

ANTI-AGING NEWS *The following articles are for informational purposes only and are not meant to offer medical advice.*



Scientists trick T-cells to resist aging, find fountain of youth within

The biological fountain of youth

Scientists at Cold Spring Harbor Laboratory worked to genetically engineer T-cells to target and destroy senescent cells. Senescent cells are linked to aging and age-related disorders such as [Alzheimer's](#) disease, obesity, diabetes, and Parkinson's disease. They are cells that are permanently stunted. The process of cellular senescence is important in healthy bodies because it stops the growth and spread of abnormal cells. However, these cells accumulate in organs and tissues over time. This makes it increasingly hard for tissue to regenerate.

Eliminate damaging cells

"Senescent cells are cells in our body that have accumulated a lot of damage and as a result they have stopped doing their normal jobs and instead become very inflammatory," says Assistant Professor Corina Amor Vegas at the Cold

Spring Harbor Laboratory and study author. *"The accumulation of these cells in tissues is really deleterious because it creates a severe pro-inflammatory microenvironment that prevents the other cells in the tissue from working properly too."*

Programing anti-aging cells

So the researchers modified T-cells with the mission to eliminate these senescent cells in mice to test for [anti-aging](#) effects. In particular, they used a drug known as CAR (chimeric antigen receptors) T-cells. The mice in the study experienced lower body weight, better glucose tolerance, boosted metabolism, and more physical activity. There was no tissue damage or toxicity as a result.

One dose for life?

What's even more noteworthy is the longevity of the CAR T-cells. After one dose, young mice retain the anti-aging effects for the rest of their lives. *"T-cells have the ability to develop memory and persist in your body for really long periods, which is very different from a chemical drug,"* says Armor Vegas. *"With CAR T-cells, you have the potential of getting this one treatment, and then that's it. For chronic pathologies, that's a huge advantage. Think about patients who need treatment multiple times per day versus you get an infusion, and then you're good to go for multiple years."*

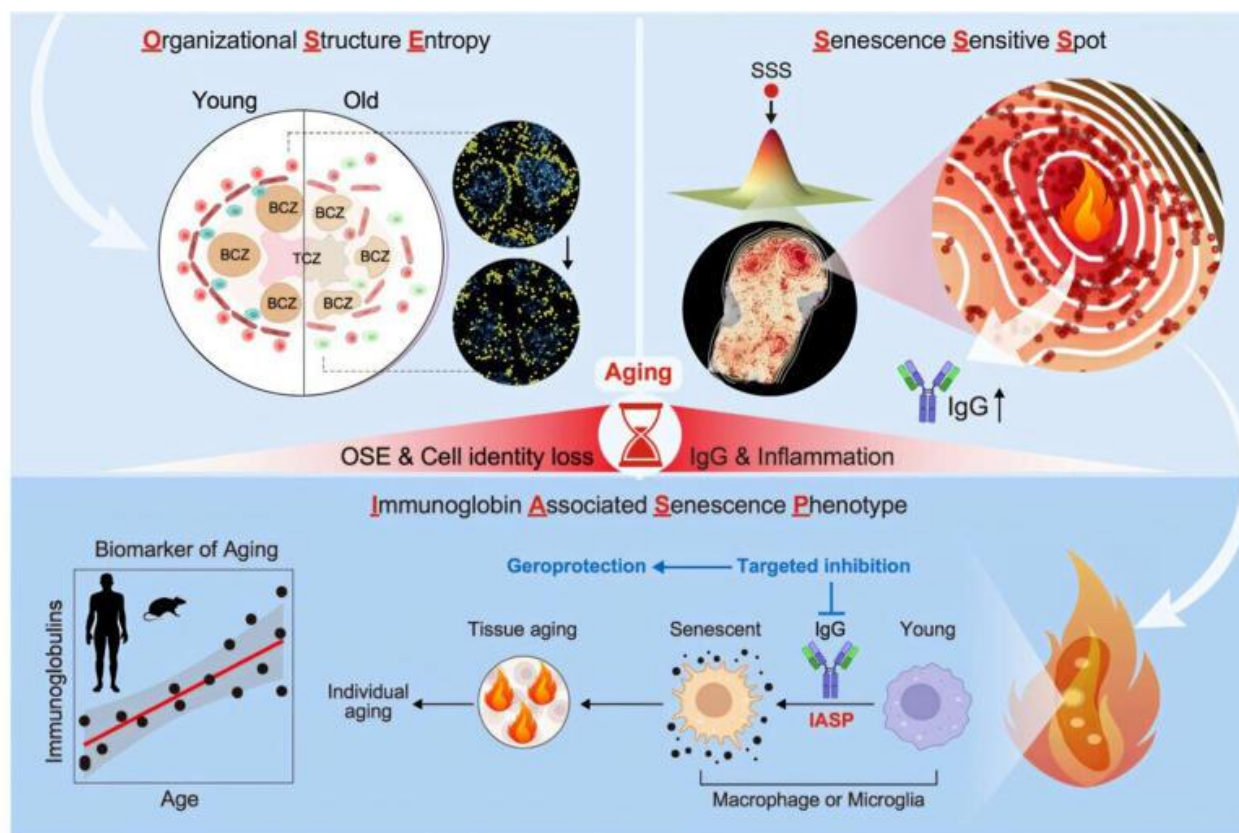
Eliminating senescent cells

There are currently medications that target and eliminate senescent cells, but they need to be taken regularly. Additionally, what's called "senolytic treatment" is new and it's unclear exactly who can benefit from it. It's likely that researchers will need to customize these drugs to target specific issues. Meanwhile, CAR T-cells seem like they have the potential to benefit a person's overall health after one dose-or at least they can benefit a mouse's health.

The future of CAR T-cell anti-aging treatment

In 2017, CAR T-cells received FDA approval as treatment for different kinds of blood cancer. But this study further investigates its medical potential. Armor Vegas and her colleagues are now researching if mice with this treatment would not only live healthier lives but longer ones. There is much to discover before CAR T-cells can be proven to be humanity's fountain of youth.

Unveiling the secrets of aging: Scientists discover dual role of immunoglobulins



A team of scientists from the Chinese Academy of Sciences (CAS) and BGI

Research has uncovered the intricate mechanisms by which immunoglobulins influence the aging process, a finding that might reshape our understanding of aging.

This research, [published](#) in *Cell* on Nov. 4, not only charts a high-precision map of aging across various organs but also reveals the dual-edged sword of immunoglobulins in systemic aging.

The quest for systemic biomarkers and key drivers of aging has been a long-standing puzzle in the field of gerontology. This study, a collaborative effort between Liu Guanghui's team from the Institute of Zoology (IOZ) of CAS, Gu Ying's team from BGI Research, Zhang Weiqi's team from the Beijing Institute of Genomics of CAS, and Qu Jing's team also from IOZ, has provided compelling answers.

By meticulously analyzing millions of spatial spots across nine organs in male mice, the team created high-precision spatial transcriptomic maps. These maps detailed the spatial distribution of more than 70 cell types, offering a vivid picture of aging's spatial characteristics.

The transcriptomic landscape, dubbed Gerontological Geography (GG), exposes the common threads of tissue structural disorder and loss of cellular identity as hallmarks of aging.

"This landscape is a significant step forward, pinpointing the epicenters of aging within multiple organs and uncovering the accumulation of immunoglobulins as a key aging characteristic and driver," said Professor Liu, one of the corresponding authors of the study.

Using the novel method of organizational structure entropy (OSE) analysis, the researchers discovered that increased spatial structural disorder and loss of cellular identity are universal signs of systemic aging, suggesting that spatial structural damage may be a primary cause of organ functional decline during aging.

The team also identified senescence-sensitive spots (SSS), which are structural regions in different tissues more susceptible to aging's effects. They found that areas closer to SSS exhibit higher tissue structural entropy and greater loss of cellular identity, indicating that SSS could be the nucleus of organ aging.

Notably, in immune organs, plasma cells, which are responsible for antibody synthesis, and cells with specific structures and functions, are the main components of the SSS microenvironment. The expression levels of immunoglobulin-related genes in these cells increase around SSS.

The study further discovered that immunoglobulin G (IgG) accumulates in multiple tissues and organs during aging in humans and mice, suggesting that IgG levels could serve as a new biomarker for aging. Moreover, IgG was found to directly induce aging in human and mouse macrophages and microglia, releasing inflammatory factors. Intriguingly, injecting IgG into young mice induced aging in multiple tissues and organs, demonstrating its potent aging effects.

In a promising development, the team developed an intervention strategy using antisense oligonucleotides (ASO) to reduce IgG content in mouse tissues, thereby delaying the aging of multiple organs.

This study is the first to map the spatial transcriptome of pan-organ aging in mammals, revealing tissue structural disorder and loss of cellular identity as key aging hallmarks and precisely locating the core regions and microenvironmental characteristics of aging sensitivity.

The Immunoglobulin-associated Senescence Phenotype (IASP) proposed by the study expands the frontiers of aging science and opens new avenues for delaying aging and preventing related diseases.

More information: Shuai Ma et al, Spatial transcriptomic landscape unveils immunoglobulin-associated senescence as a hallmark of aging, *Cell* (2024). DOI: [10.1016/j.cell.2024.10.019](https://doi.org/10.1016/j.cell.2024.10.019)

Provided by Chinese Academy of Sciences

The Superfood That Is As Close To The Fountain Of Youth As You Can Get

In the quest for everlasting youth, a remarkable ally has emerged: collagen. Often referred to as the body's scaffolding, it is a protein that not only supports the structure of our skin, hair, and nails but also plays a pivotal role in maintaining joint flexibility and a robust metabolism.¹ As the years go by, our natural production dwindles, giving rise to visible signs of aging and decreased vitality.² However, by harnessing the potential of collagen, you can embark on a journey towards a rejuvenated self, exuding radiance and vitality.

Advertisement

The Essence of Collagen's Influence

The intricate web of collagen is woven throughout our bodies, forming the foundation for skin elasticity, muscle tone, and the integrity of bones and blood vessels.³ Picture it as nature's building blocks, holding everything together in harmonious balance. Yet, as we cross the threshold into our thirties, this collagen orchestra begins to play a softer tune, leaving us susceptible to wrinkles, sagging skin, and joint discomfort. But here's the good news: the narrative doesn't have to end here. By embracing the potential of collagen, we can script a new chapter for our well-being.

The allure of collagen extends far beyond the surface – it delves into the realm of profound skin transformation, hair revitalization, and nail fortification. Recent studies have unveiled the captivating impact of the superfood's supplementation on skin's elasticity and the reduction of fine lines, a testament to its potential in promoting overall skin health. Beyond appearances, collagen emboldens hair strands, coaxing them into newfound vibrancy, while also bestowing resilience upon nails. As you weave collagen into the fabric of your daily existence, the effects of time on your skin, hair, and nails need not be feared.

Digestive Harmony and Metabolic Mastery

The saga of collagen's influence doesn't stop at its outward radiance; it's an inner symphony too. This protein partner plays a pivotal role in maintaining a harmonious digestive system and even stoking the fires of metabolism. By inviting collagen to the table of your dietary choices, you gift your body a pathway to optimal function and a metabolism that dances to its own youthful rhythm. The canvas of possibilities is rich and varied – from foods to meticulously crafted supplements, the means to rejuvenate are well within reach.

Enter the realm of collagen-boosting foods – a haven where nature's bounty collides with the intention to restore. Enriching your diet with citrus fruits, berries, verdant greens, and sulfur-rich companions like garlic can set the stage for collagen synthesis. Yet, the spotlight shines on proteins, the elemental backbone of its formation. Whether it's the nourishment of meat, the

vitality of poultry, the bounty of fish, or the promise of eggs, proteins bring forth the amino acids that lay the foundation for the superfood's revival. Vegetarians and vegans, fear not, for legumes and beans offer their plant-powered hand in this dance of rejuvenation.

Decoding Collagen

The realm of collagen supplements beckons, each type offering a distinct treasure trove of benefits. The offerings span from bovine (cow), to poultry and fish variants, and the delicate essence of egg shell membranes. These choices aren't mere supplements; they are keys to specific realms of well-being. From fostering joint health to enhancing skin's supple grace and fortifying muscles, selecting the right collagen ally can amplify the symphony of vitality in your life.

Like a sculptor with a chisel, you wield the power to shape your existence. Collagen, this fountain of youthful possibilities, invites itself into your daily tapestry. Embrace it through the vessel of nourishment, the elixirs of supplements, and the mindfulness of choices. It's a journey where your skin continues to radiate, joints find renewed flexibility, and your entire being thrives in the embrace of time.

This longevity scientist's 3 surprising predictions for the growing industry of healthy aging

"People are paying more attention to internal health, rather than external beauty," says Alina Su, CEO of Generation Lab. © STUART ISETT/FORTUNE

More people are taking extra steps to ensure optimal health as they age.

That's according to Alina Su, CEO of precision medicine and health tech company Generation Lab, at *Fortune's Brainstorm Health* conference in Dana Point, Calif. last week.

"Everyone is trying to be healthier ... People are paying more attention to internal health, rather than external beauty," Su tells *Fortune* in an interview, in which she shared the launch of the company's SystemAge test—part of its \$149 a month membership fee.

SystemAge uses epigenetic blood tests, which evaluate how someone's lifestyle and environment affect their health. These tests calculate a person's pace of aging and risk for health diseases across 19 organs and systems; Su hopes to give customers a launching pad toward optimizing their health by providing personalized lifestyle recommendations based on the data.

It's all in the name of "Health care 3.0," which Su says represents a shift from treatment to prevention and gives people the power to take control of their health, according to the company's press release. Generation Lab joins a list of companies using data science and technology with the goal of extending health and life span.

Since launching her company last year, Su, who has researched aging and regeneration at Harvard Medical School and The Conboy Laboratory at UC Berkeley, has spoken to hundreds of doctors and thousands of consumers and entrepreneurs in the longevity space.

Here are her three predictions for the evolving longevity sector and the business of living longer:

1. More young people will join the longevity craze

Longevity clinics don't just appeal to older adults. Su says their customers range from ages 20 to 70. "It's not 40 plus. It's 20 plus," Su says of their average customer, who she says is often a young, healthy adult.

The interest in how data can determine health risks and give lifestyle recommendations has given way to a growing number of preventive health and longevity clinics emerging globally. When traveling to Dubai, Su saw beauty spas rebranded to longevity centers. After talking to numerous doctors, Su learned an estimated three to four new clinics are popping up in the city each month, attracting customers across generations. "There used to be aesthetic clinics that are now transforming to longevity practices," Su says. "This was shocking."

Public figures, many of whom influence the youngest generations, seem eager to lead the charge and take scans and tests to optimize their health. Last year, Kim Kardashian was outspoken about taking Penuvo's full-body MRI for internal, preventative health reasons on her social media, Su points out.

2. You don't need to be a big-time biohacker to access longevity

Longevity has become synonymous with extreme—and expensive—biohacking, like entrepreneur [Bryan Johnson](#), who takes dozens of supplements a day, has exchanged blood with his son (which is not recommended by the FDA), and spends millions of dollars a year to reverse his age.

"Anyone can be Bryan Johnson, they just don't know how," Su says.

Su believes that, with more data, people can get simple, low-cost lifestyle recommendations.

3. Expect more standards in the future

Today, anyone can market their business as a longevity clinic. There's no certification to be considered a longevity doctor, and there are not enough standardizations in the field.

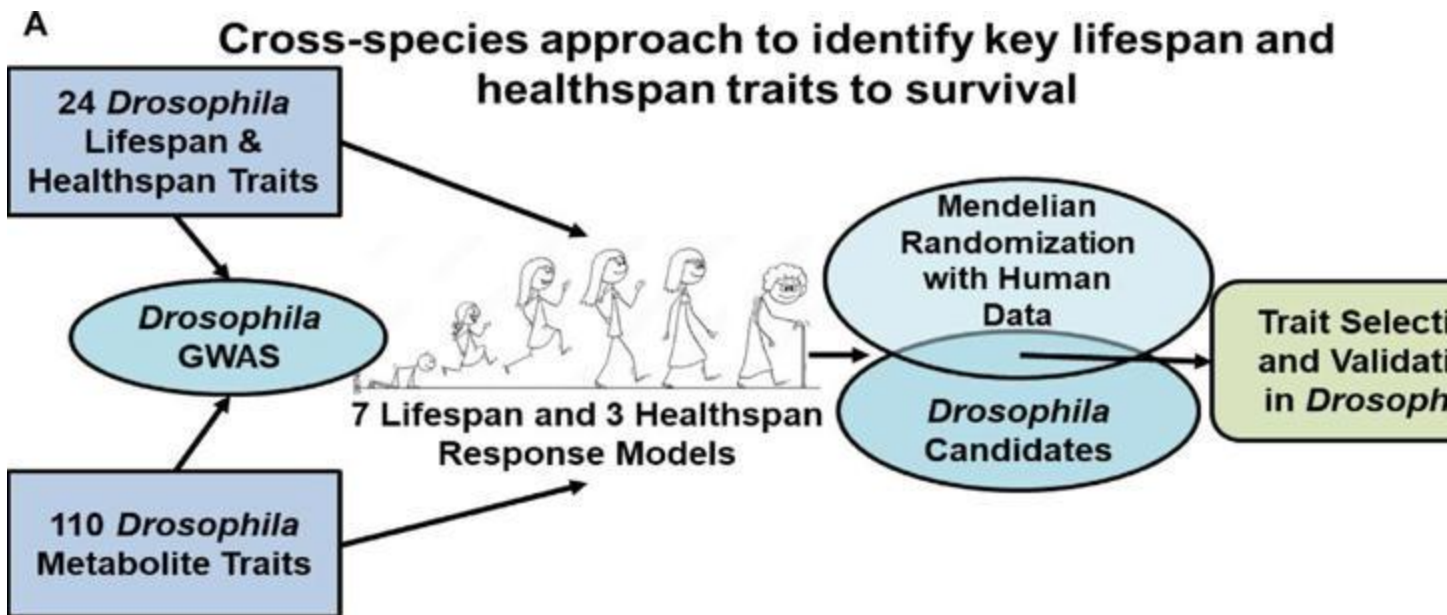
At a congressional meeting in March, Su advocated for research, clear definitions in the field, and regulatory markers as companies seek to put drugs on the market that aim to extend health span and reduce the risk of age-related diseases.

"How do you even assess if the drug on longevity is working or not? How can you even tell without a biomarker of aging that one's working or not?" Su says. "Once we define a biomarker of aging, we can tell the efficacy, and then we can tell what's actually working."

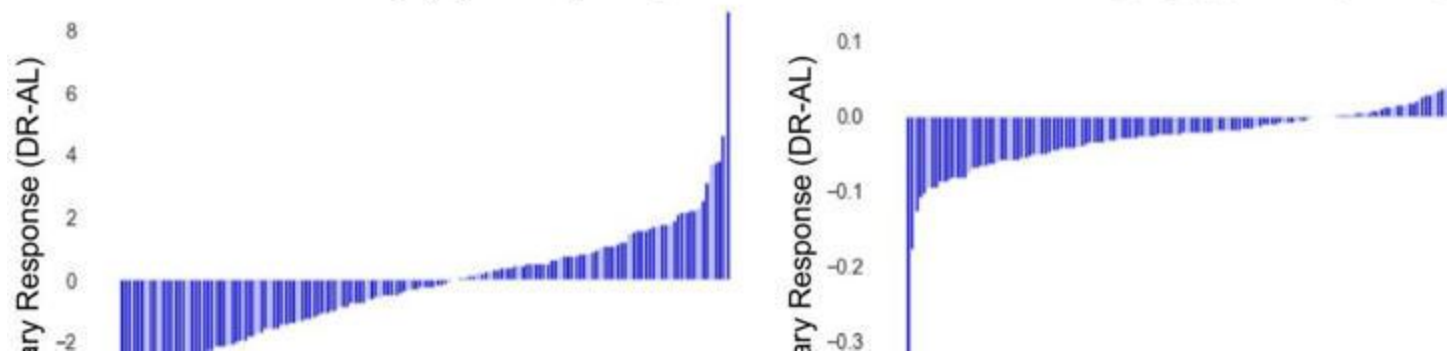
For more on how to live longer:

- 9 longevity experts share their [best advice for creating healthy habits that can help you age well](#)
- Wealthy men are spending millions to lower their [biological ages](#) and live longer. [These women are lowering their biological age with cheaper solutions](#)
- [The longevity secrets of Singapore](#), the 6th blue zone city where people are living the longest, happiest lives
- [The strict anti-aging routine of a 45-year-old CEO](#) who spends millions a year to be 18 again—from [diet](#) to [exercise](#)

Researchers identify key metabolites impacting lifespan in flies and humans



B Late-life Initial Mortality (α) Dietary Response **C** Late-life Rate of Aging (β) Dietary Response



Diet influences lifespan and healthspan in a genotype-specific manner. DGRP shows strong strain-specific responses to diet (A) Graphical workflow for modeling data from *Drosophila* and filtering traits using Mendelian randomization of human data. B DGRP strain traits on a high yeast (AL, red) or low yeast (DR, blue) diet were used to determine strain-specific dietary response (DR-AL). B–E Bar graphs of DGRP strain dietary response in B late-life initial mortality α , C late-life rate of aging β , D body weight (mg), and E max lifespan. Credit: Nature Communications (2024). DOI: 10.1038/s41467-024-52909-y

Discoveries that impact lifespan and healthspan in fruit flies are usually tested in mice before being considered potentially relevant in humans, a process that is expensive and time-intensive. A pioneering approach taken at the Buck Institute leapfrogs over that standard methodology.

Utilizing cutting-edge machine learning and systems biology, researchers have analyzed and correlated huge data sets from flies and humans to identify key

metabolites that impact lifespan in both species. Results [published](#) in *Nature Communications* suggest that one of the metabolites, threonine, may hold promise as a potential therapeutic for aging interventions.

"These results would not have been possible without this pioneering approach," says Buck professor Pankaj Kapahi, Ph.D., senior author of the paper. "There is a lot of data sitting out there that is not being correlated between species. I think this approach could be a game-changer when it comes to identifying potential interventions to improve human health."

Threonine has been shown to protect against diabetes in mice. The essential amino acid plays an important role in collagen and elastin production and is also involved in blood clotting, fat metabolism and immune function.

The method, simplified

The work began with former Buck postdoc Tyler Hilsabeck, Ph.D., crunching data (involving metabolomics, phenotypes and genomics) to analyze 120 metabolites in 160 strains of fruit flies on both restricted and normal diets. The goal was to reveal how different genotypes responded to the diets to influence lifespan and healthspan.

"This allowed us to find the 'needles in the haystack' when it came to identifying relevant metabolites," Hilsabeck says.

Vikram Narayan, Ph.D., a postdoctoral fellow then cross-referenced findings with human data from the massive UK Biobank. "Using the human data allowed us to focus on interesting metabolites to those that are conserved in both species. It also allowed us to uncover the impact of those metabolites on humans," he says. Importantly, the team then brought those relevant metabolites back into the fly to validate the results.

The results

In flies, threonine extended lifespan in a strain-and-sex-specific manner. Individuals with higher levels of threonine-related metabolites had longer, healthier lives.

"We're not saying that threonine is going to work in all conditions," says Kapahi. "Our research shows it works in subsets of both flies and people. I think most of us have stopped expecting to find a 'magic-bullet' intervention for aging. Our method provides another way to develop precision medicine for geroscience."

The results also include findings that were not so positive for both species. Orotate, which is relatively understudied and has been linked with fat metabolism, was negatively associated with aging. In flies, orotate counteracted the positive impact of dietary restriction across every strain of the animals. In humans, orotate was linked to a shorter lifespan.

Larger implications

Kapahi hopes the larger research community will begin employing this method.

"So many times we find things that work in worms and flies and then we don't have the resources to move the basic science forward. This approach allows us to say with a lot more certainty that discoveries are going to be relevant in humans." Kapahi says this method may reduce the need for studies in mice, something he welcomes.

Other Buck researchers involved in the study include Vikram P. Narayan, Kenneth A. Wilson, Enrique Carrera, and Judith Campisi. Other contributors include Daniel Rafferty, Northwest Metabolomics Research Center, University of Washington, Seattle; Daniel Promislow, Departments of Pathology and Biology, University of Washington, Seattle; and Rachel B. Brem, Department of Plant and Microbial Biology, University of California, Berkeley.

More information: Tyler A. U. Hilsabeck et al, Systems biology approaches identify metabolic signatures of dietary lifespan and healthspan across species, *Nature Communications* (2024). DOI: [10.1038/s41467-024-52909-y](https://doi.org/10.1038/s41467-024-52909-y)

Provided by Buck Institute for Research on Aging

Longevity Breakthrough: New Treatment Reverses Multiple Hallmarks of Aging

BY UNIVERSITY OF TEXAS M. D. ANDERSON CANCER CENTER SEPTEMBER 2, 2024 [28 COMMENTS](#) 5 MINS READ

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Researchers have shown that restoring youthful levels of a telomerase subunit can significantly alleviate aging signs in models, potentially impacting age-related diseases like Alzheimer's and cancer. Their study identified a compound that maintains the telomerase reverse transcriptase (TERT) levels, reducing cellular aging, inflammation, and improving memory and muscle function.

Researchers at MD Anderson have identified a molecule that diminishes age-related inflammation and enhances brain and muscle function in preclinical models.

Researchers at [The University of Texas MD Anderson Cancer Center](#) have shown that therapeutically restoring 'youthful' levels of a specific subunit of the telomerase enzyme can significantly reduce the signs and symptoms of aging in preclinical models. If these findings are validated in clinical trials, they could have important therapeutic implications for age-related diseases such as Alzheimer's, Parkinson's, heart disease, and cancer.

The study, published in *Cell*, identified a small molecule compound that restores physiological levels of telomerase reverse transcriptase (TERT), which normally is repressed with the onset of aging. Maintenance of TERT levels in aged lab models reduced cellular senescence and tissue inflammation, spurred new neuron formation with improved memory, and enhanced neuromuscular function, which increased strength and coordination.

The researchers show that TERT functions not only to extend telomeres, but also acts as a transcription factor to affect the expression of many genes directing neurogenesis, learning and memory, cellular senescence, and inflammation.

"Epigenetic repression of TERT plays a major role in the cellular decline seen at the onset of aging by regulating genes involved in learning, memory, muscle performance, and inflammation," said corresponding author Ronald DePinho, M.D., professor of Cancer Biology. "By pharmacologically restoring youthful TERT levels, we reprogrammed expression of those genes, resulting in improved cognition and muscle performance while eliminating hallmarks linked to many age-related diseases."

Loss of *TERT* is connected with aging through multiple mechanisms

Aging is associated with various epigenetic changes that influence functional and physiological decline. One of the hallmarks of aging is the gradual shortening of telomeres,

the chromosomal end structures that help maintain their stability. Free radicals also can modify and harm telomere sequences.

Ronald DePinho, M.D. Credit: The University of Texas MD Anderson Cancer Center
When telomeres become extremely short or modified, they trigger a continual DNA damage response, which can lead to cell senescence – a phenomenon in which cells release inflammatory factors that can cause tissue damage, prompting aging and cancer.

Telomerase is a protein complex responsible for synthesizing and extending telomeres. However, its activity is reduced over time due to the epigenetic silencing of *TERT*, particularly at the onset of natural aging or Alzheimer's and other age-related diseases.

The DePinho laboratory previously showed that deactivating the *TERT* gene *in vivo* led to premature aging, which could be reversed through *TERT* reactivation. The researchers also observed that certain cells, such as neurons and cardiac cells, were rejuvenated without undergoing the normal cell division required to synthesize telomeres.

Their observations led them to hypothesize that TERT had other functions beyond synthesizing telomeres and that overall telomerase levels were important in the aging process. Based on these findings, the researchers, led by DePinho and first author Hong Seok Shim, Ph.D., aimed to develop a drug to restore TERT levels.

Small molecule restores TERT levels, reversing hallmarks of aging

A high-throughput screen of over 650,000 compounds identified a small-molecule TERT activating compound (TAC) that epigenetically de-represses the *TERT* gene and restores physiological expression present in young cells.

In preclinical models equivalent to adults over age 75, TAC treatment for six months led to new neuron formation in the hippocampus (memory center) and improved performance in cognitive tests. Additionally, there was an increase in genes involved in learning, memory, and synaptic biology, consistent with TERT's ability to interact with and control the activity of transcription factor complexes regulating diverse genes.

TAC treatment also significantly reduced inflammaging – an age-related increase in inflammatory markers linked with multiple diseases – in both blood and tissue samples and also eliminated senescent cells by repressing the *p16* gene, a key senescence factor.

TAC improved neuromuscular function, coordination, grip strength, and speed in these models, reversing sarcopenia – a condition under which muscle mass, strength, and performance naturally worsen with advancing age.

Additionally, TAC treatment in human cell lines increased telomere synthesis with reduced DNA damage signal at telomeres and extended the proliferative potential of these cells, demonstrating the activity of TAC in *ex vivo* human models.

“These preclinical results are encouraging, as TAC is easily absorbed by all tissues, including the central nervous system. Yet further studies are needed to properly assess its safety and activity in long-term treatment strategies,” DePinho said. “However, our deeper understanding of the molecular mechanisms driving the aging process has uncovered viable drug targets, allowing us to explore opportunities to intercept the causes of a variety of major age-related chronic diseases.”

Reference: “TERT activation targets DNA methylation and multiple aging hallmarks” by Hong Seok Shim, Jonathan Iaconelli, Xiaoying Shang, Jiexi Li, Zheng D. Lan, Shan Jiang, Kayla Nutsch, Brittney A. Beyer, Luke L. Lairson, Adam T. Boutin, Michael J. Bollong, Peter G. Schultz and Ronald A. DePinho, 21 June 2024, *Cell*.

DOI: [10.1016/j.cell.2024.05.048](https://doi.org/10.1016/j.cell.2024.05.048)

This study was supported by the National Institutes of Health (R01 CA084628, P30 CA016672, and S10 RR029552), the G. Harold and Leila Y Mathers Charitable Foundation, and the Belfer Family Foundation Neurodegeneration Consortium. This study was a collaborative effort with Peter Schultz and Michael Bollong at the Scripps Institute.

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Age Reversal Breakthrough: Harvard/MIT Discovery Could Enable Whole-Body Rejuvenation

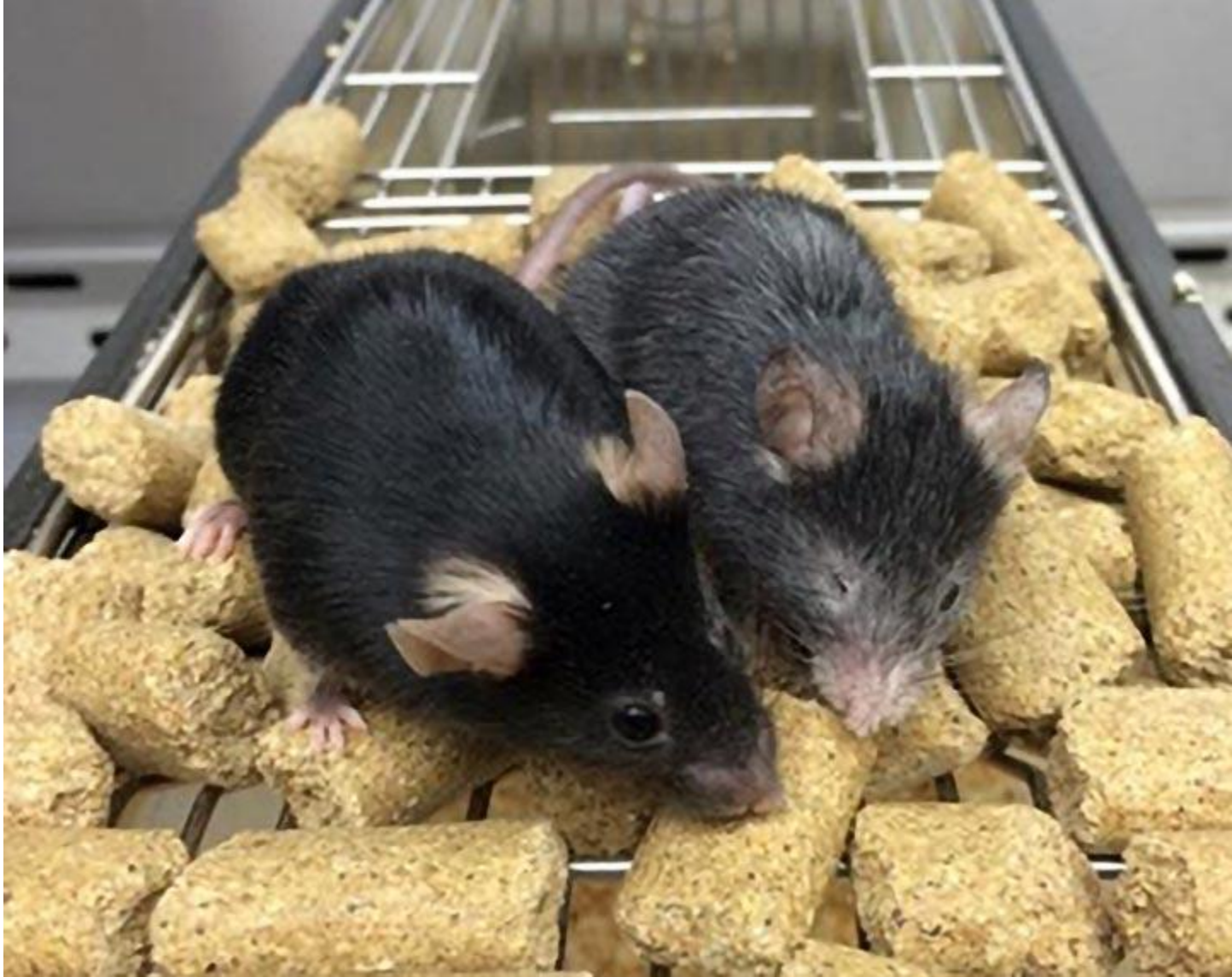


Scientists from Harvard Medical School, the University of Maine, and MIT have published a groundbreaking study revealing a chemical method to reprogram cells to a more youthful state. This technique offers a potential alternative to gene therapy for reversing aging. The implications of this research are vast, with potential applications in regenerative medicine, treatment of age-related diseases, and whole-body rejuvenation.

