



CURALINK

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thecurafoundation.org

Welcome to CuraLink—a newsletter for innovators building a healthier future for all.

Dear Cura community,

Welcome back to CuraLink, a newsletter and interview series featuring the most pressing issues in human health, unmet medical needs and the emerging innovations and technologies directed to address them.

Last month, we spoke with visionary biotech entrepreneur Dr. Noubar Afeyan about the power of the immigrant experience and the five technologies that will revolutionize the next decade of medicine. Dr. Afeyan is the co-founder and chairman of Moderna and founder and chief executive officer of Flagship Pioneering.

This month, we are fortunate to speak with leading researcher and physician [Eric Verdin, MD](#), president and chief executive officer of [The Buck Institute for Research on Aging](#) and a professor of medicine at the University of California, San Francisco, on the state of aging science.

Based on existing data, Dr. Verdin believes it is possible for most people to live to 95 years of age free of age-related diseases like Alzheimer's and cancer. Read on to learn how scientists are making this goal a reality.



Robin L. Smith, MD
*Founder, President and Chairman,
Cura Foundation*

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A conversation with Dr. Eric Verdin

Aging is an inescapable fact of life—our skin wrinkles, joints ache, arteries stiffen and bones hollow as the years go by. But aging expert [Dr. Eric Verdin](#) says it may be possible to slow or even reverse aging and its cascade of negative health effects in the near future—all with simple and accessible lifestyle changes.

In the next two decades, Dr. Verdin predicts another 10 to 20 years could be added to our lifespan. By identifying and harnessing biomarkers of aging to develop novel therapies, Dr. Verdin hopes to add quality to those extra years, enabling people to remain active and engaged later in life.

This month, Dr. Verdin outlines the three most effective anti-aging practices, how we might tweak the molecular levers of aging to live healthier longer, as well as ways to alleviate the looming aging crisis.

It's an essential conversation for everyone, no matter their age.



Eric Verdin, MD, President and Chief Executive Officer of The Buck Institute for Research on Aging and Professor of Medicine at the University of California, San Francisco

What sparked your interest in studying aging and aging-related disease?

Like the best things in life, it happened by chance. I spent much of my career in two fields: I was trained as a physician with a sub-specialization in endocrinology and metabolism, but I also studied virology. Through the work we were doing on HIV, we ended up cloning the genes for a family of proteins (discovered by someone else) that play a role in aging.

The whole field of aging changed in the 1990s. I felt that we had been given a gift—we had expertise in a family of proteins that plays a big role in aging and that everybody was interested in. At that time, I started slowly switching my lab to working almost full time on aging and this is what we have been doing for the last 20 years.

What is your ultimate vision or hope for the field of aging?

We have a big vision. In the last 150 years, our lifespan has increased from around 40 to around 80—a doubling of lifespan compared to our ancestors. The problem is that extended life does not come with the quality that many people would expect.

When I ask people: Do you want to live to 110 or 120? Most people will say no. We envision aging as a time of suffering, pain, disease and illness. We have some evidence from our work in the lab that aging does not have to be like this. We are working on further extending lifespan. There is still a lot of potential for lifespan to increase at least another 20 or 30 years. But we want those years to be healthy and productive. Our tagline at the Buck is "Live better longer."

"We don't want to live older at all costs. We want to live better in good health."

Health care providers possess an arsenal of drugs to address age-related diseases independently. Why is there still a need for new approaches to these diseases?

The most exciting thing in the field is the realization that aging by itself is really closely tied to the disease of aging. Everyone knows this if you have seen your parents or your grandparents fall ill. What's not clear is why. Why is it that aging should lead to disease?

You can use the analogy to Newton who was not the first one to see that apples fell from trees. He was the first one to ask: Why are they falling? Realizing they were falling because of the force of gravity allowed him to build a new model of the universe.

