech, postdoctoral researcher Siva Karthik Varanasi, and

colleagues took a closer look at how the immune system and liver interact. They discovered that certain bile acids in the liver were affecting the activity of cancer-fighting immune cells called T cells. But while many of these bile acids were impairing T cell function, one specific bile acid, called ursodeoxycholic acid (UDCA), was actually *boosting* their activity. And when mice were given a UDCA dietary supplement, it was enough to control liver tumor growth. Since UDCA is already available as a generic medication, the researchers are hopeful that it could be incorporated into liver cancer treatments to make immunotherapy more effective for these patients.



A scientist carrying supplements—like UDCA—climbs a ladder toward a liver containing a bile acid-surrounded tumor.



NEUROSCIENCE

Neuroscientists discover how the brain slows anxious breathing

NATURE NEUROSCIENCE 11/2024

Deep breath in, slow breath out... Isn't it odd that we can self-soothe by voluntarily slowing down our breath? Humans have long used slow breathing to regulate emotions, but scientists had yet to understand how

the brain consciously controls our breathing and whether this actually has a direct effect on our anxiety and emotional state. Associate Professor Sung Han, senior research associate Jinho Jhang, and colleagues have now, for the first time, identified a specific brain circuit that regulates voluntary breathing. Using mice, the researchers pinpointed a group of brain cells in the frontal cortex of the brain that connects to the lower brainstem, where vital actions like breathing are controlled. Their findings show that this neural pathway allows us to coordinate our breathing with our current behaviors and emotional state. Han says new therapeutics designed to target these brain cells could help prevent panic and hyperventilation in anxiety and post-traumatic stress disorders.

"By uncovering a specific brain mechanism responsible for slowing breathing, our discovery may offer a scientific explanation for the beneficial effects of practices like yoga and mindfulness on alleviating negative emotions, grounding them further in science."

ASSOCIATE PROFESSOR SUNG HAN



Boosting this molecule could help retain muscle while losing fat

About one in eight adults in the US has tried or currently uses a GLP-1 medication, and 40 percent of users cite weight loss as their main goal. But weight loss doesn't discriminate between fat and muscle. Patients using GLP-1 drugs can experience rapid and substantial muscle loss,

accounting for as much as 40 percent of their total weight loss. So how can we lose weight without also losing critical muscle? Professor Ronald Evans, postdoctoral researcher Hunter Wang, and colleagues discovered that a protein called BCL6 is key to maintaining healthy muscle mass. The experiments showed that fasting led to lower BCL6 levels and reduced muscle mass and strength in mice, but increasing BCL6 successfully reversed these losses. The researchers suggest that pairing GLP-1 medications with a BCL6-boosting drug may help counteract unwanted muscle loss. Similar therapies could also be used to treat other populations prone to muscle loss, such as older adults and patients with systemic diseases like sepsis or cancer. The stomach sends hunger signals to the brain in the form of ghrelin (blue arrow), prompting the brain to send growth hormone to muscle tissue (pink arrow). In the foreground, a closer look at the muscle reveals growth hormone (pink orbs) influencing BCL6 (purple mass) to attach to the cell's DNA (purple chain) and regulate genes involved in muscle growth.



Standing from left: Weiwei Fan, Kyeongkyu Kim, Lillian Crossley, Gabriela Estepa, and Satoshi Ogawa. Sitting from left: Ronald Evans and Hunter Wang.



PLANT BIOLOGY

Plant cells gain immune capabilities when it's time to fight disease

NATURE 01/2025 Human bodies defend themselves using a diverse set of immune cells that circulate from one organ to another, responding to everything from cuts to colds to cancer. But plants don't have this luxury. Because plant cells are immobile, each cell is forced to manage its own immunity on

top of its many other responsibilities. How these multitasking cells accomplish it all—detecting threats, responding to them, and warning others—has remained unclear. Research from Professor Joseph Ecker, postdoctoral researcher Tatsuya Nobori, and colleagues reveals that when plant cells encounter a pathogen, they enter a specialized immune state and temporarily become PRimary IMmunE Responder (PRIMER) cells, a new cell population that acts as a hub to initiate the immune response. The researchers also discovered that PRIMER cells are surrounded by another population of cells they call bystander cells, which seem to be important for transmitting the immune response throughout the plant. The findings bring us closer to understanding the plant immune system—an increasingly important task amid the growing threats of antimicrobial resistance and climate change, which both escalate the spread of infectious disease among crops.



Gene expression visualized in a section of a pathogen-infected plant leaf.



From left: Joseph Ecker and Tatsuya Nobori.



Section of a plant root showcasing the periderm and its carbon-capturing phellem cells.



From left: Charlotte Miller and Wolfgang Busch.

Two-in-one root armor protects plants from environmental stressors and fights climate change



Plants may burrow into the ground and stretch toward the sun, but they're ultimately stuck where they sprout—at the mercy of environmental threats like temperature, drought, and microbial infection. To compensate for their inability to up and move when danger strikes, many plants have evolved different ways to protect themselves,

such as building an armor called the periderm around their body and roots. Professor Wolfgang Busch, research scientist Charlotte Miller, and colleagues have debuted the first comprehensive gene expression atlas of the plant periderm at the single-cell level. The atlas provides new information about the different kinds of cells that make up the periderm and which specific genes control their development. This includes important insights into phellem cells, which are rich in suberin—a molecule that helps capture and store excess carbon dioxide from the atmosphere. Scientists can now use this information to stimulate periderm growth in plants facing environmental stress due to climate change. They can also potentially boost phellem cell genes to produce plants with enhanced carbon-capturing abilities—a central goal of Salk's Harnessing Plants Initiative.



Your immune cells are what they eat

SCIENCE 12/2024 The decision between scrambled eggs or an apple for breakfast probably won't make or break your day, but for your cells, a similar decision could determine their entire identity. Professor Susan Kaech, postdoctoral researcher Shixin Ma, and colleagues revealed new insights into the complicated

relationship between nutrition and cell identity. They found that the state of the immune system's T cells could be determined by which nutrient the cell was metabolizing. Switching from acetate to citrate could shift the cells from an active, disease-fighting "effector" state to an "exhausted" one. The findings reveal how different nutrients can change a cell's gene expression, function, and identity. They also suggest that new therapies could be designed to target these nutrient-dependent mechanisms to help T cells remain active in patients with chronic diseases like HIV or cancer.



From left: Susan Kaech, Shixin Ma, and Thomas Mann.

Symphony AT SALK

We invite you to step into a realm where science and culture converge in a celebration of human creativity. For a single night each year, the Salk Institute transforms its historic courtyard overlooking the Pacific Ocean—into a world-class concert hall under the stars, offering an experience as rare and groundbreaking as the discoveries made within its walls. The evening will unfold with a champagne reception, followed by a gourmet dinner and a performance by the San Diego Symphony, alongside Emmy® and Tony® award-winning actress and singer **Kristin Chenoweth**.