In a pioneering study, researchers from Harvard Medical School, University of Maine, and MIT have introduced a chemical method for reversing cellular aging. This revolutionary approach offers a potential alternative to gene therapy for age reversal. The findings could transform treatments for age-related diseases, enhance regenerative medicine, and potentially lead to whole-body rejuvenation.

Groundbreaking Discovery in Aging Reversal

In a monumental study, a team of researchers has revealed a novel approach to combating aging and age-related diseases. This work, undertaken by scientists at Harvard Medical School, introduces the first chemical method to rejuvenate cells, bringing them to a more youthful state. Prior to this, only powerful gene therapy could achieve this feat.

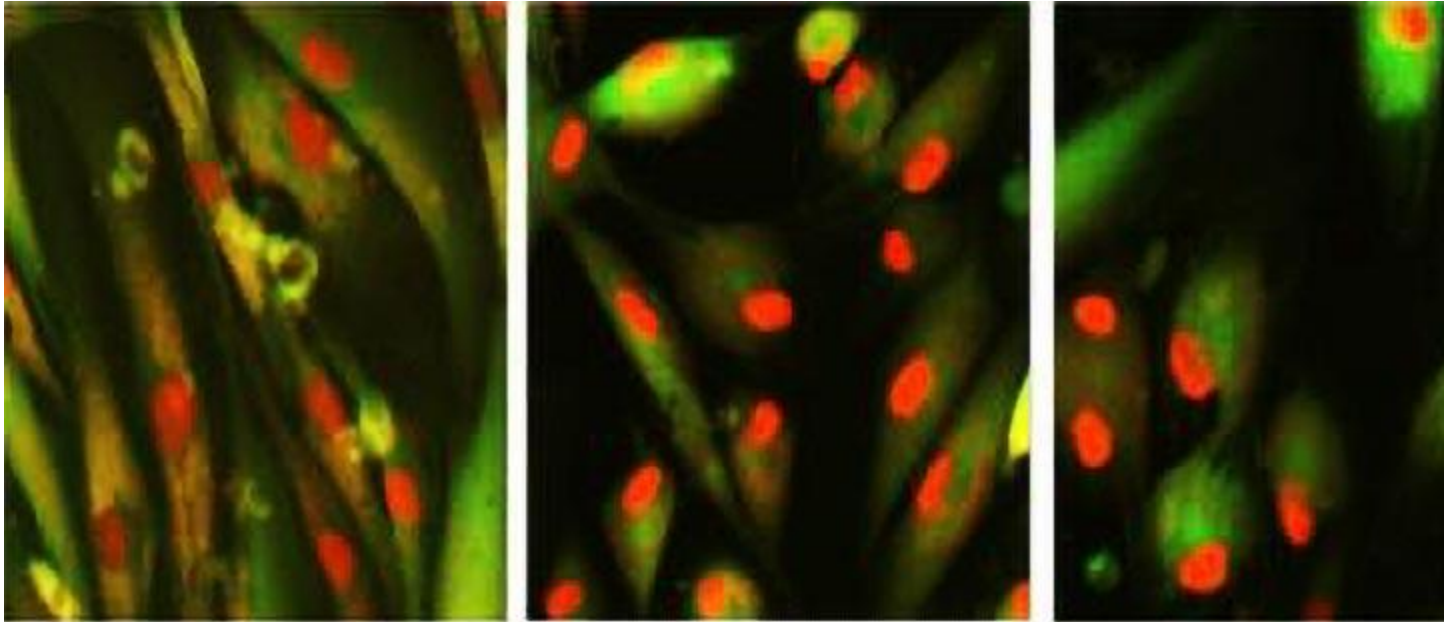


Mice in the Sinclair lab have been engineered to age rapidly to test the effectiveness of therapies to reverse the aging process. The mouse on the right has been aged to 150% that of its sibling on the left by disrupting its epigenome. Photo credit: D. Sinclair, Harvard Medical School. Credit: 2023 Yang et al.

On July 12, 2023, researchers from Harvard Medical School, the University of Maine, and the Massachusetts Institute of Technology (MIT) published a fresh research paper in *Aging*. The paper, titled, “Chemically induced reprogramming to reverse cellular aging,” extends upon a previously groundbreaking discovery. The researchers are Jae-Hyun Yang, Christopher A. Petty, Thomas Dixon-McDougall, Maria Vina Lopez, Alexander Tyshkovskiy, Sun Maybury-Lewis, Xiao Tian, Nabilah Ibrahim, Zhili Chen, Patrick T. Griffin, Matthew Arnold, Jien Li, Oswaldo A. Martinez, Alexander Behn, Ryan Rogers-Hammond, Suzanne Angeli, Vadim N. Gladyshev, and David A. Sinclair.

Exploring the Methodology

This discovery builds on the finding that the expression of specific genes, known as Yamanaka factors, can transform adult cells into induced pluripotent stem cells (iPSCs). This breakthrough, which earned a Nobel Prize, prompted scientists to question if cellular aging could be reversed without pushing cells to become too young and potentially cancerous.



Rejuvenation and age reversal of senescent human skin cells by chemical means. Cells in the right two panels have restored compartmentalization of the red fluorescent protein in the nucleus, a marker of youth that was used to find the cocktails, before the scientists confirmed they were younger, based on how genes were expressed. Image credit: J. -H. Yang, Harvard Medical School. Credit: 2023 Yang et al.

In this recent study, the scientists probed for molecules that could, in tandem, revert cellular aging and refresh human cells. They designed advanced cell-based assays to differentiate between young and old, as well as senescent cells. The team employed transcription-based aging clocks and a real-time nucleocytoplasmic protein compartmentalization (NCC) assay. In a significant development, they identified six chemical combinations that could return NCC and genome-wide transcript profiles to youthful states, reversing transcriptomic age in less than a week.

Relevance and Potential Applications

The Harvard team has previously shown the possibility of reversing cellular aging without causing unregulated cell growth. This was done by inserting specific Yamanaka genes into cells using a viral vector. Studies on various tissues and organs like the optic nerve, brain, kidney, and muscle have yielded encouraging results, including improved vision and extended lifespan in mice. Additionally, recent reports have documented improved vision in monkeys.

These findings have profound implications, paving the way for regenerative medicine and potentially full-body rejuvenation. By establishing a chemical alternative to gene therapy for age reversal, this research could potentially transform the treatment of aging, injuries, and age-related diseases. The approach also suggests the possibility of lower development costs and shorter timelines. Following successful results in reversing blindness in monkeys in April 2023, plans for human clinical trials using the lab's age reversal gene therapy are currently underway.

Views from the Research Team

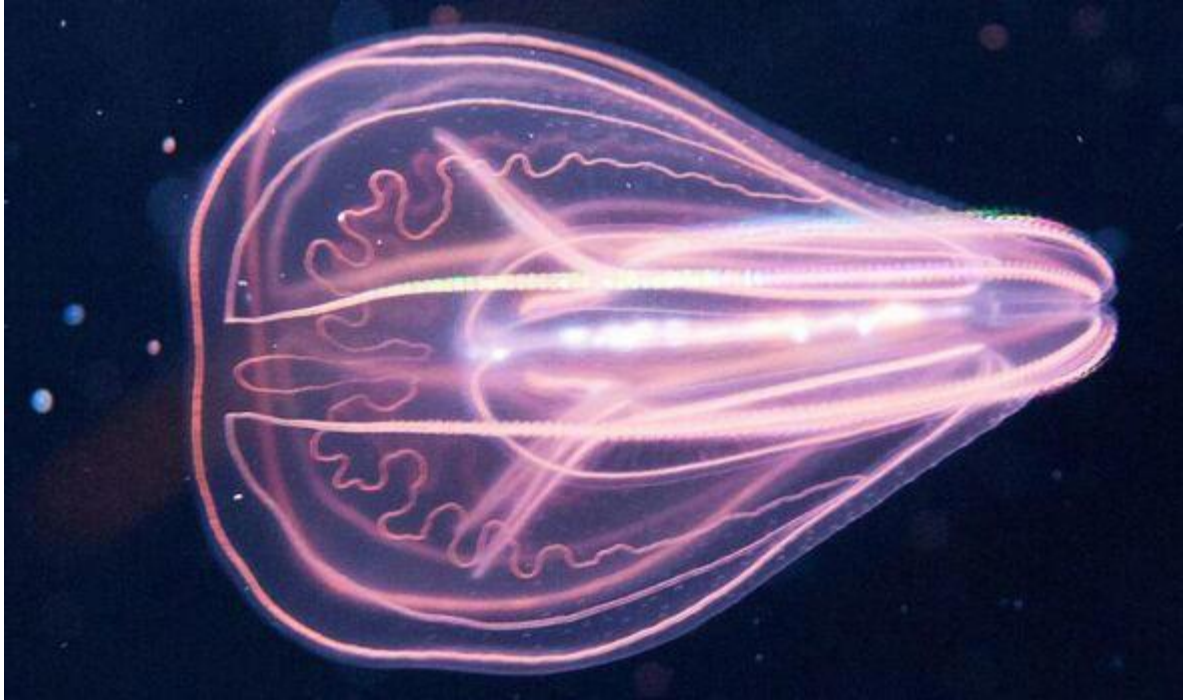
"Until recently, the best we could do was *slow* aging. New discoveries suggest we can now reverse it," said David A. Sinclair, A.O., Ph.D., Professor in the Department of Genetics and co-Director of the Paul F. Glenn Center for Biology of Aging Research at Harvard Medical School and lead scientist on the project. "This process has previously required gene therapy, limiting its widespread use."

The team at Harvard envisions a future where age-related diseases can be effectively treated, injuries can be repaired more efficiently, and the dream of whole-body rejuvenation becomes a reality. "This new discovery offers the potential to reverse aging with a single pill, with applications ranging from improving eyesight to effectively treating numerous age-related diseases," Sinclair said.

Reference: "Chemically induced reprogramming to reverse cellular aging" by Jae-Hyun Yang, Christopher A. Petty, Thomas Dixon-McDougall, Maria Vina Lopez, Alexander Tyshkovskiy, Sun Maybury-Lewis, Xiao Tian, Nabilah Ibrahim, Zhili Chen, Patrick T. Griffin, Matthew Arnold, Jien Li, Oswaldo A. Martinez, Alexander Behn, Ryan Rogers-Hammond, Suzanne Angeli, Vadim N. Gladyshev and David A. Sinclair, 12 July 2023, *Aging-US*.

DOI: [10.18632/aging.204896](https://doi.org/10.18632/aging.204896)

Sea creature with ability to defy age accidentally discovered by scientists



Sea creature with ability to reverse age accidentally discovered by scientists© Orin Zebest/Wikimedia

Scientists have [uncovered new details about the so-called immortal jellyfish](#).

The comb jelly, also known by its scientific name *Turretopsis dohrnii*, has the ability to defy age. And a new study published in [Proceedings of the National Academy of Sciences](#) suggests it may be one of a swath of species with the ability to "time travel."

"The work challenges our understanding of early animal development and body plans, opening new avenues for the study of life cycle plasticity and rejuvenation," said Joan J. Soto-Angel, a postdoctoral fellow at the University of Bergen who co-wrote the study, in a [statement](#).

"The fact that we have found a new species that uses this peculiar 'time-travel machine' raises fascinating questions about how spread this capacity is across the animal tree of life."

Soto-Angel revealed the discovery came about accidentally.

He and his colleagues were investigating the subject after a larval ctenophore suddenly appeared in the place of an adult ctenophore in a tank in his lab.

The team later discovered it was the same creature.

They decided to recreate the scenario in an attempt to trigger reverse development, which is when they discovered that an adult ctenophore can, in fact, revert to a larval stage if under extreme stress.

"Witnessing how they slowly transition to a typical cydippid larva as if they were going back in time, was simply fascinating," Soto-Angel explained.

"Over several weeks, they not only reshaped their morphological features, but also had a completely different feeding behavior, typical of a cydippid larva."

Research suggests the comb jellies are ancient animals that may be among the first to ever exist.

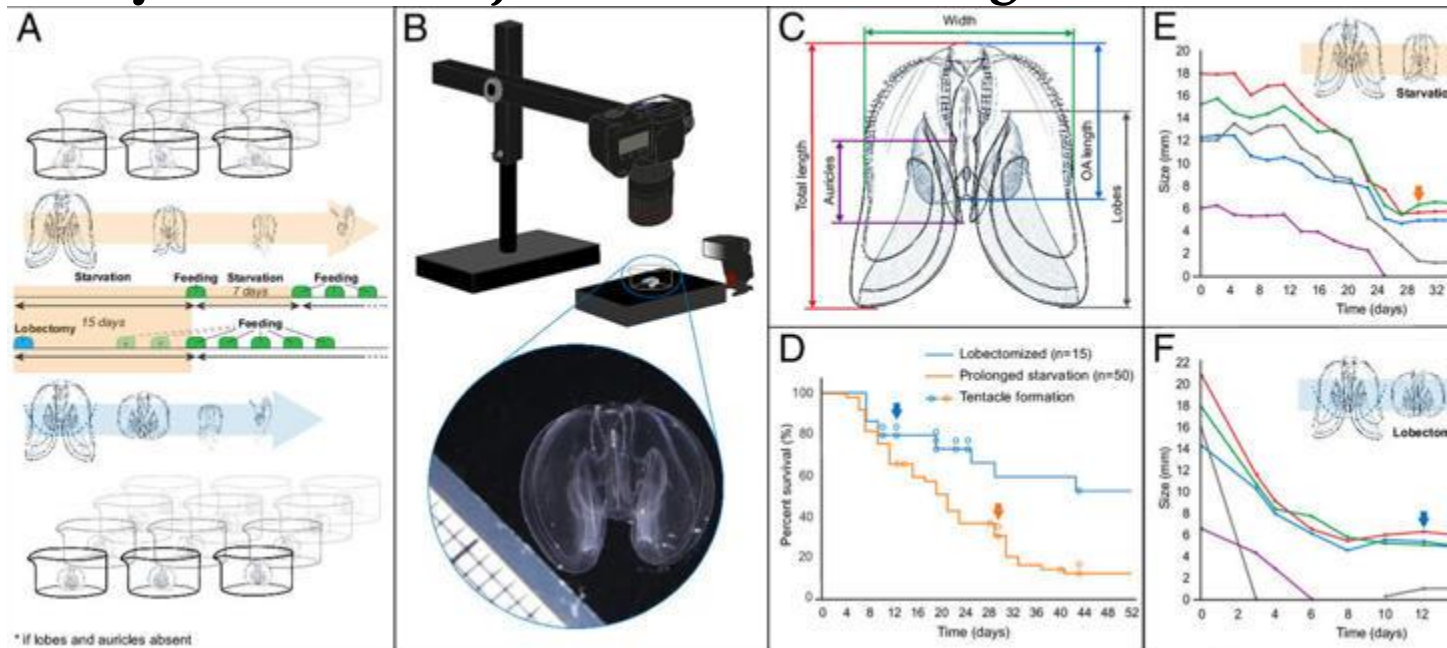
It is believed they emerged roughly 700 million years ago.

"This is a very exciting time for us," said Paul Burkhardt, a researcher at the University of Bergen who also co-wrote the study, in the statement.

"This fascinating finding will open the door for many important discoveries. It will be interesting to reveal the molecular mechanism driving reverse development, and what happens to the animal's nerve net during this process."

The researchers believe that the life cycle plasticity of the organism may be present among more animals, too.

Study finds comb jellies can reverse age

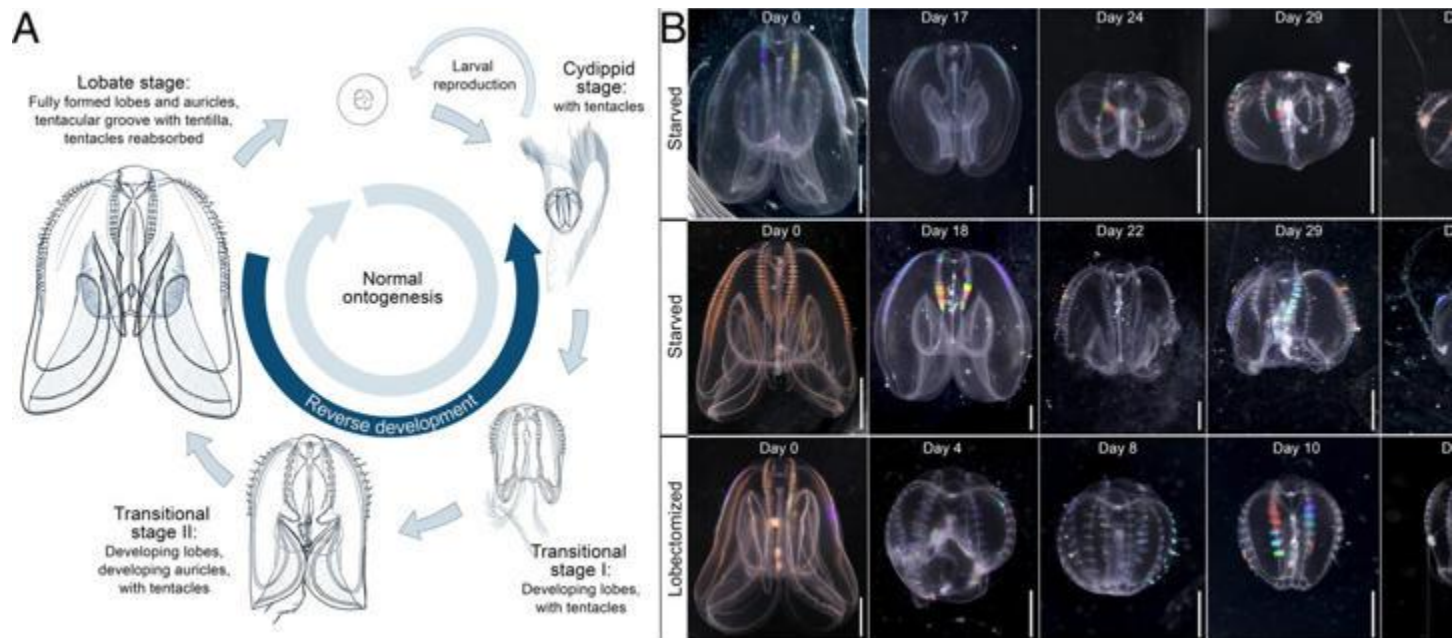


Reverse development in the ctenophore *Mnemiopsis leidyi*. (A) Experimental design for starved (above) and lobectomized (below) *M. leidyi*. (B) Imaging station to record morphometric changes over time. (C) Detail and extent of the anatomical features monitored. (D) Percentage of survival over time across the two treatments. Circles over the line indicate tentacle regeneration for all individuals that displayed reverse development (n = 20). Arrows correspond to the animals shown in panels E and F. (E) Morphometric changes for a starved individual. (F) Morphometric changes for a lobectomized individual. Arrows point to tentacle regeneration. Color code for anatomical features followed in panels E and F as shown in panel C. Credit: Proceedings of the National Academy of Sciences (2024). DOI: 10.1073/pnas.2411499121

A new article published in *Proceedings of the National Academy of Sciences* reveals the unprecedented ability for reverse development in a ctenophore, also called comb jelly. The findings suggest that life cycle plasticity in animals might be more common than previously thought.

Animal life cycles typically follow a familiar pattern of decline in countless variations: they are born, grow, reproduce and die, giving way to the next generation. Only a few species are able to deviate from this general principle, the best-known example being the "immortal jellyfish" *Turritopsis dohrnii*, which can revert from an adult medusa back to a polyp. This elusive group of animals with flexible life cycles now includes the ctenophore *Mnemiopsis leidyi*.

"The work challenges our understanding of early animal development and body plans, opening new avenues for the study of life cycle plasticity and rejuvenation. The fact that we have found a new species that uses this peculiar 'time-travel machine' raises fascinating questions about how spread this capacity is across the animal tree of life," said Joan J. Soto-Angel, a postdoctoral fellow in the Manet Team at the Department of Natural History at the University of Bergen.



Life cycle and main morphological changes of the ctenophore *Mnemiopsis leidyi*. (A) Life cycle of the ctenophore *M. leidyi*. Ordinary downstream development (normal ontogenesis, clockwise) and reverse development (anticlockwise). Note the absence of tentacles in the fully transitioned lobate stage, and the presence of newly developed anatomical features (i.e., auricles and lobes) gradually appearing during metamorphosis of the cydingid stage, and shrinking until they disappear during reverse development. Illustrations of the different life stages by Nicholas Bezio. (B) Individual trajectories and morphological changes during reverse development for three *M. leidyi* specimens that fully reversed to a typical bitentaculate cydingid stage. Note the increase of prey items in the gut when tentacles regenerated. Scale bar: 5 mm for Day 0; all others 2 mm. Credit: Proceedings of the National Academy of Sciences (2024). DOI: 10.1073/pnas.2411499121

Gelatinous time-travel

The remarkable discovery began by chance. While observing animals in the laboratory, Soto-Angel noticed that an adult ctenophore had vanished from a tank, seemingly replaced by a larva.

Curious to find out if these could be the same individual, he and Pawel Burkhardt, group leader at the Michael SARS Centre at the University of Bergen designed experiments to try and reproduce this potential reversion under controlled conditions. When exposed to the stress of starvation and physical injury, *Mnemiopsis leidyi* demonstrated an extraordinary ability to shift from its lobate form back to a cydippid larval stage.

"Witnessing how they slowly transition to a typical cydippid larva as if they were going back in time, was simply fascinating," Soto-Angel recalled. "Over several weeks, they not only reshaped their morphological features, but also had a completely different feeding behavior, typical of a cydippid larva."

An ancient model to study life cycle evolution

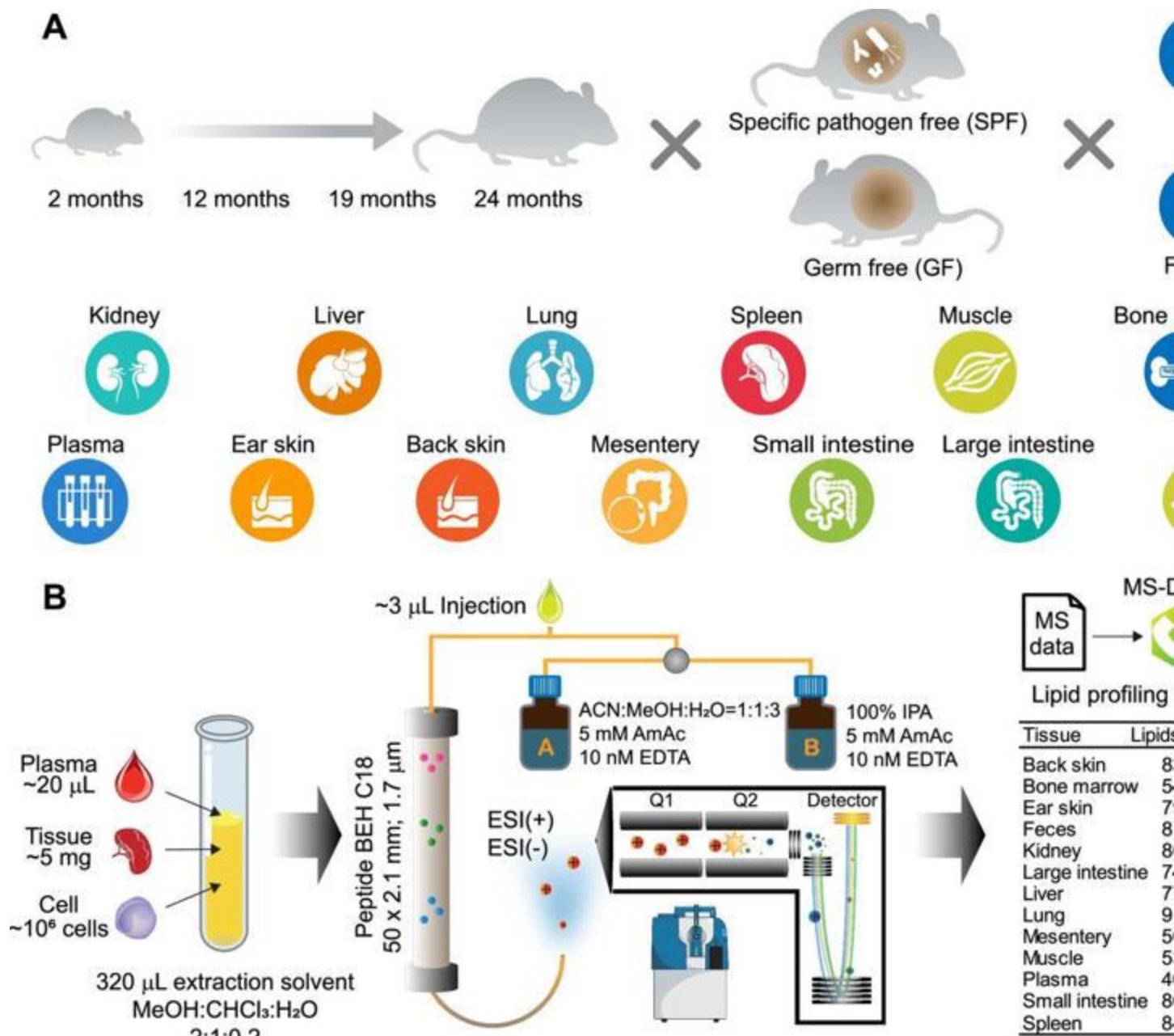
The study broadens the known developmental flexibility of ctenophores and positions *Mnemiopsis leidyi* as a valuable model for future research in developmental biology and aging. Since ctenophores are among the earliest animal lineages, the findings suggest that reverse development may represent an ancient feature in the animal kingdom.

"This is a very exciting time for us," Burkhardt said. "This fascinating finding will open the door for many important discoveries. It will be interesting to reveal the molecular mechanism driving reverse development, and what happens to the animal's nerve net during this process."

More information: Joan J. Soto-Angel et al, Reverse development in the ctenophore *Mnemiopsis leidyi*, *Proceedings of the National Academy of Sciences* (2024). DOI: [10.1073/pnas.2411499121](https://doi.org/10.1073/pnas.2411499121)

Provided by University of Bergen

Cracking the aging code: Insights into lipid changes



Summary of experimental design and lipid profiling in this study. Credit: Nature Aging (2024). DOI: 10.1038/s43587-024-00610-6 © Provided by Medical Xpress

Researchers at the RIKEN Center for Integrative Medical Sciences (IMS) have discovered numerous age-related changes in the lipid metabolism of mice, across both organs and sexes. Among these changes was the selective accumulation, throughout the body, of certain lipids produced by gut bacteria as the mice aged. They also discovered a sex difference in the kidneys and a gene responsible for it.

Published in *Nature Aging*, this [study](#) could lead to better understanding of chronic age-related conditions like Alzheimer's disease, atherosclerosis, kidney disease, and cancer.

Lipids, often in the form of fats or oils, are essential molecules for storing energy in our bodies, among other things. In addition, lipids act as signaling molecules and as components of cell membranes. Metabolism—the breakdown of biomolecules such as lipids and sugars into their component parts—slows down as we age, which helps explain why it's easier to gain weight, and more difficult to lose it, as we get older.

Although this has been known for more than 50 years, how changes in lipid metabolism in particular affect lifespan and health remains unclear. In their recent study, Hiroshi Tsugawa and his team at RIKEN IMS reasoned that before this question can be fully answered, we need to know what the actual changes are, in great detail. Only then can scientists begin looking for links between aging lipid metabolism and human health. Toward this end, they used mice to develop an atlas of age-related changes in lipid metabolites.

By using a cutting-edge technique to take multiple snapshots of the mouse lipidome—all lipid metabolites present in a biological sample—the researchers found that BMP type lipids increased with age in the kidneys, liver, lungs, muscles, spleen, and small intestine of the mice. These lipids play key roles in cholesterol transport and the breakdown of biomolecules within cellular recycling centers called lysosomes. Age-related lysosomal damage might result in cells making more BMPs, which could lead to further metabolic changes, such as increasing cholesterol derivatives in the kidney.

The researchers also investigated the impact of gut bacteria on the lipidome, discovering that while gut bacteria produced many structurally unique lipids, only

sulfonolipids increased with age in the liver, kidney, and spleen. In fact, no other group of lipid metabolites from gut bacteria were even detected in these peripheral tissues.

"As this kind of lipid is known to be involved in regulating immune responses, the next phase of our research will involve testing the gut bacteria-derived sulfonolipids to determine their structure and physiological functions," says Tsugawa.

The researchers also found age-related sex differences in the mouse lipidome, particularly in the kidneys, with levels of the lipid metabolite galactosylceramide being higher in older male mice than in older females. This discrepancy was attributed to increased expression of the UGT8 gene in male mice. Understanding sex-specific metabolic differences like this could shed light on susceptibility to age-related diseases humans.

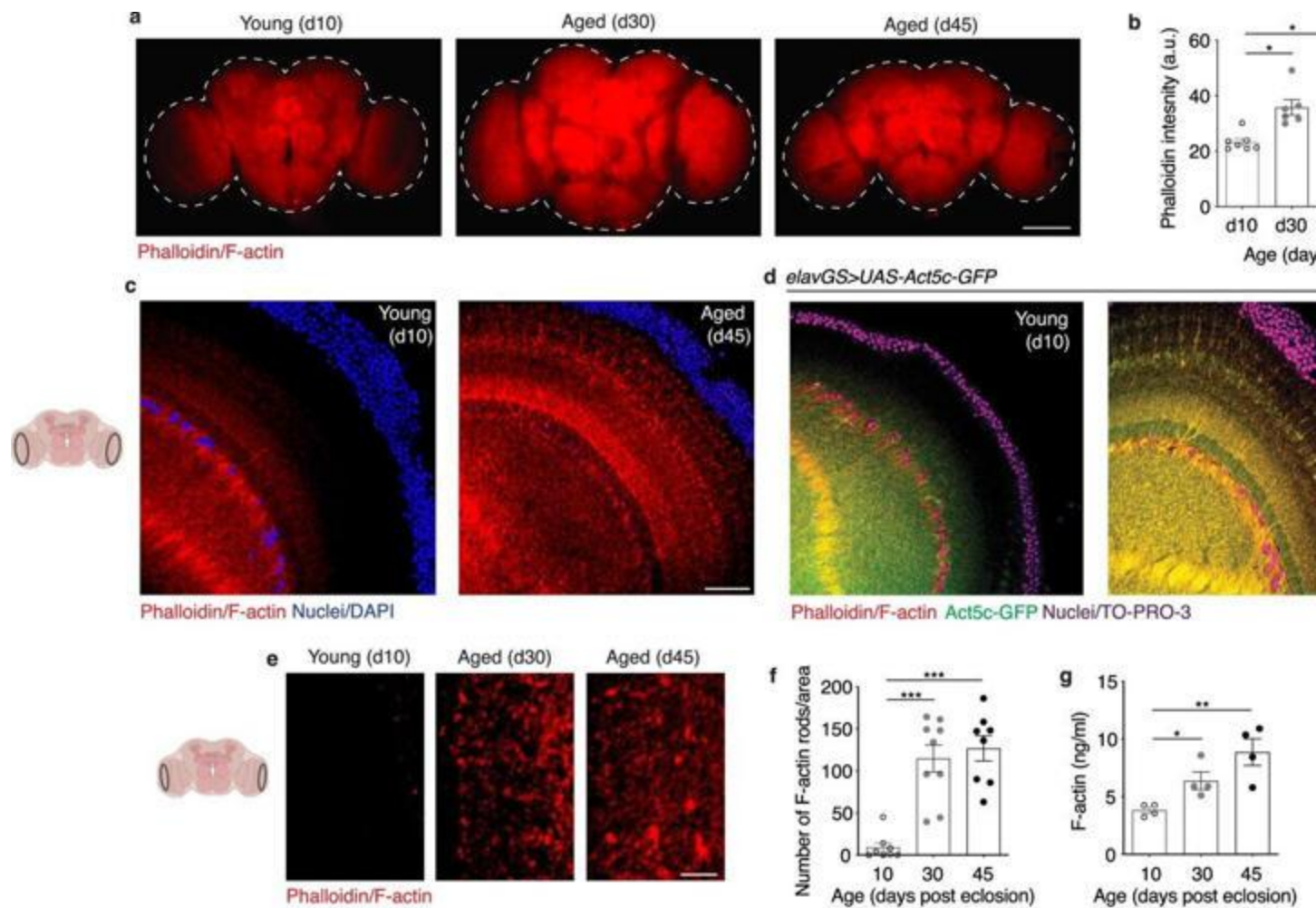
"Our research has comprehensively characterized the changes in the lipidome that occur in the mouse with aging. In doing so, we have created an atlas that will serve as an important global resource," says Tsugawa. "Next, we must extend this type of study to the human lipidome and microbiome."

The findings highlight the importance of understanding how lipid metabolism changes as we age, and the potential of targeting the lipidome when designing treatments for age-related diseases.

More information: Hiroshi Tsugawa et al, A lipidome landscape of aging in mice, *Nature Aging* (2024). DOI: [10.1038/s43587-024-00610-6](https://doi.org/10.1038/s43587-024-00610-6)

Provided by RIKEN

Scientists can reverse brain aging in fruit flies by preventing buildup of a common protein



F-actin accumulates in aged *Drosophila* brains and correlates with health. Credit: Nature Communications (2024). DOI: 10.1038/s41467-024-53389-w

Humans aren't the only ones who grow forgetful as they age—fruit flies do, too. But because fruit flies have a lifespan of only about two months, they can be a useful model for understanding the cognitive decline that comes with aging.

A new study [published](#) in *Nature Communications* shows that when a common cell structural protein called filamentous actin, or F-actin, builds up in the brain, it

inhibits a key process that removes unnecessary or dysfunctional components within cells, including DNA, lipids, proteins and organelles.

The resulting accumulation of waste diminishes neuronal functions and contributes to cognitive decline. By tweaking a few specific genes in aging fruit flies' neurons, the researchers prevented F-actin buildup, maintained cellular recycling and extended the healthy lifespan of fruit flies by approximately 30%.

Actin, a family of proteins that help give cells their shape, are abundant throughout the body. F-actin forms filaments that are essential for maintaining cell structure and many other functions. The researchers, led by former postdoctoral scholar Edward (Ted) Schmid in David Walker's lab, noticed F-actin buildup in the brains of aging fruit flies and wondered if it contributed to brain aging and overall loss of organismal health.

