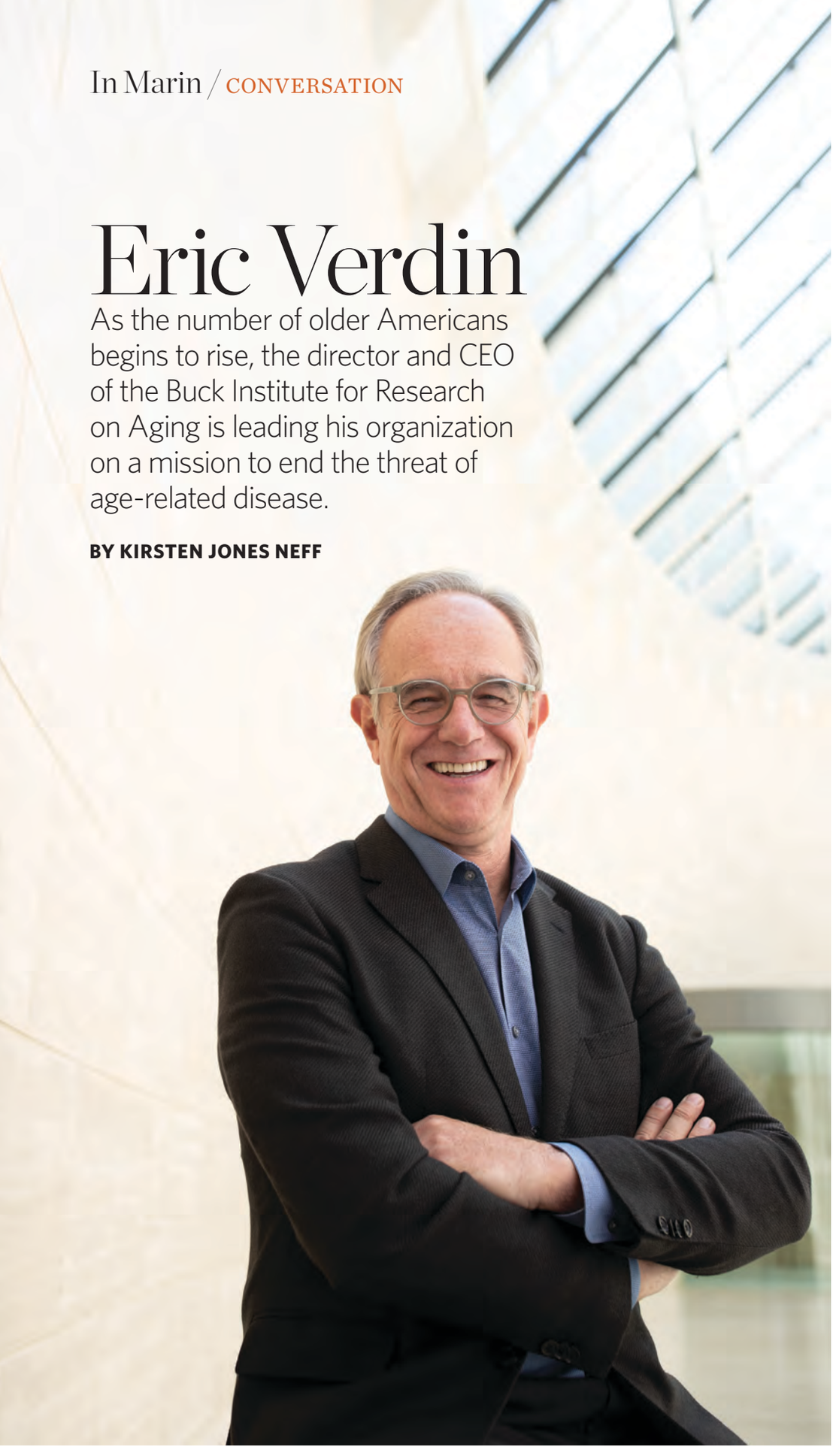
Eric Verdin

As the number of older Americans begins to rise, the director and CEO of the Buck Institute for Research on Aging is leading his organization on a mission to end the threat of age-related disease.

BY KIRSTEN JONES NEFF



JIM HUGHES

MANY OF US have seen it from the freeway — the striking white building sitting nobly atop the hills above Novato. We may be intrigued, and we may even know that it is the Buck Institute for Research on Aging. But like those captivated by Willy Wonka's mysterious factory, most Marinites have never ventured inside and cannot describe what is actually happening within those architecturally stunning walls (the center was designed by the late I.M. Pei).