This is more than an event; it is a tribute to the brilliance that shapes our future. Please join us to support Salk science and revel in the transformative power of music. Sponsorships are available now. Individual tickets will go on sale starting June 2. Find the latest information at **symphony.salk.edu**.

FRONTIERS

SEEDS OR CHANCES

The Harnessing Plants Initiative is scaling a new kind of crop that could save the future of farming-and the planet. In a nation founded by farmers and scientists, agriculture has long been a symbol of American liberty, industry, and innovation. Thanks to early investments in research and technology, the United States has grown into an agricultural powerhouse, supporting millions of jobs and a large share of the global food supply.

Today, a new generation of farmers is inheriting the land and the responsibility that comes with it.

- "First and foremost, we have a lot of people to feed," says first-generation farmer Megan Freeman, "but as it stands, we don't all have the same access to healthy food. On the farm, we believe everyone has a right to high-quality, nutrient-dense produce. Everyone deserves that dignity."
- Freeman was one of the first graduates of the Sustainable Agriculture and Food Systems program at UC Davis. Ten years later, she's a full-time farmer and education manager at Coastal Roots Farm in Encinitas, California.

She and her colleagues have joined a long-standing agricultural tradition in Southern California. Most farms in San Diego County are multigenerational family farms, and the region boasts the highest number of part-time farmers in the country. Their work continues to be a major driver of the local and state-wide economy.



From left: Coastal Roots Farm in Encinitas, California; Megan Freeman, a first-generation farmer.

But like many California farmers, the Coastal Roots team is spending increasing time and resources protecting their crops from environmental threats.

"Our biggest challenge is the inconsistency of recent weather patterns," says Freeman. "The rain came very late this year, and when it does, it's intense. We have to pull farmers off their posts to go dig trenches and lay out sandbags to try to stop the floodwaters from washing away all our soil and crops."

Coastal Roots' farming practices are based on centuries of historical weather patterns, but recent changes are making it harder for both people and plants to time their activities.

"If the temperature spikes after we've planted our cool season crops, or our fruit trees blossom early and then get pummeled by rain and hail—that's a whole harvest lost in an instant," she says.

Heat waves and wildfires recently destroyed many fields and orchards in the region, leaving farmers to rely on government assistance programs to subsidize their losses. When the last decade of prolonged droughts forced California farmers to leave hundreds of thousands of acres of farmland unused, the economic impact was well into the billions of dollars.

Extreme weather events have similarly impacted farms across the Midwest and Great Plains. In 2022, federal crop insurance paid farmers a record \$19 billion for crop losses—a more than 500 percent increase from the \$3 billion spent in 2002. Still, only about half of all losses were covered by insurance, suggesting the actual damages exceeded \$30 billion.

That's why Coastal Roots Farm has committed to using sustainable farming practices that prioritize soil health, water efficiency, and crop resiliency. The farm is now celebrating its 10th anniversary, and its soil and harvests are only getting stronger.

"(When I first joined the farm,) we had a whole area that was just backfill from a housing development—it was not productive land," says Freeman. "The team started planting pioneer trees that add carbon and nitrogen to the soil, digging swales for water retention, and using our pasture-raised chickens to clear pests and fertilize the land. Now the soil in our food forest is super rich, and we're growing these giant pieces of chard that are bigger than your face."

Freeman also finds hope in her interactions with the many school groups that visit the farm each year.

"I think this younger generation understands that we have the power to make choices that can impact the environment positively or negatively," she says. "But if we want to encourage them to become the farmers of tomorrow, we need to make agriculture a more viable and sustainable industry today."

THE PROBLEM WITH CARBON

Weather patterns may be getting harder to predict, but the source of the problem is clear.

Humans have spent the last few centuries reshaping the land to meet their needs—clearing forests, paving over grasslands, and building energy systems that release carbon into the air. These actions have enabled tremendous progress, but they've also altered the natural balance that keeps our environment and food systems stable.

Today, there's more carbon dioxide (CO_2) in the atmosphere than at any other point in recorded history. This excess carbon has been trapping heat and shifting weather patterns for years. In the US, unpredictable harvests are already disrupting the economy and raising food prices. Around the world, subsistence farmers are at risk of losing their entire livelihoods. With the global population expected to increase sharply over the next few decades, the stakes are undoubtedly high.

Countries around the world have pledged to achieve carbon neutrality by the year 2050, but these efforts require substantial investment and mutual buy-in. Current industrial sequestration methods are also ill-equipped to capture and store enough carbon in time.

So the question is: Is there another way? Could we somehow grow crops that not only survive these environmental changes, but also help reverse them?

At the Salk Institute, a team of scientists is doing just that.



Harnessing Plants Initiative faculty from left: Joseph Ecker, Lena Mueller, Joseph Noel, Julie Law, Wolfgang Busch, Todd Michael, and Talmo Pereira.



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Plants retain carbon longer when their roots are larger, deeper, and richer in suberin—a cork-like compound that decomposes slowly. By enhancing these traits, Salk is creating crops that can capture atmospheric carbon and store it underground for centuries.

A NATURAL SOLUTION

Salk's Harnessing Plants Initiative is the world's leading program for plant-based carbon capture, built on decades of foundational research from the Institute's preeminent plant scientists.

The idea is deceptively simple: enhance plants' natural ability to absorb and store carbon as a way to clean the air and restore environmental stability.

But how do you turn up the dial on plant-based carbon removal? The secret lies underground.

When plants take in CO_2 for photosynthesis, they store the carbon molecules in their leaves, stems, and roots. A lot of that carbon is eventually released back into the air, but that doesn't have to be the case.

Plants can store carbon for much longer when their roots are 1) bigger, 2) deeper, and 3) richer in suberin—a cork-like plant compound that holds onto carbon and decomposes very slowly. By enhancing these three traits, Salk is developing plants that can store carbon deep underground for several decades or even centuries.

"What makes our approach so promising is its accessibility, scalability, and sustainability," says Salk Professor Wolfgang Busch, executive director of the Harnessing Plants Initiative. "Carbon capture factories use expensive machinery that will take a lot of time and resources to expand worldwide. With plant-based methods, we don't have to create a new industry or convince people to use a new technology, because farming already exists. We can scale carbon-capturing crops quickly and relatively cheaply, which is critical if we want to make an impact in time."

In 2017, Busch left the Gregor Mendel Institute in Vienna to co-found the Harnessing Plants Initiative with Salk scientists Joanne Chory, Joseph Noel, Julie Law, and Joseph Ecker. With early support from TED's Audacious Project, Hess Corporation, and the Bezos Earth Fund, the Initiative quickly grew into one of plant biology and agriculture's most ambitious efforts.

"We need food to live, and we need a healthy environment to produce food," says Andy Jarvis, director of Future of Food at the Bezos Earth Fund. "The beauty of carbon sequestration is that nature already has the tools. We just need to scale them up, and through science and modern technology, we can boost those processes."



SUSTAINABLE SCIENCE

Salk's approach is made possible by advances in plant genetics, genomics, and epigenetics.