Their first clue of a correlation: Flies on a restricted diet both lived longer and had less F-actin buildup in their brains. Their second clue: When treated with a drug known to extend lifespan, called rapamycin, there was also less F-actin in the brains of aged flies.

"But that's correlation, not a direct demonstration that F-actin is detrimental to aging of the brain," said Walker, senior author and UCLA professor of integrative biology and physiology. "To get at causality, we turned to genetics."

Because the fruit fly genome is thoroughly mapped and understood, the group was able to target in aging fruit flies genes that are known to play important roles in the accumulation of actin filaments. That included a gene called Fhos, a member of a family of proteins known to elongate and organize actin filaments.

"When we reduced Fhos expression in aging neurons, it prevented the accumulation of F-actin in the brain," said Schmid, now an investigator at the Arkansas Biosciences Institute and assistant professor at Arkansas State University. "This really allowed us to expand our study because now, we had a direct way to target F-actin accumulation in the brain and study how it affects the aging process."

Even though the genetic intervention was targeted to just neurons, it improved the flies' overall health. They lived 25-30% longer, while showing signs of improved brain function as well as markers of improved health in other organ

systems. Preventing F-actin accumulation protected cognitive function, which shows the buildup is driving age-onset cognitive decline.

"Flies get more forgetful as they age, and their ability to learn and remember declines in middle age, just like it does in people," Walker said. "If we prevent accumulation of F-actin, it helps the flies learn and remember when older—which tells us the buildup is not benign."

Further investigation showed the F-actin was interfering with the body's "cellular garbage disposal system." Damaged or superfluous proteins and other components inside a cell are broken down in a process called "autophagy." Aging research has established that autophagy pathways become less active with age, but no one knew exactly why.

The new study shows that preventing F-actin accumulation led to much more active autophagy in the brains of aged fruit flies. The authors found that if they removed F-actin but also disabled autophagy, it did not slow aging: The primary mechanism by which F-actin drives brain aging appears to be by impairing autophagy. The researchers also showed that disrupting F-actin in aged brains can restore brain autophagy to youthful levels and reverse certain cellular markers of brain aging.

These findings may be good news for the elderly fruit flies with reduced F-actin in their brains. But it has not yet been demonstrated in humans, and developing interventions to prevent F-actin accumulation might prove more challenging. Still, the discovery directs researchers in a fruitful new direction for healthier aging in people.

"Most of us in the aging field are focused on moving beyond lifespan into what we call the healthspan," said Walker. "We want to help people enjoy good health and a high quality of life while extending the lifespan. Our study improved cognitive and gut function, activity level, and overall healthspan of fruit flies—and offers hope for what we might be able to achieve in humans."

More information: Edward T. Schmid et al, Accumulation of F-actin drives brain aging and limits healthspan in *Drosophila*, *Nature Communications* (2024). DOI: [10.1038/s41467-024-53389-w](https://doi.org/10.1038/s41467-024-53389-w)

Provided by University of California, Los Angeles

Theory About the Multiverse Suggests That it May Even Hold the Key to Immortality

In 1979, physicist Alan Guth proposed 'cosmological inflation' as one of the most developed multiverse models to answer questions about the existence of a parallel universe that had been discussed since the early 1900s. He suggested that after the Big Bang, the universe expanded rapidly for a brief moment, creating a huge zoom effect that affected the cosmic microwave background and the distribution of galaxies.

Elaborating on the same, Neil Turok, a physicist at the University of Edinburgh, UK, told [Bored Panda](#), "It was an approach that was born out of a certain sense of frustration with previous approaches. In my view, they had all become rather complicated and contrived, including my own approaches." He added, "I thought we could be on the verge of the next big revolution in theory. It would be inspired by the data, and by the failure of traditional paradigms. It would change our view of the universe."

Following Guth's proposal, many theories emerged including one from physicist Andrei Linde, who introduced chaotic inflation in 1983. This suggested that rapid expansion possibly occurred in different ways due to chaotic early conditions in the universe. [Knewz.com](#) noted that in 2013, the European Space Agency's Planck satellite map of the cosmic microwave background challenged inflation theory.

Since then, scientists have been inventing new methods to prove that there were parallel universes. Some argued in favor of the cyclic universe, which proposed that the universe went through endless cycles of formation and destruction. Additionally, Turok himself suggested a mirror universe theory in 2018, explaining that our universe had a twin where time moved backward.

According to theoretical physicist Alexander Vilenkin of Tufts University in Massachusetts, inflation didn't stop everywhere at the same time. Writing in [Scientific American](#), he explained that when inflation stopped in one area, a new bubble universe was formed. He further wrote, "This picture of the universe, or multiverse, as it was called, explained the long-standing mystery of why the

constants of nature appeared to be fine-tuned for the emergence of life. The reason was that intelligent observers existed only in those rare bubbles in which, by pure chance, the constants happened to be just right for life to evolve. The rest of the multiverse remained barren, but no one was there to complain about that."

Another theory that gained attention was Hugh Everett's 'Many-Worlds theory.' According to his theory, whenever an event had several possible outcomes, the universe split with every action. The theory surfaced more in the late 1990s through a thought experiment called 'quantum suicide,' which suggested that the Many-Worlds idea was theoretically possible. It was first suggested by physicist Hans Moravec in the 1990s and later expanded by Max Tegmark.

The experiment was created to test the idea of the 'many worlds' interpretation of quantum mechanics. Furthermore, the trials suggested that the person involved in the experiment would never experience death. This was because there would always be a version of the universe where they survived, making them 'quantum immortal.' Since then, physicists and mathematicians have continued to explore its implications. However, Many-Worlds was just one of several theories about the universe, and scientists were exploring more in search of a logical explanation.

This transparent sea creature can age in reverse

An Atlantic comb jelly known as the "sea walnut" has the ability to reverse its own aging process, a new study suggests.

When food is scarce or the sea creature is injured, the gelatinous invertebrate can develop backward into its larval form, which has two tentacles to catch food. The adult form, which looks like a small pair of transparent lungs, lacks these tentacles.

The sea walnut (*Mnemiopsis leidyi*) is the third-known animal species, and the first-known comb jelly (Ctenophora), that can revert to an earlier life stage after already reaching adulthood, according to the study, which was published Aug. 10 on the preprint database [BioRxiv](#). (It has not yet been peer-reviewed).

Scientists previously showed that a handful of cnidarians — a group that includes jellyfish, sea anemones and corals — can develop backward, but only before reaching sexual maturity. The two other documented species that can develop backward as adults are the so-called immortal jellyfish (*Turritopsis dohrnii*) and the dog tapeworm (*Echinococcus granulosus*).

Age reversal in comb jellies "confirms that reversal development might be more widespread than previously thought," researchers wrote in the study, which builds on [previous work](#) investigating the [sea walnut's hardiness](#).

Related: [Extreme longevity: The secret to living longer may be hiding with nuns... and jellyfish](#)

The sea walnut is native to the western Atlantic Ocean, but the species has spread to become an invasive nuisance in Europe and Asia. *M. leidy* can [survive in the ballast water of ships for weeks](#) despite the lack of food, which is how researchers think the comb jellies made it across the Atlantic. The species is now found in the Black and Caspian seas, where it has contributed to the collapse of fisheries by competing with native creatures for food, as well as in the Mediterranean, Baltic and North seas.

To shed light on the sea walnut's survival tactics, the researchers carried out experiments in which they starved one group of comb jellies and physically injured another by removing tissue from their lobes. (Like other ctenophores, sea walnuts can regenerate entirely from even a small chunk of flesh. The same researchers [previously found](#) that the sea walnut's nervous system is fused, which [may confer some advantage for tissue repair and healing](#).)



New research suggests the sea walnut can develop in reverse when stressed. (Image credit: dan_manila via Alamy)

Starved and amputated sea walnuts shrunk into tiny blobs, but they didn't die. When the researchers fed both groups again, they observed that 13 out of the 65 comb jellies tested had grown tentacles, a sign they had regressed to the larval stage.

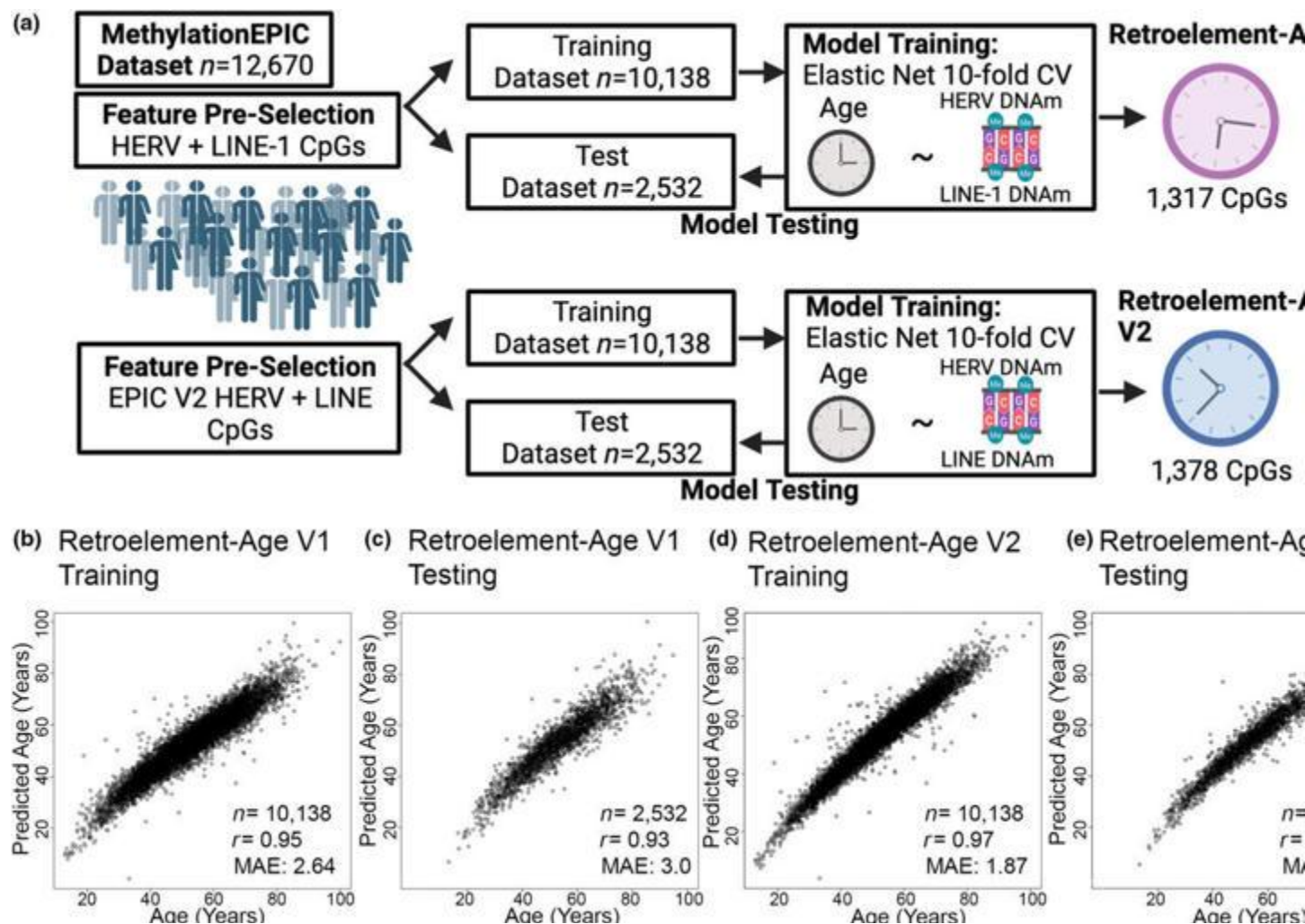
Co-author [Joan J. Soto-Angel](#), a marine biologist and postdoctoral fellow at the University of Bergen in Norway, told [Science](#) that the jellies used their tentacles to capture food to which they would not have had access as adults, tapping into a new ecological niche. With enough food, the comb jellies eventually reached their original size again and regrew their lobes. The creatures even regained their ability to reproduce, according to the study.

Finding a third animal capable of aging in reverse "was quite a surprise," Soto-Angel said. The process by which *M. leidyi* regresses to its larval form is different from how the immortal jellyfish does it, he said, but both animals could help researchers understand aging better.

Comb jellies are also one of the oldest extant animal lineages and [possibly the sister group to all animals](#), making them a unique model to study evolution.

It remains unclear whether the comb jellies really turned back the clock on their age, or whether they simply shrunk, [Yoshinori Hasegawa](#), a zoologist at the Kazusa DNA Research Institute in Japan who was not involved in the research, told Science. "It looks like an imperfect rejuvenation," Hasegawa said.

Study finds potential link between DNA markers and aging process



Construction of Composite Retroelement-Age and Retroelement-Age V2 Epigenetic Clocks. Credit: Aging Cell (2024). DOI: 10.1111/accel.14288

Researchers at Weill Cornell Medicine and the epigenetics company

TruDiagnostic have uncovered DNA markers associated with retroelements, remnants of ancient viral genetic material in our genes that act as highly accurate epigenetic clocks predicting chronological age. The results support the idea that certain retroelements in the human genome may be involved in aging.

Retroelements have been known to impact gene regulation, gene expression, genomic stability and the trajectory of various human diseases, but their potential as biomarkers for aging had been largely unexplored.

The [study](#), published in *Aging Cell*, concluded that these retroelement clocks embedded in the human genome capture unique signals of aging not previously recognized by other clocks that measure chronological age.

Most aging clocks estimate a person's biological age based on patterns of epigenetic markers—chemical tags called methyl groups that are attached to DNA and affect how genes are expressed. The pattern of methylation on retroelements seems to change as people age, causing some genes to be more active, which may lead to genomic instability, inflammation and age-related diseases.

Aging is a complex process influenced by genetic, environmental and epigenetic factors, with researchers pursuing reliable markers that can predict biological age—a snapshot of a person's age at the biochemical level that impacts health and overall well-being. On the other hand, chronological age represents the number of years a person has lived. Depending on the individual, the two may not correlate.

Building an aging clock based on retroelements

Researchers used a machine learning model from TruDiagnostic to analyze epigenetic data from 12,670 individuals with ages ranging from 12 to 100. Using the resulting DNA methylation patterns of retroelements, specifically human

endogenous retrovirus (HERV) and long interspersed nuclear elements (LINEs), they developed a composite retroelement-age clock called "Retro-Age."

"Now, with Retro-Age, we have greater insight and a fresh perspective into the aging process and a potentially powerful tool to predict biological age," said first author Dr. Lishomwa Ndhlovu, the Herbert J. and Ann L. Siegel Distinguished Professor of Medicine and professor of immunology in medicine in the Division of Infectious Diseases at Weill Cornell Medicine.

The researchers found that the Retro-Age clock remained accurate when testing various human tissues, complemented existing epigenetic clocks and even extended to other mammalian species. Their findings point to the possibility that retroelement activity might be a fundamental aspect of aging across different species.

Turning back the clock: The impact of environmental factors

The researchers also found that the DNA methylation patterns they observed were not only predictive of age but also responsive to outside factors like antiretroviral therapy taken by people living with HIV. HIV infection accelerates epigenetic aging, while antiretroviral therapy appears to reverse the clock to some degree. This suggests that retroelement activity is influenced by both the infection and its treatment, affecting the biological aging process in people living with HIV.

"The reactivation of specific retroelements increases with age, potentially leading to biological hallmarks of aging such as inflammation, cellular senescence and genomic instability," said corresponding author Dr. Michael Corley, assistant professor of immunology in medicine in the Division of Infectious Diseases at Weill Cornell Medicine.

"Our findings indicate that retroelement clocks capture previously undetected facets of biological aging and may open the door to future treatments for these and other age-related conditions."

Monitoring the activity of retroelements could help track the effectiveness of anti-aging therapies, health outcomes in aging populations and the impact of lifestyle changes on biological aging, said the researchers.

Drs. Ndhlovu and Corley plan to explore new treatments or therapeutic interventions for age-related diseases by targeting the epigenetic states of specific retroelements in the human genome. This approach, they noted, may eventually reverse or mitigate the biological effects of aging, improving an individual's health span and lifespan.

More information: Lishomwa C. Ndhlovu et al, Retro-age: A unique epigenetic biomarker of aging captured by DNA methylation states of retroelements, *Aging Cell* (2024). DOI: [10.1111/ace.14288](https://doi.org/10.1111/ace.14288)

Provided by Weill Cornell Medical College

Study: Certain nutrients may slow brain aging



Chronological versus brain age. Credit: npj Aging (2024). DOI: 10.1038/s41514-024-00150-8© Provided by Medical Xpress

Scientists have long been studying the brain with the goal of aiding healthier aging. While much is known about risk factors for accelerated brain aging, less has been uncovered to identify ways to prevent cognitive decline.

There is evidence that nutrition matters, and a novel study [published](#) in *npj Aging*, from the University of Nebraska–Lincoln's Center for Brain, Biology and Behavior and the University of Illinois at Urbana-Champaign further signals how specific nutrients may play a pivotal role in the healthy aging of the brain.

The team of scientists, led by Aron Barbey, director of the Center for Brain, Biology and Behavior, with Jisheng Wu, a doctoral student at Nebraska, and Christopher Zwillig, research scientist at UIUC, performed the multimodal study—combining state-of-the-art innovations in neuroscience and nutritional science—and identified a specific nutrient profile in participants who performed better cognitively.

The cross-sectional study enrolled 100 cognitively healthy participants, aged 65–75. These participants completed a questionnaire with demographic information, body measurements and physical activity.

Blood plasma was collected following a fasting period to analyze the nutrient biomarkers. Participants also underwent cognitive assessments and MRI scans. The efforts revealed two types of brain aging among the participants—accelerated and slower-than-expected. Those with slower brain aging had a distinct nutrient profile.

The beneficial nutrient blood biomarkers were a combination of fatty acids (vacenic, gondoic, alpha linolenic, elcosapentaenoic, eicosadienoic and lignoceric acids); antioxidants and carotenoids including cis-lutein, trans-lutein and zeaxanthin; two forms of vitamin E and choline. This profile is correlated with nutrients found in the Mediterranean diet, which research has previously associated with healthy brain aging.

"We investigated specific nutrient biomarkers, such as fatty acid profiles, known in nutritional science to potentially offer health benefits. This aligns with the extensive body of research in the field demonstrating the positive health effects of the Mediterranean Diet, which emphasizes foods rich in these beneficial nutrients," Barbey, Mildred Francis Thompson Professor of Psychology, said.

"The present study identifies particular nutrient biomarker patterns that are promising and have favorable associations with measures of cognitive performance and brain health."

Barbey noted that previous research on nutrition and brain aging has mostly relied on food frequency questionnaires, which are dependent on participants' own recall. This study is one of the first and the largest to combine brain imaging, blood biomarkers and validated cognitive assessments.

"The unique aspect of our study lies in its comprehensive approach, integrating data on nutrition, cognitive function, and brain imaging," Barbey said. "This allows us to build a more robust understanding of the relationship between these factors. We move beyond simply measuring cognitive performance with traditional neuropsychological tests.

"Instead, we simultaneously examine brain structure, function, and metabolism, demonstrating a direct link between these brain properties and cognitive abilities. Furthermore, we show that these brain properties are directly linked to diet and nutrition, as revealed by the patterns observed in nutrient biomarkers."

The researchers will continue to explore this nutrient profile as it relates to healthy brain aging. Barbey said it's possible, in the future, that the findings will aid in developing therapies and interventions to promote brain health.

"An important next step involves conducting randomized controlled trials. In these trials, we will isolate specific nutrients with favorable associations with cognitive function and brain health, and administer them in the form of nutraceuticals," Barbey said.

"This will allow us to definitively assess whether increasing the levels of these specific nutrient profiles reliably leads to improvements in cognitive test performance and measures of brain structure, function, and metabolism."

More information: Christopher E. Zwillling et al, Investigating nutrient biomarkers of healthy brain aging: a multimodal brain imaging study, *npj Aging* (2024). DOI: [10.1038/s41514-024-00150-8](https://doi.org/10.1038/s41514-024-00150-8)

Provided by University of Nebraska-Lincoln

Spineless awareness: Comb jellies can fuse and reverse age, new research reveals



Warty Comb jellyfish *Mnemiopsis leidyi* Getty Images/Oxford Scientific

In 1641, French philosopher René Descartes, writing his famous "[Meditations on First Philosophy](#)," observed that a [mind is fundamentally different from the body](#) which contains it. He reasoned that, while physical objects like flesh and bone can be divided or merged together, [consciousness](#) is intrinsically different because it cannot be quantified. Scientists have long known that it is impossible to separate or fuse a conscious mind — at least, that is what they thought.

Yet a pair of recent studies about comb jellies raise provocative questions about Descartes' maxim. The first is a [study](#) from the journal *Current Biology* found that ctenophores, a phylum of aquatic invertebrates better known as comb jellies, can successfully fuse together after being injured. (Though the animals have a striking weirdness and similarity to jellyfish, [they are not technically related](#).) The scientists studied a population of warty comb jellies (*Mnemiopsis leidyi*) in a tank, gazing in amazement as two organisms bonded with one another with the flesh, seamlessly integrating as if to form a single new animal.

"While maintaining a population of *M. leidyi* in a seawater tank, we noticed an atypically large individual with two aboral ends [referring to the area farthest from the mouth] and two apical organs [areas closest to the animal's apex]," the authors wrote in a statement. To test whether this comb jelly was actually two individuals who had fused together, the scientists tested individual ctenophores collected at different sites on separate dates. After cutting off a part of each animal's lobe and placing different creatures together, they found on nine out of ten occasions (90%) "independent grafting experiments were successful, and all fused ctenophores survived for the full holding time of about three weeks in the holding tank."

Previous research has demonstrated that *M. Leidyi* fuse within themselves whenever they need to defecate, squashing together their outer skin and digestive system fuse to form an opening— essentially creating a "[disappearing anus](#)" — yet this is the first evidence for two separate jellies becoming one. But If these two individuals are now one, does that mean their minds literally melded — or that perhaps they were never even sentient in the first place?

"We know that comb jellies (aka: ctenophores) are sentient in that they can sense their surroundings to find food and change the direction of their swimming if they bump into something," study co-author and Colorado State University biologist Mariana Rodriguez told Salon. "We don't know much else beyond this basic type of sentience. It's hard to answer what this implies for consciousness of two animals fusing into one since it depends on how we define consciousness."

Fellow co-author Kei Jokura, a biologist at the University of Exeter, initially discovered the fused comb jelly. Jokura told Salon that although no other animal has demonstrated “functional fusion” in the manner seen with the comb jellies, other organisms like corals, sponges and ascidians can physically behave as if they are a single entity despite containing numerous individuals.

“However, this differs from our finding, where previously independent organisms fused in just a few hours, merging nervous and digestive systems functionally,” Jokura said. “This ability is largely influenced by a lack of an allo-recognition system, which usually differentiates self from non-self and triggers immune rejection. In our experiments, nearly 90% of individuals exhibited fusion, suggesting that comb jellies might lack this allo-recognition mechanism.”

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Jokura added he was most intrigued by “the synchronized contraction of the muscles, which indicates that nerve cells fused quickly, allowing the sharing of electrical signals or action potentials. This could imply a form of shared consciousness, making this phenomenon a valuable experimental model for studying integration mechanisms.”

Jokura was not the only scientist to make a milestone discovery after wandering past a tank containing a gelatinous animal. While studying comb jellies in a different tank, University of Bergen natural historian Joto J. Soto-Angel [noticed](#) that an adult ctenophore, also the species *M. leidy*, had vanished from his tank and seemingly replaced by a larva. Working with Pawel Burkhardt, group leader at the University of Bergen’s Michael SARS Centre, Soto-Angel designed experiments to see if the comb jelly reverted to its larval form much like the so-called “[immortal jellyfish](#)” *Turritopsis dohrnii*.

Like Jokura, Soto-Angel’s curiosity was rewarded. After being exposed to the stress of starvation and physical injury, the comb jellies in Soto-Angel’s care reverted back to a cydippid larval stage.

"Witnessing how they slowly transition to a typical cydippid larva as if they were going back in time, was simply fascinating," Soto-Angel said in a statement. "Over several weeks, they not only reshaped their morphological features, but also had a completely different feeding behavior, typical of a cydippid larva."

"This is a very exciting time for us," Burkhardt added in the statement. "This fascinating finding will open the door for many important discoveries. It will be interesting to reveal the molecular mechanism driving reverse development, and what happens to the animal's nerve net during this process."

Even scholars who are not involved in the pair of papers agree that they reveal the immense potential in studying ctenophores. University of Florida neuroscientist Leonid L. Moroz, who specializes in ctenophores but was not involved in either recent study, told Salon that "we know more about rocks on the Moon than about our oceans. It is estimated that we only know ~10% of marine inhabitants."

Pointing out that this is disastrous for humanity from the perspective of our basic survival, Moroz added that "support for basic science, and marine biology in particular, is the only reasonable and cost-efficient way to ensure a healthy life for our children and grandchildren."

As Rodriguez succinctly put it, "Comb jellies may be the oldest animal group that exists and so they provide a unique opportunity to study basic but fundamental aspects of how animals move and interact in the world." Because of their remarkable abilities like fusing together and reversing their own aging process, they "can teach us new ways to think about the evolution of regeneration and sentience."

We're entering a 'new age' of aging research with ability to 'enhance health spans,' scientists say

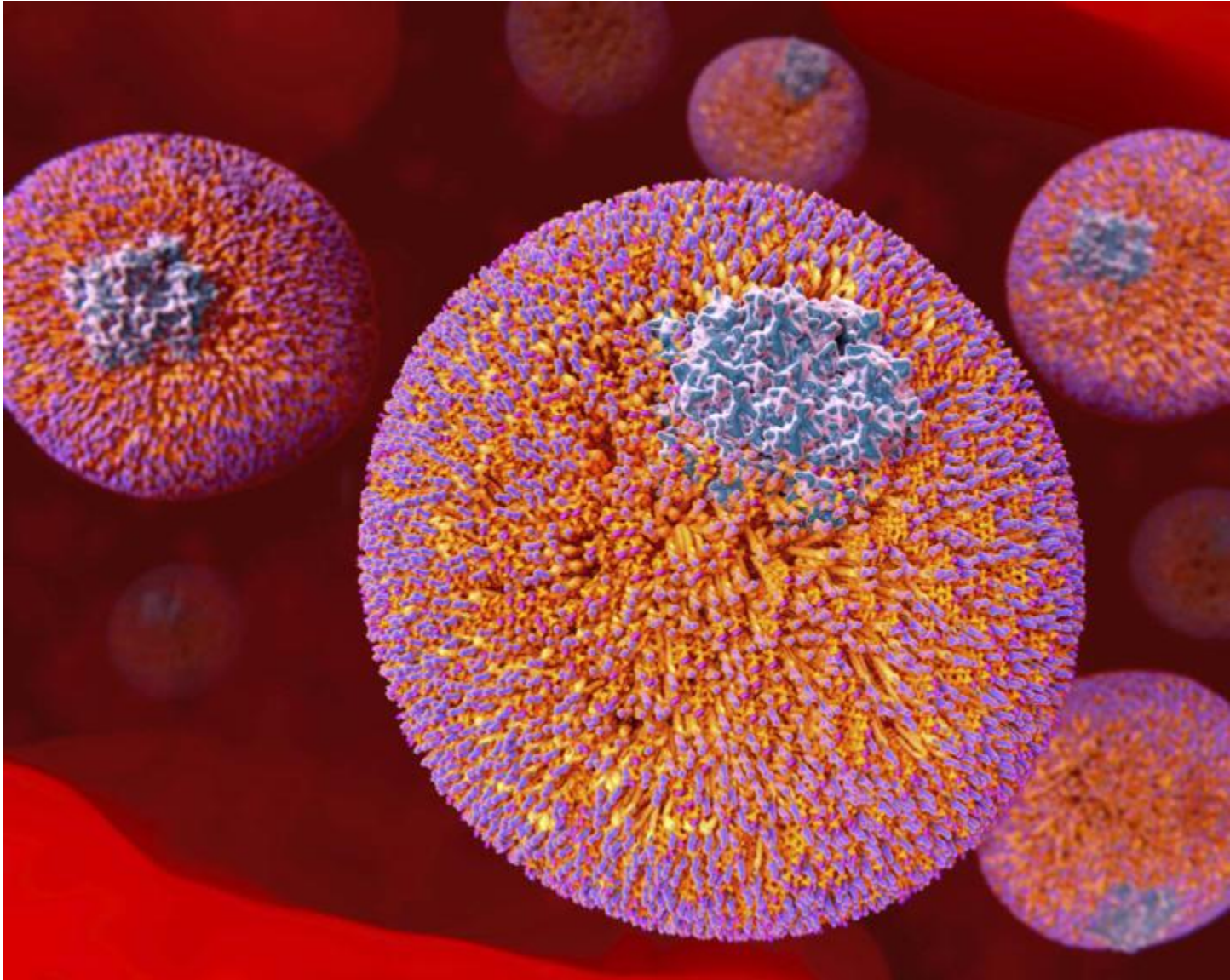


We're entering a 'new age' of aging research with ability to 'enhance health spans,' scientists say© The Focus

A group of Chinese scientists has claimed we're entering a "new clinical age of aging research," with developments showing "significant potential" to "enhance health spans."

There are dozens of things we can do to boost our own potential to live a long and [healthy](#) life. Whether it be [adopting daily habits to help manage stress and](#)

boost our immune system, or deciding to remove certain things from our lives, such as smoking or drinking alcohol, our fate is, at least in part, in our hands. But progress goes further than that. Science has been delivering innovations that have serious potential to improve longevity, the researchers say.



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New approaches allow us to get rid of cells that have stopped dividing

"Innovative approaches have been developed to eliminate senescent cells," reads the [paper](#), published on September 2, 2024, in the academic journal Trends in Endocrinology & Metabolism.

This is one of three anti-aging interventions they studied. The other two are the "targeting of inflammaging" (explanations will follow!) and the "harnessing of endogenous metabolites and precursors with anti-aging properties."

- **HUH:** [Three common mistakes causing premature aging that skin expert warns against](#)

They also touch on rapamycin, which they call an "anti-aging molecule," which possesses anti-inflammatory effects. In clinical contexts, rapamycin (sold under the brand name Rapamune, and also called Sirolimus) is used to coat stents, prevent organ transplant rejection, and treat a rare form of lung disease.

Recent developments in medicine have led to the advent of senolytics. These are compounds that can be used to eliminate the negative effects of chronic senescent cells and kill them specifically.

Senescent cells, aka "zombie cells," have stopped dividing but aren't dead. The word "senescence" refers to the process by which a cell ages and permanently stops dividing. As a person ages, senescent cells build up in tissues throughout the body. Removing zombie cells without damaging other cells will prevent the buildup of what are essentially useless bits of matter in the tissues of the body.

What are 'inflammaging' and 'endogenous metabolites' and how are they used in anti-aging?

Inflammaging is a word for chronic inflammation. Its drivers include problems with immune cells, increased stress, and increased production of inflammatory cytokines, which are proteins the body produces to regulate the immune system.

The researchers say a “wide range” of anti-inflammaging therapies are currently in development. We know now, for example, that the long-term use of aspirin “can reduce the incidence and mortality rate of colorectal cancer by 33%.”

It can also decrease the chance a cancerous tumor will metastasize.

“Endogenous metabolite” is a fancy name for a molecule that fits somewhere in the process of metabolism, and is produced by the body. It includes loads of things: sugars, vitamins, fatty acids, and amino acids. *Exogenous* metabolites are not produced by the body and include food additives and various toxins and drugs.

The researchers praise various recent clinical advancements in the field of metabolism for being “promising” for the future of anti-aging. These include research into NAD+, which is found in all living cells and is central to energy metabolism; something called AKG, which plays a vital role in energy metabolism and physiology; and spermidine, which is found in its highest concentrations in cereals, legumes, and soy derivatives.

However, the researchers highlight that translating [scientific insights](#) into effective anti-aging interventions remains a “formidable challenge.” In other words, it may take some time for the science to trickle down to the rest of us. Still, hope is on the horizon! Watch this space.

A New Study Inched Closer to Discovering the Antidote for Death

- A new study out of Sweden investigated the blood of centenarians to understand what biomarkers indicate the potential for longer life.
- A group of biomarkers were noted for their differences across the 100-year-olds, largely associated with lower levels of sugar and a healthy liver and kidney.
- The researchers found that “centenarians overall displayed rather homogenous biomarker profiles.”

The biomarkers don't lie, and now we have a little more science that could show us how to [live longer](#).

A team of researchers from Sweden studied [blood](#)—specifically, the biomarkers in the blood—from 44,000 individuals over the age of 64, including about 1,200 people who were at least 100 years old. The study, [published](#) in *GeroScience*, examined the largest dataset of individuals to date in order to be able to contrast the long-lived against their shorter-lived peers.

They found discrepancies.

“The differences in biomarker values between centenarians and non-centenarians more than one decade prior to [death](#) suggest that genetic and/or possibly modifiable lifestyle factors reflected in these biomarker levels may play an important role for exceptional longevity,” the authors wrote.

Karin Modig, associate professor of epidemiology at Karolinska Institutet, [wrote](#) about the team's conclusions in *The Conversation*. She noted a key finding—that people reaching their 100th birthday tended to have lower levels of glucose, creatinine, and uric acid from their 60s onward. And, uniquely enough, “centenarians overall displayed rather homogenous [biomarker](#) profiles” without extremely high or low values.

In short, limit the [sugar](#) and take care of your liver and kidneys. The older you get, the more important this advice may become.

“Higher levels of total cholesterol and [iron](#) and lower levels of glucose, gamma-glutamyl transferase, alkaline phosphatase, lactate dehydrogenase, and total iron-binding capacity were associated with reaching 100 years,” the authors wrote.

Modig said that while the team didn’t draw any conclusions about lifestyle factors or genes responsible for the biomarker values, it is “reasonable to think that factors such as nutrition and alcohol intake play a role.” She suggested watching [kidney](#) and liver health, as well as glucose and uric acid levels.

