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Science > Health

# Is the Hack to Human Longevity Within Reach?

Scientists say we should focus more on achieving healthier lives instead of totaling up our years.

BY CONNIE CHANG NOV 7, 2023

Fountains of youth, elixirs bestowing immortality—our stories and myths have long chased everlasting life. But science didn't follow suit until the mid-1990s, when researchers tweaked a gene and doubled the lifespan of the humble *C. elegans*—a worm that lives, reproduces and dies in 3 weeks. Soon, scientists were creating long-lived yeast, flies and mice; and headlines heralded the end of aging.

Decades later, however, we're still not blowing out a Noah-sized number of candles on our birthday cakes. "It's great to increase lifespan in worms, if you

have a pet worm, but humans are a lot more complicated than worms and mice," Eric Verdin tells *Popular Mechanics*. Mice, moreover, are more short-lived than their body size predicts, so it's quite easy to increase their lifespan. "Humans, though, are already the naked mole rat" of their weight class, says Verdin, the chief executive of the Buck Institute for Research on Aging—citing that species' remarkable longevity among similarly sized rodents.

**Ageotypes**

**Biogerontology**

**Epigenetic reprogramming**

**Healthspan**

**Molecular gatekeeper**

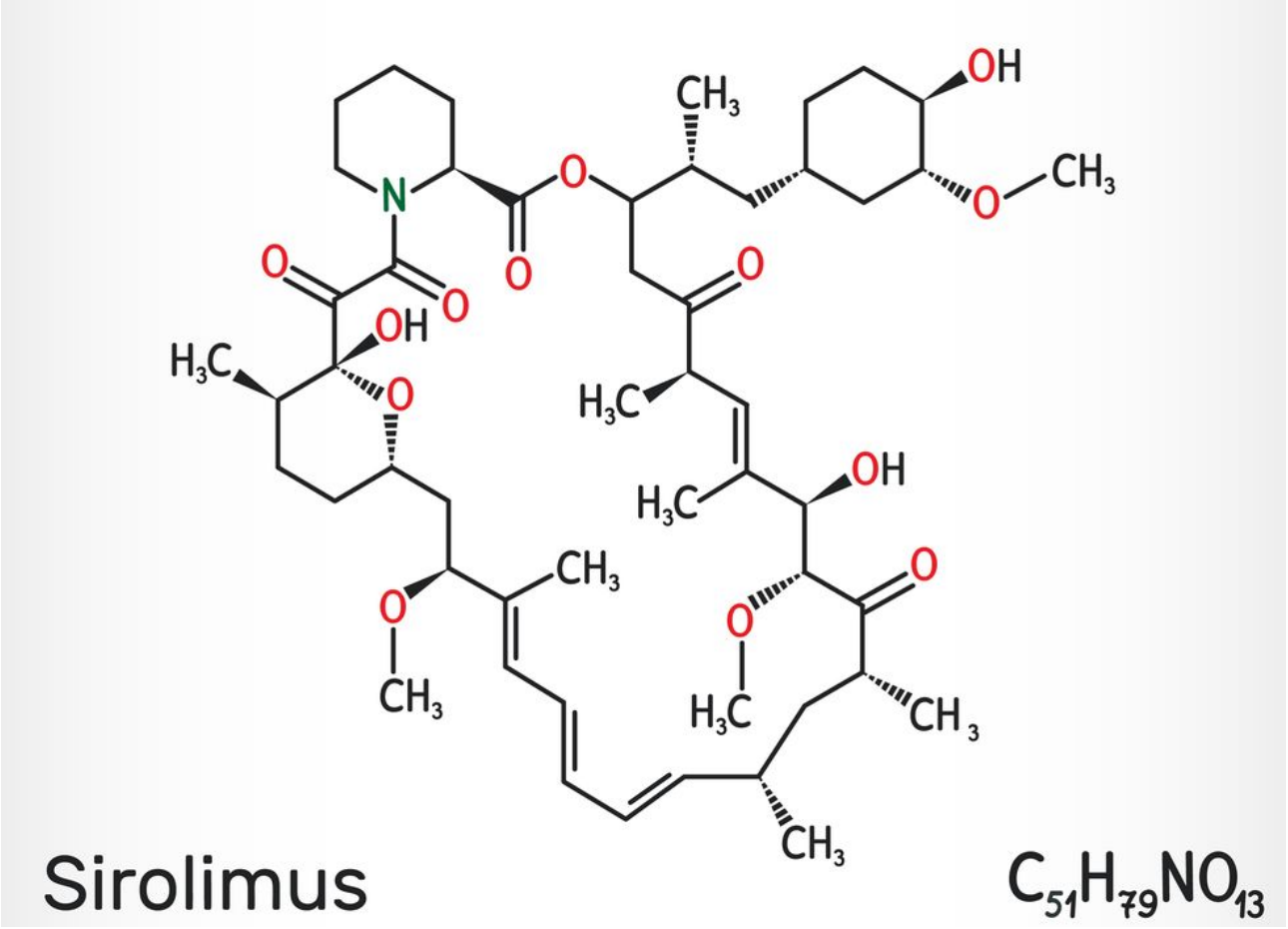
Matt Kaeberlein, a biogerontologist at the University of Washington, thinks immortality is possible, but that we're "nowhere near dramatic increases in human longevity." Instead, he and like-minded colleagues are most excited about the field's potential impact on healthspan, or the period of time we're in good health and free from disease. "Almost all of the major causes of death and disability have age as their greatest risk factor," Kaeberlein tells *Popular Mechanics*. So the influx of money and interest to study the biology of aging could kill multiple birds with one stone.

