The power to...
Leverage diversity to improve health span

It’s not enough simply to live longer; we want to live healthier. And that will take an investment in research that examines diverse influences on aging at every level—from molecular drivers to lifestyles and the environment.

The challenge
Aging is one of life’s most complex puzzles. For different people, aging has different consequences. For some, their golden years may be disrupted by cancer, diabetes, heart disease, neurodegenerative disorders or any number of conditions. Yet other people seem more resilient, gliding through their elder years healthy and fit. This is not necessarily luck. There are biological and environmental factors that keep some people more resistant to disease as they age.

Salk researchers are deeply committed to figuring out how these resilient cellular circuits operate and to finding ways to keep them running smoothly. They are focused on improving both life span (living longer) and health span (living free from disease) so people can have more healthy and productive years.

This is critically important work. And yet aging research has historically been approached with tunnel vision, each discipline studying the issue in a silo. For some, their golden years may be disrupted by cancer, diabetes, heart disease, neurodegenerative disorders or any number of conditions. Yet other people seem more resilient, gliding through their elder years healthy and fit. This is not necessarily luck. There are biological and environmental factors that keep some people more resistant to disease as they age.

The Salk approach
In Salk’s Paul F. Glenn Center for Biology of Aging Research and the collaborative San Diego Nathan Shock Center, scientists are working to better understand how each individual’s aging process is driven by their unique biology, background, environment and lifestyle. This approach will allow scientists to target these drivers of aging with personalized interventions to improve resilience and increase health span.

To achieve this, we are diversifying the way we think about aging. We are shifting research programs to better account for the diversity of environments in which we live; diversity in the gender, racial and ethnic backgrounds of the people we study; diversity in lifestyle; and diversity in the molecules we consider drivers of aging.

New health span-enhancing interventions that arise from our research must work for everyone, not just the privileged few.

Empowering diversity in: molecular drivers of aging. Over the past 50 years, researchers around the world have been investigating the various biological mechanisms that contribute to aging. Some may play a bigger role in driving aging and health span for some people than others, but all are intertwined. Here are just a few molecular drivers of aging studied by Salk scientists:

- **DNA damage** accumulates while cellular repair mechanisms slow, contributing to cancer and other conditions that become more common with age.
- **Epigenetic** changes are chemical modifications cells make to chromosomes, not altering the DNA sequence itself but determining which genes are turned “on” or “off” at a given time. These switches can be influenced by environmental exposures, diet and many other factors, and in turn, they may determine how cells behave, how organs function and, how disease develops.
- **Telomeres**, the protective DNA caps at the end of chromosomes, get shorter over time, with each cell division. When telomeres get too short, cells cease to divide or even die, profoundly affecting neighboring cells and the whole body.
- **Mitochondria**, the body’s all-important cellular power plants, become less efficient as cells age, thereby affecting the whole body.
- **Inflammation** becomes widespread throughout the body, affecting many organ systems and influencing virtually every age-related disease.

None of these mechanisms work alone. There is constant crosstalk, which can make bad situations worse. However, by understanding these mechanisms, we are better equipped to find ways to control them and lengthen our health span.
Empowering diversity in: gender, racial and ethnic backgrounds.
Science must work for everyone, not just those with the privileges that allow them to participate in research. We must work to build trust in science and increase accessibility to both participation in research, and the ultimate benefits.

At the Salk Institute, this means proactively seeking human research samples—biopsies, for example—from a variety of sources. Even in mice, a ubiquitous research model, scientists have preferentially used males to reduce the number of variables in their work. Times are changing. The results may be more complex as we broaden our criteria for research models, but they'll also be more interesting and more broadly applicable.

Empowering diversity in: our environments. Like much of our health, the way our bodies age is influenced by our diets, abilities to exercise, the type of work we do, and our exposures to germs and environmental toxins. Yet historical, political and racial factors, rather than merely personal choice, have long determined who lives in the healthiest neighborhoods—those with more green space, better access to healthy foods, clean water, and less air and noise pollution—and who doesn't.