The research included data from 44,000 Swedes who underwent health assessments between the ages of 64 and 99. They were then followed for up to 35 years, with 1,224 of them hitting 100 years old. Of note, 85 percent of the people who reached centenarian status were female. Modig wrote that the team studied 12 blood-based biomarkers related to inflammation, metabolism, liver and kidney function, and malnutrition and anemia—all associated with [aging](#) or mortality in previous studies. Of those 12, the team believes 10 of them show a connection to the likelihood of turning 100.

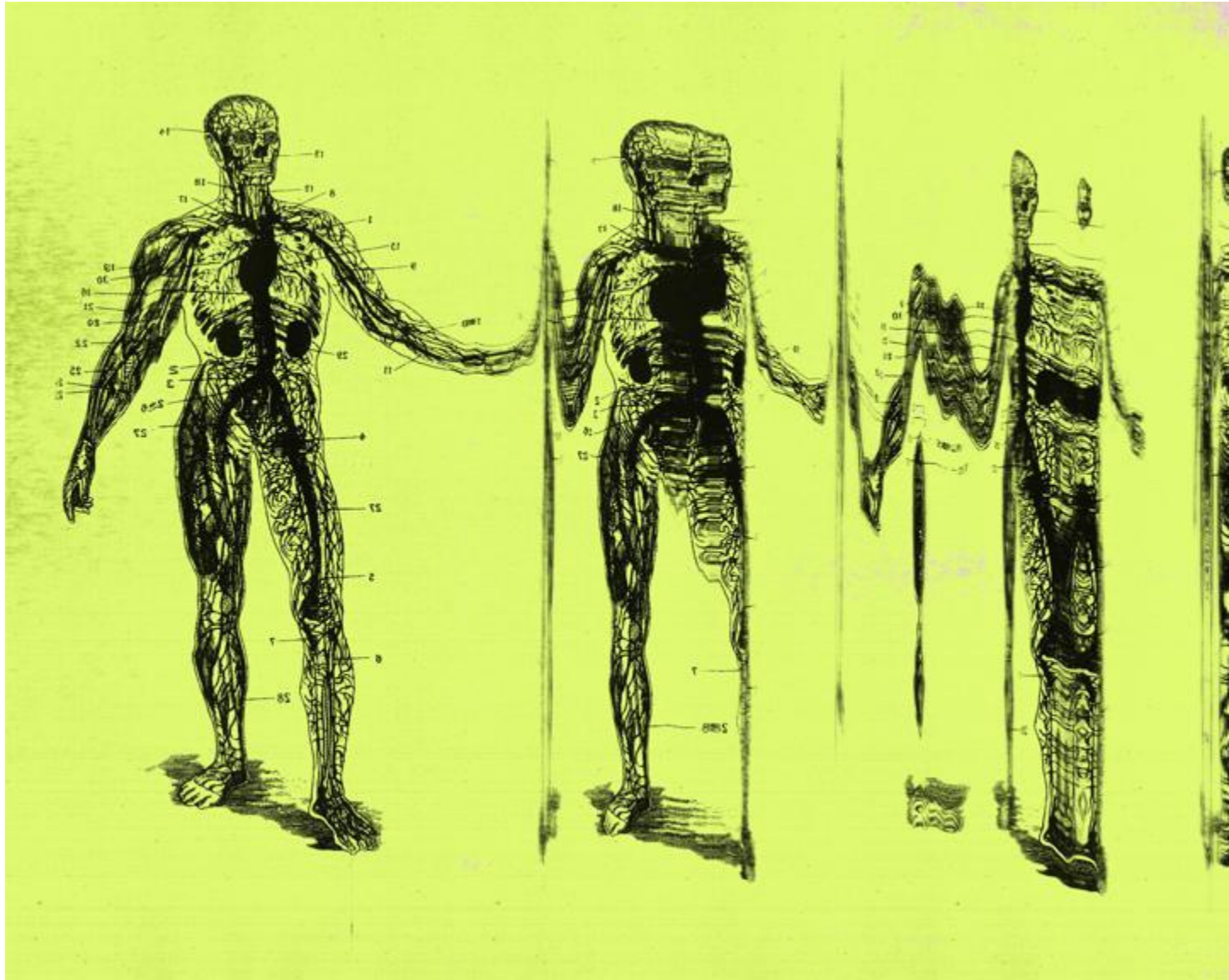
Overall, those who celebrated a 100th birthday had lower levels of glucose, creatinine, and uric acid from their 60s onward. Modig wrote that both centenarians and non-centenarians had values outside the range considered normal in clinical guidelines, likely because those guides are set on a younger and healthier [population](#).

“Even if the differences we discovered were overall rather small,” Modig wrote, “they suggest a potential link between metabolic [health](#), nutrition, and exceptional longevity.”

Modig acknowledged that “chance probably plays a role at some point in reaching an exceptional age,” but with observed differences in biomarkers, there’s a likelihood that [genes](#) and lifestyle are also significant.

Long live biomarkers.

Why We Can't Age in Reverse (And Why We Might Not Want to Anyway)



Why We Can't Age in Reverse (And Why We Might Not Want to Anyway)© Michael Houtz; Getty Images

For anyone overwhelmed by the discourse around longevity and the seemingly constant “breakthroughs” in the quest to vanquish the march of time, Nobel Prize–winning biologist Venki Ramakrishnan’s new book [Why We Die: The New Science of Aging and the Quest for Immortality](#) is meant to help make sense

of it all. It seeks to provide, as Ramakrishnan puts it, a “hard, objective look at our current understanding of aging and death.”

Because of the natural human fear of death—and its inevitability—the appeal of *Why We Die* is evergreen. But the book also comes at an opportune moment for a longevity reality check: A few days before it was published earlier this year, [David Sinclair](#), perhaps longevity medicine’s most visible exponent, stepped down from the Academy for Health and Lifespan, which he founded. Scientists had resigned in droves from the academy because Sinclair had claimed his veterinary supplement company [Animal Biosciences](#) had reversed aging in dogs. One former colleague, Matt Kaeberline, went as far as describing Sinclair's behavior as that of a “[snake oil salesman](#).” (Snake oil seems to be the hottest supplement in longevity right now. Even Dr. Peter Attia, who wrote *Outlive: The Science and Art of Longevity*, told the [New Yorker](#) the term longevity itself “just smells of snake oil.”)

Why We Die gets back to basics. Ramakrishnan, a former president of the [Royal Society](#), goes to great lengths to back up his modest take, which boils down to: There’s some exciting research being done, we’re far from being able to “reverse aging,” and we should wonder if that’s something we actually want to do. He points out that cell death, for example, can also be seen as a mechanism to [protect against cancer](#)—so a compound that reverses [aging at a cellular level](#) isn’t necessarily a good thing.

Ramakrishnan also covers some of the interpersonal rifts in the space between aging researchers and the people he calls “immortality merchants.” Though Ramakrishnan identifies a large part of gerontology (the study of aging) as important, legitimate work, he takes issue with the people he feels have monetized our fear of death by keeping a fluid relationship between their marketing and underlying science.

For any casual Attia or Huberman listener, some key terms will be familiar: TOR pathways, sirtuin, resveratrol, and all types of -phagy’s. But the windup does not end with a pitch or a protocol. In *Why We Die*, Ramakrishnan tempers our expectations on the longevity hype, and wonders what would happen if the most optimistic claims actually came true.

He spoke with GQ to talk a little more about the hype around life extension and what might *actually* help you live longer.

GQ: It seems like there's a groundbreaking development in the longevity space about twice a week.

Venki Ramakrishnan: Part of it is that there's human anxiety about aging and about death. A lot of people actually might be willing to accept death—although you never know until you're close to it—but they really dread to be incapacitated, the decrepitudes of old age. And so a lot of the anti-aging industry tries to monetize that anxiety by selling them supplements or this, that, or the other. Some of the supplements might do something useful, others probably not.

Many of these supplements might have promise on some mechanistic level, but the long-term research hasn't been done.

Correct.

And some people are just like, Hey, I'm gonna run an N-of-1 long-term study on myself.

Exactly. And some people will openly say that. [Bryan Johnson](#) says, "I'm a longevity pioneer," and he's trying all of these things.

That I find very interesting, because I'm like, OK, you're running an N-of-1, but how are you controlling for all of these variables?

It's a completely unscientific study. Even if Johnson lives for extraordinarily long time, it's simply because he's rich and has very good medical care. We have no idea how much of the intervention actually worked.

How would you describe the philosophy and approach of gerontology versus the longevity and anti-aging space?

I would have thought they're both the same. Gerontology is the study of what happens as we age. And anti-aging is simply an application of that: They're trying to intervene in those processes. So I wouldn't make a strong distinction between the two.

Most of the sane end of the spectrum, and certainly most of the governmental support—the NIH, the Medical Research Council, and so on—their support for aging research is really to ensure that people try to stay healthy as they get older. And that's a serious social issue, because we're getting older—societies are getting older. When Social Security was instituted, the median age was below 65. More than half of people wouldn't even reach Social Security age. And now, people are living well over 15 years, maybe two decades, beyond Social Security age, so there's an issue of *how can you keep older people healthy?* And also, *how can you keep them independent?* Because you don't want them to be dependent. And then, *how can you keep them productive?* So those are all questions about what you can do about aging, the processes of aging, and the diseases connected with aging.

So the philosophy in the community shifted between tackling individual diseases like cancer, diabetes, dementia, et cetera—which, of course, we have to tackle. But maybe they felt if you tackle the underlying causes of aging, then you would help with all of those things, because all of those things get worse—the chances of developing it get worse—with age. I would say that most sane people?...that's what they're aiming at.

Then there's this highly optimistic or aggressive end of the spectrum, [those] who just want to "solve" aging, or they want to "abolish" aging, or indefinitely

postpone it. They're very prominent, but for most of the community, that's not what it's about.

To that point: When you were talking about aging as a societal issue, and something that governments have a real financial interest in figuring out— that's an interesting motivation. And then you have the very individual motivation of billionaires who are trying to recapture the youth that they wasted building their fortune.

[Laughs] That's a good phrase.

You put it better in the book, writing “when they were young, they wanted to be rich, and now that they’re rich, they want to be young.”

That's actually a paraphrase of a fellow journalist of yours. A guy named [Antonio Regalado](#). He often writes for the *MIT Technology Review*, and I got it from one of his articles. I've cited him. I've reworded it, but that's his basic idea. When they were young, they wanted to be rich. And when they're rich, they want to be young.

That chase has a knock-on effect: Even if you look at popular health podcasts, some of these longevity findings, like when something new comes out on NAD or whatever it is, it's discussed.

Absolutely. And NAD precursors, like NMN [nicotinamide mononucleotide], or NR [nicotinamide riboside], there are two main precursors that are being marketed. They have the sales that are \$280 million a year and expect it to go to a billion dollars by 2030, so it's highly monetizable. But anything that can be monetized always gets a lot of press, and nobody wants to wait for the human clinical trials to ask, Is it really improving?

First of all: One thing that field has a problem with is defining how to measure aging. Because if you only measure it by mortality, you have to wait an awfully long time for clinical trials—20 years to see any effect, right? Or even longer. So what they do is they want to have other markers like blood markers or epigenetic markers.

There *are* a bunch of molecular changes that occur with age. But what the community has to decide is to agree on a set of markers that everybody says, Okay, this set of markers is measuring aging, and these are the criteria for how we would measure aging. But aging is somewhat complex. Somebody could be high in one marker, but low in another marker; so what does that mean? And people now also monetize markers, they sell tests to determine biological age for \$500 or \$1,000 a pop? You could give them a sample of your blood, and they tell you, *oh, your biological age is this*. And there's a bit of snake oil in that, because these markers work on a population level.

We know that a population as a whole develops epigenetic changes with age. But [for] an individual, a single marker can't actually tell you—and also, different parts of an individual may have aged to different degrees. Your liver may be older than your kidney or your lung. If you're a smoker, maybe your lung ages very fast. These things need to be sorted out by the community before that's ready.

But getting back to the supplements and these treatments, if they can agree on a set of markers, and use that to measure aging, then they can measure what is the effect of all these various therapies, and see how effective they are, et cetera. And some people are trying to do that, but others are jumping the gun and just selling their stuff based on some animal trials and preliminary reports, and some very preliminary studies.

Something similar to the biomarker tests that I've seen is [continuous glucose monitors](#) being used in this way. The technology is ahead of the education, especially where people promoting a ketogenic diet will put it on, and then they'll eat bread and be like, "Look! It spiked. That means bread is bad."

I'll give you a quote from a famous guy. He said it was "a way of separating money from the worried well." He said that the effect of wearing a CGM monitor 24/7, giving you feedback on the effects of every mouthful you eat on your glucose level is likely to be sizable and have a substantial influence on behavior. He said the worried well—the upper-middle classes—are ripe for financial exploitation of this kind. And he said that the CGM device is great for diabetics because they have to know how to control their glucose and when to take insulin and things like that. So it's a very useful tool for diabetics, and allows them to have much better control over their blood sugar. But for ordinary people? It's just crazy. It's just a waste of money.

It's a medical technology that became a consumer gadget.

Yeah, and making lots of money: They can sell hundreds of thousands of these devices with minimal real benefit.

There's this trickle-down interest in longevity and whatever you can do to pursue anti-aging, even at the normal person level, via podcasts. I'm thinking of the *Huberman Lab* podcast, and Peter Attia's podcast. They aren't singularly focused on longevity, but it's obviously a large part of their interests. I'm curious if (a) you listen to them and (b)—

No, I have not listened to them. I've taken a look at Attia's book, *Outlive*, it's a big bestseller. It's highly prescriptive. He says, You've got to do these 10 things that'll get you to be able to do this, this, and that. And he's also a very big fan of rapamycin, beyond what's clinically tested. I don't want to say too much except: He's also involved in pushing advice, and various supplements and so on. I wouldn't want to say anything too directly, because I don't want any lawsuit on my hands. But I would just say that's a very different approach from mine, which is to just simply look at the biology and point out: What are the limits of our understanding today? And what do we need to progress beyond to something that's applicable? I'm not saying that rapamycin is never going to be useful, but I think they need to establish long-term safety, long-term efficacy, dosing, all these things. Maybe it's not the best compound, maybe you need a different compound that also inhibits TOR, but in a safer way. So I think there are a lot of issues there.

From the academic and research perspective, is this focus on longevity influencing what gets funded—taking money from other places?

It's not a huge fraction. The amount of money going into longevity has really exploded, but it's still a very small fraction of the overall research budget. So I'm not too worried about that. As we discussed, it is a real social issue that societies need to address. So I am not against longevity research; I think it's a very good thing to have. I think we need to have serious longevity research and really take a look at what will improve health best in old age: What are the interventions that are the most effective and the safest in old age?

One thing that is influencing it is the amount of private money going into longevity research, and how some of that private money is actually attracting some of the best scientists away from academia into these private institutes which are potentially for-profit institutes. That creates certain conflicts of interest, and also influences the agenda slightly about turnaround times, speed, priority of problems; all of those things can be influenced once you have private investors backing things. I think there really is a danger that longevity is being influenced by private money, but the public side I think is okay.

You urge people in the book to exercise a bit of skepticism or caution when they see a study go viral in the news.

One of the purposes for the book is saying that aging is complicated and involves a lot of biology, and it has to do with how we evolved. So what I've done is walk the reader through, in hopefully a very accessible way, all of the underlying biology for why we age and why we die. And the goal is, first of all, that understanding the biology also gives them the tools for how to live. What should they do if they know these are the things that cause aging, and these are things that can help. It's not a recipe book, like some of these aging books that say "Do

this, this, and this," but rather say, *this is what happens*. So you can take it in your hands to do the right things to help the process and be more healthy. So that's the first thing.

The second is giving them the understanding that the biology of aging means that every time they come across these articles, they can have a mental framework now of how to evaluate an article. If it's NMN, then they know what NMN is doing—they've read about it, so they can go back to the book and look it up. And so they can have a mental framework to evaluate new findings and see if they're hyped, or if there's something there. And if there's something there, is it ready for prime time? Or what other work needs to be done before it's useful. It's really to empower the general reader.

Obviously, gerontology has been around for a long time. Was there a tipping point where the longevity field changed?

Well, there have always been these extreme-longevity advocates for a long time. That's not new. It's not new in human culture, either. There was always the Fountain of Youth, and things like that. This is just the latest act in a long-running play. But what has changed is that there's now serious science. I would say 50 years ago, aging was considered a slightly backwater field—maybe even disreputable. Mainstream biologists didn't really want to go into that.

And then because of social pressures, because of social requirements, because the NIH and all these government agencies said, Hey, we have to do something about this, we need to understand the biology, then serious biology started getting done. It still has its shaky science, but lots of fields, especially which involve human health, have that, and I would say there is quite a lot of rigorous science going on in the aging field.

Do you have concern for the average person really focusing on optimizing everything for longevity? Beyond the reasonable things like eating well and moving around.

[Longevity advocates] would say, if you talk to them, they would say longevity is really about health. It's the health that makes them live longer. And so that's not a bad aim. I don't want to be too hypocritical, because I'm taking two or three anti-aging medicines, as I pointed out in my book: I'm taking blood pressure medicines, I'm taking statins. [The third medication is aspirin.] Now, you could say I could've tried to control that purely with diet and exercise. And I did try, but it eventually caught up with me until my doctor said, "Look, I would really advise you to go on statins and take blood pressure medicine, or you're gonna get a stroke or a heart attack."

If somebody came with a pill and said, "Look, this is going to give you 10 years extra of healthy life," now, most of us will take that, right? Who would want to become sick and die right away instead of being healthier for 10 years? So we can't be too hypocritical, but I think the focus on radical life extension is completely misguided.

You mention the rushed rollout of social media and AI, and the impact that's had on our world. Are there any nascent technologies that give you some optimism?

AI has a lot of potential to do good in science. In my field, it's having a pretty major impact in predicting protein structures; it could be useful in genomics, and pattern recognition in cells, and so on. I can imagine AI being potentially very useful, but AI is so hyped and, unfortunately, the biggest use of AI is going to be in extracting more money from the consumer, and that's a problem. The

priorities, especially in Silicon Valley, are not well-aligned with what is good for the consumer or good for society. Maybe we may think it's good for the consumer: Okay, we can connect with our friends, I can talk to you online, and it's all due to computer technology. But it also has a lot of downsides: social isolation, the spread of disinformation. The problem is that these people in Silicon Valley, especially, but just generally tech people everywhere, tend to jump in without thinking of all the potential consequences. If you go slowly, you can deal with consequences as they arise. If you just rush out stuff, then things happen that you're not in control of.

One problem with aging is that, if they make big breakthroughs—I'm not saying they will—but let's say we all start living to be 95, 100. Everybody just starts living longer. It'll change society in many ways, and we need to be prepared for that. How do we deal with society where people are older? What about intergenerational fairness? What about turnover? What about regeneration? What about economic disparity? The rich already live 15 years longer or more than the poor, and they live more of their lives healthily, much more of their lives healthily. So the poor are not only living shorter lives, but they're spending more of it in poor health. So now, if you have even more disparity, then you can see how it would really diverge, because the rich will accumulate power. And as they get older, they'll accumulate even more wealth, pass on more wealth to their offspring. And you can just have this sort of two-tier system. I think people need to be aware of these things.

I'm curious if there's anything beyond eating well and exercising that you think—

Sleep. Americans always seem to forget sleep, but sleep is very important for repair and maintenance and so on. The other things I didn't mention is that simple checkups for blood pressure, blood markers like cholesterol, lipid, hemoglobin, and other inflammation markers, markers for diabetes. Those are all very important. And if people catch those early, there are useful interventions—like how I'm taking medications for blood pressure—that can really allow you to live a healthier life when they're older. I mean, if you are a stroke patient and

you've recovered, your life is still not as good as if you'd never got the stroke. And same with a heart attack.

Those are very obvious measures which are already available. I didn't talk about the social markers, which is being connected socially, having a network of friends and support and regular social interactions, and having a sense of purpose in life. Those are also quite important for healthy aging. So, there are a number of things we can do, but not easily—if you're poor, all of these things are harder to do. The poor don't have time, and they can't eat very good food, whatever cheap food that they can get; they don't have enough time to exercise or don't have a place to exercise. And they often don't get enough sleep, they're working two, three jobs at the same time. So all these things are easier for rich people than for poor people. And so how do we as a society make it more equitable? That's an issue.

I have to ask: Why do we die?

Well, that too is interesting. So while we're alive, millions of cells in us are dying all the time, we don't even notice it. And some of them have to die because they're part of the normal function of living. So they're programmed to die at certain points. At the same time, when we die, most of our cells are still alive, paradoxically. In fact, entire organs are alive—you can donate organs for transplant patients.

So what does it mean when we die? Well, we're not talking about cellular death. When we say *humans dying*, we're talking about the inability to function as a coherent, conscious individual. And that means we get a series of damages, a series of defects that build up with age. And at some point, it affects a critical function that leads to critical systems failure. For example, if you get really frail with old age, you get heart failure; heart failure will then lead to loss of blood to the brain, the brain will stop working, and then you won't be able to function as an individual. It's this inability to function as a coherent whole—that is how I define death.

Discovery of New Biological Law May Explain Aging and Evolution



Artist's impression of a strand of DNA. Tower's law suggests that our cells exist in two states: one with an unstable component, such as a genetic mutation, and one without. And the existence of these two states may have contributed to our evolution over time. © jes2ufoto/Getty

A new biological law has been proposed offering key insights into the processes of evolution and aging.

Biological laws are recognized patterns that hold true for a group of living organisms. For example, Allen's rule, formulated by zoologist Joel Allen in 1877, states that warm-blooded animals in colder climates have shorter, thicker limbs than those in hotter areas, in order to conserve body heat.

Now, in a paper published in the journal *Frontiers in Aging*, biologist John Tower, a professor at the University of South Carolina, has proposed a new biological law challenging long-held assumptions over stability in biological systems.

"Rules of biology typically involve conservation of resources," Tower wrote. "For example, common patterns such as hexagons and logarithmic spirals require minimal materials, and scaling laws involve conservation of energy. Here a relationship with the opposite theme is discussed, which is the selectively advantageous instability of one or more components of a replicating system."

In other words, Tower's law postulates that instability and volatility in biological components—such as our cellular machinery—may be beneficial to our survival.

This "selectively advantageous instability" allows for the rapid turnover of old and damaged cellular components, breaking them down into building blocks that can be used to create new structures.

"Even the simplest cells contain [enzymes that break down DNA, RNA and proteins] and regularly degrade and replace [these key biological molecules], indicating that selectively advantageous instability is essential for life."

He adds that this process plays a key role in evolution. As cells live in this constant flux of instability, they can exist in one of two states: one with an unstable component present and one in which the unstable component is absent. Natural selection may act differently on these two cell states.

"This can favor the maintenance of both a normal gene and a gene mutation in the same cell population, if the normal gene is favorable in one cell state and the gene mutation is favorable in the other cell state," Tower wrote.

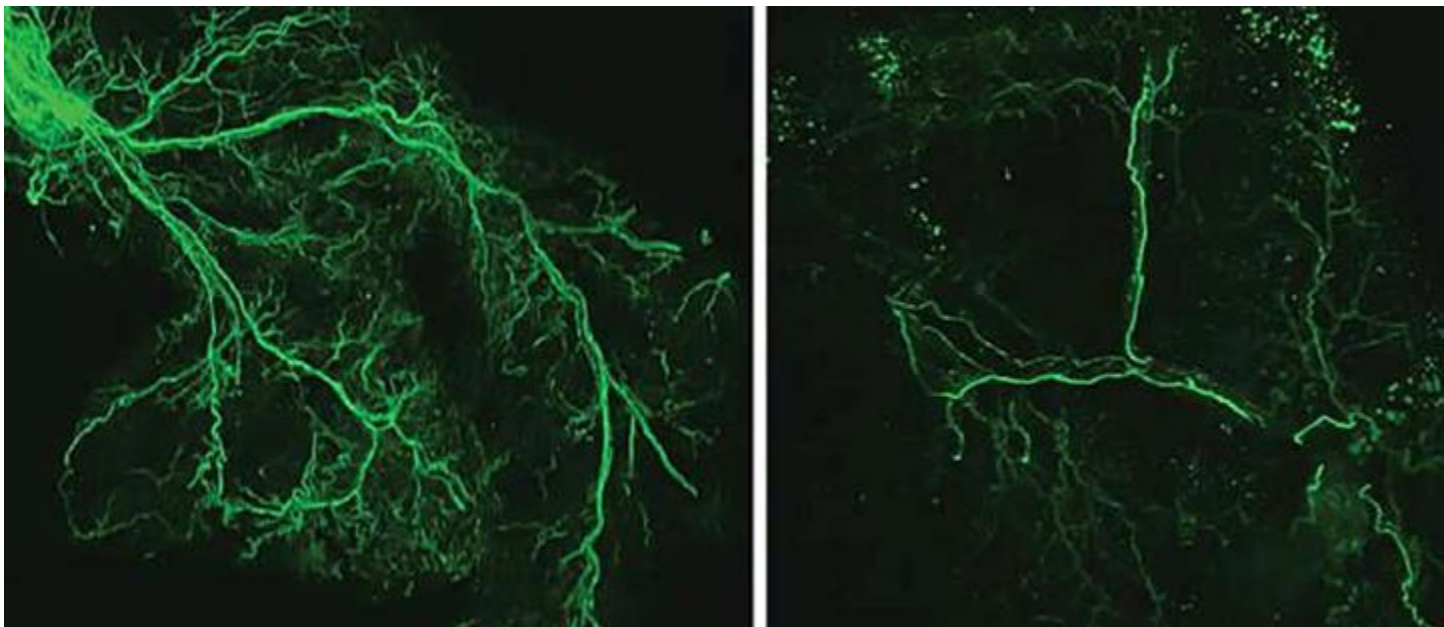
This, he argued, creates genetic diversity and makes cells and organisms more adaptable to changes in their environment.

However, selectively advantageous instability may also take a toll when it comes to aging. Over time, building and breaking down these unstable components within our cells uses up materials and energy, and may induce wear and tear on our cellular machinery. The existence of cells in two states can also allow harmful mutations to emerge and linger in our bodies, which Tower said may contribute to aging.

"In summary, selectively advantageous instability promotes replicator genetic diversity and reproductive fitness, and may promote aging through loss of resources and maintenance of deleterious alleles," he wrote.

Tower hopes that this new rule, if proven, will aid in the design of synthetic cells in the future.

Activating One Specific Brain Cell Extended Lifespan in Mice by 70 Days



Lines of green glowing nerves branching densely on the left but sparsely on the right.© Provided by ScienceAlert

Aging might have advantages in wisdom, experience, [and even evolution](#), but the gradual breakdown of biology that comes with growing old is rarely much fun for anybody.

A new study in mice suggests it may not always have to be this way.

"We demonstrated a way to delay aging and extend healthy lifespans in mice by manipulating an important part of the brain," [says](#) Washington University developmental biologist Shin-ichiro Imai.

Our brains control a vast number of bodily functions, primarily by way of nervous impulses, which can manage communication networks based on the ebb and flow of hormones.

The infrastructure carrying these communication signals and their surroundings deteriorate as we age, causing increasing faults.

So our organs and tissues start to miss out on signals needed to maintain themselves.

Signaling chemicals that form parts of the pathway between our brains and fat tissues, specifically [white adipose fat](#), [have been associated](#) with aging in mice previously, so Imai and colleagues took a closer look at the critical early steps in this communication network.

They allowed one group of rodents to age naturally while tweaking the neurons at the beginning of the brain to fat pathway so they remained active. These cells, DMHPpp1r17, are tucked away in our brain's [hypothalamus](#), an important conduit between our nervous system and the body's hormone system.

Incredibly, the mice that received the neuron activation treatment lived 60 to 70 days longer than the control mice, who died within the typical laboratory mouse lifespan of about 1,000 days.

More importantly, the mice that underwent neural treatment had thicker, shinier coats and were more active during their old age, suggesting they were healthier for longer too.

Further investigation revealed parts of the mechanism at play.

When the DMHPpp1r17 neurons are on, they can activate our body's fight or flight response – our sympathetic nervous system using the [Ppp1r17](#) molecule. This promotes the use of our body's white adipose stores that release a protein called eNAMPT, which in turn regulates hypothalamus neurons, completing the circuit.

"Ppp1r17 is also well conserved in various vertebrate species such as human, chimpanzee, monkey, rat, mouse, bovine, rabbit, chicken, xenopus, and zebra finch, suggesting that Ppp1r17 carries some essential functions throughout evolution," the researchers [explain in their paper](#).

This is a vital circuit for fueling our bodies, but the normal aging mice started producing less Ppp1r17, activating fewer fat stores.

With less activity, the nerves through our adipose tissues begin to degrade, meaning even less eNAMPT is produced, so even fewer hypothalamus neurons are activated, creating a self-propagating system of deterioration.

There are still many details to hash out, including if eNAMPT works directly on the hypothalamic neurons or if there are more intermediary steps. The team is also keen to discover if this feedback loop influences communication between other tissue types within our bodies, like skeletal muscle.

If so, this could explain an awful lot, as many known factors of biological aging, including [stress](#) and [stress mitigators](#), weight, and [exercise](#), all influence some part of this brain to fat system – another example of just how physiologically linked we are to the world around us.

This research was published in [Cell Metabolism](#).

Anti-Aging Discovery May Pave the Way to Treatments for Longer Life



Aging is a complex process that scientists don't fully understand. However, recent developments in biotechnology have allowed us to piece together this ancient puzzle. © sezer66/Getty

Why do we age? It's a simple question with a not-so-simple answer. But with the help of modern biotechnology, scientists have been able to slowly piece together the biochemical basis of this long-held mystery.

Our cells are like tiny molecular factories, working to carry out all of the essential processes our bodies need to survive. However, like factories, the machinery in our cells gets worn out over time, which is what causes our cells to age.

Our cellular machinery is split into different substations, called organelles. And, when it comes to aging, two organelles are particularly important: a) the mitochondria—the energy-producing powerhouses of the cell, and; b) the lysosomes—the cell's internal garbage disposal station.

During the energy-making process, mitochondria can produce dangerous waste products, which [build up over time and damage our DNA](#). Lysosomes, meanwhile, contain a soup of digestive enzymes that breakdown worn-out cellular components. If the lysosomes themselves become damaged, these enzymes can leak out into the rest of the cell and cause havoc on the remaining healthy cellular components. Therefore, damage to either of these cellular stations has been associated with aging, cell death and many age-related diseases.

Clearly, keeping these organelles in ship shape is essential for the health and longevity of our cells. But exactly how our bodies maintain and repair these cellular substations is still unknown.

That may all be about to change. In a recent study, published in the journal [Proceedings of the National Academy of Sciences](#), researchers from Osaka University in Japan have identified a protein that plays an important role in the maintenance of these molecular machines, and their disposal should they go wrong.

In previous research, scientists had identified a cellular switch involved in the maintenance and removal of damaged mitochondria and lysosomes. However, exactly how this molecular switch, called TFEB, was able to interact with these organelles was unclear.

Now, the team at Osaka have discovered that TFEB acts by increasing the production of a protein called HKDC1, which increases in concentration in the cell during times of mitochondrial and/or lysosomal stress. But then the question remains: what does this protein actually do?

Together with TFEB, HKDC1 is involved in the controlled removal of damaged mitochondria—in other words, it helps take out the mitochondrial trash. HKDC1 also appears to play an important role in allowing cross-talk between these two cellular structures, supporting the [repair of damaged lysosomes](#).

Dysfunction of either of these repair pathways is linked to aging and age-related disease, suggesting that HKDC1 may offer a useful target for anti-aging treatments in the future.

Study finds heart healthy behaviors may help reverse rapid cell aging



Credit: Pixabay/CC0 Public Domain© Provided by Medical Xpress

The benefit of better heart health may be associated with the positive impact of heart healthy lifestyle factors on biological aging (the age of the body and its cells), according to research published in the *Journal of the American Heart Association*.

"Our study findings tell us that no matter what your actual age is, better heart-healthy behaviors and managing heart disease risk factors were associated with a younger biological age and a lower risk of heart disease and stroke, death from heart disease and stroke and death from any cause," said Jiantao Ma, Ph.D., senior study author and an assistant professor in the division of nutrition epidemiology and data science at the Friedman School of Nutrition Science and Policy at Tufts University in Boston.

This study analyzed whether a chemical modification process known as DNA methylation, which regulates gene expression, may be one mechanism by which cardiovascular disease health factors affect cell aging and the risk of death. DNA methylation levels are the most promising biomarker to estimate biological age.

To some degree, biological age is determined by your genetic makeup, and it can also be influenced by lifestyle factors and stress.

Researchers examined health data for 5,682 adults (mean age of 56 years; 56% of participants were women) who were enrolled in the Framingham Heart Study, an ongoing, large, multigenerational research project aimed at identifying risk factors for heart disease.

Using interviews, physical exams and laboratory tests, all participants were assessed using the [American Heart Association's Life's Essential 8](#) tool. The tool scores cardiovascular health between 0-100 (with 100 being the best) using a composite of four behavioral measures (dietary intake, physical activity, hours slept per night and smoking status) and four clinical measurements (body mass index, cholesterol, blood sugar and blood pressure).

Each participant was also assessed using four tools that estimate biological age based on DNA methylation and a fifth tool that assesses a person's genetic tendency towards accelerated biological aging. Participants were followed for 11–14 years for new-onset cardiovascular disease, cardiovascular death or death from any cause.

The analysis found:

- For each 13-point increase in an individual's Life's Essential 8 score, the risk of developing cardiovascular disease for the first time was reduced by about 35%, death from cardiovascular disease was reduced by 36% and death from any cause was reduced by 29%.
- In participants with a genetic risk profile making them more likely to have an accelerated biological age, the Life's Essential 8 score had a larger impact on outcomes potentially via DNA methylation, i.e., DNA methylation accounted for 39%, 39%, and 78% reduction in the risk of cardiovascular disease, cardiovascular death and all-cause death, respectively.
- Overall, about 20% of the association between Life's Essential 8 scores and cardiovascular outcomes was estimated to be due to the impact of

cardiovascular health factors on DNA methylation; in contrast, for participants at higher genetic risk, the association was almost 40%.

"While there are a few DNA methylation-based, biological age calculators commercially available, we don't have a good recommendation regarding whether people need to know their epigenetic age," Ma said. "Our message is that everyone should be mindful of the eight heart disease and stroke health factors: eat healthy foods; be more active; quit tobacco; get healthy sleep; manage weight; and maintain healthy cholesterol, blood sugar and blood pressure levels."