Currently, we have a group of chronic diseases of aging, from heart attacks to macular degeneration to some cancers, that are being treated and looked at as individual entities. Medicine does a pretty good job at treating them, but it treats them as if they were independent occurrences, whereas we know that the underlying mechanism is aging. By understanding the molecular levers and the mechanisms by which aging is linked to



The Buck Institute

these diseases, we hope to allow people to live longer in better health. We think that by probing the question—what is it about aging that causes disease?—we're going to be able to change the course of human aging.

Now, what is the evidence that is making this possible? Centenarians, those lucky humans who live to 100, live on average 20 years longer than most of us. They also spend a much smaller fraction of their lives affected by diseases. Typical centenarians would start to be sick around 95 and then spend five years ill in the terminal part of their life. For the rest of us, we live to 80, and we start being sick around 65. So if you're looking at the delta of what we call the healthspan—the healthy years of life—it's between 65 and 95. That's 30 years of potentially healthy lifespan that we can gain. This is the focus of our work.

I'm excited about the future of the field, but when people ask me: How long are we going to live? It does not make any sense to talk about the lifespan of 150, because today we don't have any evidence that it is possible. I am confident, however, that we're going to be able to help most people live to 95 in good health. And that to me is exciting enough for today.

Can you share the origin story of the Buck Institute and how has it evolved since its founding?

We were the first research institute founded and established to study only aging. The instigator of this was a woman named Beryl Buck who was a nurse and lived in Marin County where we are located. She left part of her fortune in an endowment to create an institute focused on the biology of aging.

This was in the 1990s when people were thinking that aging was becoming a very different entity than what we thought it would be. Before this, aging was considered the same way we think about entropy. Nobody thinks that we're going to be able to fight entropy. Entropy is one of the two immutable laws of thermodynamics. The idea that aging is an irreversible process because it's a law of nature really changed in the 1990s when we began to look at aging as a regulated process for which we have levers. We can tweak it.

In the last couple of years, there has been a lot more talk about age reversal, which would have seemed a bit crazy 10 years ago. Now it's becoming our focus as well as many others in the field. The idea is that not only can you slow down aging, or age at different rates, but now you can reverse it. I think that's truly exciting.

For 20 years we have been studying aging using animal models—mice, fruit flies and other models—which allows work to be done very quickly, but the drawback is that you don't know if this is going to work in humans. It is now time to take all of these discoveries and bring them to bear in humans and start implementing this aging revolution. We hope the Buck Institute continues to be the leader in the area of translational biology of aging.

You've said in the past: "Science is showing that while chronological aging is inevitable, biological aging is malleable." How much of the aging process is dictated by lifestyle and environmental factors versus genetics? How much control do individuals have in influencing their longevity, and how much might we have in the future?

That's my favorite question, and it's probably one of the most important ones. Many of us have a somewhat fatalistic approach to our aging. People think: My parents died young, and therefore, I might as well enjoy life and have another cigarette or another glass of wine. Until recently, based on twin studies, people used to think that your lifestyle versus genetics split was about 80 percent lifestyle versus 20 percent genetics. But we've just discovered that some of these studies were flawed. A new study came out about two years ago based on studying the longevity of millions of people using ancestry.com. They found that it is 93 percent lifestyle and seven percent genetics.

"Genetics are not very important unless there is a centenarian in your family."

If you have a first-degree relative that is a centenarian, the likelihood you're going to live above 90 is extremely high. Frankly, many of these families who have a strong genetic influence on aging don't even have healthy lifestyles. They can do whatever they want.

For most of us, it's about lifestyle. The question is: what kind of lifestyle? The Buck is working on finding drugs that are going to increase lifespan and healthspan, but there are no drugs today that are proven to do this in humans. But certain interventions are showing the same effects: exercise, nutrition, sleep and stress management. At the Buck, we are studying the effects of these on the mechanism of aging. Everyone knows you should exercise. What's not clear is which type of exercise is benefiting your health or how much is necessary to optimize your lifespan and healthspan.