# Yes, We Can Slow Aging, With Difficulty

The most effective intervention to slow aging was discovered decades ago in the 1980s, says Kaeberlein. Mice that were fed 60 percent fewer calories survived 60 percent longer than their normally fed peers. "As the body's starving, it exits normal life in the fast lane and goes into standby mode, which

prioritizes survival," Valter Longo, the Director of the USC Longevity Institute, explains to *Popular Mechanics*.

But that degree of deprivation is untenable for most people and difficult to pull off safely. So scientists raced to find the cellular mechanisms that explained caloric restriction's power. What they uncovered were molecular gatekeepers like mTOR, a protein that senses the level of nutrients in the cellular environment. In times of abundance, it promotes growth and reproduction; while in times of famine, it emphasizes longevity and repair.




Molecular structure of Rapamycin, also called Sirolimus, which is used to suppress and regulate the immune system to treat cancerous tumors and help patients accept organ transplants. It's also used in longevity research.

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Most intriguing, mice fed rapamycin—a drug that blocks mTOR, "tricking the cell and the organism into thinking that there's not very much food around"—lived as much as 30 percent longer than control mice, said Kaberlein. He is currently testing the compound in dogs, but preliminary results indicate heart

function and blood pressure improved in animals given rapamycin. And a small study of rapamycin use in the elderly shows that it boosts flu vaccine response and offers protection against respiratory infections—highlighting its effect on immune functions that decline with age.

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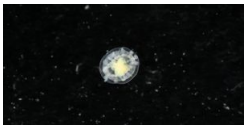


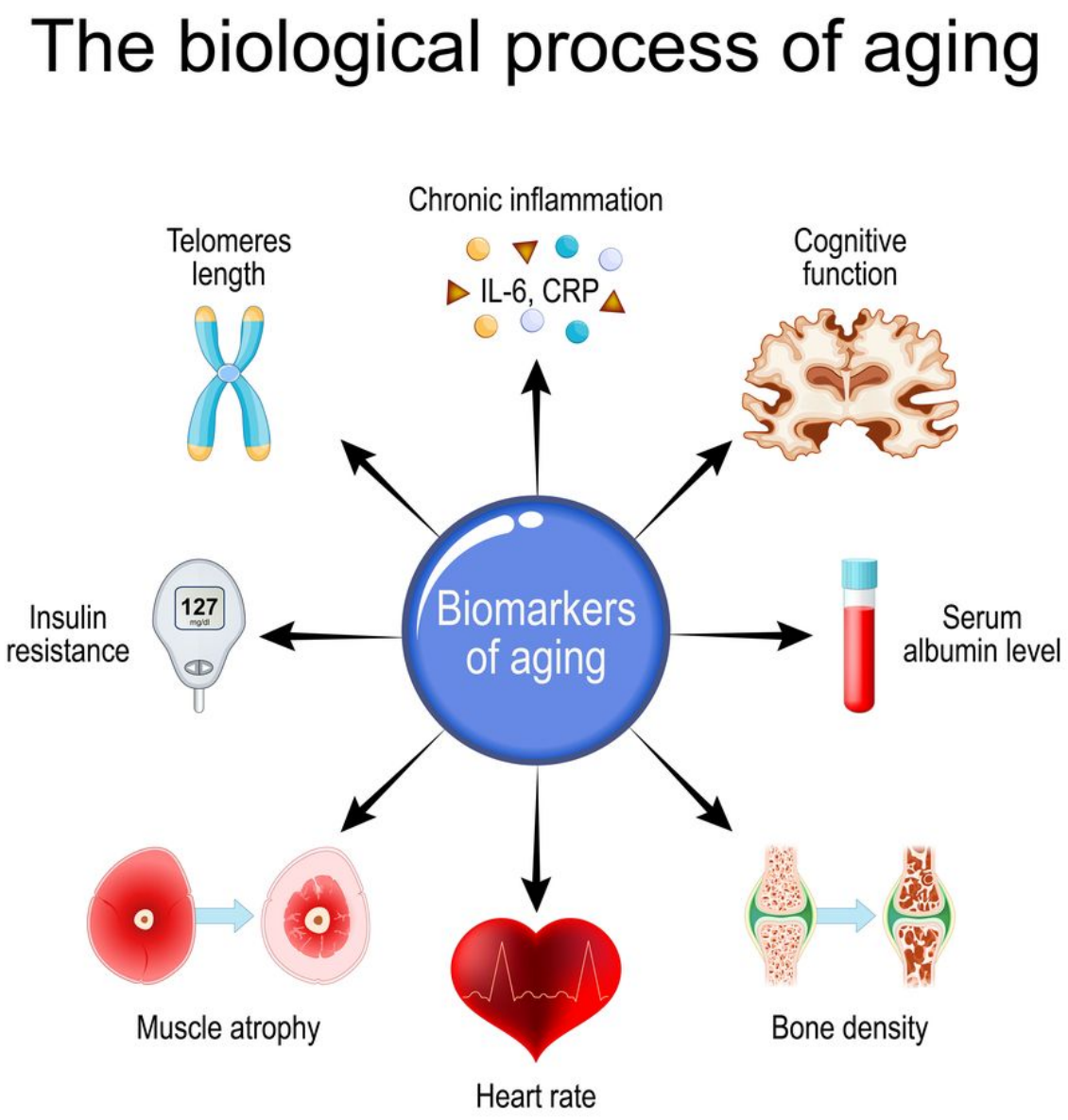
What These Immortal Jellyfish Can Teach Us