The idea came together through their early experiments with thale cress, a mustard species commonly used in plant biology research. Chory and Busch discovered genes that could more than double the size and depth of the plant's roots, while Law and Noel were making progress on boosting its suberin levels. Encouraged by these results, the group wondered whether this could also be done in other plants.

The team has been conducting huge trials to explore the natural diversity of other crop species, searching for varieties that already have some of the characteristics they're looking for. Using the latest tools in plant and molecular biology, they can then identify the specific gene variants that produce these traits and transfer them to the next generation of crops.

The process is conceptually similar to the standard breeding techniques that farmers have long used to cultivate new crop varieties, but it's much more precise and efficient in practice (a major advantage when time is of the essence).



Top photo: Salk Ideal rice enters its first large-scale field trial in Palmira, Colombia, in partnership with CIAT. Bottom photo: Scientists tend corn at the greenhouse.

The team has already successfully identified more than 345 promising gene candidates for enhancing root mass, depth, and suberin content, far surpassing their initial goal of 50 genes per trait.

These genes are now being tested in several key agricultural species. The resulting carbon-capturing crops are called Salk Ideal Plants[®], and their catalog is quickly expanding.

"This field trial is a huge step forward for us. In the race to rescue air quality, food stability, and global public health, we clearly have the best shot of making an impact on a timescale that matters."

PROFESSOR WOLFGANG BUSCH

THE FIRST FIELD TESTS

The Harnessing Plants Initiative currently spans eight major crop species: rice, corn, wheat, sorghum, alfalfa, soybean, canola, and pennycress.

Salk Ideal versions of each crop are first planted in small laboratory growth chambers, where the researchers can evaluate whether each candidate gene is producing the desired trait. If a plant looks particularly promising, it's then advanced to the greenhouse stage, where it can be observed in a larger variety of soil and climate conditions. The most successful crop lines are finally tested in open field trials, where they must brave the elements across an entire agricultural season.

In their first five years of funding, the team has already developed 38 different Salk Ideal crop lines spanning five different species, each containing a different gene to enhance root size, depth, or suberin content.

In the fall of 2024, the Initiative reached another major milestone. The first translational field trial of Salk Ideal rice was launched in Palmira, Colombia, in collaboration with the International Center for Tropical Agriculture (CIAT).

More than half the world's population depends on rice as their primary source of calories. Studies have shown that growing rice and other staple crops at elevated CO_2 levels significantly reduces their protein content and critical nutrients like iron, zinc, calcium, and magnesium. If these grains become even 5–10 percent lower in iron and protein, developmental impairments, malnutrition, and anemia will increase to the point of a humanitarian crisis.

"This field trial is a huge step forward for us," says Busch. "In the race to rescue air quality, food stability, and global public health, we clearly have the best shot of making an impact at a timescale that matters."

HARNESSING PLANTS INITIATIVE BY THE NUMBERS



GLOBAL Collaborations



PLANT GENOMES SEQUENCED



GENE CANDIDATES IDENTIFIED



SALK IDEAL CROPS IN DEVELOPMENT



PAPERS PUBLISHED 2023–24



INSIDE SALK SPRING 202

PARTNERS IN PROGRESS

Salk scientists have teamed up with leading industry experts to accelerate the transition from **potential** to **tangible** impact.

In 2022, the Harnessing Plants Initiative helped launch Cquesta, a biotechnology spinoff company tasked with commercializing Salk Ideal Plants. With sites in La Jolla, Chicago, and St. Louis, Cquesta serves as the bridge between nonprofit research and the agricultural industry.

"Cquesta's mission is to turn these discoveries into real-world products that farmers can easily access," says Cquesta CEO Tim Ulmasov. "Our job is to work directly with agricultural businesses to make sure these crops are scalable, reliable, and profitable to them."

The business model works as follows: Research partners like Salk identify genetic strategies to enhance desirable traits in important crops. Cquesta's scientists then make these changes in specific crop varieties of interest—mainly proprietary seeds designed and owned by major seed companies. The resulting crops then go through multiple trials to confirm that the genetic enhancements preserve the original integrity of the plant while also boosting root systems and carbon sequestration.

Capturing carbon can be profitable to farmers in the form of carbon credits, and Cquesta supports farmers in calculating and reporting this benefit. But while incentivization programs do exist for certain crops, carbon credits can't currently drive business on their own. Farmers and seed companies are still most interested in traits that will directly support their crops, yields, and profits. Fortunately, the larger, deeper root systems of Salk Ideal Plants benefit farmers in many important ways.

"These stronger root systems don't just retain more carbon," says Ulmasov. "They also support soil health, absorb more water and nutrients, and help crops survive intense heat, droughts, and floods. That's why we're getting so much traction—these are agronomically meaningful traits."

"Cquesta's mission is to turn these discoveries into real-world products that farmers can easily access. Our job is to work directly with agricultural businesses to make sure these crops are scalable, reliable, and profitable to them."

CQUESTA CEO TIM ULMASOV



Cquesta's field trial of three new lines of Salk Ideal CoverCress.

Once these auxiliary benefits are fully validated, Cquesta will license the traits to major seed companies, who will then sell and distribute the enhanced seeds to their established networks of agricultural customers.

Ulmasov says tapping into these existing markets is the most efficient way of getting Salk Ideal Plants out to farmers across the world—and word is already spreading fast.

"We're getting a lot of interest," he says. "Major US seed companies are giving us their seeds to test these traits in. They haven't seen these kinds of traits before, and they recognize the novel opportunity. Having the Salk name behind us also gives them confidence in our approach."

Cquesta also launched its own field trial in Illinois this past fall, surveying three new lines of Salk Ideal CoverCress. Additional trials are being planned for 2025 while their staff make progress on new lines of corn, soybean, and canola.

When it comes to scaling this technology, Salk and Cquesta are aiming big. There are currently more than 1.4 billion acres of land across the world perfectly suited to grow Salk Ideal crops. That's a landmass the size of Australia that could be used to sequester carbon without having to change any land use or cultivation practices. When all is said and done, Cquesta is planning to achieve commercialized carbon removal at the gigaton scale.

THE FUTURE OF FARMING

With the next round of field trials in development, Salk scientists are getting a head start at advancing their techniques even further.

The team is developing a new software called RootGPT, an artificial intelligence platform that uses their massive datasets to better predict which genetic interventions will work best in different crop varieties, soils, and climate zones.

"Think of it as personalized agriculture," says Busch. "Instead of designing one-size-fits-all solutions, Root GPT will help us tailor our methods to the specific needs of each crop species and farming region. This will massively speed up the breeding process and help us get farmers the best plants in the shortest amount of time."

Speed and efficiency are constant priorities in Busch's leadership strategy. The other major factor on his mind is funding. With less than 2 percent of US federal funding going toward environmental and climate research, the Harnessing Plants Initiative will continue to rely on philanthropic support.

"In just five years, we have built the world's most advanced program for plant-based carbon capture," says Busch, "but that won't matter if we can't see our mission through. The next five years of research and funding will be what finally gets these plants to the farmers who need them. If we are successful, every human being on the planet will benefit."