Currently, a big focus in the field of aging is identifying biomarkers of aging. Starting from the first point—aging causes disease and eventually death—how do you measure aging? You cannot intervene if you don't know what you are affecting. One way to do this is through a long-term clinical study that follows 10,000 people for 20 or 30 years. Those studies have shown that, globally, exercise makes you live longer. But I'm convinced that there are modalities of exercise that would take less time and create more benefits. If you had a biomarker of aging, that should allow you to recapitulate all of this work in a much shorter and more granular way. Instead of saying you should exercise, we could tell people if you walk 25 minutes a day, every day, here's what you can expect in terms of life expectancy.

Imagine taking this approach for exercise and bringing it to nutrition, sleep, stress management, meditation or yoga. Biomarkers of aging is an area that will help reveal the best modalities in the next five to 10 years.

Right now we just have glimpses. We're looking at a universe where we can recommend some things to people, but it's not very specific and the net result is that most people don't do it.

For example, look at an area like Marin County, which has one of the longest life expectancies in the country. You might ask why the county's average life expectancy is 87 years of age, which is 10 years higher than expected? The answer is it's a high-income county where many people exercise, have access to organic food and have strong family support. A lot of the social determinants of health are at work here. What excites me is the fact that living here, I know not everybody exercises and not everybody eats well, which tells me that we are reaching this number of 87 with only a fraction of the population being optimized toward their health. That makes me really optimistic that this initial goal of everyone living to 95 in good health is not a pipe dream. It's something that we can do, and it would be absolutely remarkable.

Is there a central question that most aging scientists are pursuing or one development that could blow the field open scientifically?

Imagine you have found a car and you don't even know what it's used for. So, you start taking it apart. And you find all of these pieces: computers, wheels, nuts, bolts, etc. This is where the field of aging is. We have taken the whole engine apart, but we don't understand how it works.

There are the hallmarks of aging—nine key modifications that are associated with aging: telomere attrition, genomic instability, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, abnormal proteostasis, deregulated nutrient sensing, epigenetic drift and altered intercellular communication. We have all of these pieces, but we don't understand how they fit together. We know that the engine is used to power the car, but we don't know how to start it.

We have all these pathways and the molecular understanding of how it happens. But we don't understand what is going to be the most effective therapy. What is the most effective aspect to target? What combination of drugs should we be contemplating?

There is still a need for some grand unifying theory that will pull all of this together.

What are the top three most effective anti-aging interventions people can use to age better and prolong their life? What are you doing personally day-to-day?

1. First, everyone should exercise, hopefully every day for a minimum of 20 minutes. Walk for 20 minutes every day, and it doesn't even need to be brisk. Regular everyday walking will suppress cancer, heart attacks, Alzheimer's disease and other chronic diseases of aging. The annual risk for all of these diseases is decreased by 40 percent

for someone who walks 35 to 40 minutes a day. If you can engage in even more vigorous activities, even better.

2. In terms of nutrition, which is probably the second most important along with sleep, many of us eat too much and we eat constantly. Most people get up at seven in the morning and eat their breakfast. They'll finish at 11 o'clock at night with a glass of milk, a nightcap, or a piece of chocolate. So they're essentially eating for 16 hours a day and fasting for eight hours a day. The evidence shows that doing exactly the opposite, fasting for 16 hours a day and eating for eight, improves your health. If you talk to most people in the aging field, almost everybody does it. It's called time-restricted feeding—the idea is restricting the number of hours that you are feeding during the day. Practically, it means you get up at seven, but you don't eat any food until noon. You can drink coffee without any sugar or cream. By noon, you have your first meal. By eight o'clock at night, you have to be finished except for water or tea.
3. Then there's sleep. Something amazing happened in the 1900s, with the advent of electricity and artificial lighting, further compounded by computers and telephones and televisions and tablets. Many of us are now stimulating our brain with light at times when light should be slowly diminishing. Light is the strongest inhibitor of sleep. As a society, it's estimated that 80 percent of people are chronically sleep-deprived. Personally, if I have a bad night and I sleep four or five hours, the next day I'm craving carbohydrates, all of my good resolutions go out, I'll have a glass of wine... I'll do all of the bad things.