We believe these differences must be acknowledged and woven into every level of basic, translational and clinical research.

See the Salk approach at work
Aligning the environment and the body's clock to improve health span. Professor Satchin Panda studies circadian rhythms, the body's 24-hour biological clock. Because circadian rhythms govern how and when cells and tissues get repaired, these studies have great potential to promote health span.

To function normally well into old age, our organs need both sleep and a break from eating. Panda recently led a study to explore the effects of time-restricted eating—eating only in a 10-hour window—on the health span of San Diego's firefighters. Firefighters are at high risk for many chronic diseases because working and eating at all hours of the day disrupts their circadian rhythms.

This study and others have helped inform methods for circadian optimization—adjusting our lifestyles to collaborate with our internal clocks. Changing a few simple habits can reduce the risk of diabetes, cardiovascular disease, colon cancer and chronic inflammation. In addition to providing guidance for disease prevention, circadian rhythms might also be harnessed to help treat certain cancers, neurodegenerative conditions and other diseases.

Targeting molecular drivers of aging to prevent tumor formation.
In most labs, telomeres and mitochondria are studied as separate drivers of aging. But at Salk, Professors Jan Karlseder and Gerald Shadel have teamed up to explore crosstalk between the two.

Karlseder is an expert in telomeres, the protective DNA caps at the end of chromosomes. While short telomeres are associated with aging, Karlseder found that forcing cells to generate overly long telomeres can also be harmful, leading to stress and potentially cancer. Lengthening telomeres to reverse aging is not as simple as it might seem, his team concluded.

Shadel is an expert in mitochondria, the organelles that generate energy for cells. He's especially interested in reactive oxygen species, toxic by-products of the process by which mitochondria generate energy. These molecules are normally thought of as detrimental to cells, but his lab is finding they actually have a second function—triggering beneficial adaptive responses.

Now working together, Karlseder and Shadel have discovered that shortening telomeres kick off a cascade of molecular signals that reach the cell's mitochondria. These signals ultimately trigger inflammation and cell death. This way, aging and unstable cells with critically short telomeres are efficiently removed by the body, preventing them from becoming cancerous. Stabilizing this pathway could offer a new approach for preventing age-related cancers.

Why Salk
For more than 60 years, the Salk Institute has pursued Jonas Salk's vision of fearless, interdisciplinary science tackling some of the biggest challenges facing humankind.

One of the Institute's strengths is that each faculty member is a world expert in their specific discipline. Salk is home to leading biologists representing almost every known angle to aging and health span—cellular behavior and communication, telomeres, genomics, epigenomics, and mitochondria. What's more, the Institute's distinguished strength in the neurosciences provides the opportunity for special focus on age-related cognitive decline.

When this expertise is combined to address big-picture issues, incredible things can happen. For example, throughout much of the 2000s a team led by former Salk Professor Juan Carlos Izpisua Belmonte pioneered the use of stem cell reprogramming factors to regenerate tissues and reverse the aging process in mice.

Why now
In 2019 the Salk Institute launched the Campaign for Discovery—a seven-year, $750 million effort to accelerate Salk's critical research.

The Campaign is focused on driving discoveries in six Centers of Excellence: Cancer Center, Center for Healthy Aging, Center for Plant Biology, Center for Neuroscience, NOMIS Center for Immunobiology and Microbial Pathogenesis, and Crick-Jacobs Center for Theoretical and Computational Biology.

To continue to lead the field in these areas, Salk is recruiting new faculty and other experts, investing in new technologies, and creating new collaborative spaces, including construction of the Joan and Irwin Jacobs Science and Technology Center.

As it has always been at Salk, there will be no barriers between disciplines. New ideas from multiple areas can mix and flourish, generating the most innovative, multipronged approaches to redefining aging.

Join us
Science is a collaborative pursuit, and we invite you to join us in accelerating life-changing discoveries: www.salk.edu/campaign.