It's easy to take science and agriculture for granted in a country that's historically invested heavily in both. Will future generations get to benefit from the same forward thinking?

"A healthy environment underpins a strong economy—it's as simple as that," says Jarvis, who facilitates Salk's strategic and funding support from the Bezos Earth Fund. "Investing in sustainable agriculture creates jobs, stabilizes rural economies, and protects the resources farmers rely on."

Imagine a future where fields of rice, wheat, and corn don't just feed the world—they help restore it. A future where crops are designed not just for yield but for nutrition, resilience, and renewal.

Thanks to the Harnessing Plants Initiative and its supporters, that future is no longer just an idea. It's already taking root.



Scan the QR code to donate to the Harnessing Plants Initiative today.

celebrating JOANNE

The Salk Institute recently honored the memory of Professor Joanne Chory, founding director of the Harnessing Plants Initiative (HPI). On March 19, which would have been her 70th birthday, the community held a celebration of her extraordinary life and accomplishments.

Chory passed away on November 12, 2024, at the age of 69 due to complications from Parkinson's disease. She was a beloved member of the Salk community, an influential advocate for environmental sustainability, and one of the greatest scientific innovators of our time.

"As we mourn Joanne's loss, we are also strengthening our resolve to achieve the ambitious goals she envisioned for HPI. Joanne's life was a testament to the power of curiosity, kindness, courage, and perseverance, and we will carry her spirit forward in all that we do. Everyone in HPI is more determined than ever to bring her vision to life, and I am confident we will succeed. We owe it to her and to the world."

HPI EXECUTIVE DIRECTOR WOLFGANG BUSCH

SPECIAL FEATURE

The day polio met its match CELEBRATING 70 YEARS OF THE SALK VACCINE



Seventy years ago, on April 12, 1955, a scientific breakthrough changed the course of public health and inspired hope worldwide. The polio vaccine developed by Jonas Salk and his colleagues was officially declared "safe, effective, and potent"—a moment heralded as a triumph of medicine over one of the most feared diseases of the 20th century.

"The most successful public health interventions are often overlooked or underappreciated—we take them for granted because you don't see what's not there," says Salk President Gerald Joyce. "The near-total absence of polio in the US over the past several decades makes it difficult for most of us to understand just how terrible it was and too easy to devalue the heroic efforts that went into eradicating it.

"On this anniversary, join us in remembering what polio took away from many families and communities, the hope and security that Jonas Salk brought us, and the value of vaccines to the past, present, and future of humanity."

On this milestone anniversary, here are some key things to know:

Polio was terrifying.

In the first half of the 20th century, poliomyelitis, or polio, struck fear into families around the globe. The victims of the disease—primarily children could face paralysis, lifelong disabilities, or even death. Several polio epidemics occurred between 1948 and 1955 in the US. The outbreak of 1952 was particularly devastating, claiming more than 3,000 lives and leaving another 21,000 people paralyzed. The sight of children in wheelchairs and iron lungs (large machines that helped them breathe) and of parents keeping their children away from public spaces like swimming pools and fairs underscored the desperation for a cure.

> From left: Louis Kahn and Jonas Salk engage in a discussion over the Salk Institute model.

Jonas Salk continues to be a hero to many.

Jonas Salk, then a young virologist and researcher, took on the challenge of defeating polio. Unlike other vaccine developers of the time, who experimented with live or weakened viruses, Salk pursued a vaccine based on killed poliovirus. This innovative approach—safer and simpler to produce—became the cornerstone of his work.

By 1954, Salk's vaccine underwent rigorous testing in one of the largest clinical trials in history. Nearly 2 million children, affectionately called the "Polio Pioneers," participated. When the announcement came in Ann Arbor, Michigan, on April 12, 1955, that the vaccine was both safe and effective, celebrations erupted across the nation. It was a day many compared to V-E Day or V-J Day, signaling victory in a battle against a relentless enemy.

BULLETIN

ADVANCE FOR USE AT 10:20 A.M. TODAY POLIO (TOPS 3) (ADVANCE) ANN ARBOR, MICH., (AP)-THE SALK POLIO VACCINE IS SAFE, EFFECTIVE AND POTENT, IT WAS OFFICIALLY ANNOUNCED TODAY. END ADVANCE JC919A 4/12

Bulletin clipping announcing the polio vaccine to be safe and effective.

Salk's decision not to patent the vaccine ensured its widespread distribution. This act of altruism exemplified his commitment to humanity. In the 1960s, Salk furthered his vision of advancing science for the public good by founding the Salk Institute for Biological Studies. Designed in collaboration with renowned architect Louis Kahn, the Institute continues to be a hub for life-changing research.







Bγ 1954, Salk's vaccine was tested in one of the largest clinical trials, involving nearlγ 2 million children known as the "Polio Pioneers."

The polio vaccine's impact still resonates today.

The introduction of Salk's vaccine led to an unprecedented drop in polio cases. In the US, the average annual number of cases plummeted from 45,000 before the vaccine to just 910 by 1962. Worldwide, polio cases have fallen by more than 99 percent since the vaccine's introduction, thanks to expanded immunization programs and collaborative global efforts. Today, polio is on the verge of eradication, a testament to the power of vaccines and public health initiatives.

The work of safeguarding humanity is never truly done.

Seventy years later, the success of the Salk vaccine serves as a powerful reminder of what science and collaboration can achieve. It also underscores the importance of global vaccination efforts in preventing disease and protecting public health. While polio has been nearly eradicated, the continued fight to eliminate the disease entirely reminds us that the work of safeguarding humanity is never truly done.

As we celebrate this landmark anniversary, let us honor Jonas Salk and all those who contributed to this extraordinary achievement. Their efforts not only conquered polio but also paved the way for future scientific innovations—at the Salk Institute and elsewhere—that save lives and bring hope to millions worldwide.

An artistic rendering on a Salk Institute chalkboard paying tribute to Jonas Salk.

OUR GREATEST RESPONSIBILITY /S TO BE GOOD ICESTORS.

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SPECIAL FEATURE

CELEBRATING 50 YEARS OF DISCOVERY Professor Tony Hunter's half-century legacy at Salk

Cancer biology pioneer honored at February 21 event

Tony Hunter first arrived at the Salk Institute in 1971 as a postdoctoral trainee from the University of Cambridge. He immediately embraced the Institute's collaborative culture and the Southern California lifestyle (and hairstyle!), forming lifelong connections with colleagues. Long hours in the lab were balanced with adventurous outings like desert camping and river rafting—hobbies he continues to this day.

SPECIAL FEATURE | TONY HUNTER

After two years at Salk, Hunter returned to Cambridge but soon found his prospects there lacking. Following a challenging year of living with friends and his lab burning down, he decided to rejoin Salk as an assistant professor in 1975.

"When I came back to Salk, I didn't have long-term plans or a clear vision for my career," Hunter says. "I never imagined I'd still be here 50 years later, but I'm happy with how things worked out. The collaborative and innovative spirit of the Institute keeps me inspired."