At the end of the day, your brain controls your whole organism. It does not only help you think but also controls your digestion, immune system and all of your healthy decisions. So when people think about sleep, they say: It's okay. I can skip a night or I can sleep less, and I'll catch up on the weekend. But all the damage in between is done. In our lab, we see that just one month of sleep deprivation changes mice in an irreversible way. Chronic sleep deprivation leads to senescence—an irreversible state. The data concerns me, because it shows that with one month of chronic sleep deprivation, the senescence cell burden in mice increases significantly.

Having the amount of sleep that you need every day is critical for your brain to function well. When you do this, you feel wonderful, which is the other net result of all this.

Much of the research on fasting has included animals or male populations. Do the potential benefits extend to women despite their underrepresentation in the data pools?

The point that you're raising is important, because it turns out that many women do not respond to fasting the same way as men do. So there might be some tweaking that needs to be done. Going back to time-restricted feeding that I was discussing a minute ago. Most people can tolerate time-restricted feeding. If you are doing the opposite, *i.e.*, eating for 16 hours and fasting for 8 hours a day, you don't want to completely switch your diet in one day. I tell people to switch it an hour a day for a week and then continue doing this. Eventually, you're going to find yourself eating only for eight hours a day and feeling better.

The net effect of fasting is that it triggers a repair process in your body, which we think is beneficial for lifespan. Most of this work is done in animal models. But when you look at the pathways that regulate aging in humans and mice, you see we are wired in the same way. So there is no reason to think that fasting is going to have these amazing benefits in animals and no effect on us. Of course, there needs to be some degree of personalization.

Unfortunately, as in much of medical care and medical research, a lot of this work has been done either in mice or in older white males. There's a need to expand this into the whole population. We go back to the biomarkers of aging. If we had biomarkers that work across all humans, then you could follow your biomarkers and decide whether this is working for you.

"What I would advocate is for people to do some degree of self-experimentation."

That's really what many of us are doing in the field. If what you are doing makes you feel miserable, it probably doesn't make any sense to do it. If your markers are not changing, it probably doesn't make any sense to keep doing it. The problem is, how does someone who is not a medical doctor or who is not familiar with the field get access to all of this knowledge?

This is our biggest challenge: How do we take this knowledge and make it something that people are excited to do? The reason I'm optimistic again is Marin County. When you're dealing with a group of people who are

educated and provided with the information and who see it around themselves, these healthy behaviors become contagious. If everyone around you is fit and healthy, you don't want to be the one who is overweight and unable to exercise. There is social pressure to be healthy. In the long run, this is going to become a very powerful driving force for everything that we are trying to do.

Recently, a new study in the New England Journal of Medicine suggested that intermittent fasting or time-restricted eating led to zero weight-loss benefits compared to eating the same diet throughout the day. What thoughts do you have about these results?

Clearly, fasting works independently of weight loss. There are two different kinds of overweight people—there are healthy overweight people and unhealthy overweight people. The data in terms of your weight and your survival is not a clear, linear response. So it's not being the skinniest that leads to a longer life. There's actually a U-shaped curve, for reasons that we frankly don't understand.



Dr. Eric Verdin with a colleague in his lab

What is the pivotal role of senescence and chronic inflammation in contributing to age-related diseases? Can we tamp down on these underlying causes using dietary or lifestyle interventions?

There are two ways to think about it. First, there's preventing senescence from occurring in the first place. We know a lot of the healthy living concepts that we discussed so far play a role in this. Then, if you have a certain number of senescent cells, can you remove them? That's the whole field of senolytics. Clinical trials are ongoing for this. So we still don't have the full answer in humans whether these are actually going to work. But there's good reason to be optimistic that some of these will yield completely novel therapies against the disease of aging.

Chronic inflammation is one of the unifying causal factors of age-related disease. When you look at what people call the hallmarks of aging, including senescence, many of their end products are a state of chronic inflammation from an overactive immune system. We think this overactive immune system is one of the major drivers that lead to aging. There's a lot of evidence that senescence cells secrete a series of factors called the SASP (senescence-associated secretory phenotype), which are contributing to aging and chronic inflammation. When you remove the senescent cells, this chronic inflammation disappears.