Longo, meanwhile, is investigating fasting-mimicking-diets (low calorie, low protein)—which are easier to tolerate than water-only diets but yield similar benefits. In mice, "after 5 days on this diet, multiple systems—cholesterol, triglycerides, metabolism—seem to reset" as damaged cells are swept away, Longo says. And during the refeeding phase, stem cells generate new healthy cells and rejuvenated organs. He is currently testing the diet in a large-scale study on people, but a smaller experiment on 71 healthy subjects showed that BMI, blood pressure, cholesterol and fasting glucose all improved when participants followed the diet five days each month for three months.

## Biomarkers Could Unlock the Keys of Living Longer

Other researchers are harnessing the might of big data and AI to extract insights on how we age. Michael Snyder, a geneticist at Stanford, has been following a cohort of 109 people for more than 10 years—drawing blood,

collecting fecal samples, and using wearables like the Apple Watch or the Fitbit to evaluate the myriad of biological markers that might impact aging. "If your health is a 1,000-piece jigsaw puzzle, we're trying to measure five or six-hundred pieces to get a much clearer picture versus the five or six we measure today," Snyder tells *Popular Mechanics*.

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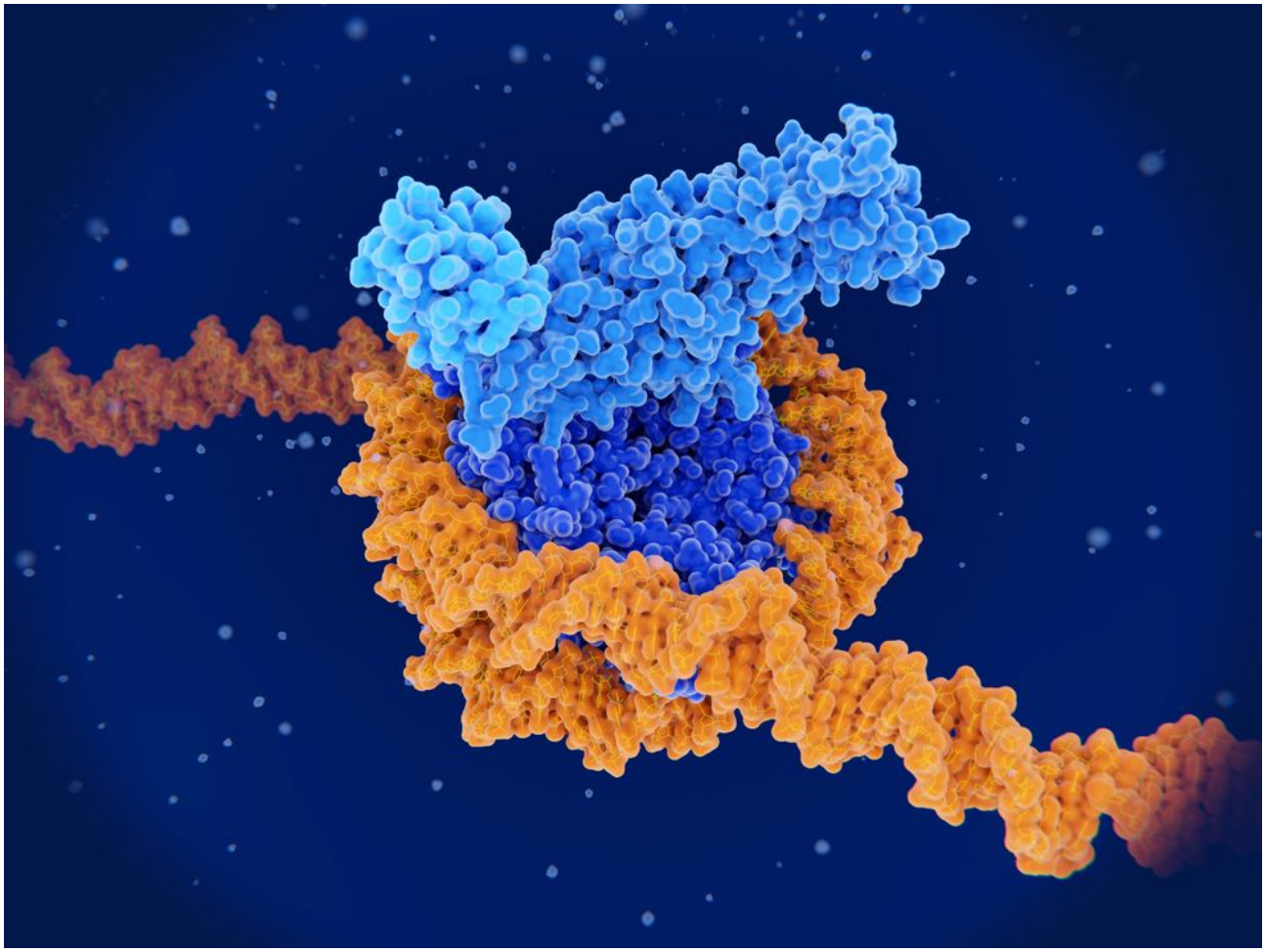
"Everybody ages differently" and there's power in knowing what type of "ager" you are, Snyder says. According to Snyder, there are four main ageotypes: metabolic, immune, hepatic (liver), and nephrotic (kidney). "So if you're a kidney ager, for example, maybe you should be drinking a lot more water." His