On February 21, Salk celebrated Hunter's 50 years as a cancer biology pioneer with a symposium titled "50 Years of Rafting the River of Life." The event featured lab alumni, colleagues, and other cancer research luminaries sharing their science, memories, and tributes.



Tony Hunter stands in front of a small sampling of his enormous collection of science and symposia T-shirts, displayed during his 50th anniversary symposium.

"Tony Hunter is a towering figure in science," says Salk President Gerald Joyce. "His discoveries have transformed cancer biology and led to therapies that have saved countless lives. His dedication, collaborative spirit, and brilliance have left an indelible mark."

In 1979, while studying tumor viruses in his Salk lab, Hunter serendipitously discovered a molecular switch that controls cell growth and division, known as tyrosine phosphorylation. It quickly became a landmark study in cancer biology.



Tony Hunter in a Salk lab, 198

"I never imagined I'd still be here [at the Salk Institute] 50 years later, but I'm happy with how things worked out. The collaborative and innovative spirit of the Institute keeps me inspired."

PROFESSOR TONY HUNTER

Hunter's research later revealed how certain tyrosine kinases, the enzymes that drive this switch, become overactive in cancers, spurring uncontrolled cell proliferation.

> Hunter's discovery inspired the development of more than 80 FDA-approved cancer drugs that target protein kinases. One of the most notable drugs in this class is imatinib, commonly known as Gleevec, which has transformed chronic myeloid leukemia (CML) from a fatal disease into a manageable chronic condition.

Over the decades, Hunter's research has spanned a remarkable breadth of scientific areas, from pancreatic cancer to DNA tumor viruses to protein phosphorylation and beyond. One recent Salk study builds on several decades of research in the Hunter lab. In 1996, Hunter's team discovered a protein called PIN1. Now, the team has uncovered how it drives bladder cancer development by increasing cholesterol production. Hunter's team

is now exploring drug combinations that can target PIN1 and reduce cholesterol to block bladder tumor growth (see page 6).

Beyond his scientific achievements, Hunter has mentored more than 100 trainees, many of whom have become scientific leaders. "I'm proud of the science we've accomplished, but also of the people I've trained and collaborated with," he says.



"Find something you're passionate about. Choose a problem where your success will make an impact. Science is a long journey, but if you follow your curiosity, you'll never be bored."

PROFESSOR TONY HUNTER

Known for his long beard, witty science-themed T-shirts, and extensive collection of handwritten notebooks, Hunter has helped define Salk's culture.

"Tony is not just a brilliant scientist but an incredibly generous and collaborative colleague," says Salk Professor Ronald Evans. "When I first arrived at Salk, Tony was the first person I met. He even lent me his car until I could get my own. He revolutionized cancer treatments, but what sets Tony apart is his willingness to share insights and tools, elevating the work of everyone around him."

Reflecting on Hunter's career, longtime colleague Salk Professor Emeritus Geoffrey Wahl is reminded of a famous quote by Jonas Salk—"Our greatest responsibility is to be good ancestors"—although Wahl recalls Salk saying "wise ancestors."

"Either way, Tony has always been both good and wise," Wahl says. "Despite his fame, he's humble and accessible. You can always ask him a question, and if he doesn't know the answer, he'll help you find it."

This is Hunter's advice to young scientists: "Find something you're passionate about. Choose a problem where your success will make an impact. Science is a long journey, but if you follow your curiosity, you'll never be bored."

Members of Hunter's lab pay tribute to his favorite hobby by "rafting" in the Salk Courtyard's River of Life water feature.

OBSERVATIONS PALLAV KOSURI Making magic out of molecules

Salk Assistant Professor Pallav Kosuri's work sounds like it's straight out of science fiction. A physicist-turnedbioengineer, Kosuri is developing nanoscale technologies that are on their way to transforming how we diagnose and treat diseases. But it's his choice of building material that is especially surprising—these mini-machines are made almost entirely out of DNA.

Kosuri's lab is using DNA to create a suite of biosensors, diagnostic tools, and drug delivery systems. He's even teamed up with NASA-engineer-turned-YouTuber Mark Rober to create the world's smallest NERF gun—a microscopic device modeled after a real toy gun, just three million times smaller. (Versatility is clearly a strong suit of the technique.)

Inside Salk sat down with Kosuri to hear more about his DNA designs and how they're bringing biology and medicine into the future.



When did you first become interested in science?

PK: I was one of those kids who devoured books encyclopedias, science fiction, fantasy, anything I could find. Science fiction was particularly magical for me. I loved the idea of alien technologies and discovering new worlds. At some point, it hit me that the "magic" of science fiction wasn't entirely fiction. The world around us—whether it's biology, physics, or technology—already operates like magic, and the key to understanding this magic is science.

That drive to "understand the magic" shaped everything. In high school, I thought I'd end up building rockets or particle accelerators because physics seemed like the ultimate way to explore the unknown. I was so inspired by the golden age of physics when scientists like Ernest Rutherford or Marie Curie could have an idea and conduct their own experiments, and their personal findings could change the course of history.

But over time, I came to see that I was actually living in a *different* golden age. These days nearly all the most transformative discoveries are happening in biology. A scientist can use a new tool and suddenly reveal something that totally changes the way we think about the nature of life. I realized I could make a much bigger impact if I applied my engineering skills to these questions in biology, and it's been an incredibly exciting journey ever since.

What part of your training most inspired the work you do today?

PK: It really started during my PhD. I came to the United States from Sweden as a Fulbright Scholar to work in biochemistry and biophysics, but after years of studying lasers and subatomic particles, I had a lot of biology to catch up on. Thankfully, I found an incredible mentor at Columbia University, Professor Julio Fernandez, who helped me find my footing in this new field between physics and biology.

Together, we studied how a spring-like protein called titin helps our muscles stretch and contract. To study this protein, we built a new kind of atomic force microscope that could measure and apply forces to a single molecule. Using this ultra-precise instrument, I could grab an individual titin molecule and measure its stiffness under different conditions. To my surprise, we discovered that certain chemical changes have a strong effect on titin's stiffness. What's more, changing the stiffness of this one protein could change the overall stiffness of the entire muscle. This discovery turned out to be very important for understanding how muscles work and how we can tune their mechanics. We can now use this information to study muscle conditions such as heart disease or design better robotics and artificial limbs. It was fascinating work, but while I was engineering these molecule-manipulating microscopes, I kept thinking, *Why are we building such massive machines to study something so small*? If we want to study molecules, why don't we build tools at the molecular scale? That question led me straight into the world of nanotechnology.

Why is nanotechnology so important?

PK: We've made huge advances in computer science by shrinking electrical circuits down to the microscopic level and then to the nanoscale. That's why our smartphones and other devices are so much smaller, faster, and more powerful. It's inevitable that nanotechnology will have a similar impact on biology. It's the direction that a lot of bioengineering is headed in.