One of my colleagues at the Buck Institute, David Furman, has identified a novel biomarker that measures chronic inflammation. This is an immune-signaling protein or cytokine known as CXCL9. He has shown that this is a very strong predictor of heart disease and other chronic diseases associated with aging. He's now doing clinical trials studying interventions to see if we can suppress the inflammatory age. If so, this could lead to a slowing of aging and a reversal of some of these chronic diseases of aging.

The global aging population is predicted to grow from seven to 20 percent in the next few decades. Worldwide, what changes are needed to avoid a full-blown aging care crisis?

Everyone is so panicked about what's happening, because the fraction of the population that is older is growing and growing and getting sicker and sicker. Data from countries like Japan and Germany suggests we're going to have a crisis of epic proportions. In Japan, by 2050, people are predicting that 40 percent of the population will be above 65. That means 40 percent of the population will be chronically ill. Who's going to work? Who's going to pay for all of their care?

This is where healthy aging completely changes the equation. Imagine all of these people being active and productively involved in society. Imagine older individuals helping teach kids in the classroom. To me, one of the consequences of healthy aging is that there will be expectations for people to stay more engaged in society. One of the strongest predictors of a long lifespan is social engagement. It is a sense of purpose and a sense that you are contributing to not only your well-being but the well-being of your family and society at large.

In the same way that we have reinvented the normal life cycle in the last 100 years, we will continue to change the way we think about the future of aging.

This interview has been edited for length and clarity.



Faith, Science and Francis Collins

[*The New Yorker*](#), April 2022

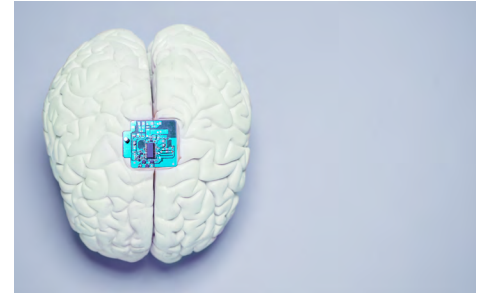
Throughout the entirety of his influential career as NIH director, Dr. Francis Collins has built bridges across America's cultural and political divides. Science writer and physician Dhruv Khullar explores the possible wake of Dr. Collins' retirement asking: Will these bridges hold, or have they already burned?



A 'Silent Victim': How Nature Becomes a Casualty of War

[*The New York Times*](#), April 2022

A fascinating dive into past military conflicts suggests that the war in Ukraine could have a profound environmental impact—threatening biodiversity and wildlife, damaging chemical plants and storage facilities, oil depots, coal mines, gas lines and other industrial sites, and causing a collapse of environmental governance. When Ukraine recovers and rebuilds from the Russian invasion, conservation will need to be an essential priority.



The Brain-Reading Devices Helping Paralyzed People to Move, Talk and Touch

[*Nature*](#), April 2022

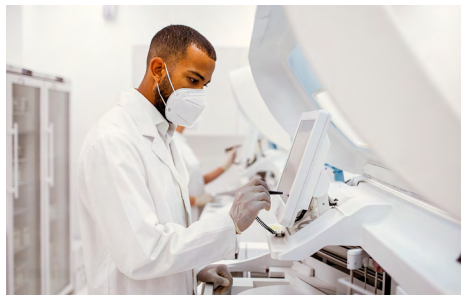
A look at the explosion of brain-computer interfaces advancing at lightning speed to restore the abilities of people with paralysis. Implants are rapidly becoming more sophisticated and are attracting commercial interest.