Randi Foraker, Ph.D., M.A., FAHA, co-author of the [Life's Essential 8: Updating and Enhancing the American Heart Association's Construct of Cardiovascular Health](#), said the findings are consistent with prior research.

"We know that modifiable risk factors and DNA methylation are independently associated with cardiovascular disease. What this study adds is that DNA methylation may serve as a mediator between risk factors and cardiovascular disease," said Foraker, who is a professor of medicine at the Institute for Informatics, Data Science and Biostatistics and director of the Center for Population Health Informatics, both at Washington University School of Medicine in St. Louis, Missouri.

"The study highlights how cardiovascular health can impact biological aging and has important implications for healthy aging and prevention of cardiovascular disease and potentially other health conditions."

Study details, background and design:

- The study analyzed health data for a subgroup of participants who attended the Framingham Heart Study exams in the offspring group from 2005 to 2008 and the third-generation group from 2008 to 2011.
- Participants were followed for an average of 14 years for children of original participants and 11 years for the grandchildren.
- Health outcomes for the analysis included the development of cardiovascular disease (coronary heart disease, heart attack, stroke or

heart failure), death from any cardiovascular disease or death from any cause.

- Results were adjusted for sex, age and alcohol use. Results for all-cause death were adjusted for the presence of cancer (excluding non-melanoma skin cancer) or heart disease at study enrollment. Participants already diagnosed with heart disease at study enrollment were excluded from the analysis of new-onset cardiovascular disease.
- The four tools to measure DNA methylation-based epigenetic age scores were based on established algorithms for DunedinPACE Score, PhenoAge, DNAmTL and GrimAge. A fifth tool, GrimAge PGS, assessed genetic tendency towards accelerated biological aging.

Because the study is an analysis of previously collected health data, it cannot prove a cause-and-effect relationship between cardiovascular health risk factors and DNA methylation. In addition, DNA methylation measures were from a single time point, which limits the validity of the mediation effect. The study's findings are also limited because the participants were predominantly of European ancestry, so the interactions of Life's Essential 8 and genetic aging found in this study may not be generalizable to people of other races or ethnicities.

"Currently, we are expanding our research to include people of other racial and ethnic groups to further investigate the relationship of cardiovascular risk factors and DNA methylation," Ma said.

According to the [American Heart Association's 2024 Heart Disease and Stroke Statistics](#), heart disease and stroke claimed more lives in the U.S. in 2021 than all forms of cancer and chronic lower respiratory disease combined, and also accounted for approximately 19.91 million global deaths.

More information: Epigenetic Age Mediates the Association of Life's Essential 8 With Cardiovascular Disease and Mortality, *Journal of the American Heart Association* (2024). DOI: [10.1161/JAHA.123.0327431](https://doi.org/10.1161/JAHA.123.0327431)

Provided by American Heart Association

Scientists discover four simple things that everyone can do to live beyond 100

Defying our age is something that's preoccupied humans for decades – in fact, some people go to such extreme lengths to look younger than they become [figures of ridicule online](#).

But what if there were certain habits that could extend all of our lives, perhaps even helping us live past 100?

Centenarians have become the fastest-growing demographic group in the world, with numbers approximately doubling every 10 years since the 1970s.

A new [review](#) featuring 34 observational studies since 2000 [via [The Conversation](#)] found some illuminating results – and certain habits that many people who reached the landmark age shared.

Essentially, the habits focus on diet, medication, sleep and living conditions.

The research found that in general people who lived to more than 100 consumed around 57-56 per cent of their energy through carbohydrates, as well as 12-32 per cent from protein and 27-31 per cent from fat. They also generally had moderate levels of red meat consumption and preferred a diet low in salt.

In terms of medications taken, the people in the study took on average 4.6 medications, which is fewer than the threshold for polypharmacy, which is pretty common and defined as taking five or more medications at the same time.

Sleep, as you might expect, played a big factor in the health data for people who lived longer lives. A healthy 68 per cent of the centenarians in the data were satisfied with the quality of their sleep.

And finally, living conditions and surroundings played a major role too. Incredibly, more than 75 per cent of people who lived to more than 100 lived in rural areas – something which the links between nature and wellbeing could

explain. In fact, the highest concentrations of people living for more than a century like Okinawa in Japan and Sardinia in Italy were all rural areas.

Research in this area is developing all the time, and earlier this year scientists discovered that [people who live past 90 have key differences in their blood](#).

The next breakthrough for longevity obsessives: measuring organ age

From peptide treatments to luxury longevity clinics here are the biggest anti-aging trends sweeping the nation

- The quest for longevity has gone mainstream as more people seek ways to reverse the aging process.
- People are resorting to peptide treatments, cold plunges, and luxury longevity clinics to extend their lifespan.
- Here are some of the top longevity trends right now, according to industry experts.

While the quest to [live longer](#) has long been a focus of the world's wealthiest entrepreneurs, these days, it's gone mainstream.

People across the country are taking a host of prescription pills like Metformin, seeking out treatments like peptide injections, and implementing a range of behavioral practices [in the hopes of reversing aging](#). By 2028, the global longevity market is expected to reach close to \$183 billion, [according](#) to a market report by business intelligence firm Grand View Research.

Research shows that several of these trends [can slow down the process of cellular aging](#), increase cognitive function, and even delay the onset of chronic diseases. Still, it's important to view any of these practices simply as tools, similar to "hammers or screwdrivers," that are neither inherently good nor bad, said Anant Vinjamoori, the chief medical officer at longevity-focused healthcare company, Modern Age. Their value ultimately depends on the context in which they're implemented, and it's worth tailoring your approach to suit your individual needs, he added.

From peptide treatments to luxury longevity clinics, here are some of the most popular longevity trends sweeping the country.

There is a growing body of scientific evidence that supports cold exposure as an anti-aging hack.

Whether you plunge into a pool of ice-cold water or try [cryotherapy](#) — which involves spending a few minutes in a below-freezing chamber — cold exposure has benefits that may help slow down the clock.

Anant Vinjamoori, chief medical officer of longevity-focused healthcare company [Modern Age](#), told Insider that cold exposure produces effective results in the short and long term.

A plunge into an ice-cold bath results in "a surge in the production of neurotransmitters such as epinephrine and dopamine," which have immediate rejuvenating and energizing effects, he said.

"Over the medium to long term, there is some evidence that cold exposure may reduce systemic inflammation, which is known to be a driver of many chronic diseases," Vinjamoori added.

High-end longevity clinics that offer everything from genetic testing to cocktails of supplements are growing in popularity — especially among high-income groups.

Many of these [longevity centers offer packages](#) or retreats that can be pretty pricey — sometimes upwards of tens of thousands of dollars a week — but longevity experts contend that they are some of the best places to get practical longevity guidance.

"The truth is that most people are probably wasting time and money on products that will never materially help them," Matt Fellowes, an advisory council member at the Stanford Center on Longevity and cofounder of health insights platform BellSant, told Business Insider by email. "One exception are some of the clinics that cater to high-income adults, which are actually science-based and, most importantly, create highly personalized assessments and guidance for people — meaning, they only focus on what their specific bodies need."

At [Clinique La Prairie](#) — a more than 90-year-old longevity center in Switzerland — the seven-day, six-night "premium revitalization" package includes longevity consultations, sleep quality assessments, DNA tests, personalized nutrition guidance, and personal training sessions, alongside luxury accommodation and limousine service for about \$53,000. The program "stimulates cell regeneration, fights the signs and causes of aging, and reinforces the immune system through a four-pillared approach of medicine, nutrition, wellbeing, and movement," a spokesperson for Clinique La Prairie previously told BI.

There are less expensive options, however.

Time-restricted eating has been shown to have a host of health benefits.

Research suggests that time-restricted eating patterns can result in [health benefits for those with diabetes and obesity](#) or even [enhance the body's defenses against oxidative stress](#).

"For me, the primary benefit of time-restricted eating is regulating circadian rhythms. Sleep quality almost always improves by limiting the consumption of calories in the evening hours," said Modern Age's Vinjamoori.

Try skipping the meat and adopting a plant-based diet, instead.

Those who cut out animal protein— and stick to a relatively plant-based diet— are likely to live longer and healthier lives, according to studies.

David Sinclair, a Harvard Medical School professor and longevity researcher, said that high animal protein diets really only help people feel better in the short term.

"I'm convinced, and the data shows it from population studies, that a carnivorous diet is not a longevity-producing diet in the long run," he [said](#) on an episode of "The Knowledge Project Podcast."

In many of the world's [Blue Zones](#)— [areas where people tend to reach the age of 100](#)— people are likely to have a relatively plant-focused diet.

Red light therapy uses LED lights or lasers to expose the body to red light—the longest wavelength of light on the visible spectrum.

There is research to suggest that [exposing oneself to red light](#) for five to 20 minutes may increase production of adenosine triphosphate, which is a compound that provides and stores energy for the cells.

"While more research is needed to understand the full benefits and mechanisms of red light therapy, there is evidence to suggest it may be beneficial in improving certain skin conditions including acne, aging, hair loss, wound care, and sun damage," dermatologist Laura Buford previously [told](#) Insider.

body to improve cellular function.

NMN, or Nicotinamide Mononucleotide, is a supplement that can help boost levels of a critical coenzyme in the body called NAD+.

NAD+ is vital in facilitating metabolic processes and maintaining healthy cellular function.

Harvard Medical School professor Sinclair — who has studied the relationship between NAD+ and aging — [said](#) in an interview with the YouTube channel Reverse Aging Revolution that the human body uses NAD+ as "a measure of adversity." As humans get older, NAD+ levels decrease, which means the body's defense enzymes and repair enzymes take a hit, and humans "succumb to aging," Sinclair [said](#).

Since NAD+ is a large molecule, it's difficult to take it directly. Sinclair recommends taking its building blocks like B3, Nicotinamide riboside (NR), or NMN.

"What we've discovered in people, in clinical trials, is that the closer you get to the NAD itself, the better the boost in NAD that you get," Sinclair [said](#), which is why he recommends NMN.

Or try Ashwagandha, an herb that's long been used for anti-aging in Ayurveda, an ancient system of holistic medicine originating in India.

The herb, often classified as an adaptogen, has a host of health benefits that range from easing anxiety and stress to soothing arthritis to boosting cognitive function. Modern Age's Vinjamoori said that ashwagandha has been shown in research studies to reduce cortisol, a hormone associated with stress, and improve sleep in people with insomnia.

Recent research has also shown that ashwagandha could be a [promising agent in anti-aging treatments](#). A [study](#) published in the Journal of Clinical Medicine in 2020 found that ashwagandha may help maintain the length of the key proteins at end of chromosomes known as telomeres. Telomeres are often shortened in the process of DNA replication which has been pointed to as the main factor that "speeds up cell ageing and promotes degeneration processes" the study [noted](#).

People that are serious about aging are also turning to prescription pills like Metformin.

[Metformin, a pill prescribed for diabetes, is increasingly being used by biohackers](#) as a way to improve how humans age and slow the onset of diseases like cancer, cognitive decline, and vision loss.

The drug helps regulate blood sugar and decrease appetite, essentially giving the metabolism a boost and stimulating a cellular clean-up process known as autophagy, Insider [reported](#).

In his book [Lifespan](#), Harvard professor Sinclair said he takes a gram of metformin every morning along with his yogurt in the hope that it will regulate his metabolism and help his organs remain younger and healthier, Insider [reported](#).

OpenAI CEO Sam Altman also [said](#) his personal antiaging regimen includes metformin.

And Rapamycin, an immunosuppressive drug used to help treat some cancers.

It's also used in kidney transplants to help an organ recipient's body accept new kidneys, Insider [reported](#).

The pill can slow down cellular growth and reproduction which means it might be a way to "turn down troublesome age-related inflammation," which can contribute to age-related diseases like cancer and Alzheimer's, Business Insider [reported](#).

Business Insider also previously [reported](#) that researchers have already seen rapamycin slow aging in [flies, crustaceans, yeast, and mice](#). In humans, studies have shown that it may [help improve immune function](#), especially in older adults.

Despite its potential to be a "fountain of youth," no one has really nailed down the right way to regulate the drug for aging.

Matt Kaeberlein, a longevity researcher studying rapamycin's effects on humans, previously [told](#) Insider that "the doses that people are taking off-label are all over the place," adding that, "it's the wild west."

Treatments like hormone therapy, in the form of pills or injections, have also surged in popularity.

The body's balance of hormones can shift with age and spur a variety of age-related conditions like weight gain, mood swings, fatigue, and lower sex drive, two longevity-focused doctors told Insider. As a result, they've seen an increasing patient interest in hormone therapy.

Modern Age's Vinjamoori told Business Insider that testosterone replacement has gained popularity among men and women as it has become clear that optimal testosterone levels can impact mood, libido, and even metabolism.

"The importance of testosterone for women, in particular, is underappreciated — testosterone is actually the most abundant hormone in a woman's body and is the first hormone to decline with age," Vinjamoori told Business Insider.

It's not just testosterone, but also sex hormones like estrogen and progesterone that are being sought out by patients. Vinjamoori said the options for hormone therapy range from pills to creams to patches to pellets.

Peptides are another buzzy anti-aging treatment these days.

[Peptides](#), a broad class of anti-aging and performance-enhancing treatments, have taken off in recent years among bodybuilders, athletes, and biohackers.

They're [essentially short chains of amino acids](#) that neuroscientist Andrew Huberman has described as a "new kind of wedge in between supplements and prescription pills." Some of the most popular peptide treatments are ones that release [human growth hormone](#) and can improve fat loss and muscle repair.

"Indeed, biohackers are very excited about it because you can practically make your body do certain things," [Christian Angermayer](#), a major investor in the longevity sector, previously told Insider.

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There may come a day when patients can measure the age of their organs through a blood test.
DIGICOMPHOTO/SCIENCE PHOTO LIBRARY/Getty© DIGICOMPHOTO/SCIENCE PHOTO LIBRARY/Getty

- A study measured the age of specific organs in 5,676 adults and found that 20% had advanced aging in one.
- The study found that those with accelerated heart aging have a 250% higher risk of heart failure.
- The study builds on the idea of "[biological age](#)," a measure of your age based on biochemistry.

A growing body of evidence suggests age is more than just a number.

Take [multimillionaire Bryan Johnson](#). On paper, he's 46 years old. But he's been making headlines by contesting the idea that it means something about his health — and lifespan. Through a rigorous antiaging regimen that involves eating a strict vegan diet, exercising regularly, and taking more than 100 pills a day, Johnson's doctors told [Bloomberg](#) his test results show that he's achieved the heart of a 37-year-old, the skin of a 28-year-old, and the lung capacity of an 18-year-old.

So, how old is he, exactly? Johnson's doctors told Bloomberg that he's reduced his "biological age" by about five years. Biological age has become a buzzword in

longevity circles and is "the true age that our cells, tissues, and organ systems appear to be, based on biochemistry," [according](#) to the National Institute on Aging. But the idea that a singular number can represent it is controversial partly because there's no standard for normal aging, as [BI previously reported](#). Even Johnson's test results prove that organs don't all age at the same rate.

The latest breakthrough in longevity research suggests there may be a way to measure the age of specific organs. A recent [study](#) in Nature utilized machine learning models to analyze the age of 11 major organs for 5,676 adults. One of the study's key findings was that about 20% of people had accelerated aging in one organ, associated with a 20 to 50% higher mortality risk.

Knowing your "oldest organ" might also tell you more about your health trajectory — and the age-related diseases you could develop — than your biological age. The study found that individuals with accelerated heart aging, for example, have a 250% higher risk of heart failure. Every additional four years of age increased an individual's risk of developing heart disease by almost 2.5-fold over 15 years, the study noted. It also found that accelerated brain and vascular aging in an individual can predict the progression of Alzheimer's disease as strongly as the best biomarker test for the disease.

The technology to measure age organ-by-organ is far from ready to mainstream. Still, the concept has attracted the interest of those in longevity circles, according to [The Wall Street Journal](#). Some researchers told the Journal that there may be a day when patients can test the age of their organs through a simple blood test. It's not a far-off idea, given that there are already [blood tests that can test for cancer](#).

However, some scientists believe there's little merit in providing patients with these details before we devise interventions for them.

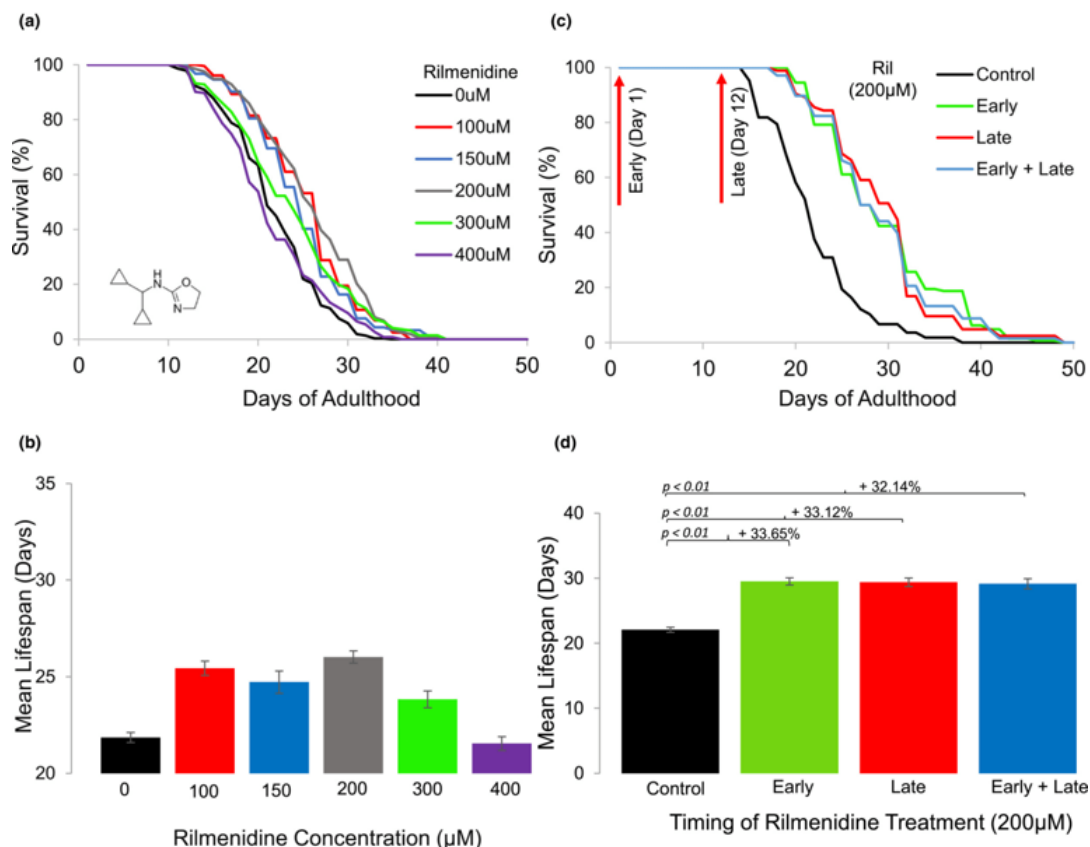
"It's not going to be terribly helpful for someone to know they might arguably get a particular age-related disease early unless there are preventive steps or other interventions they can take to help that," Dr. James Kirkland, a physician and professor whose research focuses on aging at the Mayo Clinic, told the Journal.

Common hypertension drug slows down aging and can increase life expectancy

Researchers have discovered that a drug commonly used to treat [hypertension](#) can [extend lifespan](#) and slow down aging.

The study, which was published in [Aging Cell](#), found that rilmenidine, a medication that is already prescribed for hypertension, can increase lifespan and improve health markers in animals that were treated with it. The drug was found to mimic the effects of caloric restriction, a well-known anti-aging intervention that has been shown to promote longevity across species.

The researchers found that rilmenidine could provide a promising [anti-aging strategy](#) due to its rare and non-severe side effects, making it a potential treatment for humans. Unlike other drugs that were previously studied for their anti-aging effects, rilmenidine has the potential for future translatability to humans, due to its widespread use and fewer side effects.



The study was led by Professor João Pedro Magalhães, who worked on the research while at the [University of Liverpool](#) and is now based at the [University of Birmingham](#).

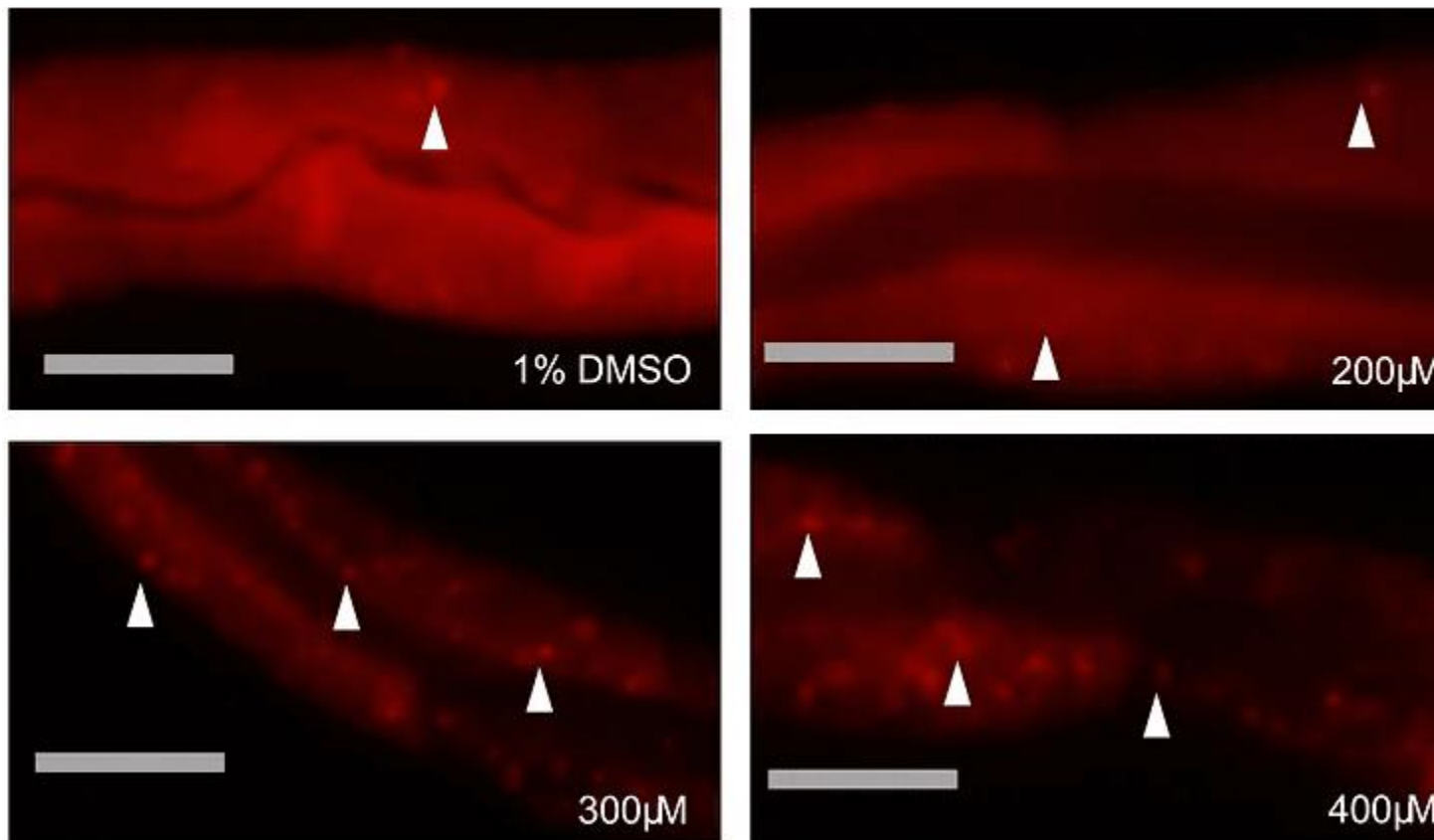
The research involved collaboration with scientists from [ETH Zürich](#) and [Harvard Medical School](#). The research was funded by the Swiss National Science Foundation, LongevityCity, and the Biotechnology and Biological Sciences Research Council.

[Caloric restriction](#) has been the most robust anti-aging intervention to date. However, studies of caloric restriction in humans have had mixed results and side effects. Therefore, finding medications like rilmenidine that can mimic the benefits of caloric restriction is considered the most reasonable anti-aging strategy.

The researchers found that the [healthspan and lifespan benefits](#) of rilmenidine treatment in the roundworm *C. elegans* were mediated by the I1-imidazoline receptor nish-1. They identified this receptor as a potential longevity target. This suggests that rilmenidine could provide a promising approach to slow down the aging process in humans by targeting the nish-1 receptor.

Professor Magalhães commented, "With a global aging population, the benefits of delaying aging, even if slightly, are immense. Repurposing drugs capable of extending lifespan and healthspan has a huge untapped potential in [translational geroscience](#). For the first time, we have been able to show in animals that rilmenidine can increase lifespan. We are now keen to explore if rilmenidine may have other clinical applications."

The study's findings have important implications for the development of [new anti-aging therapies](#). The ability to use a commonly prescribed medication to slow down the aging process could revolutionize the field of aging research. Rilmenidine's safety and effectiveness could also make it a viable alternative to caloric restriction, which is often difficult to follow and has unwanted side effects.



Induced autophagy by rilmenidine perturbed polyQ aggregation. (a) Representative images of day 2 adult transgenic animals, expressing the intestinal specific autophagy reporter gene. (CREDIT: Aging Cell)© The Brighter Side of News

The researchers hope to further investigate the potential benefits of rilmenidine for human aging. In the meantime, they recommend that further research is conducted to explore the full range of health benefits that the drug could offer.

The researchers' findings could have a significant impact on the field of aging research, which is rapidly expanding as the [global population ages](#). With the number of people over the age of 65 expected to triple by 2050, there is a growing need to develop effective anti-aging therapies that can improve health and extend lifespan.

Rilmenidine's potential as an anti-aging drug could revolutionize the field of aging research and provide a new avenue for improving human health and extending lifespan. The researchers' findings have important implications for the future of anti-aging research and could lead to the development of new, more effective anti-aging therapies in the future.

Lifechanging enzyme reverses muscle loss due to old age

Researchers have published findings that contribute to future therapeutics for muscle degeneration due to old age and cancer.

Enzyme GCN5 is key in skeletal muscle loss due to aging. (CREDIT: Creative Commons)

An international team led by uOttawa Faculty of Medicine researchers have published findings that could contribute to future therapeutics for muscle degeneration due to old age, and diseases such as cancer and muscular dystrophy.

In a study appearing in the [Journal of Cell Biology](#), which publishes peer-reviewed research on cellular structure and function, the authors said their work demonstrates the importance of the enzyme GCN5 in maintaining the expression of key structural proteins in skeletal muscle. Those are the muscles attached to bone that breathing, posture and locomotion all rely on.

"We found that if you delete GCN5 expression from muscle it will no longer be able to handle extreme physical stress," says Dr. Keir Menzies, a molecular biologist at the Faculty of Medicine's Biochemistry, Microbiology and Immunology department and cross-appointed as an associate professor at the Interdisciplinary School of Health Sciences.

Over the span of roughly five years, the uOttawa-led international collaboration painstakingly experimented with a muscle-specific mouse "knockout" of GCN5, a well-studied enzyme which regulates multiple cellular processes such as metabolism and inflammation. Through a series of manipulations, scientists produce lab mice in which specific genes are disrupted, or knocked out, to unveil animal models of human disease and better understand how genes work.

In this case, multiple experiments were done to examine the role the GCN5 enzyme plays in muscle fiber. What they found with this line of muscle-specific mouse knockouts was a notable decline in muscle health during physical stress, such as downhill treadmill running, a type of exercise known by athletes to cause micro-tears in muscle fibres to stimulate muscle

growth. The lab animals' muscle fibers became dramatically weaker as they scurried downhill, like those of old mice, while wild-type mice were not similarly impacted.

Dr. Menzies, the senior author of the study, says the findings are akin to what is observed in advanced aging, or myopathies and muscular dystrophy, a group of genetic diseases that result in progressive weakness and loss of muscle mass. It was supported by human data, including an observed negative correlation between muscle fiber diameter and Yin Yang 1, a highly multifunctional protein that is pivotal to a slew of cellular processes and found by the Menzies lab to be a target of GCN5. Ultimately, the team's research found that GCN5 boosts the expression of key structural muscle proteins, notably dystrophin, and a lack of it will reduce them.

(a) Bar graph showing all positively correlated musculoskeletal diseases obtained from BSCE by using all differentially expressed genes from the *Gcn5^{skm}-/-* bioset as an input for the meta-analysis. (CREDIT: Rockefeller University Press) This is significant because dystrophin is the body's most important protein for maintaining the membrane of muscle cells, serving as a kind of anchor and cushioning shock absorber in cells of muscles. Without it, muscles are very susceptible to physical stress, and the withering of muscles can lead to crippling and deadly consequences.

"Our publication shows that if you knock out GCN5 the one major thing we see is a lack of dystrophin, without seeing any real disruption of any other mechanisms," says Dr. Menzies. He noted that the paper also reaffirmed other research showing that GCN5 doesn't alter the content of muscle mitochondria, the powerhouses in cells, and another major influencer of muscle health.

Dystrophin acts as a shock absorber within the muscle cells, reducing any damage caused by muscle contractions. (CREDIT: Shutterstock)

The research builds on data showing that dystrophin is "important for maintaining general muscle integrity and muscle health," according to Dr. Menzies.

Dr. Menzies suggests the research could help to create a foundation for developing therapeutics down the line. "These findings may therefore be

useful for the discovery of new therapeutics that regulate GCN5 activity, or its downstream targets, for maintaining healthy muscle during cancer, myopathies, muscular dystrophy or aging,” he says.

What are the symptoms of muscle atrophy?

According to the Cleveland clinic, the symptoms of muscle atrophy differ depending on the cause of your condition. The most obvious sign of muscle atrophy is reduced muscle mass. Other signs of muscle atrophy may include:

- One arm or one leg is smaller than the other.
- Weakness in one arm and or one leg.
- Numbness or tingling in your arms and legs.
- Trouble walking or balancing.
- Difficulty swallowing or speaking.
- Facial weakness.
- Gradual memory loss.

What causes muscle atrophy?

The cause of muscle atrophy depends on the type you have according to the Cleveland Clinic. Disuse (physiologic) atrophy is caused by not using your muscles enough. If you stop using your muscles, your body won't waste the energy it needs to take care of them. Instead, your body will start to break your muscles down, which causes them to decrease in size and strength.

Disuse atrophy may affect you if you:

- Lead a sedentary lifestyle.
- Are malnourished.
- Don't get enough exercise.
- Sit at a desk job all day.
- Are on bed rest.
- Have a genetic disorder such as muscular dystrophy or Charcot-Marie-Tooth disease.
- Can't move your limbs due to a stroke or other conditions such as dermatomyositis.
- Have age-related atrophy (sarcopenia).

Neurogenic atrophy is caused by an injury or disease affecting nerves that connect to your muscles. When these nerves are damaged, they can't

trigger the muscle contractions that are needed to stimulate muscle activity.

When your muscles don't contract, your body thinks you don't need them anymore. So your body starts breaking them down, which causes them to decrease in size and strength. Diseases and other conditions that can affect these nerves include:

- Amyotrophic lateral sclerosis (ALS).
- Guillain-Barre syndrome.
- Carpal tunnel syndrome.
- Polio.
- Spinal cord injury.
- Multiple sclerosis.

Note: Materials provided above by [University of Ottawa](#)

Scientists show how to boost muscle regeneration and rebuild tissue

One of the many effects of aging is loss of muscle mass, which contributes to disability in older people.

One of the many effects of aging is loss of muscle mass, which contributes to disability in older people. To counter this loss, scientists at the Salk Institute are studying ways to accelerate the regeneration of muscle tissue, using a combination of molecular compounds that are commonly used in stem-cell research.

In a study, in [Nature Communications](#), the investigators showed that using these compounds increased the regeneration of muscle cells in mice by activating the precursors of muscle cells, called myogenic progenitors. Although more work is needed before this approach can be applied in humans, the research provides insight into the underlying mechanisms related to muscle regeneration and growth and could one day help athletes as well as aging adults regenerate tissue more effectively.

"Loss of these progenitors has been connected to age-related muscle degeneration," says Salk Professor Juan Carlos Izpisua Belmonte, the paper's senior author. "Our study uncovers specific factors that are able to accelerate muscle regeneration, as well as revealing the mechanism by which this occurred."

The compounds used in the study are often called Yamanaka factors after the Japanese scientist who discovered them. Yamanaka factors are a combination of proteins (called transcription factors) that control how DNA is copied for translation into other proteins. In lab research, they are used to convert specialized cells, like skin cells, into more stem-cell-like cells that are pluripotent, which means they have the ability to become many different types of cells.

"Our laboratory previously showed that these factors can rejuvenate cells and promote tissue regeneration in live animals," says first author Chao Wang, a postdoctoral fellow in the Izpisua Belmonte lab. "But how this happens was not previously known."

Muscle regeneration is mediated by muscle stem cells, also called satellite cells. Satellite cells are located in a niche between a layer of connective tissue (basal lamina) and muscle fibers (myofibers). In this study, the team used two different mouse models to pinpoint the muscle stem-cell-specific or niche-specific changes following addition of Yamanaka factors. They focused on younger mice to study the effects of the factors independent of age.

In the myofiber-specific model, they found that adding the Yamanaka factors accelerated muscle regeneration in mice by reducing the levels of a protein called Wnt4 in the niche, which in turn activated the satellite cells. By contrast, in the satellite-cell-specific model, Yamanaka factors did not activate satellite cells and did not improve muscle regeneration, suggesting that Wnt4 plays a vital role in muscle regeneration.

Induction of Yamanaka factors (OKSM) in muscle fibers increases the number of myogenic progenitors. Top, control; bottom, treatment. Red-pink color is Pax7, a muscle stem-cell marker. Blue indicates muscle nuclei. (Credit: Salk Institute)

According to Izpisua Belmonte, who holds the Roger Guillemin Chair, the observations from this study could eventually lead to new treatments by targeting Wnt4.