In biology, nanotechnology lets us design devices that work at the same scale as the molecules we're trying to study and manipulate. Our cells are made of tiny molecular machines that work together in incredibly precise ways. If we want to truly understand biology or develop new medical solutions, we need tools that work at that scale. In the end, these new tools will also be much faster, cheaper, and more accessible than our current technologies.

How do you build machines out of DNA?

PK: DNA might seem like an unusual choice, but it's an incredible material for this purpose. It's relatively simple in structure yet highly programmable and very precise in its assembly. It's also 100 percent biocompatible and nontoxic. We use a technique called DNA origami to fold the strands into different shapes. Think of it like molecular LEGO. DNA is the building block, and we can design it to self-assemble into specific structures that carry out important functions with high efficiency.

How will this technology help advance health and medicine?

PK: There are so many potential applications, but I can share a few that we're especially excited about.

My lab is currently developing a range of DNA-based nanosensors, which are tiny devices that can detect molecules, electrical currents, physical forces—all sorts of things that scientists want to measure. They're super sensitive and extremely precise, so they have the potential to advance a lot of the research here at Salk.

For example, we know that nearly half of all adults in the US have high blood pressure, but how exactly does this pressure affect the heart? Which cells are most vulnerable to being damaged by this mechanical stress, and how can this lead to heart disease? To study this, we're developing a nanosensor that glows when it senses a certain amount of pressure. Our vision is to use such sensors to create a detailed map of how mechanical stress is distributed across the heart. Being able to measure these aspects of biology will help us better understand and treat many different diseases.

What's even more exciting is that these kinds of nanosensors can also be used as diagnostic tools. Imagine going to the doctor, and instead of having multiple vials of blood drawn and waiting days for the results, the clinicians only need to take a tiny sample and can analyze it instantly. And they're not just doing 1 or 2 or 10 different tests that the doctor specifically ordered. They're using thousands of different sensors at a time to give you a much fuller picture of your health. Most experts in the field of molecular diagnostics agree that this will be possible at some point in our future; my personal conviction is that DNA sensors will be the fastest way to get there.

But most importantly, because DNA-based sensors can detect single molecules, they can spot a disease before symptoms even appear. For example, a nanosensor would only need to find a single piece of viral RNA to detect an infection and could even identify the specific strain. This has huge implications, especially for cancer, for which early detection is so critical. If we could catch cancers when they're still just a few cells, we could dramatically improve treatment outcomes and save millions of lives.

We could also potentially use DNA origami to design better therapeutics. Instead of flooding the patient's body with a systemic drug, we could develop tiny drug-delivery systems that bring the medication directly to the specific cells that need it. This level of precision could make treatments more effective while avoiding all the unwanted side effects that can come with traditional therapies.

What excites you most about DNA origami?

PK: I think we're on the verge of a revolution in molecular diagnostics and medicine. The tools we're building with DNA origami will help transform how we detect and treat diseases. But beyond these clear applications, what excites me most is the unknown. When you start working on this scale—building devices out of molecules—you're opening an entirely new frontier of engineering. I mean, who would have thought that studying molecular mechanics would lead us to develop better cancer diagnostics? To paraphrase Jonas Salk, the possibilities are only limited by our imagination and our ability to work hard to turn those dreams into reality.



Left: A rendering of the DNA origami motor created by the Kosuri lab.

What excites me most is the unknown. When you start working on this scale—building devices out of molecules—you're opening an entirely new frontier of engineering."

ASSISTANT PROFESSOR PALLAV KOSURI



Why is Salk the right place for you to pursue this work?

PK: What really sets Salk apart is its focus on big, bold science. Everyone here is driven by Jonas Salk's vision of being "good ancestors." We all want to leave a legacy of discovery that truly benefits future generations. That ethos allows us to pursue high-risk, high-reward ideas—like using DNA to build molecular machines—that might not fit into traditional academic settings or receive sufficient federal funding.

Salk is also a unique institute because it doesn't confine researchers to a single discipline. Here, we don't have departments—we're encouraged to collaborate across fields. That's critical for my work because it sits at the intersection of biology, physics, and engineering. I can walk down the hall and talk to a cancer biologist, an immunologist, or a neuroscientist, and each conversation sparks new ideas and directions that no individual field could achieve alone.

What we've all come to recognize is that the biggest advances we can make stem from the cross-pollination of different disciplines, where everyone brings something to the table and the result is much greater than the sum of the parts.

It's just like biology, really. Most of nature is made of just four elements: oxygen, carbon, hydrogen, and nitrogen. You have these few well-defined things, but when you mix them together in the right way, the complexity that arises is beyond our wildest imagination.

It's magic—and that's what inspires my work here at Salk. $\textcircled{\textbf{S}}$



In September 2023, The Kosuri Lab at the Salk Institute collaborated with YouTuber@MarkRober to use DNA origami to make the world's smallest NERF blaster. Scan the QR code to watch the video that has been viewed over 35 million times on YouTube.





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INSIDE SALK SPRING 2025

ASSISTANT PROFESSOR PALLAV KOSURI

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INSIGHTS Uprooting, replanting, and blooming again

In October 2024, the Salk Institute named Suzanne Page as its new Vice President and Chief Operating Officer. Page is a lawyer, a businesswoman, and a research executive. Before all that, she was a girl from Indiana.

"It was just your typical small-town Midwest upbringing where people knew each other. You would stay outside with the other kids until the streetlights came on—it was one of those neighborhoods."

Page is the daughter of Norwegian immigrants, who, according to Page, took a typical route into the US through Minnesota before finally settling in Indiana. Her childhood was marked by activity and adventure, with time spent in nature, rising through the ranks of her Girl Scout troop, or on the court perfecting her basketball shot.

Page has a strong background in key areas for Salk: research operations, finance, and legal in the for-profit and nonprofit sectors. From studying finance and law at Indiana University and traveling the world as a corporate lawyer

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to leading executive operations at scientific institutes in Miami, Vail, and San Diego—she's done it all.

Along the way, Page has cultivated a one-of-a-kind skill set in optimizing resources and helping organizations reach their goals. Now at Salk, her unique perspective will help the Institute's scientists do what they do best: make groundbreaking discoveries across the life sciences. As a key member of the Executive Leadership Team, Page leads administrative initiatives at Salk.

Following work and family

After law school, Page left Indiana and landed at Getty Images, where she served as senior vice president and general counsel for the world's leading provider of visual media. At Getty, she spent a lot of time acquiring other companies in the industry around the world and raising funds to make that happen.

Following Getty Images was Microsoft, where she served as the platform's business manager, handling licenses and "buy versus build" strategic decisions. Following this amazing opportunity, she was soon recruited by the University of Miami to create a new division in the School of Medicine, which also placed her closer to her family. She excelled quickly, taking a leadership role for all the university's campuses and participating in the purchase and integration of a new hospital, which became the top National Institutes of Health-funded organization in the state.

> Page's dealmaking and relationship-building brought her to her next opportunity: working with her university colleagues to build a biotechnology company that spun out of the university, Longeveron, Inc.