The Science of Connection

[*A Slight Change of Plans Podcast*](#), March 2022

In her podcast exploring the fallout and learning opportunities that come with life-altering change, Dr. Maya Shankar speaks with Dr. Dixon Chibanda, a psychiatrist based in Zimbabwe. For years, Dr. Chibanda has been on a mission to expand access to mental health care in his country, home to only one psychiatrist for every 1.5 million people. To bridge the gap and provide people with the help they need, Dixon turned to a rather unorthodox group for help: grandmothers.



The Future of Cancer Research

[*Nature Medicine*](#), April 2022

Cancer research is moving at a breakneck pace and is now poised to prevent, diagnose, and treat cancer more effectively than ever before. In a special issue of the journal *Nature Medicine*, physicians, scientists and expert commentators share the latest breakthroughs in novel therapeutics to early detection strategies and how progress hinges on making these breakthroughs accessible to all.



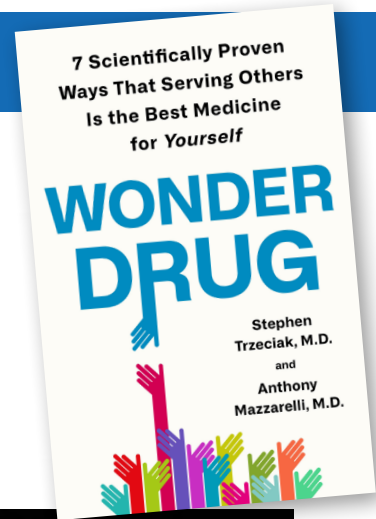
'It's Life or Death': The Mental Health Crisis Among U.S. Teens

[*The New York Times*](#), April 2022

The pandemic has intensified an already alarming trend: teenagers dealing with skyrocketing rates of anxiety, depression and suicidality. Fueled by a range of factors including social isolation and social media, the problem is hitting record highs. This special series shows the depth of this devastating problem and offers vital tools for loved ones to help.

Updates & Events

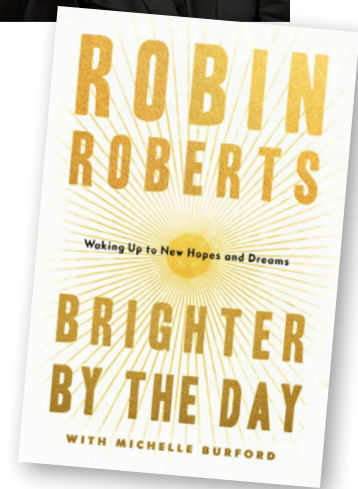
- Physician scientists Dr. Stephen Trzeciak and Dr. Anthony Mazzarelli recently explored the vast health benefits tied to service in his new book *Wonder Drug: 7 Scientifically Proven Ways That Serving Others Is the Best Medicine for Yourself*. "Wonder Drug is a journey through the scientific evidence that serving others is not just the right thing to do, it's also the smart thing to do for your physical health, mental health, happiness and well-being, and even your professional success," Dr. Trzeciak tells *CuraLink*. Read more about *Wonder Drug* at <https://us.macmillan.com/books/9781250809049/wonderdrug>



- Life Itself, the three-night retreat hosted by Dr. Sanjay Gupta and Marc Hodosh, will take place May 31st-June 3rd, 2022, in San Diego, California. The event celebrates extraordinary minds and ideas intersecting health and medicine and includes speakers Dr. James Allison, Dr. Deepak Chopra, Dr. Anthony Fauci, Reed Jobs, Dean Kamen, Dr. Martine Rothblatt, John Sculley, Dr. David Sinclair, Dr. Rudolph Tanzi, Dr. Rochelle Walensky and Dr. Michelle Williams among many others. Learn more about Life Itself at <https://lifeitself.health/>



- Congratulations to beloved host Robin Roberts on celebrating 20 years on Good Morning America and publishing her uplifting new book, *Brighter by the Day: Waking Up to New Hopes and Dreams*. The book offers practical wisdom and inspiring insights from her own life, giving readers ways to inject more joy into their lives. Learn more about *Brighter by the Day* at <https://www.grandcentralpublishing.com/titles/robin-roberts/brighter-by-the-day/9781538754627/>



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