company, January AI, commercializes this research by designing personal diet and exercise recommendations, informed by individual glucose monitoring and biometric data from wearables.

Saul Villeda, a neurobiologist at the University of California, San Francisco, is also interested in aging biomarkers. His group has connected the circulatory systems of young and old mice and identified both the factors that accelerate aging—and those that slow it. This includes factors that help grow new neurons, lower inflammation, and increase vascularization, or blood flow. The researchers are currently characterizing the factors or combinations of factors that deliver the most bang for the buck across organs like the brain, liver, and muscles.

## Futuristic, But Optimistic Lines of Research



A molecular model of a process that can activate or repress gene transcription— the copying of DNA to fulfill various cellular functions—without changing the actual genetic sequence. It is an example of an epigenetic change.

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Then there are tantalizing hints of interventions that could result in multi-fold increases in lifespan. Epigenetic reprogramming, for example, is the new kid on the block that everyone's excited about, says Villeda. As we age, our DNA accumulates chemical marks that control which genes are expressed. Over time, these marks can impair how our cells function, leading to diseases of aging like neurodegeneration, cardiovascular disease, and cancer. Reprogramming cells, using four master genes, returns old cells to a younger state with chemical marks resembling those of embryonic stem cells. But the logistics are daunting. Researchers "have shown in a very nice paper that you can increase nerve regeneration in the eye and reverse vision loss in mice, but that was a very local administration," says Verdin. The challenge is to rejuvenate an entire organism without turning it into a bag of cancer, or jelly.

> "If we can increase the average healthspan of a hundred million people by 10 years, that's a billion years of human healthspan." –Matt Kaeberlein

Villeda hopes his work and others' will someday translate to a pill that can mimic the effect of these ideas, but he warns that progress will be slow—pointing to the decades of work that preceded the concerted push that yielded the COVID-19 mRNA vaccines. With aging research, "we're still at a stage where we're developing the mechanisms and the biology," Villeda says. But he believes we'll get our mRNA vaccine moment.

## 💪 WHERE THERE'S A WILL...

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“But while we wait for a magic pill, there’s a lot we can do now to improve our health and longevity,” Luigi Ferruci, a geriatrician at the NIH’s National Institute on Aging and the Director of the Baltimore Longitudinal Study on Aging, tells *Popular Mechanics*. By not smoking, controlling blood pressure, eating sensibly, and exercising, you can increase your life expectancy by up to ten years. Throw in periodic fasting three times a year or simply limit when you eat to a 12-hour window, and you could probably add another decade.

“I don’t want to get lost in this idea that we’re only successful as a field if we double lifespan,” Kaeberlein says. If we can increase the average healthspan of a hundred million people by 10 years, that’s a billion years of human healthspan. Think of what society can do with that—“that’s a big deal.”

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