> > "The company founders trusted me to establish this biotechnology company from the ground up, which included building out research and development and manufacturing facilities, as well as leading clinical trials, finance, legal, and everything that goes with running a new business," explains Page. "I was humbled that the founder, one of my investigators from the university, selected me and believed in me to establish and help manage his company, which eventually went public."

> > > After 12 action-packed years in Miami, Page started a position as vice president of the Steadman Philippon Research Institute in Vail.

This also enabled Page, a lifetime skier and Colorado vacationer, to live closer to her sister and mother.

Like Salk, Steadman Philippon had unique needs related to its small campus and intimate atmosphere. Page managed its federal grants, clinical trials, and facilities, inadvertently shaping her skill set into a perfect match for Salk.

From slopes to surf

Page's move to Salk was motivated by the opportunity to help advance some of the world's best science.

"I knew immediately. My husband said I manifested this job," Page laughs. "There's a certain energy at Salk. I saw this framed handwritten letter from Francis Crick to his son, and I just thought this is such a special place. I am proud to be part of Salk and its amazing community."

By the time she arrived at the Institute, Page had more than 20 years of experience working with scientists. She says staying informed about the research has been key to supporting its development.

"I have enjoyed meeting with faculty one-on-one, learning about their science and touring their labs. Understanding what they do and how they do it is important to my success in fostering their science. We're here for the labs, and we have shared goals. When you have shared goals, strategizing and optimizing is easier for everyone."

Many dreams

Outside of work, Page's family takes precedence. She beams when she talks about them—especially her daughter, who is in her final year of college in Boulder, Colorado, studying business and data analytics. Her family also loves to travel, prioritizing trips that pull them outdoors for adventures like skiing or kayaking.

Page's work at Salk not only fulfills her dream but will fulfill many dreams as she helps the Institute's scientists get the resources and infrastructure they need to bring their ideas to life. S

Irene López Gutiérrez

AFTER EVERY STORM COMES SUNSHINE-AND SCIENCE

It was winter in Irene López Gutiérrez's seaside hometown in northern Spain, and yet another storm was pouring rain over the houses and streets, trapping everyone inside. With little else to do, 11-year-old Gutiérrez sat in front of the television, searching for something interesting to watch. Then, it happened.

"I found this **Spanish science** show where they interviewed researchers from all disciplinesbiologists, physicists, mathematicians," says Gutiérrez. "After that, I was really into scientists."

"Alzheimer's disease is not just something going on with your neurons—your immune system is also perturbed. But scientists are often trained to be very focused, very specialized. We need to step out of that to see the big picture and full complexity of the disease." —IRENE LÓPEZ GUTIÉRREZ

She may have been stuck indoors, but her mind was now traveling through nature, space, and time. When the storm clouds passed, Gutiérrez was still buzzing with curiosity.

Teachers nurtured her interest in science in the years that followed. Gutiérrez loved to learn, so she didn't narrow her sights onto any one field just yet.

Then, another dark cloud cast its shadow over her family: Her grandfather was diagnosed with a brain tumor.

"I spent a lot of afternoons watching him in his house because it's a very tough disease," says Gutiérrez. "Suddenly my grandfather couldn't see, couldn't hear, couldn't move, couldn't speak. I was losing him."

Gutiérrez helped care for her grandfather as he gradually lost his faculties and entered a vegetative state. Doctors warned he would only survive a few months longer. Instead, the family watched him live another three years.

"I remember my mother and uncles asking the doctors, 'Can he hear us? Does he know we're here?" Gutiérrez recalls. "That's when I realized how amazing and important the brain is, and I decided that I would study biology when I went to university."

> Gutiérrez was the first in her family to attend university. She specialized in biochemistry, looking to understand life at a molecular level. When it was time to join a lab, she decided on a neuroscience lab that studied Alzheimer's disease.

"I realized that I loved research," she says, "and I loved research in neuroscience."

After earning her bachelor's, Gutiérrez moved on to master's and doctoral degrees. She spent six years studying Alzheimer's at the Universidad Complutense de Madrid, supplementing her training with prestigious internships in Texas, Germany, and Belgium. She was never one to be confined, and her research soon expanded beyond the boundaries of neuroscience. She realized she was ready for a big move—a new place, with new perspectives. That place was Professor Susan Kaech's lab at Salk, where she now works as a postdoctoral researcher exploring the new frontier of neuroimmunology.

"Working with immunology experts in Sue's multidisciplinary lab has been immensely helpful," she explains. "Alzheimer's disease is not just something going on with your neurons—your immune system is also perturbed. But scientists are often trained to be very focused, very specialized. We need to step out of that to see the big picture and full complexity of the disease."

Gutiérrez is working to see that big picture using a new human research model of Alzheimer's disease.

"I used mouse models throughout my doctoral studies, so the human model is what really excites me now."

Working in collaboration with Salk Professor Rusty Gage's lab, Gutiérrez uses miniature models of the human brain, called organoids, to explore the differences between healthy brains and those with Alzheimer's disease. The team recently succeeded in adding immune cells to these organoid models, allowing them to observe how human brain and immune cells interact.

"For many years, we thought that the peripheral immune system couldn't enter the brain, since the brain has its own specialized immune cells," says Gutiérrez. "Now we realize there's a lot of communication happening between the immune system and our brain cells that we don't yet understand."

The researchers are now working to add larger functional immune systems to their brain organoids. Once these models are up and running, Gutiérrez has plenty of questions she'd like to answer.

"We get sick with infectious diseases throughout our lives. We know that can alter our immune system, but how might it also contribute to brain disease?" asks Gutiérrez. "We already have evidence that there's some accumulation of specific proteins in the brains of mice and humans with Alzheimer's disease. I want to find out what immune cells are doing there."

By looking at the brain through the lens of immunology, Gutiérrez and her colleagues are helping us understand neurodegeneration in a whole new way.

"Being a part of this neuroimmunology movement is very, very exciting," she says. "There's so much knowledge just over the horizon, and I cannot wait to get there." **S**

Hear more at www.salk.edu/podcast.



Luddy founded ServiceNow, a leading intelligent platform driving end-to-end digital transformation. Under his leadership, ServiceNow became the fastest-growing enterprise software company to achieve more than \$10 billion in annual revenue organically. Today, Luddy continues to innovate as a technology visionary, focusing on projects to revolutionize spreadsheets and improve the diagnosis and treatment of rare genetic diseases in children.



FRED LUDDY

"Fred's innovative spirit and experience in technological advancement align well with Salk's mission to advance high-impact science, especially our ambitions in biocomputation," says Salk President Gerald Joyce. "We are excited to welcome him to our Board and look forward to the unique perspective he will bring."



DETLEF WEIGEL

Plant geneticist Detlef Weigel named Salk Nonresident Fellow

As a Nonresident Fellow, Weigel joins a group of eminent scientific advisors who guide the Institute's leadership. Weigel is a director and scientific member at the Max Planck Institute for Biology Tübingen in Germany and a former Salk faculty member. He uses genomic techniques to study developmental and evolutionary plant biology.