"Our laboratory has recently developed novel gene-editing technologies that could be used to accelerate muscle recovery after injury and improve muscle function," he says. "We could potentially use this technology to either directly reduce Wnt4 levels in skeletal muscle or to block the communication between Wnt4 and muscle stem cells."

The investigators are also studying other ways to rejuvenate cells, including using mRNA and genetic engineering. These techniques could eventually lead to new approaches to boost tissue and organ regeneration.

Other authors included: Ruben Rabadan Ros, Paloma Martinez Redondo, Zaijun Ma, Lei Shi, Yuan Xue, Isabel Guillen-Guillen, Ling Huang, Tomoaki Hishida, Hsin-Kai Liao, Concepcion Rodriguez Esteban, and Pradeep Reddy of Salk; Estrella Nunez Delicado of Universidad Catolica San Antonio de Murcia in Spain; and Pedro Guillen Garcia of Clinica CEMTRO in Spain.

The work was funded by NIH-NCI CCSG: P30 014195, the Helmsley Trust, Fundacion Ramon Areces, Asociacion de Futbolistas Espanoles (AFE), Fundacion Pedro Guillen, Universidad Catolica San Antonio de Murcia (UCAM), the Moxie Foundation and CIRM (GC1R-06673-B).

Note: Materials provided above by the [Salk Institute](#).

Protein discovery unlocks the secret to reversing muscle aging

Researchers at the University at Buffalo have unveiled a groundbreaking discovery that may hold the key to reversing cellular aging.

In the relentless pursuit to slow or even reverse the aging process, scientists at the [University of Buffalo](#) have made a groundbreaking discovery. This new study, published in the renowned [journal Science Advances](#), centers around a protein named NANOG, drawing its name from the mythical Irish land of Tír na nÓg, a place steeped in legends of eternal youth and vitality. Their research offers a promising path to combat the age-related decline of skeletal muscle cells. By overexpressing NANOG in senescent myoblasts—the embryonic precursors to muscle tissue—the research team achieved a remarkable reversal of key cellular aging markers. These improvements were observed in autophagy, energy homeostasis, genomic stability, nuclear integrity, and mitochondrial function.

One of the most striking results was the increase in muscle stem cells in prematurely aging mice, showcasing the potential of rejuvenating aging cells within the body. Importantly, this approach avoids the need to reprogram cells to an embryonic pluripotent state, a process often associated with tumor risks in stem cell therapy.

Dr. Stelios T. Andreadis, the study's corresponding author and a SUNY Distinguished Professor in the Department of Chemical and Biological Engineering at the [UB School of Engineering and Applied Sciences](#), explained the broader goals of their research: "Our work focuses on understanding the mechanisms of NANOG's actions in hopes of discovering druggable targets in signaling or metabolic networks that mimic the anti-aging effects of NANOG. Ultimately, the work could help lead to new treatments or therapies that help reverse cellular senescence, and aid the many people suffering from age-related disorders."

Understanding Cellular Senescence and Its Impact

Cellular senescence is a critical factor in aging and age-related diseases. Senescent cells are unique in that they stop dividing but don't die when they should. Instead, they linger and secrete chemicals that can cause inflammation. Similar to a single moldy fruit spoiling the entire batch, a few senescent cells can spread inflammation and damage to surrounding healthy cells.

Interestingly, not all senescent cells are harmful. The compounds they release, known as the senescent secretome, play important roles

throughout life, such as during embryonic development, childbirth, and wound healing.

Fluorescent confocal image of NANOG Polyclonal Antibody. (CREDIT: Abcepta) However, as we age, the number of senescent cells increases. The immune system's efficiency declines over time, allowing these cells to accumulate and affect nearby healthy cells. This accumulation impacts the body's ability to handle stress, recover from injuries, and maintain cognitive functions, as senescent cells in the brain can impair learning and memory.

Senescence has been linked to numerous age-related conditions, including cancer, diabetes, osteoporosis, cardiovascular disease, stroke, Alzheimer's disease, and related dementias, as well as osteoarthritis. It also contributes to the decline in vision, mobility, and cognitive abilities.

Moreover, researchers suggest that senescent skin cells may be behind the sagging and wrinkling of aging skin. They also play a role in the severe inflammation seen in older adults with COVID-19, known as the cytokine storm.

The Role of NANOG in Combating Aging

The discovery of NANOG's powerful anti-aging properties is a significant breakthrough in the study of cellular senescence. By overexpressing this protein in senescent myoblasts, the researchers were able to reverse many aging hallmarks, offering hope for combating age-related disorders without the risks associated with reprogramming cells to an embryonic state.

The research could help lead to treatments for atherosclerosis, osteoporosis and other age-related disorders. (Credit: University of Buffalo)

One key improvement was in autophagy, the cell's internal cleaning system, which ensures that damaged cellular components are efficiently removed. Energy homeostasis, essential for maintaining cellular functions, was also restored to a youthful state. Additionally, genomic stability, nuclear integrity, and mitochondrial function—all critical for cell health—showed marked improvements.

A particularly promising result was the increase in muscle stem cells in prematurely aging mice. This finding suggests potential future therapies

not only for muscle cells but possibly for other tissues and organs. Developing targeted drugs that mimic NANOG's effects opens exciting possibilities for treating a wide range of age-related disorders.

The Future of Anti-Aging Research

As the scientific community delves deeper into the mechanisms of cellular senescence and NANOG's rejuvenating effects, the potential for new anti-aging treatments becomes more tangible. While we are still unraveling the complexities of aging at the cellular level, this discovery is a significant step toward understanding longevity and vitality.

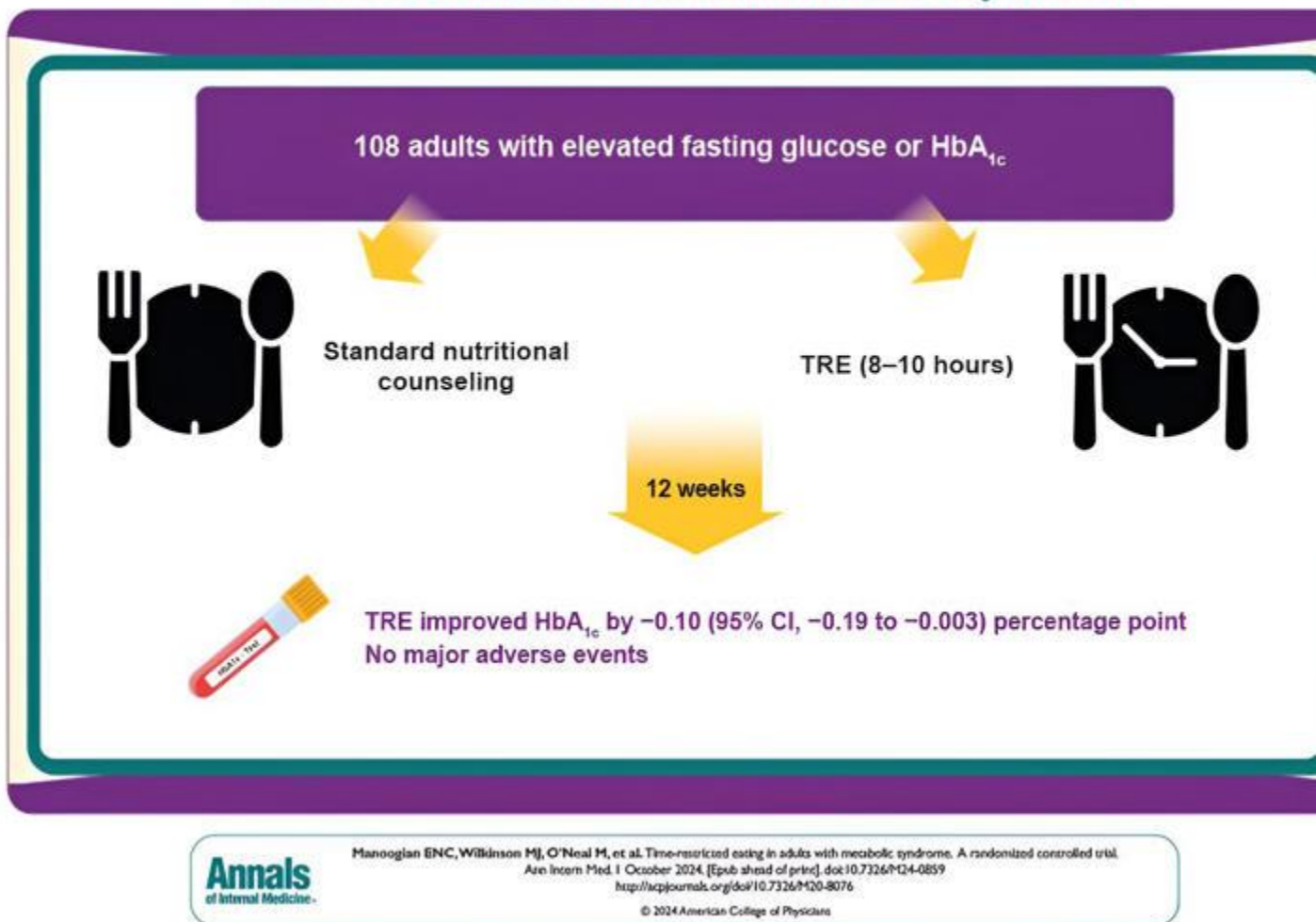
This illustration shows a senescent muscle cell (left), including the numerous factors that led to its declining ability to divide and grow. (CREDIT: University at Buffalo)

The potential for harnessing NANOG and similar proteins as therapies for age-related diseases underscores human ingenuity and our relentless pursuit of healthier, longer lives. In the near future, we might see revolutionary treatments that can turn back the clock on cellular aging, offering hope to countless individuals burdened by age-related conditions. The mythical land of Tír na nÓg, symbolizing eternal youth, may soon move from legend to reality, thanks to scientific progress. This journey toward harnessing NANOG and similar proteins is a testament to the remarkable advances in our understanding of aging and the potential for groundbreaking treatments.

As research progresses, the dream of finding effective anti-aging treatments that can improve the quality of life for many is becoming more attainable. This study represents a significant milestone in the quest for longevity and health, bringing us closer to a future where age-related decline can be effectively managed and perhaps even reversed.

One in three Americans has a dysfunctional metabolism: Clinical trial suggests intermittent fasting could help

What is the effectiveness of time-restricted eating (TRE)—limiting daily dietary intake to a consistent 8–10 hours without mandating calorie reduction—to improve cardiometabolic factors in adults with metabolic syndrome?



Time-restricted eating in adults with metabolic syndrome. Credit: Annals of Internal Medicine (2024). DOI: 10.7326/M24-0859

More than one-third of adults in the United States have metabolic syndrome, a cluster of conditions that significantly raise a person's risk of heart disease, stroke, and type 2 diabetes. These conditions include high blood pressure, elevated blood sugar, excess abdominal fat, and abnormal cholesterol levels.

In a new clinical trial, researchers at the Salk Institute and University of California San Diego School of Medicine found that time-restricted eating—also known as intermittent fasting—could offer significant health benefits to adults with metabolic syndrome.

Patients who ate within a consistent eight-to-ten-hour window each day for three months saw improvements in several markers of blood sugar regulation and metabolic function compared to those who received standard treatments.

"Our bodies actually process sugars and fats very differently depending on the time of day," says Salk Professor Satchidananda Panda, co-corresponding author of the study and holder of the Rita and Richard Atkinson Chair. "In time-restricted eating, we are re-engaging the body's natural wisdom and harnessing its daily rhythms to restore metabolism and improve health."

The TIMET study is the first to evaluate the benefits of a customized time-restricted eating schedule in patients taking medication for metabolic syndrome. The results are published in [*Annals of Internal Medicine*](#).

"For many patients, metabolic syndrome is the tipping point that leads to serious and chronic diseases like diabetes and heart disease," says co-corresponding author Pam Taub, professor of medicine at the UC San Diego School of Medicine and a cardiologist at UC San Diego Health.

"There is an urgent need for more effective lifestyle interventions that are accessible, affordable, and sustainable for the average American."

Western diets high in sugar, salt, and fat, combined with increasingly sedentary lifestyles, are thought to have contributed to the rising rates of metabolic dysfunction. While the initial recommendation may be to "eat less and move

more," these lifestyle changes are difficult for most people to sustain long-term. The researchers say time-restricted eating offers a more practical approach accessible to a wider range of patients, including those already on medication.

"Unlike expensive pharmaceuticals like Ozempic, which require lifetime use, time-restricted eating is a simple lifestyle change that doesn't cause side effects and can be maintained indefinitely," says first author Emily Manoogian, a staff scientist in Panda's lab at Salk. "Patients appreciate that they don't have to change 'what' they eat, just 'when' they eat."

In the new study, time-restricted eating protocols were customized to each participant's eating habits, sleep/wake schedules, and personal commitments. The resulting regimen had them reduce their eating window to a consistent eight to ten hours per day, beginning at least one hour after waking up and ending at least three hours before going to sleep.

Manoogian says this personalized approach made the intervention easier for patients to complete, compared to other intermittent fasting studies, which typically assign the same strict time window to all participants.

The TIMET study also accepted participants who were on medication for metabolic syndrome—a group usually excluded from such trials. This makes it the first study to measure the benefits of time-restricted eating in addition to existing standard-of-care pharmacological treatments.

In the study, 108 adults with metabolic syndrome were randomly sorted into either the time-restricted eating group or the control group. Both groups continued to receive standard-of-care treatments and underwent nutritional counseling on the Mediterranean diet. Participants also logged their meals using the "myCircadianClock" mobile app, developed at Salk.

After three months, patients who had completed the time-restricted eating regimen showed improvements in key markers of cardiometabolic health, including blood sugar and cholesterol. They also saw lower levels of hemoglobin A1c, a marker of long-term blood sugar control. This reduction was similar in scale to what is typically achieved through more intensive interventions by the National Diabetes Prevention Program.

The time-restricted eating group also showed 3–4% greater decreases in body weight, body mass index (BMI), and abdominal trunk fat, a type of fat closely linked to metabolic disease. Importantly, these participants did not experience significant loss of lean muscle mass, which is often a concern with weight loss.

The TIMET trial adds to a growing body of evidence supporting the use of time-restricted eating as a practical, low-cost intervention to improve cardiometabolic health.

The promising results suggest that health care providers could consider recommending the lifestyle intervention to patients with metabolic syndrome as a complement to existing treatments, though additional long-term studies are needed to determine whether time-restricted eating can sustain these benefits and ultimately reduce the risk of chronic disease.

More information: Emily N.C. Manoogian et al, Time-Restricted Eating in Adults With Metabolic Syndrome, *Annals of Internal Medicine* (2024). DOI: [10.7326/M24-0859](https://doi.org/10.7326/M24-0859)

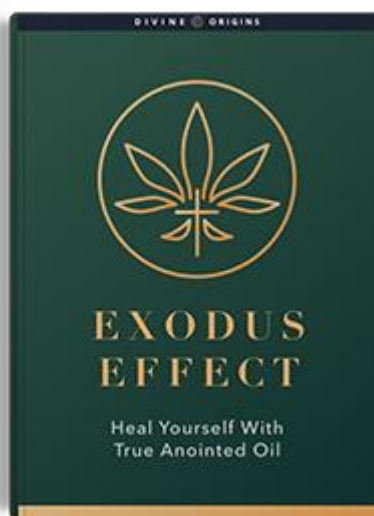
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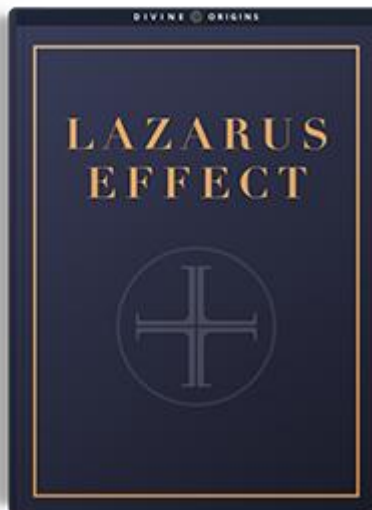
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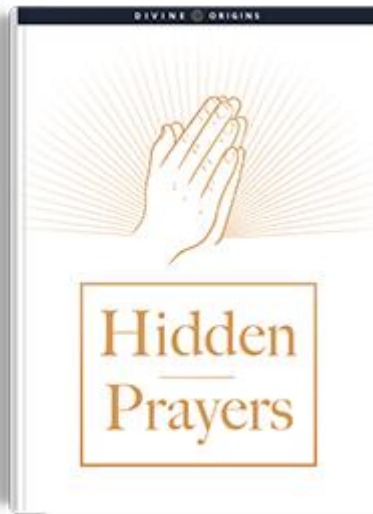
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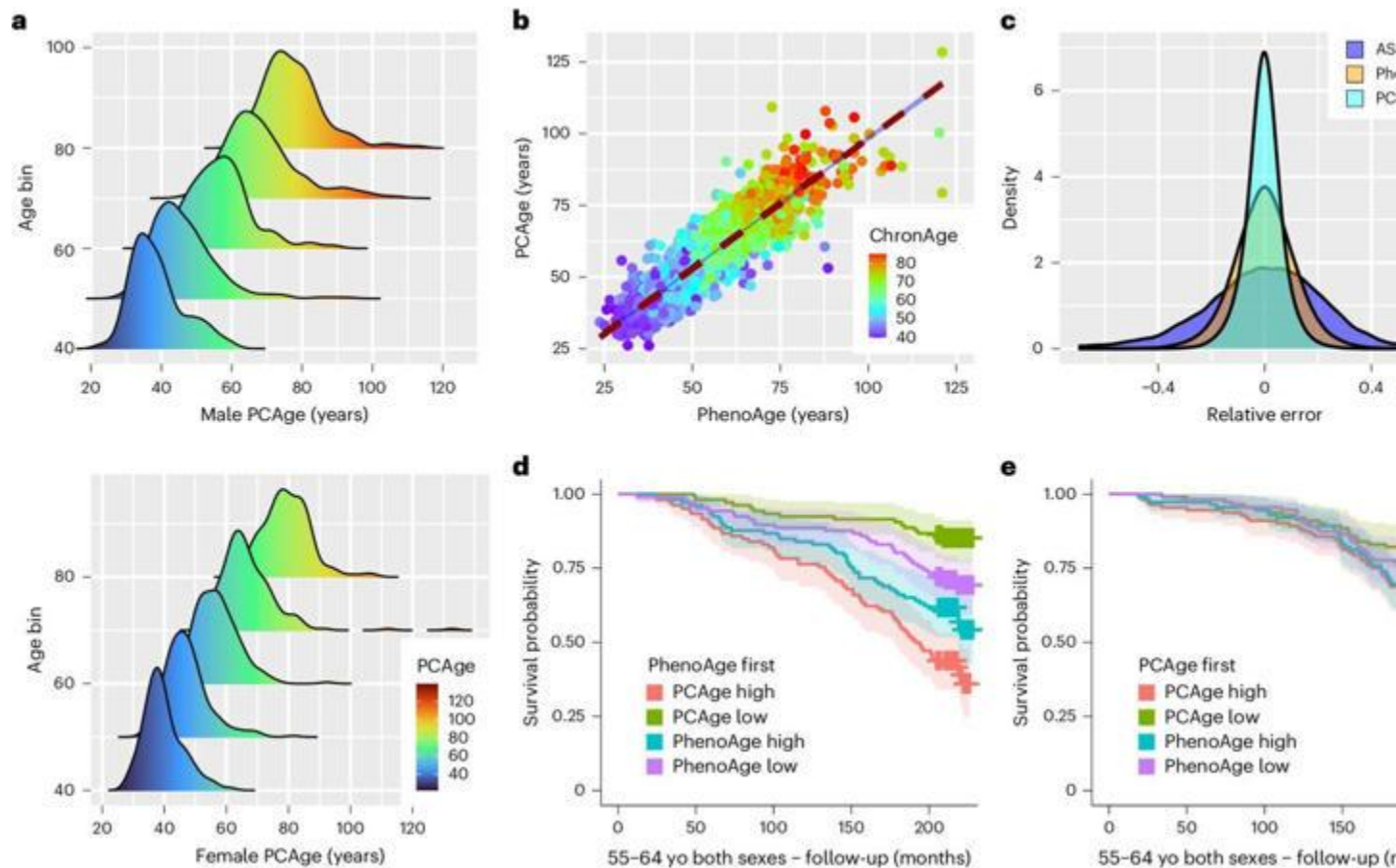
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Data analysis shows that adopting therapeutic changes can lead to longer lifespan



Testing PCAge for robustness and precision. a, Ridgeline plots of male and female populations binned by decade for CA. b, Scatter plot and linear regression of PhenoAge versus PCAge for males and females. c, Impact of random errors in clinical parameters on BA clocks and disease score. d, Kaplan–Meier survival curves over 20-year follow-up for subjects with PhenoAges of 55–64 years, stratified by PCAge or PhenoAge. e, Equivalent to d but showing Kaplan–Meier survival curves for subjects with PCAs of 55–64 years. Credit: Nature Aging (2024). DOI: 10.1038/s43587-024-00646-8© Provided by Medical Xpress

A combined team of longevity specialists, gerontologists and biochemists from Singapore General Hospital, National University of Singapore and Yale-NUS College, Singapore, has found that people who take appropriate steps to promote their longevity can live longer if they follow certain guidelines.

In their [study](#), published in the journal *Nature Aging*, the group analyzed aging-related data from several sources.

Over the past several years, medical researchers have come to believe that humans have both a chronological age and a biological age. The former is fixed by year and works the same for everyone. The latter is dependent on a host of factors, most of which are based on hereditary, environmental and lifestyle choices.

For many years, the medical community has assumed that people who choose to make certain changes in the way they live can lengthen their lifespan—eating healthier foods, getting exercise and avoiding dangerous activities, for example. For this new study, the researchers sought concrete evidence showing such assumptions are correct.

The researchers analyzed training datasets from the National Health and Nutrition Examination Survey containing medical information for 1,476 men and 1,536 women between the ages of 40 and 84.

They documented outcomes for people who had undergone treatment for diseases or conditions that are known to impact longevity, such as cardiac and renal problems and/or conditions that cause chronic inflammation, and compared them with those who had not. They found close correspondence between the two aging benchmarks, though they noted that there were some significant residuals.

The researchers next compared what they describe as a streamlined aging clock and compared it with what they describe as a clinical aging clock and found they both performed in similar ways when used to measure the likely longevity of a given person. They also found that both were better predictors of longevity than chronological age clocks.

The team then looked at data from the CALERIE study, which involved the impact of a restricted diet on longevity, and found that just two years on the diet led to significant reductions in biological age.

More information: Sheng Fong et al, Principal component-based clinical aging clocks identify signatures of healthy aging and targets for clinical intervention, *Nature Aging* (2024). DOI: [10.1038/s43587-024-00646-8](https://doi.org/10.1038/s43587-024-00646-8)

Want to live forever? Be sure to preserve your brain

It's 2146 and you're commuting to your retail job on Mars from one of Elon

Musk's fancy new teleportation machines on Earth. You're put to sleep; the machine scans the position and other properties of every subatomic particle in your body and brain, and beams the information to Mars, where an identical new body and brain is created, while the original is dematerialised in a flash of light. You wake up on Mars and order a Cybercab to the depressing, hermetically sealed mall. Hey ho, another day.

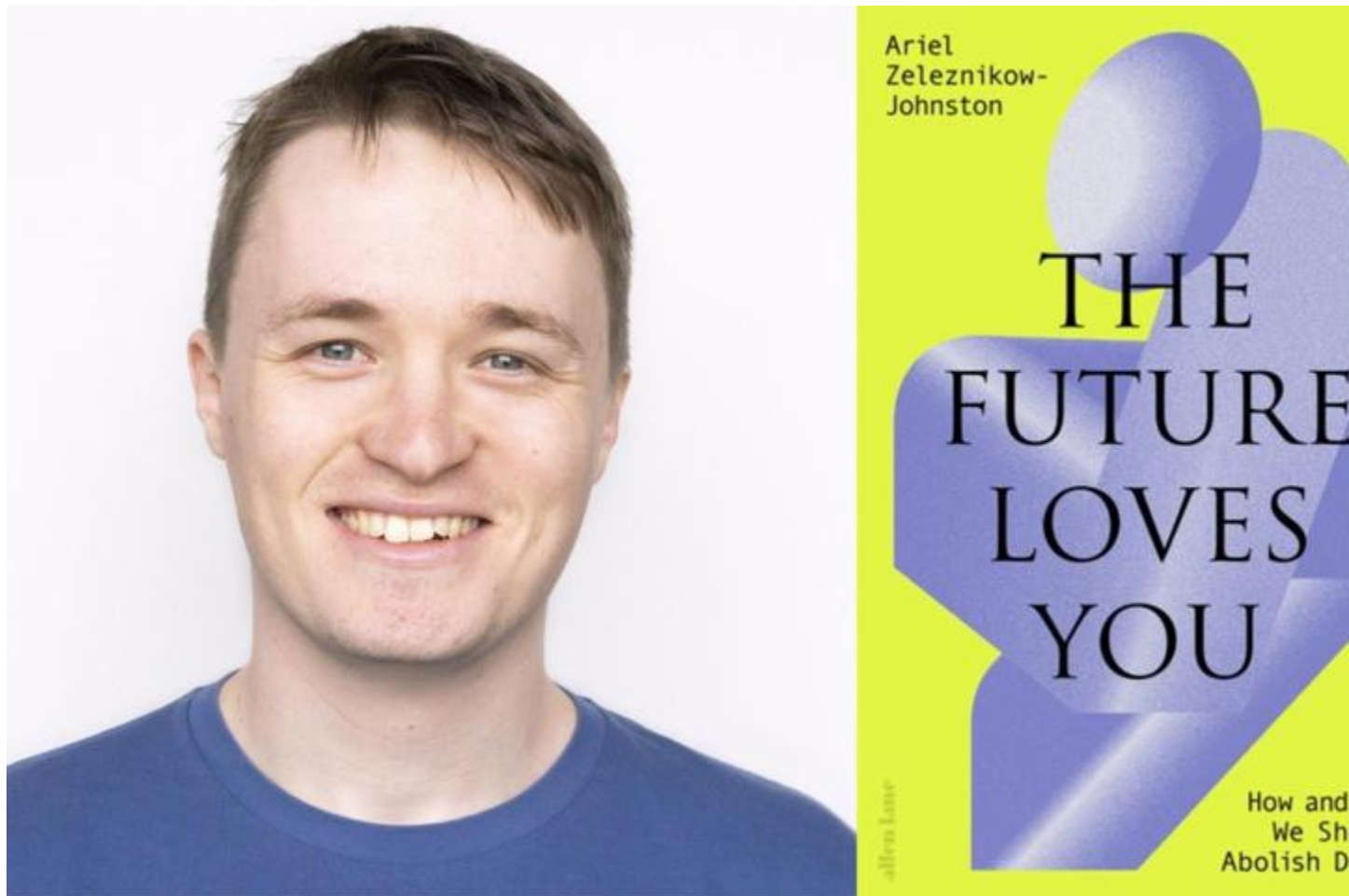
It took people a while to get used to the idea of teleportation, but now it's routine. One day, however, there's a glitch. You wake up in the machine, but you're still on Earth. A soothing female AI voice explains that, while there's now an identical copy of you going to work on Mars, the machine failed to vaporise your original body as usual. Of course, the voice says, we can't have two identical citizens wandering around at any one time, or society would cease to function. The Teslaportation Company regrets to inform you, therefore, that you must now report to an assisted-death pod to be killed.

Is this fair? And which of these identical humans is the real you? Most normal people would reply that I am still the person on Earth, and that the copy on Mars, despite waking up with all my memories, my personality, and exactly the same body, is not me. The idea that he will go on to live his life just as I would is no consolation for my own impending execution. Indeed, all those times the teleportation process worked normally, wasn't I already being murdered time and time again?

A version of this [sci-fi thought experiment](#) was originally devised by the celebrated English philosopher Derek Parfit and reappears in *The Future Loves You*, a new book about "abolishing death" by the young neuroscientist Ariel Zeleznikow-Johnston. His argument is that the version on Mars is really me, too: any system that can fully recreate the workings of your brain, in all its electrochemical complexity, is you. This view has the advantage, he explains, of

implying that we might be able to defeat death, even if it does offend ordinary intuitions about what makes us who we are.

For Zeleznikow-Johnston, this recreation of your brain could happen via a high-powered computer, or by growing a new one in a vat with stem cells, or any kind of cyborg combination of the two. Philosophers call this “the assumption of substrate independence”, a notion that is, like many of Zeleznikow-Johnston’s premises in this book, controversial – after all, no one has yet made a consciousness out of any material other than biological neurons.



The Future Loves You is published by Allen Lane

But if he’s right, and it were possible to perfectly record the “connectome” of a person – a high-resolution map of all their brain connections – before they died, then it would follow that we might one day be able to revive them with advanced technology, and reboot their consciousness inside a robot. This is a more Matrix-like vision of immortality than the one offered by cryonics, whereby rich people currently pay to have their whole bodies – or, if they’re penny-pinching, just their

heads – deep-frozen at death in the hope that future generations will figure out how to revive them.

None of what Zeleznikow-Johnston describes is possible at the moment. But he does spend many interesting pages on the current state of neuroscientific recording and the preservation of tissues. It turns out that, with a combination of chemical “vitrification” and low temperatures, we could already preserve a person’s brain in such a state that, at least in principle, future technology would be able to read its connectome perfectly and recreate it, so waking it up into a baffling future.

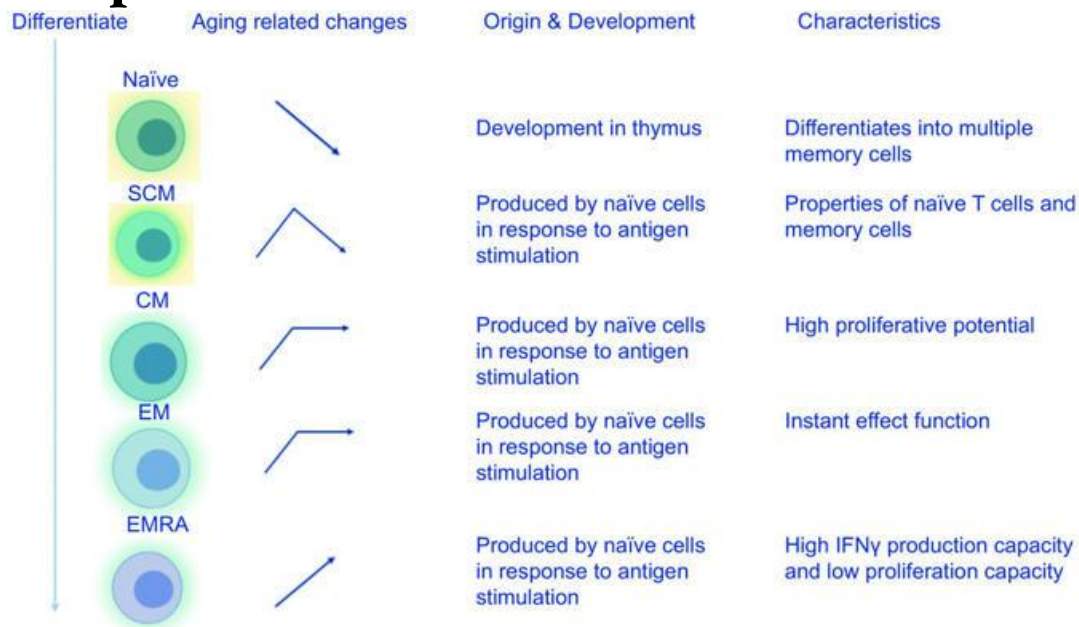
The author pursues these implications with admirable doggedness. If it’s possible to preserve people’s [brain-identities](#) in such a way now, then, he says, we ought to be doing it. Remarkably, according to his calculations, it should cost only about \$13,000 (£10,300) per person for the preservation procedure and a further \$1,300 per year in cold storage – or, as he works out for us, only about an extra 4 per cent of the total annual NHS budget. Now there’s something for Rachel Reeves to think about.

How seriously should we take all of this? Well, aside from all the tech-utopian speculation – which depends on the future invention of impressive technologies, as well as the willingness of our descendants to resuscitate lots of dead people, and, indeed, the survival of the human race itself – there are some excellent, concrete chapters. These focus on what we currently know about how memory, ageing and awareness work, making this book, additionally, an engaging description of modern brain science.

And then there might even be some readers who agree with Zeleznikow-Johnston’s desire to [“abolish involuntary death”](#). As for all those poets and philosophers who have argued that death is what makes life meaningful, Zeleznikow-Johnston proposes that they’ve simply succumbed to a state of “learned helplessness” in the face of calamity. (The scientific journal *The Lancet*’s “Commission on the Value of Death” in 2022 even claimed, with a straight face, that “it is healthy to die”.) Even so, if you would hesitate to step into the teleportation machine, this book will not convince you that any kind of happy immortality awaits.

The Future Loves You is published by Allen Lane at £25. To order your copy for £19.99, call 0330 173 0523 or visit [Telegraph Books](#)

T cells and aging: Unraveling the complexities of lifespan



Linear differentiation characteristics of T cells in peripheral circulation and changes with aging. SCM: stem cell memory T cells; CM: central memory T cells; EM: effector memory T cells; EMRA: effector memory CD45RA T cells. Credit: Aging Research (2024). DOI: 10.26599/AGR.2024.9340021© Provided by Medical Xpress

Aging significantly impacts the immune system, notably through the involution of the thymus, which reduces T cell production. This decline weakens immune responses, making older adults more susceptible to infections and diseases. Aged T cells also exhibit reduced recognition and responsiveness to antigens, impairing immune surveillance and memory.

The thymus, essential for T cell maturation, undergoes structural and functional changes over time, further diminishing immune function. Due to these issues, there is an urgent need for in-depth research to explore strategies for enhancing immune function in the elderly.

Researchers from Jinan University and Johns Hopkins University, led by Xiao Sean Leng, [published](#) their findings in *Aging Research*. The study delves into T cell development and aging, focusing on thymus development, T cell subset differentiation, and their implications for immune health in older adults.

The study provides an in-depth analysis of T cell development, beginning with their migration from bone marrow to the thymus, where they undergo critical selection and maturation processes. It highlights the differentiation of various T cell subsets, including conventional naïve T cells, regulatory T cells, effector T cells, and memory subsets, as well as unique subsets like $\gamma\delta$ T cells, MAIT cells, and NKT cells.