It turns out a lot is happening inside the Buck Institute these days. As it celebrates its 20th anniversary, the Buck is a world-renowned leader in research on aging. The institute's mission to "end the threat of age-related disease" has become increasingly relevant as our world population ages; a 2017 United Nations report predicts that by 2050 there will be more people 60 or older on the planet than there are adolescents and young adults ages 10 to 24, which will make it important that societies cope with chronic age-related disease. While the relevance of the Buck Institute's research spans the globe, Director and CEO Eric Verdin, M.D., who arrived there from the UCSF Gladstone Institute for Virology and Immunology three years ago, is also working to increase that work's visibility and accessibility here in Marin County. The 62-year-old Mill Valley resident instigated a new approach that includes outreach and efforts to connect Buck Institute research to people's daily lifestyle and health choices.

We sat down with him to learn more about the institute's current research and his vision for its future.

You took the helm three years ago. What is your vision for the Buck Institute? We are the only large independent medical research institute in Marin and we have the potential to change medicine. Today medicine is very organ-centric. We call it "whack-a-mole" medicine, treating every disease of aging as if each were independent. You see a heart doctor, then a neurologist, and so on, and we are currently treating these diseases as if they were independent problems. Our message is that all these diseases of aging are driven by

the same pathways, the pathways that we have discovered that control aging, and by targeting the pathways we will be treating all of these diseases. Our drug research is part of the equation, and there is also a long-term desire to open a clinic and become more directly relevant to humans, and so we are hiring people interested in human biology.

We also want to become a voice in the community that provides evidence-based recommendations that people can actually trust and follow. We believe the Buck Institute can be a leader not only in research, but also in terms of the dissemination of simple, clear, science-based information. And we have been ramping up our programs. We created the "Live Better Longer" blog, offering evidence-based information about supplements, ketogenic diet, calorie restriction, fasting, exercise and other aging-related subjects. We are also offering community seminars, which are available online, and tours — community engagement opportunities. We should be the pride of Marin. People have told us, "I had no idea that this was right in my backyard," and so we are working hard to let people in Marin know they have a gem in their midst.

What are the most significant breakthroughs in the study of aging at the moment? In the mid-'90s, new research showed that we could modify an organism and, with one single mutation, double its life span. If you could double life span by making such a small modification, we realized that there are pathways and systems on the cellular level that we could modify to control aging in organisms. This changed the way we thought about aging. Twenty years ago the Buck was founded on the promise of these discoveries, [presented in] just a few research articles at the time. This was incredibly gutsy, to found an entire institute on this idea. And it turned out that it was true: we can manipulate aging in simple animals. At the Buck Institute we study *C. elegans*, a small worm about the size of a comma, fruit flies and mice. People ask, how could a tiny worm have any relevance to us? Well, this little worm lives 20 days and in those 20 days it recapitulates a whole life span — childhood, teenage years, adulthood and then old age and death. All of the work on these worms has yielded an understanding of the aging pathways in our cells. A pathway is a series of proteins all talking to each other and controlling the rate of aging. If you tinker with them, you can accelerate aging or you can slow it down.

Two surprising things came out of this research. One, we found the pathways are conserved, meaning they are not unique to the worm. They actually are the same in fruit flies, in mice and in humans, so we can learn a lot by studying these systems. And second, aging is plastic — it can be modulated and regulated. If we (scientists) can make mutations, we can find drugs that do the same thing. Our scientists Gordon Lithgow, Ph.D., and Simon Melov, Ph.D., were the first to show you can increase life span with a drug. And now there are many of these drugs — the NIH (National Institutes of Health) has a program that tests drugs that increase life span in mice and there are eight or nine of these so far. Several are already being used with humans.

I have heard you use the term "healthspan." What does this mean? Everybody focuses on life span, but our primary focus is healthspan, or increasing the healthy years of life. There's a whole series of diseases as you age, the chronic diseases of aging: cancer, heart attack, stroke, macular degeneration, osteoporosis, Alzheimer's, Parkinson's, osteoarthritis, for example. The link between aging and disease is something we've internalized as the order of things — you get old, you get sick, and then you die.

"We want to become a voice in the community that provides evidence-based recommendations that people can actually trust and follow."

Most of us have a life expectancy of around 78 (although it is on average almost 10 years more here in Marin), and we will live 15 percent of our lives affected by disease. By the time we are 65, about 80 percent of us are afflicted with a chronic disease of aging and close to 60 percent are afflicted by two of these diseases. So when we think about aging, most of us are dreading it. Here at the Buck Institute we are not focused on radical life extension — that is not what we are after — but we have discovered that disease is not a necessary part of aging.

Healthspan has enormous implications for both quality of life and the cost to society. As the population ages, our cost of health care is going up. This could bankrupt our Social Security, our Medicare and Medicaid, the whole system. What we have learned in studying these simple animals is that when we slow down aging, we don't only make the animals live longer, but they live healthier. They see what we call the "compression of morbidity," meaning the disease years are compressed, a smaller percentage of their lives.