Innovation and Collaboration Grants

Salk's Innovation Grant Program was launched in 2006 by then-Board chair Irwin Jacobs and his wife, Joan. These grants are designed to fund unconventional and forward-looking ideas that don't fit the mold of more traditional funding sources. The Collaboration Grant Program was launched in 2019 to foster new collaborative efforts between Salk scientists. Inspired by the success of the Innovation Grant Program, these awards support team-science approaches for tackling important challenges, laying the foundation for large research grants.

Three new Innovation and Collaboration Grants were recently awarded: Salk President **Gerald Joyce** and Associate Professor **Dmitry Lyumkis** have proposed a new method to capture, for the first time, how RNA remodels itself through evolution; Assistant Professor **Daniel Hollern** is developing an innovative strategy to help the immune system recognize tumor cells by prompting B cells to release anti-tumor antibodies that can mark the cells as cancerous; and Research Professor **Todd Michael** is generating plant artificial chromosomes that hold hundreds to thousands of genes to revolutionize scientists' ability to address fundamental questions about plant evolution—a critical line of inquiry as Salk researchers work to improve crop plant stability and resilience in the face of climate change.





GERALD JOYCE

DMITRY LYUMKIS





DANIEL HOLLERN

TODD MICHAEL



JOSEPH ECKER



SATCHIN PANDA



RONALD EVANS



REUBEN SHAW



RUSTY GAGE



KAY TYE

Seven Salk scientists named among most highly cited researchers in the world

Professors **Joseph Ecker**, **Ronald Evans**, **Rusty Gage**, **Satchin Panda**, **Reuben Shaw**, and **Kay Tye**, as well as research assistant **Joseph Nery**, were named to the Highly Cited Researchers list by Clarivate. The 2024 list included 6,636 researchers from 59 countries who have demonstrated "significant and broad influence in their fields of research," as reflected by their publication of multiple papers over the past decade that rank in the top 1 percent by citations for their fields.



JOSEPH NERY

SPOTLIGHT



RUSTY GAGE

Professor Rusty Gage received 2024 Ogawa-Yamanaka Stem Cell Prize

Gladstone Institutes selected Gage for his pioneering work in stem cell biology of the central nervous system, which he studies using reprogrammed cells to help scientists understand age-related neurological diseases and psychiatric disorders. He was celebrated in a ceremony last December, where he received \$150,000.

Professor Tony Hunter honored with 2024 Prince Mahidol Award

Awarded this year in the field of medicine, Hunter joined the prestigious list of 94 individuals who have earned the prize over the past 31 years—several of whom have gone on to earn Nobel Prizes. The award is given by the Prince Mahidol Award Foundation, which annually awards individuals and institutions with "outstanding and exemplary contributions to the advancement of international medical and public health services." Hunter received a medal, certificate, and \$100,000 prize.



TONY HUNTER



Tony Hunter visits Bangkok, Thailand, to receive the Prince Mahidol Award.

Professor Ronald Evans received 2025 Kimberly Prize and Rolf Luft Award

Evans was awarded the 2025 Kimberly Prize from the Northwestern University Feinberg School of Medicine and the Simpson Querrey Institute for Epigenetics, as well as the 2025 Rolf Luft Award from the Karolinska Institute in Sweden. Both awards pay tribute to his discovery and functional characterization of the superfamily of nuclear hormone receptors. This work was hugely impactful in uniting the field of endocrine physiology and led to the development of new drugs to treat leukemia, liver disease, inflammation, type 2 diabetes mellitus, cancer, and more.



RONALD EVANS



President Gerald Joyce elected honorary member of the Royal Irish Academy

Founded in 1785, the Royal Irish Academy serves to advance learning and scholarship in Ireland. Among the Academy's duties is to recognize outstanding research achievements and promote awareness of the positive impact science has on our lives. Joyce will now be a part of this mission and will be formally inducted at a ceremony in Dublin.

EVENTS

Biotech Sisterhood

On November 5, 2024, Biotech Sisterhood, a group of female CEOs in the biotech industry, gathered for a panel at Salk to share their journeys through the STEM pipeline, followed by a networking lunch. The panel featured Nancy Whiting, cofounder, president, and CEO of NextRNA Therapeutics; Dominique Verhelle, president and CEO of Recludix; Kay Watt, director of program management for Salk's Harnessing Plants Initiative; and Deepshika Ramanan, assistant professor and reproductive immunologist at Salk. By bringing together varied perspectives and experiences, we not only celebrate the achievements of women in science but also inspire the next generation to pursue their passions in STEM fields.



From left: Deepshika Ramanan and Nancy Whiting







← Salk Women & Science

The annual Salk Women & Science Awards empowers the next generation of leaders, innovators, and visionaries in the scientific community. With \$175,000 in funding generously provided by the program, these awards provide critical support for travel, research, and childcare or in-home care needs for early-career scientists. On November 8, 2024, we honored the following awardees based on innovation, impact, and alignment with the program's goals:

Jessica Arzavala, Margarita Behrens' lab

How viral infections during pregnancy can affect perinatal brain development

Lara Labarta-Bajo, Nicola Allen's lab

The long-term effects of infection: How inflammation in the body contributes to brain aging and motor decline

Deryn LeDuke, Kay Tye's Lab

Do dieting and exercise influence emotional processing differently in men and women?

Ayesha Rustom Thanawalla, Eiman Azim's lab The effects of anxiety on movement and coordination

ightarrowLunar New Year

On January 29, 2025, the Asian, Pacific Islander and Desi at Salk (APIDAS) affinity group hosted a special event to usher in the Year of the Snake. Attendees enjoyed delicious food, a live Southern Sea Dragon performance, an interactive calligraphy station, a wishing tree to manifest good luck in the new year, and trivia to learn more about Lunar New Year traditions.

"Lunar New Year is important to me because it is a time when family gathers, near and far, to create new memories," said Pek Sze Baird, Salk's events operation supervisor. "As an immigrant, I understand the longing that comes with not being able to go home every year to celebrate with loved ones. This makes it even more rewarding to experience this special occasion with my fellow Salkies. By bringing [a] Lunar New Year event to campus, it feels like I'm home for it, and I am grateful to share this tradition with others."





Listen to all-new episodes of Salk's podcast: **Beyond Lab Walls**

In Salk's Year of Alzheimer's Disease Research,

we're sitting down with the experts on brain aging and sharing their latest discoveries with you. In two new episodes, hear how Salk scientists are getting to the root of Alzheimer's and why postdoctoral researcher **Irene López Gutiérrez** (page 34) is listening in on conversations between immune cells and the brain. Subscribe and stay tuned to learn more about Salk's bold new approach to studying Alzheimer's. BEYOND LAB WALLS a Salk Institute podcast

Beyond Lab Walls is a production of the Salk Office of Communications and can be heard on Apple and Google podcasts, Stitcher, Spotify, or anywhere you listen to podcasts.



Scan the QR code to visit www.salk.edu/podcast.

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