The research emphasizes the vital roles these subsets play in maintaining immune function, particularly in older adults. The study also explores the impact of thymic involution on T cell functionality, demonstrating that aged T cells exhibit reduced antigen responsiveness and result in increased susceptibility to infections and cancers in older adults. Additionally, it suggests potential strategies to address the challenges in studying T cell development and aging, aiming to enhance immune function and resilience in the elderly.

Dr. Xiao Sean Leng, the lead researcher, states, "Our study sheds light on the intricate processes of T cell development and aging. Understanding these mechanisms is crucial for developing strategies to enhance immune function in older adults, potentially improving their healthspan and resilience against diseases."

The findings underscore the need for innovative approaches to boost immune function in the elderly. Potential strategies include enhancing thymus function, promoting T cell regeneration, and developing targeted therapies to improve T cell responses. This research paves the way for future studies aimed at mitigating the effects of aging on the immune system, ultimately contributing to better health outcomes for older adults.

More information: Lipeng Mao et al, Human T cell development and aging: Remodeling throughout the lifespan, *Aging Research* (2024). DOI: [10.26599/AGR.2024.9340021](https://doi.org/10.26599/AGR.2024.9340021)

Provided by Tsinghua University Press

Study warns bad sleep in middle age can speed up brain aging

Poor sleep in our 30s and 40s can speed up brain aging, warns a new study. American researchers found that people in early middle age who suffer from sleeping issues - including having difficulty falling or staying asleep - have more signs of poor brain health in late middle age.

Study co-author Dr Clémence Cavallès, of the [University of California, San Francisco](#), said: "Sleep problems have been linked in previous research to poor thinking and memory skills later in life, putting people at higher risk for dementia.

"Our study which used brain scans to determine participants' brain age, suggests that poor sleep is linked to nearly three years of additional brain aging as early as middle age."

The study included 589 people with an average age of 40 at the start of the study.

Participants completed sleep questionnaires both at the beginning of the study and again five years later. They also underwent brain scans 15 years after the study began.

Researchers reviewed the participants' responses to questions such as "Do you usually have trouble falling asleep?" "Do you usually wake up several times at night?" and "Do you usually wake up far too early?"

The team recorded the number of six poor sleep characteristics for each participant: short sleep duration, bad sleep quality, difficulty falling asleep, difficulty staying asleep, early morning awakening and daytime sleepiness.

The participants were divided into three groups. Those in the "low" group had no more than one poor sleep characteristic. People in the "middle" group had two to three, and those in the "high" group had more than three.

At the start of the study, around 70% were in the low group, 22% were in the middle and 8% were in the high group.

The research team examined the participants' brain scans where the level of brain shrinkage corresponds to a specific age.

They then used machine learning to determine the brain age of each participant.

After adjusting for factors including age, sex, high blood pressure and diabetes, researchers found people in the middle group had an average brain age that was 1.6 years older than those in the low group, while those in the high group had an average brain age 2.6 years older.

Bad sleep quality, difficulty falling asleep, difficulty staying asleep and early morning awakening were the characteristics linked to greater brain age - especially when people consistently had those poor sleep characteristics over five years, according to the findings published online by the journal [Neurology](#).

The researchers say their study doesn't prove that poor sleep accelerates brain aging, rather it only shows an "association" between poor sleep quality and signs of brain aging.

But study co-author Professor Kristine Yaffe said: "Our findings highlight the importance of addressing sleep problems earlier in life to preserve brain health, including maintaining a consistent sleep schedule, exercising, avoiding caffeine and alcohol before going to bed and using relaxation techniques."

Yaffe, also of the University of California, San Francisco, added: "Future research should focus on finding new ways to improve sleep quality and investigating the long-term impact of sleep on brain health in younger people."

How pregnancy may speed up the aging process



How pregnancy may speed up the aging process© iStock/iStock

The fatigue and pangs of pregnancy have made many women feel older than their years. Now there's new research that suggests pregnancy may, in fact, accelerate the aging process.

Two new studies of genetic markers in the blood cells of pregnant women suggest that their cells seem to age at an exaggerated clip, adding extra months or even years to a woman's so-called biological age as her pregnancy progresses.

But one of the studies also suggests this process may reverse itself once a woman gives birth, rewinding time so that some mothers' cells seemingly end up

biologically younger afterward than they'd been during gestation, especially if a mother breastfeeds her baby.

Together, the studies underscore how physically demanding pregnancy is. But they also raise important questions about aging itself and whether it really can be sped up, slowed or reversed by pregnancy.

Aging in pregnancy

The [newest of the studies](#), published today in Proceedings of the National Academy of Sciences, found pregnancy “has a big impact on a woman’s body” and biological age, said Calen P. Ryan, an associate research scientist at the Columbia Aging Center at Columbia University in New York, who led the new research.

In it, scientists used several different biological-age “clocks” and other measures to analyze DNA markers in blood samples. These clocks aren’t timepieces but, instead, algorithms, developed using artificial intelligence programs, that examine the patterns of specialized chemical markers found on the outside of some genes. These markers accumulate and change in response to our age, health and lifestyles, a process known as epigenetics.

The algorithms can use these epigenetic markers to estimate the relative age of cells. This measure, often referred to as biological age, can differ from someone’s chronological age, which just means how long he or she’s been alive.

In the new study, the researchers checked blood samples from 825 young women in the Philippines, all born in the same year. Some had been or were pregnant, and others hadn’t conceived. Analyzing these samples, the epigenetic clocks broadly agreed that the biological age of the young women who’d been or were pregnant tended to be higher than that of the others, by at least several months, even after the researchers controlled for economic disparities and other social and health factors.

Pregnancy as a stress test

Similarly, the other new study, published [in March in Cell Metabolism](#), used several different epigenetic clocks to estimate the changing internal age of pregnant women at several points during their pregnancies.

"We were very interested in looking at the impacts of pregnancy as a naturally occurring stress test," said Kieran J. O'Donnell, an assistant professor at the Yale Child Study Center and Yale School of Medicine, who oversaw one of the new studies.

With blood samples from 119 pregnant American women and five different clocks, the researchers tracked the epigenetic changes related to the women's biological age, starting early in gestation and ending three months after they'd given birth.

The clocks again agreed that pregnancy seemed to be aging the incipient moms as they approached full term, making their blood cells' DNA appear to be as much as two years older than it had been earlier in the pregnancy.

More encouraging, though, O'Donnell said, is that this aging seemed to reverse for most of the women within three months after birth. In general, their patterns of DNA markers soon reverted to an earlier, more-youthful state, and for some new moms who'd breastfed exclusively in the first three months postpartum, overshot the mark, leaving them apparently "younger" biologically than before, by as much as eight years, the study's authors wrote, "indicating a pronounced reversal of biological aging."

Disagreement about aging

But some researchers who study aging, longevity and epigenetics are skeptical of the studies' findings and conclusions. "It seems unlikely to me that pregnancy induces a whole-body acceleration of biological aging which is then reversed soon after pregnancy," said Matt Kaeberlein, a longtime longevity researcher who serves as CEO of Optispan, a company that promotes longevity and produces the "Optispan" podcast.

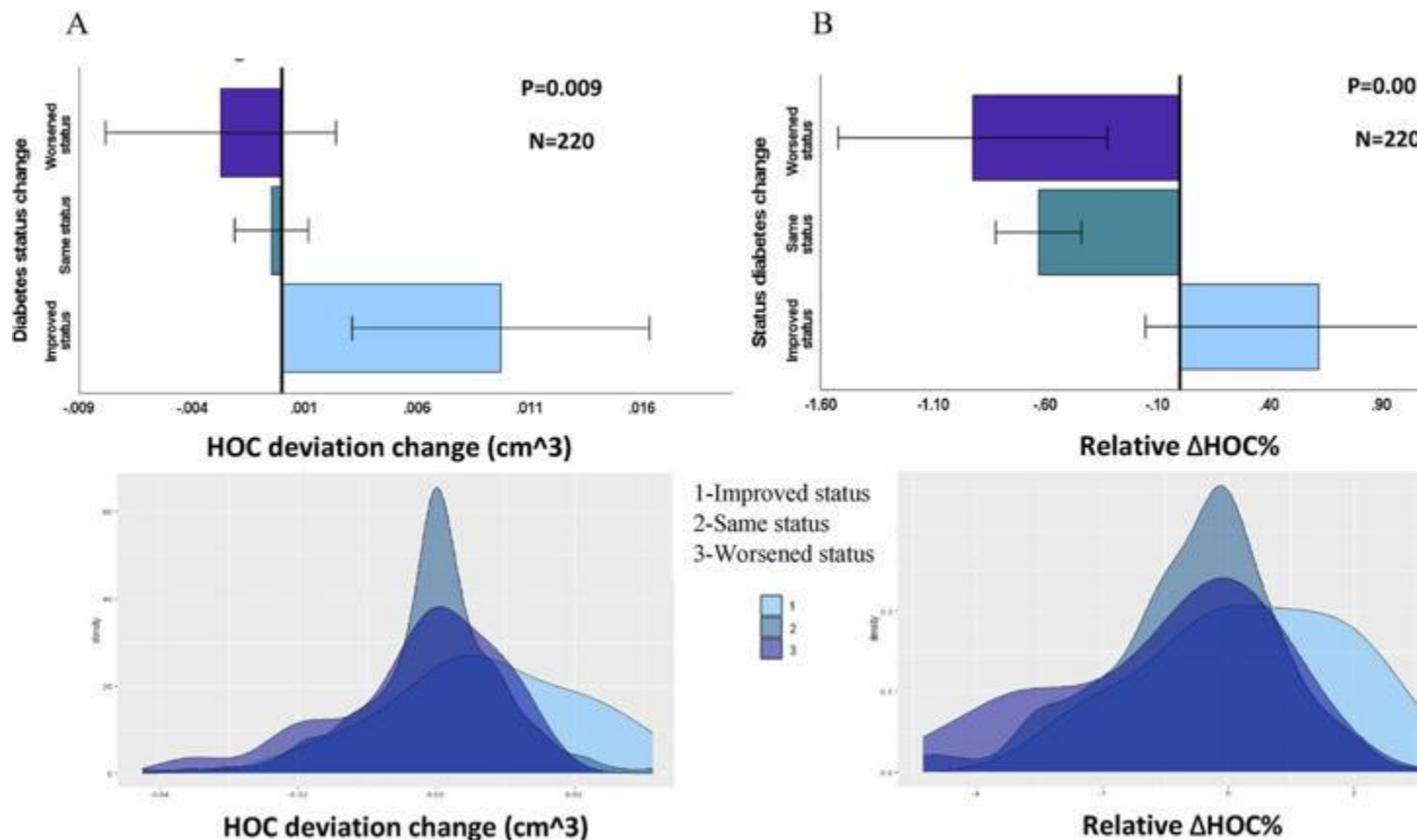
Charles Brenner, who studies metabolism, cancer and aging at the Beckman Research Institute of the City of Hope National Medical Center in California was blunter in an email. "100%, it's a misuse of aging biomarkers," he wrote.

Both scientists, as well as others who've discussed the studies online, speculate that the epigenetic shifts seen during pregnancy probably reflect the profound physiological demands of carrying a child. They're "a transient response to the stress of pregnancy, particularly in the immune system," Kaeberlein said.

What they aren't is evidence that pregnant women suddenly get older and then younger, these researchers say, or experience lasting effects that could directly shorten or lengthen their life spans.

But the cellular changes being picked up and analyzed by the epigenetic clocks might someday be useful health indicators. If a pregnant woman's epigenetic markers don't soon bounce back once she's no longer pregnant, she and her doctor might want to closely monitor her blood pressure, blood sugar and other standard measures of health, not because she suddenly seems older after becoming pregnant, but because, Ryan said, "pregnancy is such a big deal, physically."

Study reveals blood sugar control is key factor in slowing brain aging, highlighting benefits of Mediterranean diet



(A) HOC deviation change across diabetes status change following 18 mo of intervention. (B) HOC change across diabetes status change following 18 mo of intervention. MRI-assessed hippocampal occupancy score (HOC) 18-mo change deviation from expected for chronologic age (A), and MRI-assessed HOC 18-mo related change (B) with 18-mo diabetes status change during the intervention. Credit: The American Journal of Clinical Nutrition (2024). DOI: 10.1016/j.ajcnut.2024.09.013

Age-related brain atrophy, the gradual loss of neurons and shrinkage of brain tissue, is a natural part of aging, which can lead to cognitive decline and other neurological issues. While so far aging cannot be prevented, recent research from an 18-month dietary intervention offers hope that lifestyle and dietary changes can slow brain aging. A new international study, led by Ben-

Gurion University of the Negev as part of the DIRECT PLUS Brain MRI trial, has brought to light how blood sugar control can significantly impact brain health.

Brain age, as evaluated by MRI measurements of the hippocampus and lateral ventricles, reflects the biological aging of the brain, which can differ from a person's chronological age. Chronological age is the number of years lived, while brain age indicates the brain's actual health.

Typically, as we age, the hippocampus shrinks and the lateral ventricles expand, serving as markers of brain aging. Some individuals have a brain age younger or older than their chronological age. A younger brain age suggests better cognitive health, while an older brain age may indicate accelerated aging and increased risk of cognitive decline.

The study, which was [published](#) recently in *The American Journal of Clinical Nutrition*, was conducted by an international team of brain and nutrition experts, including researchers from Ben-Gurion University, Harvard University, Leipzig University, and more. The research was primarily carried out by Ph.D. student Dafna Pachter and overseen by Prof. Iris Shai, along with several international collaborators.

A [previous study](#) published two years ago, reported that Mediterranean (MED) and green-MED diets significantly attenuated age-related brain atrophy by ~50% within 18 months.

In the current study, the researchers aimed to understand the mechanism by which the slowing of brain atrophy occurs.

The study found that a decline in HbA1c, and key markers of long-term blood sugar levels, are associated with significant positive changes in specific brain regions commonly affected by age-related atrophy. Brain MRI results showed that lower HbA1c levels corresponded to greater deviations in the thalamus, caudate nucleus, and cerebellum—areas crucial for cognitive function, motor control, and sensory processing.

The study suggests that improved blood sugar control could be one of the most important factors in slowing down age-related brain changes.

Earlier research has highlighted the benefits of the Green Mediterranean (Green-Med) diet, including better blood sugar control. The Green-Med diet is rich in polyphenols from plant-based sources like Mankai (a high-protein aquatic plant) and green tea, while being low in red and processed meats. The current study further strengthens this connection by suggesting that the Green-Med diet may not only support metabolic health but also exert protective effects on brain structure and function.

DIRECT PLUS Trial—One of the largest brain MRI intervention studies in the world

The DIRECT PLUS trial, one of the longest and largest brain MRI studies conducted to date, involved approximately 300 participants who were divided into three dietary groups. Whole-brain MRI measurements were taken before and after the 18-month trial to track changes in brain health.

The researchers used Hippocampal Occupancy (HOC), as a proxy for brain age which predicts future risk of dementia. HOC typically decreases with age. Interestingly, some participants exhibited a brain age either younger or older than their chronological age.

Using NeuroQuant, an FDA-authorized fully automated tool, the research team quantified and segmented the brain MRI-derived data. The study aimed to examine whether improved glycemic control and specific dietary components could slow down brain aging.

The results indicated that participants who managed to improve their blood sugar levels and achieve normal glucose status experienced a more pronounced attenuation of brain aging. Notably, those who consumed higher amounts of green tea and Mankai duckweed shakes demonstrated the most significant improvements in both blood sugar levels and brain health.

Glycemic control and polyphenols: The key to a younger brain age?

The study's senior researcher, Prof. Iris Shai, from Ben-Gurion University, an adjunct professor at Harvard University, and an Honorary Professor at Leipzig University, explains, "Maintaining low blood sugar levels, even within the normal range, shows promise for preserving a younger brain, especially when combined with a healthy diet and regular physical activity. Specifically, polyphenols found in plant-based foods may cross the blood-brain barrier and help reduce brain inflammation, which is crucial for memory."

Dafna Pachter, a Ph.D. student and the first author of the paper, adds, "This trial offers a safe approach to potentially slow down our brain aging—by adopting the components of a green-Mediterranean diet."

This study is one of the first large-scale trials to directly link dietary changes, particularly those associated with the Green-Med diet, to improved glycemic control and slower brain aging. While further research is needed to fully understand the mechanisms at play, these results suggest a potential avenue for reducing the risk of age-related cognitive decline through relatively simple dietary adjustments.

More information: Dafna Pachter et al, Glycemic control contributes to the neuroprotective effects of Mediterranean and green-Mediterranean diets on brain age: the DIRECT PLUS brain-magnetic resonance imaging randomized controlled trial, *The American Journal of Clinical Nutrition* (2024). DOI: [10.1016/j.ajcnut.2024.09.013](https://doi.org/10.1016/j.ajcnut.2024.09.013)

Provided by Ben-Gurion University of the Negev

Eating less more effective than fasting for living longer: study

Eating less long-term is more likely to help people live longer than periodic fasting, according to new research.

Consuming fewer calories had a greater impact on lifespan than fasting, say scientists.

They concluded that a "more moderate" level of calorie restriction might be the way to balance long-term health and living longer following a [study of mice](#).

However, losing weight may not be an indicator of a longer lifespan.

One surprising finding of the American study, published in the journal [Nature](#), was that mice that lived the longest on restrictive diets were those that lost the least weight despite eating less.

The mice that lost the most weight on restrictive diets tended to have low energy, compromised immune and reproductive systems, and shorter lives.

For nearly a century, lab studies have shown consistent results: eat less food, or eat less often, and an animal will live longer.

But researchers have struggled to understand why restrictive diets work to extend lifespan, and how to best implement them in humans.

For the new study, scientists at [The Jackson Laboratory](#) (JAX) in Bar Harbor, Maine, tracked the health of more than 900 mice on a range of diets.

The research was designed to ensure that each mouse was genetically distinct, which allowed the team to better represent the genetic diversity of humans.

The study concluded that eating fewer calories had a greater impact on lifespan than periodic fasting, revealing that very-low-calorie diets generally extended the mice's lifespan regardless of their body fat or glucose levels - both typically seen as markers of metabolic health and aging.

Research leader Professor Gary Churchill, of JAX, said: "Our study really points to the importance of resilience.

"The most robust animals keep their weight on even in the face of stress and caloric restriction, and they are the ones that live the longest.

"It also suggests that a more moderate level of calorie restriction might be the way to balance long-term health and lifespan."

Churchill and his colleagues assigned female mice to any of five different diets: one in which they could freely eat any amount of food at any time, two in which the animals were provided only 60% or 80% of their baseline calories each day, and two in which the animals were not given any food for either one or two consecutive days each week but could eat as much as they wanted on the other days.

The mice were then studied for the rest of their lives with periodic blood tests and extensive evaluation of their general health.

Overall, mice on unrestricted diets lived for an average of 25 months, those on intermittent fasting diets lived for an average of 28 months, those eating 80% of their normal diet lived for an average of 30 months, and those eating 60% of their previous diet lived for 34 months.

But within each group, the range of lifespans was wide with mice eating the fewest calories, for example, having lifespans ranging from a few months to 4.5 years.

When the research team analyzed the rest of their data to try to explain the wide range, they found that genetic factors had a "far greater" impact on lifespan than diets.

They say their findings highlight how underlying genetic features, yet to be identified, play a major role in how these diets would affect an individual person's health trajectory.

The team pinpointed genetically encoded resilience as a "critical" factor in lifespan; mice that naturally maintained their body weight, body fat percentage and immune cell health during periods of stress or low food intake, as well as those that did not lose body fat late in life, survived the longest.

Churchill said: "If you want to live a long time, there are things you can control within your lifetime such as diet, but really what you want is a very old grandmother."

The study also cast doubt on traditional ideas about why some diets can extend life.

For example, factors such as weight, body fat percentages, blood glucose levels and body temperature did not explain the link between cutting calories and living a longer life.

Instead, the study found that immune system health and traits related to red blood cells were more clearly connected to lifespan.

The researcher says their findings mean that human studies of longevity - which often use metabolic measurements as markers for aging or youthfulness – may be overlooking more important aspects of healthy aging.

Churchill added: "While caloric restriction is generally good for lifespan, our data show that losing weight on caloric restriction is actually bad for lifespan.

"So when we look at human trials of longevity drugs and see that people are losing weight and have better metabolic profiles, it turns out that might not be a good marker of their future lifespan at all."

Foods that slow brain aging and how to incorporate them in your diet

A new study has shown that specific nutrients, similar to those found in the Mediterranean diet, can play a crucial role in slowing brain aging, according to Healthline.

Foods that slow brain aging

Scientists have found that fatty fish should be included in your diet.

"**Fatty fish**, like salmon, mackerel, sardines, and trout, are rich in omega-3 fatty acids, and we should aim to have at least one portion of oily fish a week," the researchers say.

Leafy greens like spinach, kale, and broccoli are also excellent choices. They provide carotenoids, such as lutein and zeaxanthin.

Nuts and seeds are another product worth stocking up on. Almonds, sunflower seeds, and flaxseeds contain vitamin E and ALA (alpha-linolenic acid).

To add more choline to your diet, try including **eggs and liver**. Filling your plate with **colorful vegetables** and fruits is also a good idea. Peppers, tomatoes, and oranges are rich in antioxidants and vitamin C.

How to incorporate more brain-healthy foods into your diet

You don't need to completely overhaul your diet to prioritize your brain's health. You can start with small steps in the right direction.

Dietitian Ludlam-Raine advises choosing one or two days a week to include **salmon, sardines, or mackerel in your meals**.

You can also increase your intake of **leafy greens** by adding spinach or kale to smoothies, salads, and side dishes.

For snacks, Ludlam-Raine recommends keeping **almonds, sunflower seeds, and flaxseeds** on hand.

You can eat them alone or add them to yogurt, cereal, or porridge for a more complete meal.

Breakfast is a great time to increase your choline intake by having **eggs**. Finally, Ludlam-Raine advises adding plenty of color to your plate with an array of fresh **fruits and vegetables**.

Aim for a variety of colorful foods to ensure a good mix of antioxidants and carotenoids.

The key is to consume whole, minimally processed foods as much as possible.

"Try to eat at least five portions of fruits and vegetables a day and 30 different plant-based foods a week. Eat the rainbow to obtain all the nutrients you need," advises the expert.

Longevity Escape Velocity: The Theory Having Scientists Believe Humans Could Live Forever

The idea of living forever has been a recurring thought in humanity's collective mind since the dawn of civilization. From the era of the Sumerian Epic of Gilgamesh to Medieval alchemists, scholars and researchers have pondered the possibility of eternal life.

Now, scientists who've been working on the "Longevity Escape Velocity" theory believe that all symptoms of aging could be eradicated by 2030, essentially allowing humans to live forever.

The "Longevity Escape Velocity" Theory

The "Longevity Escape Velocity" theory centers on the idea that humans will one day be able to defy death and essentially become immortal.

The hypothetical idea takes its name from the basic physics principle of escape velocity, which dictates that an object can defy the law of gravity when it reaches a certain speed. Likewise, humans may one day be able to escape the pull of death and live forever.

Reaching a Near Immortal State

While LEV remains nothing more than a theory, scientists and researchers worldwide are working on various projects that could make this a reality one day.

As scientists increase their knowledge in fields such as cell rejuvenation, the life expectancy of humans will continue to rise until it reaches a near-immortal state.

LEV Could Become a Reality by the 2030s

Futurist Ray Kurzweil believes humanity may reach a huge breakthrough in the LEV field by the year 2028 or 2029, yet many researchers have deemed this hopeful.

According to Aubrey de Grey, one of the leading longevity researchers and proponents of the theory, the best-case scenario is that LEV could become a reality by the 2030s

President of the Longevity Escape Velocity Foundation

de Grey currently sits as the president and chief science officer of the Longevity Escape Velocity Foundation. In a statement to the New York Post, he [said](#), "We wanted to put this out there because everyone knows aging is bad. Everyone says it's bad, but nobody does anything about it."

He [continued](#), "Like bad weather, people are stuck in the assumption that nothing can be done, even if we try. We wanted to put that assumption to rest."

"Dublin Longevity Declaration"

Now, many of the world's leading authorities on longevity have gathered together to join the new "[Dublin Longevity Declaration](#)." This collection of scientists claims they will work on reversing biological aging at the cellular level.

According to the website, they believe the efforts of scientists who have attempted to slow down aging the old-fashioned way by attacking one disease at a time are "overly pragmatic."

Harvard Geneticist Believes LEV Will Come in Our Lifetime

Revered Harvard geneticist George Church believes that LEV may see significant breakthroughs in our lifetime, and people could reap the benefits of the research before the end of the century.

Another proponent of the theory, Sourav Sinha, head of strategy at the Longevity Vision Fund, shares opinions similar to those of the church. During a recent [discussion](#), she admitted that with the right kind of investment, LEV could become a reality in as little as a few decades.

LEV is Backwards and Silly, Says Expert

Not everyone agrees with de Grey and the scientists who have signed up to the Dublin Longevity Declaration, however. Dr. Thomas Perls admits that while the pursuit of preventing age-related disease is a great cause, the idea that LEV may lead to eternal life is silly.

"These billionaires, of course, they've seen: if you throw enough money at a particular problem, you solve it," Perls told

Perls Claims Scientists Are Getting Ahead of Themselves

While Pearls admits he's on board with pouring billions of dollars into projects that could help scientists cure or reduce the chance of age-related illnesses such as dementia and Alzheimers, it claims the search for immortality is a waste of time.

The geoscientists argue that it's simply a waste of time to invest money in living forever when the greatest researchers have yet to find a way to ensure that people in their 80s and 90s remain in good health.

The Pursuit of Delaying Aging

According to Pearls, researchers should realign their focus and look into delaying aging rather than getting rid of it. "We want to do what we can to delay or even avoid aging-related diseases that may increase life expectancy or life span a little bit for people," [said](#) Perls.

He [continued](#), "But in no way do I think that's going to lead to the notion of living forever."

Philosopher Believes Healthy Living Can Result in Increased Longevity

Futurist and philosopher Nick Bostrom has proposed that humans should opt to live healthier as they age and believes humans in the future could live to surpass 1,000 years with the help of AI.

He claims humanity needs to place AI in control and allow it to do what's necessary to create new drugs and find cures for all illnesses and aging. Should this be successful, he claims humanity could achieve an "indefinite lifespan."

Biological Limits

Regarding living to 200 or even 1,000 years old, Perls again doesn't see any future in which this becomes a reality.

According to the scientist, we can't outlive our biological limits no matter how advanced humans become. Nor does he think rejuvenation is theoretically possible. Instead, he [recommends](#): "Let's keep going with the healthspan."

Our mind, body and soul are interconnected in ways that we may not fully understand. We often tend to focus on one aspect, neglecting the other two. However, it is crucial to understand that they are all equally important and work together to create a harmonious balance within us.

 The mind is where our thoughts are born, and it plays a significant role in how we perceive the world around us.

 Our body is the vessel through which we experience life, and our senses enable us to interact with the environment.

 Our soul is the intangible aspect of our being that connects us to our higher self and the universe.

 It is essential to pay attention to the signals our body gives us as it is a storehouse of information that our mind may not have access to.

 To develop synchronicities between the mind, body, and soul, here are a few techniques that can be beneficial:👇

 Mindfulness - Mindfulness is the practice of being present in the

moment and observing our thoughts, emotions, and physical sensations without judgment.

 Meditation - Meditation is a powerful tool that can help us connect with our soul. It is a practice that involves focusing on a single object or thought to achieve a state of deep relaxation and inner peace.

 Exercise - Physical activity is essential for maintaining a healthy body and mind. It can help release endorphins that elevate our mood and reduce stress levels.

 Nutrition - Our diet plays a significant role in our physical health and mental well-being. Eating a balanced diet rich in nutrients can provide the energy needed to function optimally.

  In conclusion, developing synchronicities between our mind, body, and soul is crucial for overall well-being.

 Taking care of each aspect equally can lead to a harmonious balance within us, enabling us to lead a fulfilling life.

So, let us pay attention to the signals our body gives us, listen to our thoughts, and connect with our soul.

What is ageing? Even the field's researchers can't agree

Survey of scientists who study ageing finds no consensus on the fundamentals.



When ageing begins is one of many questions researchers cannot agree on. Credit: mrPliskin/iStock via Getty

Researchers studying [ageing](#) disagree on just about everything — including what ageing is, whether it is a disease and when it starts — according to a survey of about 100 scientists working in the field.

A key goal of ageing research is to help people live longer, healthier lives. But the exact causes of ageing, as well as effective approaches to slow or reverse it, remain elusive. For the field to tackle these challenges, researchers need to speak a common language, says Alan Cohen, who studies ageing at Columbia University in New York City. “There doesn’t have to be perfect consensus, but we need to sort things out quite a bit,” he says.

Vadim Gladyshev, another researcher in the field who is based at Harvard Medical School in Boston, Massachusetts, and his colleagues agree. They decided to survey participants at an international conference on ageing in Newry, Maine, in 2022, to better understand the views of those researching the topic. Respondents included early-career researchers, established scientists and industry professionals. The results are described in *PNAS Nexus* today¹.

Most researchers are clear in their own minds about what ageing is — but their perspectives don’t align with those of others, says Gladyshev. “People joke in the field that there are more theories than people.” Despite this, Gladyshev says he was surprised by the scale of the problem.

The latest results reflect those of a similar survey of 37 researchers conducted in 2019 by Cohen and his colleagues². Now “it’s unquestionably clear that there’s a huge disagreement”, says Cohen.

What is ageing?

When asked to describe ageing, one-third of respondents considered it to be a loss of function over time, from declines at the cellular level to a decrease in overall health and fitness. Others saw ageing as a [gradual accumulation of deleterious changes](#). Not all respondents associated ageing with negative connotations, with some seeing it as a change in state — reversible or otherwise — or a continuation of development. And others approached the subject from a demographic standpoint, describing ageing simply as an [increased chance of dying](#).

A question about the causes of ageing also elicited a broad range of responses, from the build-up of damage to evolutionary constraints, and from

changes to the regulatory system to a deterioration in repair mechanisms. A few admitted they did not know what underlies ageing.

Researchers also disagree on whether ageing is a disease. More than one-third of respondents said it is, another 38% said it isn't and the remaining 28% were neutral. Cohen doesn't favour describing ageing as a disease because it implies that it is something that needs to be eliminated, although many researchers in the field are, to some extent, [working towards this goal](#).

For Gladyshev, the answer to the question is more complicated. "Ageing is not a disease, but it is also not not a disease," he says. He sees many [diseases](#) as essentially accelerated ageing taking place in specific organs or in the body as a whole.

When does ageing start?

Respondents generally said that ageing starts early in life, but they couldn't agree on how early.

Some said the process begins before conception, when eggs and sperm are being produced. According to this theory, if your parents are older when you are conceived, you are already more advanced in your ageing, says Cohen. The problem with that view of when ageing starts, he says, is that it can go back in time forever. Cohen thinks that ageing starts from the point at which egg and sperm meet — at conception.

Others think that ageing starts on the day of birth. A few said it starts when puberty hits. Some consider that ageing begins only when the body stops developing, when a person reaches their twenties, or a few years later, when the body reaches peak performance, in the mid-twenties.

Ultimately, Gladyshev says, the vast diversity of responses reflects the many unknowns in the field. Gladyshev expects rapid advances in efforts to define ageing, including the development of [biomarkers](#) to track [biological age](#). "It's a time of opportunity."

doi: <https://doi.org/10.1038/d41586-024-03936-8>

Lacking purpose in life linked to cognitive decline, study suggests

Older people who feel that their life lacks purpose may be more prone to memory loss and thinking problems as they age, a study suggests.

The new study adds to mounting evidence linking psychological wellbeing to healthy ageing.

A new paper, published in the Journal of Neurology, Neurosurgery and Psychiatry, examined long-term data on hundreds of older adults in Illinois in the US.

Some 910 people were tracked for an average of 14 years to assess whether they developed mild cognitive impairment or dementia.

An annual psychological wellbeing assessment was conducted on people involved in the study.

These assessments gathered information on purpose in life, positive relation with others, personal growth, self-acceptance, autonomy and "environmental mastery".

During the follow-up, some 29% were diagnosed with mild cognitive impairment – the stage between an age-related decline in memory and thinking and dementia.

And among this group, 34% were diagnosed with dementia.

The international team of researchers found that people who developed mild cognitive impairment had a faster decline in psychological wellbeing compared with people who were "cognitively intact".

This led to overall lower wellbeing scores two years before they were diagnosed with mild cognitive impairment, experts found.

Looking at the different elements of psychological wellbeing, the researchers found that people who developed mild cognitive impairment (MCI) were found to lack a purpose in life some three years before diagnosis.

And they had lower levels of personal growth some six years before diagnosis.

"Psychological wellbeing (specifically purpose in life and personal growth) became significantly lower before MCI diagnosis," the research team said.

"Reduced psychological wellbeing may serve as a predictor for impaired cognitive function. And post-diagnostic psychological support should be planned for people diagnosed with dementing disorders."

Longevity Breakthrough: New Protein Discovery Could Be the Key to Healthier Aging

New research found that the protein MANF helps cells manage toxic protein clumps, improving cellular health and potentially aiding treatments for age-related diseases like Alzheimer's and Parkinson's.

Researchers at [McMaster University](#) have uncovered a previously unidentified cell-protective role of a protein, potentially paving the way for new treatments for age-related diseases and promoting healthier aging.

The team has found that a class of protective proteins known as MANF plays a role in the process that keep cells efficient and working well.

The findings appear in the journal *Proceedings of the National Academy of Sciences*.

Our cells make proteins and discard them after they perform their jobs. This efficient, continuous maintenance process is known as cellular homeostasis. However, as we age, our cells' ability to keep up declines.