What role does genetics play in how we age? The old consensus about genetics has been replaced by data from a research institute called Calico that is very strong. They used data from ancestry.com and it indicates that only about 7 percent of longevity is determined by genes and 93 percent by the environment. This is incredible because it means longevity is determined by environmental factors. That is a powerful message that places the responsibility on each of us to do what we can to stay healthy. Now there is an exception to this. If someone in your family has lived to 100, then it becomes

very favorable that you will live to at least 90. The genetics become very strong. And these people who do live to 100, they can essentially do whatever they want and they still live to 100. But for the rest of us, everything from the air we breathe to exercise to sleep to diet to loneliness or depression — everything that is not your genes — will be strong determinants of life expectancy. In fact, the strongest determinants of life expectancy are a sense of purpose in life and first-degree relationships — children, spouse, close friends — and being surrounded by these people.

What are you currently most excited about at the Buck Institute? I am excited about everything! One especially exciting thing is that with $6 million in seed money from Nicole Shanahan (an attorney, Silicon Valley entrepreneur and philanthropist married to Google founder Sergey Brin), we have recently established a Center for Reproductive Longevity and Equality. We have hired four faculty researchers, and their work of the center focuses on ovarian aging in women. It turns out, menopause is a strong predictor of longevity and ovarian aging is woefully understudied, completely ignored by modern medicine, even though ovarian aging is in fact the earliest manifestation of aging. It happens before muscle failure or brain failure and so on. By the age of 35, 10 percent of women will be infertile, so Nicole's interest is in creating more equality in terms of reproductive choices for women.

> "Here at the Buck Institute we are not focused on radical life extension — that is not what we are after — but we have discovered that disease is not a necessary part of aging."

What do you personally do to slow down your aging process on a cellular level? Fasting is important. Continuously eating from the moment you wake up to the time you go to bed is the worst thing you can be doing. So the concept is called "time-restricted feeding," the idea that you restrict the number of hours that you eat throughout the day. A lot of people here at the Buck, I and many of my colleagues, are on something called 8-16, which means you eat during eight hours of a day, and the other 16 hours you do not put food in your mouth. Water, tea, coffee is OK, but no food [or drink] that brings calories.

There is research behind this — we are studying calorie restriction, the ketogenic diet and fasting. If you want to do something important for your health, start this 8-16 fasting tomorrow. A lot of us wake up in the middle of the night and have a glass of milk or orange juice. I tell people, don't do it, that is poison. Your body should be fasting. People who fast for 16 hours will tell you, I used to have heartburn, I had this or I had that. Everything goes away. Type 2 diabetes goes away. People lose weight, which is amazing because they don't go on a diet, as you can eat whatever you want to in that eight-hour period. I do make exceptions, like a brunch with friends on the weekend — we shouldn't let this regimen interfere with social connections, which are so important — but I do it in general.

Do you have other recommendations? We hear about so many interventions, not all of them science-based. For instance, with diets, people wonder, should I restrict carbohydrates or restrict fat? Should I supplement with protein or not? People have no ability to make a decision based on the literature because the literature is often conflicted and complicated.

There is a lot of debate in the field about what are the main [health-impairing] culprits in our diet. For instance, the guidelines put out by the government, for a number of years, have encouraged people to restrict their fat, and we have a cottage industry of low-fat diets and food. Yet we have the largest obesity epidemic we have had in years. To me, this is an indication that there is something wrong about our recommendations.

The Buck Institute is an iconoclast in the sense that we believe we should be revisiting these questions. We are revisiting questions like, what is it about fat that is toxic? And, can protein be toxic? I worry when I see these huge bottles of protein supplements in GNC — who is buying this much protein and how much protein are they actually ingesting when they take these supplements? It is scary. People do this without real guidelines. The indication in the labs is that a mild degree of protein restriction is beneficial for your health, unless you are over 70 years old, in which case protein supplementation makes people more healthy.

For exercise, we all know that we should be physically active. Exercise is an antiaging medicine that protects us from disease. When you are physically active, your rate of cancer, heart disease, osteoporosis, they all go down by 40 percent. So why don't people exercise? Less than 10 percent of people over 60 are regular exercisers — in Marin County it's more, but nationwide it is 10 percent. Why is this? I believe marketing for things like Fitbit are a problem. Fitbit recommends you do 10,000 steps a day, which is a number that comes from nowhere; it is not science-based. And it takes about an hour and a half of walking every day to do this, which most people cannot do. But a recent study shows that you get most of the benefit in just 4,400 steps a day. So instead we can recommend something people can do; they can walk for 20 minutes and get most of the bang for the buck. M