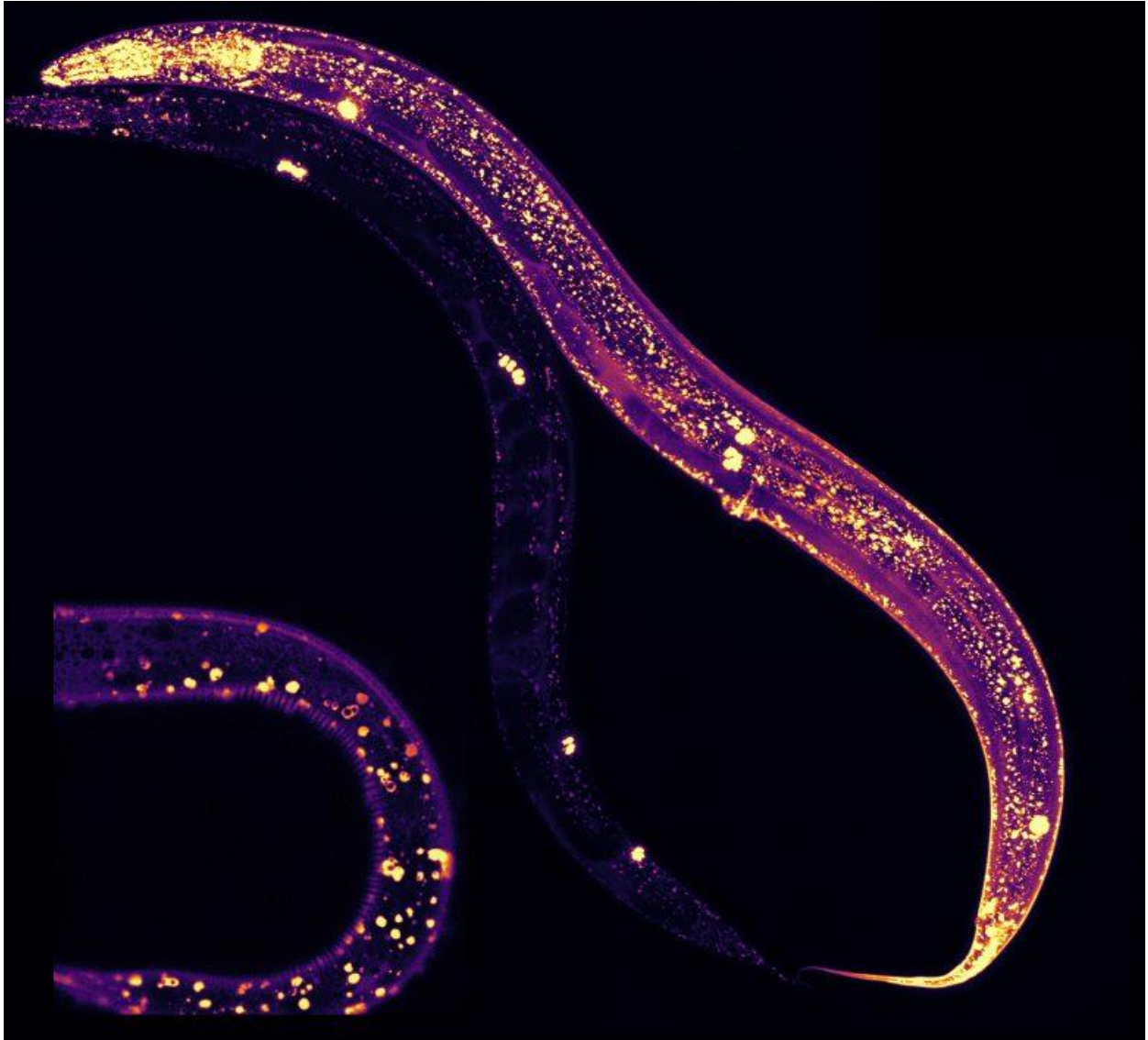
Cells can create proteins incorrectly, and the cleanup process can become faulty or overwhelmed. As a result, proteins can clump together, leading to a harmful buildup that has been linked to such diseases as Alzheimer's and Parkinson's.

"If the cells are experiencing stress because this protein aggregation has started, the endoplasmic reticulum, which is where proteins are made and then released, gets the signal to stop making these proteins," explains biology professor Bhagwati Gupta, who supervised the research.

"If it can't correct the problem, the cell will die, which ultimately leads to degeneration of the neurons and then neurodegenerative diseases that we see."

MANF's Role in Cellular Maintenance

Previous studies, including one from McMaster, had shown that MANF protects against increased cellular stress. The team set out to understand how this happens by studying microscopic worms known as *C. elegans*. They created a system to manipulate the amount of MANF in *C. elegans*.



C. elegans examined under a microscope. The yellow and purple dots are the regions where MANF protein is located. Credit: McMaster University

“We could literally see where MANF was expressed in the worms because they are translucent. We could see it in all different tissues. Within these tissues, MANF was present in structures known as lysosomes which are associated with lifespan and protein aggregation,” said Shane Taylor, now a post-doctoral fellow at the University of British Columbia who worked on the project for his PhD while at McMaster.

Activating the Natural Cellular Clean-Up System

The team discovered that MANF plays a key role in the cell’s disposal process by helping to break down the accumulated proteins, keeping cells healthier and clutter-free.

Increasing MANF levels also activates a natural clean-up system within cells, helping them function better for longer.

“Although our research focused on worms, the findings uncover universal processes. MANF is present in all animals, including humans. We are learning fundamental and mechanistic details that could then be tested in higher systems,” said Taylor.

To develop MANF as a potential therapy, researchers want to understand what other players MANF interacts with.

“Discovering MANF’s role in cellular homeostasis suggests that it could be used to develop treatments for diseases that affect the brain and other parts of the body by targeting cellular processes, clearing out these toxic clumps in cells, and maintaining their health,” said Gupta.

“The central idea of aging research is basically can we make the processes better and more efficient. By understanding how MANF works and targeting its function, we could develop new treatments for age-related diseases. We want to live longer and healthier. These kinds of players could help that.”

Reference: “The neurotrophic factor MANF regulates autophagy and lysosome function to promote proteostasis in *Caenorhabditis elegans*” by Shane K. B. Taylor, Jessica H. Hartman and Bhagwati P. Gupta, 17 October 2024, *Proceedings of the National Academy of Sciences*.

DOI: [10.1073/pnas.2403906121](https://doi.org/10.1073/pnas.2403906121)

Scientists discover that people who live past 90 have key differences in their blood

The Study Behind the Discovery

In a groundbreaking study published in [GeroScience](#), researchers analyzed health data from 44,000 Swedes aged between 64 and 99. This dataset, which spanned over 35 years, revealed significant insights about the blood profiles of individuals who lived to be 100 years old.³ A total of 2.7% of participants (1,224 people) reached the century mark, and 85% of these centenarians were female. The study focused on a range of biomarkers, including cholesterol, glucose, and creatinine levels, among others, to explore how these metrics correlated with exceptional longevity.

Biomarkers Linked to Longevity

The research unveiled that certain blood biomarkers-particularly lower levels of glucose, creatinine, and uric acid-were consistently associated with individuals who lived past 90 years of age. These markers are linked to metabolic health, kidney function, and the body's ability to process food. Remarkably, centenarians typically had blood glucose levels below 6.5 mmol/L and creatinine levels under 125 $\mu\text{mol/L}$. These findings suggest that maintaining metabolic health could be key to a longer life.

The Role of Cholesterol and Liver Function

The study also examined other important biomarkers, such as total cholesterol and liver function markers like alanine aminotransferase (Alat) and gamma-glutamyl transferase (GGT). The data showed that individuals with lower cholesterol and better liver function had a higher likelihood of reaching 100 years. Interestingly, the connection between cholesterol and longevity was more nuanced, as people with very low levels of cholesterol also had a decreased chance of reaching 100. This highlights the delicate balance required for long-term health.

The Complex Interaction of Genetics and Lifestyle

While the study offered significant insights into the biomarker profiles of centenarians, it did not conclusively identify which specific lifestyle factors or genetic predispositions influenced these results. However, the researchers suggested that factors like nutrition and alcohol intake likely play a role. For example, lower uric acid levels were linked to higher chances of longevity, indicating that diet and kidney health are important considerations.

The Bigger Picture: Metabolic Health and Longevity

The findings from this research suggest that monitoring glucose, creatinine, and uric acid levels may be important for individuals hoping to live a longer life. Although the differences in biomarker values between centenarians and non-centenarians were not drastic, they were significant enough to indicate a potential link between metabolic health and exceptional longevity. As researchers continue to explore the biological mechanisms behind aging, these discoveries offer a promising direction for future health interventions.

A Path Forward for Longevity Research

The study's findings underscore the complexity of aging and the importance of continued research into biomarkers that could help unlock the secrets of a long, healthy life. While lifestyle factors such as diet and alcohol intake may play a role, genetic predispositions and random chance also contribute to one's ability to reach 100. Tracking and managing key biomarkers from an early age may be a crucial strategy for those hoping to join the ranks of the world's centenarians.

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The post Scientist Discover Key Longevity Difference in Blood of Those Who Live Past 90 appeared first on [The Hearty Soul](#).

Breathtaking Painting Shows Human Aging as Vantage Point Changes

June 13, 2024



The human aging painting by the Spanish artist. Credit: Instagram/Sergi Cadenas

A superb painting created by Spanish artist Sergi Cadenas shows human aging as you move from one side of the piece to the other.

In the artwork, which has become viral on social media, the face of a woman ages many years when you take a few steps in the opposite direction.

In another, the piercing blue eyes of a young girl morph into the inky black ones of a little boy.

The self-taught artist takes a unique and thoroughly modern approach to this age-old tradition by creating paintings that contain dual images; they transform as you move from one side of the piece to the other.



Human aging painting inspired by flip images from childhood

Though Cadenas didn't begin his career as an artist until his thirties, his curiosity and experimentation quickly led him to developing his own distinctive technique.

Inspired by flip images he'd seen on cards as a child, the artist was struck with the idea to mimic that effect in his [oil paintings](#). Using a piping bag intended for decorating cakes, the artist creates vertical ridges on the canvas to provide a relief upon which he can produce two separate images.

In an interview for Home & Decor, the artist describes his pictorial design as minimalist, with an air of 1900s modernism.

He uses kinetic optics, painting vertical strips of paint paste on a canvas. Once the paste has dried, he paints the two sides differently, using oil paints.

The result is an extremely detailed three-dimensional painting, so much so that it almost looks like a photograph. The protagonist appears to be a single person at first glance, but it isn't: looking at the painting from right to left, the subject changes.

Each subject in Cadenas' paintings can be individually viewed by simply observing the artwork from one side or the other. However, the transformative nature of his work allows him to address deeper themes and meanings.

Some of his paintings confront complex subjects, such as the fleeting nature of youth, mortality, the dichotomy of emotions, and even racial equality.

Others simply provide the viewer with two distinct vantage points of the same image, revealing previously unseen

elements as the new image emerges in view. No matter the subject, each canvas forces the viewer to actively engage with the artwork and contemplate their own interpretations from a different perspective.

According to [Galeria Jordi Barnadas](#), Sergi Cadenas is one of the world's leading optical art artists, and his paintings are in the Swiss museum [Porrentruy Optical Art](#) (POPA).

Cadenas' work has acquired great international acclaim, and his paintings are part of private collections around the world.



Groundbreaking 21-Million Cell Study Revises Our Understanding of Aging

BY ROCKEFELLER UNIVERSITY DECEMBER 21, 2024



A large-scale single-cell study shows aging happens in specific stages driven by molecular cues, offering targets to modify the aging process and revealing key age and sex-related cellular differences. Credit: SciTechDaily.com

Aging happens in distinct stages marked by synchronized cellular changes across organs, as shown in Rockefeller’s largest-ever mammalian aging atlas. Their findings offer clues for targeting aging processes and reveal key age and sex differences in cellular dynamics.

If you compared photos of a maple tree taken in July and December, the difference would be striking: a vibrant green canopy in summer versus bare, stark branches in winter. What those images wouldn’t reveal is how the transformation unfolded—whether it was gradual or sudden. In reality, deciduous trees usually wait for environmental cues, such as changes in light or temperature, before shedding all their leaves within a brief span of one to two weeks.

When it comes to aging, we may be more like these trees than we realized.

Groundbreaking research from [Rockefeller University's Laboratory of Single-Cell Genomics and Population Dynamics](#) has revealed that aging follows a similar trajectory at the cellular level. In a study recently published in *Science*, lab leader Junyue Cao and his team employed single-cell sequencing to analyze over 21 million cells from all major organs of mice at five distinct life stages. This unprecedented effort has produced the world's largest cellular atlas compiled within a single study.

Their findings reveal that certain cell populations change in every organ, both in the same way and at the same time, during specific stages of life. This suggests that aging is not a linear process but instead a developmental stage sparked by specific molecular cues.

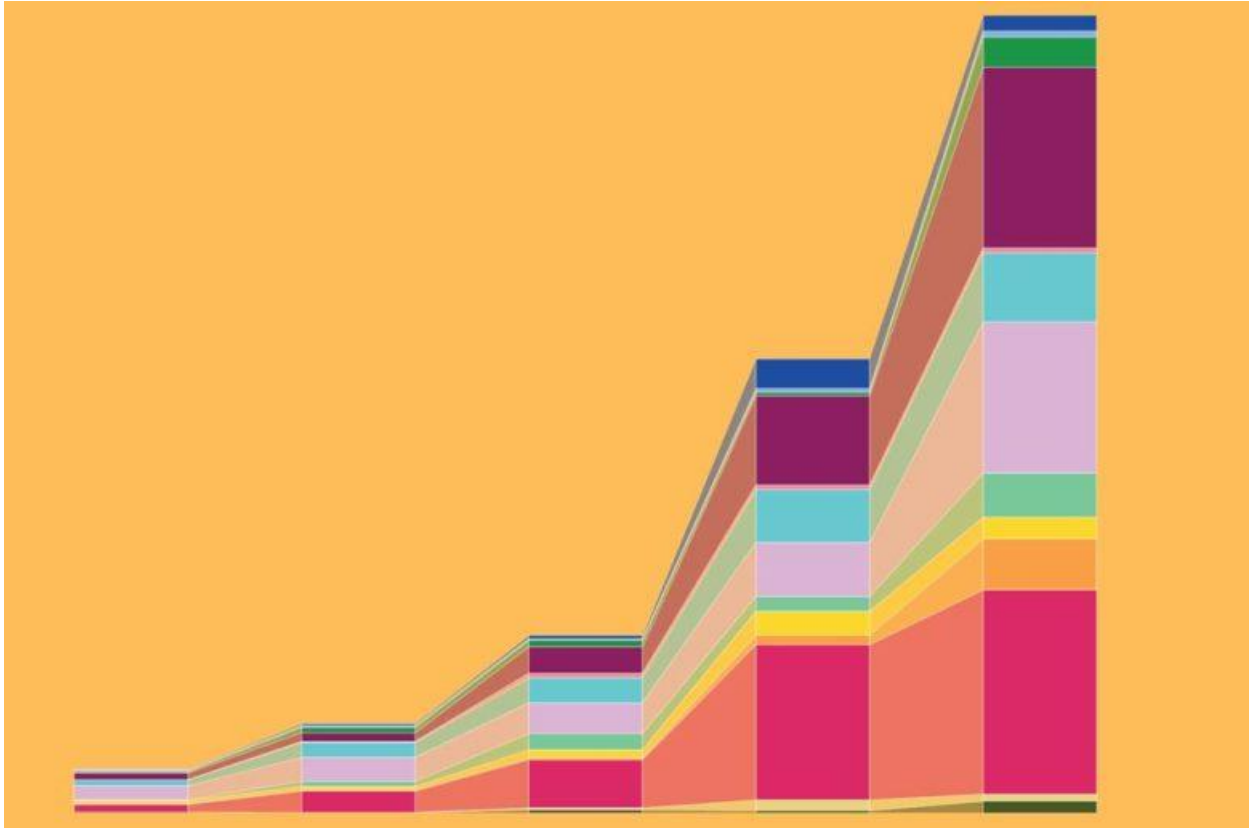
"Some cells greatly expand in number while others drop off, and the cells that go through such changes are different depending on age," says Cao. "What's more, some of these changes are controlled by the same molecular features, so we might be able to target them to delay or even reprogram the aging process itself."

From bespoke technique to universal platform

Single-cell sequencing, a specialty of Cao's lab, is a method of genetic analysis that focuses on the genetic expression and molecular dynamics of individual cells, simultaneously revealing the identity of every cell studied. His team has previously used single-cell sequencing to discover new [rare brain cell types](#) and to [track how brain cells age, among other purposes](#).

In the brain study, they also found different cell populations and cellular dynamics specific to different ages. For the current study, led by graduate student Zehao Zhang, they were curious to see if similar changes occurred elsewhere in the body.

To do that, Zhang adapted EasySci, a single-cell sequencing method developed by the group and used in their aging-brain study, to expand its cellular reach to include all the major organs of a mouse—a daunting task that Zhang managed single-handedly.



A chart showing the explosive expansion in proportion of Granzyme K+ CD8+ T cells in mice across multiple organs as they age. Credit: Laboratory of Single-cell Genomics and Population Dynamics

“The most challenging aspect was optimizing EasySci to work across diverse mammalian organs while maintaining high-quality data,” he says. “Since most previous studies often focused on specific organs or used different protocols for different organs, developing a universal protocol required testing thousands of conditions across different organs before we could even begin the real experiment.”

As a result of Zhang’s efforts, EasySci is now a unified profiling platform for major mammalian organs, capable of systematically dissecting aging and disease mechanisms across an entire organism.

For the current study, they used it to reveal the single-nucleus transcriptome profiles of some 21 million cells taken from more than 600 samples of both male and female mice at five different life stages, from young to elderly.

Critical time windows

The team discovered more than 10 main cell types and 200 cell subtypes that consistently undergo significant age-associated depletion or expansion.

In early adulthood, for example (3 to 12 months in mice), specific cell subtypes within fat, muscle, and epithelial tissues saw a marked drop-off in number, while in advanced adulthood (12 to 23 months in mice), different types of immune cells explode in number.

Intriguingly, many of these changes were linked with specific gene expressions by the cells, regardless of where they were found. “We identified cell subtypes in different organs, where they may have different functions,” Cao says. “But they seem to be controlled by the same molecular process.”

“We’ve essentially identified the cellular basis of each phase change, and documented that they don’t happen gradually over time, but at specific stages of life,” he adds. “Now that we’ve identified the critical time windows that show very strong changes in distinct cell populations, this provides us important clues about how to intervene in the aging process.”

Immune cells in particular showed population booms in later life. “We found many different B cell and T cell subtypes that get strongly expanded in different organs,” Cao says. Excesses of these cells are known to cause inflammatory and autoimmune conditions. In fact, when the researchers examined two immunodeficient mice lacking such cells, they found that the depletion of B cells and T cells reversed changes in several other cell types associated with aging, highlighting cell regulatory networks in the aging process, Cao says.

They also found extraordinarily small clusters of new cell types, some numbering as few as 500 cells. What role they play in aging remains to be studied, but some extremely rare cell types have been shown to orchestrate critical functions, Cao says. “Take pituitary gland cells: this very small population secretes important hormones essential to growth, reproductive development, and organ function.”

Age and sex differences

Unexpectedly, they also found hundreds of cellular states that differed between male and female mice in every organ, Zhang says. These include adipocyte progenitor cells, which exhibit distinct molecular states between males and females, as well as a female-specific expansion of aging-associated B cells.

Put together, these age and sex differences may help explain why women, and especially older women, suffer from autoimmune conditions at a higher rate than men do.

They also underscore the importance of having sex-balanced cell samples in aging and disease studies, Zhang says. “Many studies focus on one sex to reduce costs and maintain consistency, but this finding highlights the importance of including both sexes to uncover generalized mechanisms or to develop sex-specific treatments.”

A goldmine for future research

The study's 21-million-cell dataset, called PanSci, represents the largest single-cell-sequencing atlas of mammalian aging ever created, and Cao's lab is already planning several future projects based on this resource. For instance, they intend to look deeper into the hundreds of cellular subtypes that show robust differences between male and female mice, as well as those involved in the aging process, many of which remain poorly characterized or studied.

"I think our findings could potentially be used to identify the cellular basis for some sex-specific diseases," Cao says.

Scientists around the world are also welcome to mine PanSci for their own research, Zhang adds. "Researchers studying specific organs can extract organ-specific data, while those focusing on specific cell lineages such as immune or endothelial cells can extract the same cell types from different organs," he says. "And because the dataset is well-curated and annotated, it's ideal for training large machine-learning models for applications like age prediction, finding rare cell types, and building virtual cells for *in silico* perturbation studies."

Reference: "A panoramic view of cell population dynamics in mammalian aging" by Zehao Zhang, Chloe Schaefer, Weirong Jiang, Ziyu Lu, Jasper Lee, Andras Sziraki, Abdulraouf Abdulraouf, Brittney Wick, Maximilian Haeussler, Zhuoyan Li, Gesmira Molla, Rahul Satija, Wei Zhou and Junyue Cao, 28 November 2024, *Science*.

DOI: [10.1126/science.adn3949](https://doi.org/10.1126/science.adn3949)

Brain stimulation breakthrough: Natural learning ability — not age — determines success

LAUSANNE, Switzerland — When it comes to learning new motor skills, like playing the piano or mastering a golf swing, conventional wisdom suggests that older adults might have a harder time than their younger counterparts. But new research reveals that age may not be the deciding factor in who benefits from brain stimulation techniques designed to enhance learning. Instead, it's your natural learning ability that determines whether such interventions will help or potentially hinder your progress.

The study, conducted by researchers at École Polytechnique Fédérale de Lausanne and other institutions, challenges our assumptions about aging and learning while offering a potential pathway to more personalized [brain stimulation](#) treatments. The research team investigated how a technique called anodal transcranial direct current stimulation (atDCS) – which involves passing a weak electrical current through specific areas of the brain – affects people's ability to learn a new motor skill.

Think of atDCS as a gentle dimmer switch for your brain cells. By applying a mild electrical current to specific areas of the brain, researchers can make neurons more or less likely to fire. This technique has shown promise in improving various cognitive and motor functions, particularly in older adults who may be experiencing age-related decline. However, the results of such interventions have been notably inconsistent across different studies and individuals.

They discovered that electrical brain stimulation works dramatically differently depending on [a person's learning capacity](#). Contrary to expectations, age was not the determining factor in how individuals responded to treatment.

The researchers studied a total of 153 healthy volunteers across three age groups. For the main modeling portion of the study, they included 41 young adults aged 18-30, 34 middle-aged adults aged 50-65, and 38 older adults aged over 65. They then validated their findings with an additional group of 40 participants (20 middle-aged and 20 older adults). All participants were right-handed and were tasked with performing a sequential finger-tapping task using their left (non-dominant) hand. The task involved replicating a shown nine-digit numerical sequence as quickly and accurately as possible using four buttons, similar to learning a simple melody [on a piano](#).

Natural learners don't benefit from brain stimulation?

What makes this study particularly interesting is that the researchers developed a machine learning model to predict who would benefit from brain stimulation based on their initial performance. They discovered that individuals who struggled more with learning the sequence initially showed the greatest improvements with atDCS, regardless of their age. Conversely, those who were naturally efficient learners either saw no benefit or, in some cases, actually performed worse with the stimulation.

"By leveraging different methods in [machine learning](#), we were able to untangle the influence of different factors on the individual effects of brain stimulation," says study author Pablo Maceira in a media release.

Researchers compare the brain stimulation effect to turning up the volume on a stereo system. For someone with a less efficient learning system (like trying to hear music through interference), amplifying the signal helps clarify the message. However, for someone with an already optimal system (like listening to perfectly clear music), adding more amplification might actually distort the sound.

The study also revealed something unexpected about [older adults](#): some performed just as well as their middle-aged counterparts, challenging stereotypes about age-related decline in motor learning. This finding suggests that maintaining cognitive and motor abilities into older age might be more common than previously thought.

The research, published in the journal [npj Science of Learning](#), promises a paradigm shift in neurorehabilitation, suggesting that tailored interventions based on individual learning mechanisms — not age — could help people recover lost skills more effectively.

"Clinicians could apply a more advanced version of our algorithm to determine whether a patient will benefit from a brain stimulation-based therapy," envisions study leader Friedhelm Hummel.

The message is clear: in the world of brain enhancement, being a natural prodigy might actually be a handicap. Sometimes, having room for improvement is the best improvement of all.

Paper Summary

Methodology

This study explored how brain stimulation affects motor skill learning across different learner categories. Researchers conducted a randomized, placebo-controlled, double-blind experiment involving middle-aged and older adults. Participants practiced a finger-tapping task requiring precision and speed, with daily 20-minute sessions over ten days.

During training, some received anodal transcranial direct current stimulation (atDCS) over their motor cortex, while others received a placebo. Baseline performance data were used to classify participants into “optimal” and “suboptimal” learners using a machine-learning model. The study aimed to determine how individuals’ initial learning capabilities influenced their response to brain stimulation.

Key Results

The study found that atDCS had varying effects depending on the learner’s baseline abilities. Suboptimal learners, characterized by delayed accuracy improvements during training, showed significant benefits from stimulation. They achieved faster accuracy optimization compared to those receiving placebo.

In contrast, optimal learners, who demonstrated rapid accuracy improvements without stimulation, experienced minimal or even detrimental effects from atDCS. These findings suggest that atDCS has a restorative effect, aiding those with less efficient learning mechanisms rather than enhancing already optimal systems.

Study Limitations

First, the sample size within specific learner categories was small, particularly among older adults, leading to variability in results. Additionally, the study focused exclusively on motor skill acquisition using a finger-tapping task, limiting generalizability to other types of learning.

The long-term effects of atDCS and its applicability to broader populations, such as younger adults or clinical groups, remain uncertain. Finally, the algorithm's predictions were based on a specific dataset, which may not perfectly translate to diverse settings or tasks.

Discussion & Takeaways

The study highlights the importance of tailoring brain stimulation interventions to individual learning profiles. The differential effects of atDCS underline the need for personalized approaches in neurorehabilitation and skill acquisition training. Suboptimal learners benefited the most, reinforcing the idea that brain stimulation can act as a compensatory tool rather than a universal enhancer.

However, the potential for harm in optimal learners cautions against indiscriminate use of such technologies. Future research should explore broader applications and refine predictive models to maximize the benefits of brain stimulation while minimizing risks.

Funding & Disclosures

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Cutting Back on One Amino Acid Increases Lifespan in Middle-Aged Mice Up to 33%



Generic shot of white supplement powder

Research in mice shows limited intakes of one particular essential amino acid can slow the impacts of aging and even lengthen their lifespan.

Scientists are now wondering if these findings could help people improve their longevity and quality of life.

Isoleucine is one of three branched-chain amino acids we use to build proteins in our bodies. It is essential for our survival, but since our cells can't produce it from scratch, we have to get it from sources like eggs, dairy, soy protein, and meats.

But there can always be too much of a good thing. [Earlier research](#) using data from a 2016-2017 survey of Wisconsin residents had found dietary isoleucine levels were linked with metabolic health and that people with higher BMIs were generally consuming much greater quantities of the amino acid.

"Different components of your diet have value and impact beyond their function as a calorie, and we've been digging in on one component that many people may be eating too much of," metabolism researcher Dudley Lamming from the University of Wisconsin, US, who was involved in both studies, [explained](#) in 2023 when the newest findings were published.

"It's interesting and encouraging to think a dietary change could still make such a big difference in lifespan and what we call 'healthspan,' even when it started closer to mid-life."

In the most recent study, a genetically diverse group of mice was fed either a diet containing 20 common amino acids as a control, a diet where all amino acids were reduced by about two-thirds, or a diet where only isoleucine was reduced by the same amount.

The mice were around six months old at the start of the study, which is the equivalent age of a 30-year-old person. They could eat as much as they wanted, but only from the specific kind of food provided to their group.



Our cells can't produce isoleucine from scratch – we have to get it from foods such as soy protein. (ArtStudio Images/Canva)

Restricting dietary isoleucine increased the lifespan and healthspan of the mice, reduced their frailty, and promoted leanness and glycemic control. Male mice had

their lifespans increased 33 percent compared to those whose isoleucine was not restricted, and females had a 7 percent increase.

These mice also scored better in 26 measures of health, including muscle strength, endurance, blood sugar levels, tail use, and hair loss.

The male mice in this group had less age-related prostate enlargement, and were less likely to develop the cancerous tumors that are common in the diverse mice strains.

Curiously, the mice given low isoleucine food also ate significantly more calories than the others. But rather than gaining weight, they actually burned more energy and maintained leaner body weights, even though their activity levels were no different.

The researchers think restricting isoleucine in humans, either by diet or pharmaceutical means, has the potential to yield similar anti-aging effects - although, as with all mice studies, we won't know for sure until it's actually tested in humans.

This is easier said than done. Although the food provided to the mice was controlled, the researchers noted that diet is an incredibly complex chemical reaction, and there may be other dietary components involved in producing these results.

Restricting protein intake in general, for instance, has detrimental effects on the body, mouse or human. Translating this research for real-world human use is more complicated than just reducing intake of high-protein foods, even though this is the simplest way to limit isoleucine intake. The amino acid restriction level was constant in all experiments, and they acknowledge that more fine-tuning may be required for optimum effects across different mice strains and sexes – when it comes to diet, one size does not fit all.

"We can't just switch everyone to a low-isoleucine diet," Lamming [said](#).

"But narrowing these benefits down to a single amino acid gets us closer to understanding the biological processes and maybe potential interventions for humans, like an isoleucine-blocking drug."

The research was published in [Cell Metabolism](#).

Scientists discover major link between sugar consumption and aging

Researchers at [UC San Francisco](#) discovered a link between diets rich in vitamins and minerals, especially those with minimal added sugar, and a younger biological age at the cellular level. They studied three different measures of healthy eating and their effects on an “epigenetic clock” – a biochemical test that estimates both health and lifespan.

The results revealed that better diets corresponded with younger-looking cells. However, even healthy diets were impacted by added sugar, as each gram consumed was associated with an increase in epigenetic age.

“The diets we examined align with existing [recommendations for preventing disease](#) and promoting health, and they highlight the potency of antioxidant and anti-inflammatory nutrients in particular,” said Dorothy Chiu, PhD, a postdoctoral scholar at the UCSF Osher Center for Integrative Health and the study's first author. “From a lifestyle medicine standpoint, it is empowering to see how heeding these recommendations may promote a younger cellular age relative to chronological age.”

This study is among the first to show a link between added sugar and epigenetic aging, particularly in a diverse group of midlife women, including both Black and white participants. Most previous studies have focused on older white individuals.

Table 1. Characteristics of 624 Participants Within the Overall Follow-Up Sample, Analytic vs Nonanalytic Sample

Characteristic	Proportions ^a		P value of difference
	Analytic sample (n = 342)	Nonanalytic sample (n = 282)	
Current age, mean (SD), y	39.2 (1.1)	39.9 (1.4)	<.001 ^b
Race and ethnicity			
Black	171 (50.0)	136 (48.2)	.66
White	171 (50.0)	146 (51.8)	
Annual household income at age 9-10 y, \$			
<10 000	60 (17.5)	52 (18.4)	.90
10 000-19 999	58 (17.0)	51 (18.1)	
20 000-39 999	97 (28.4)	76 (27.0)	
≥40 000	110 (32.2)	93 (33.0)	
Missing	17 (5.0)	10 (3.6)	
Highest parental educational attainment at age 9-10 y			
<High school graduate	79 (23.1)	54 (19.2)	.29
Some college	162 (47.4)	129 (45.7)	
College graduate or higher	101 (29.5)	98 (34.8)	
Missing	0	1 (0.4)	
Single parent household at age 9-10 y	119 (34.8)	88 (31.2)	.34
No. of siblings at age 9-10 y, mean (SD)	1.2 (1.1)	1.4 (1.2)	.11
Current BMI, mean (SD)	32.5 (10.0)	30.7 (7.8)	.02 ^b
Missing	0	6 (2.1)	.007 ^b
Current status of ever smoking			
Yes	150 (43.9)	124 (44.0)	.09
No	192 (56.1)	154 (54.6)	
Missing	0	4 (1.4)	
Chronic health condition diagnosed	164 (48.0)	123 (43.6)	.28
Current medication usage	58 (17.0)	34 (12.1)	.09
Total energy intake, mean (SD), kcal	2019.4 (786.4)	NA	NA
Dietary exposures, mean (SD)			
aMED score	3.9 (1.9)	NA	NA
AHEI-2010 score	55.4 (14.7)	NA	NA
ENI score	13.5 (5.0)	NA	NA
Added sugar, g	61.5 (44.6)	NA	NA
GrimAge2, mean (SD), y ^c	61.3 (5.7)	NA	NA

Abbreviations: AHEI-2010, Alternate Healthy Eating Index 2010 (possible score range, 0-110); aMED, Alternate Mediterranean Diet (possible score range, 0-9); BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); ENI, Epigenetic Nutrient Index (possible score range, 0-24); NA, not applicable.

^a Unless otherwise noted, data are given as number (percentage).

^b Statistically significant result ($P < .05$).

^c Epigenetic clock measure.

Characteristics of 624 Participants Within the Overall Follow-Up Sample, Analytic vs Nonanalytic Sample (CREDIT: Jama Network)© The Brighter Side of News

The findings enhance our understanding of sugar's harmful effects on health, noted co-senior author Elissa Epel, PhD, a UCSF professor in the Department of Psychiatry and Behavioral Sciences.

“We knew that high levels of added sugars are linked to [worsened metabolic health and early disease](#), possibly more than any other dietary factor,” Epel said.

"Now we know that accelerated epigenetic aging is underlying this relationship, and this is likely one of many ways that excessive sugar intake limits healthy longevity."

Participants reported consuming an average of 61.5 grams of added sugar daily, with a range from 2.7 to 316 grams. For context, a bar of milk chocolate contains about 25 grams of added sugar, while a 12-ounce can of cola has about 39 grams. The U.S. Food and Drug Administration recommends that adults consume no more than 50 grams of added sugar per day.

Related Stories

[Scientists find a surprising link between high-carb diets and longevity](#) [This small dietary change has a major impact on lowering blood pressure](#) [New study reveals major link between sugar and Alzheimer's disease](#)

In this cross-sectional study, researchers analyzed food records from 342 Black and white women, averaging 39 years old, from Northern California. They compared their diets with epigenetic clock measures derived from saliva samples.

The women's diets were scored based on their adherence to a Mediterranean-style diet rich in anti-inflammatory and antioxidant foods and a diet linked to lower risk for chronic disease.

Additionally, researchers created the "Epigenetic Nutrient Index (ENI)," based on nutrients linked to antioxidative or [anti-inflammatory processes](#) and DNA maintenance and repair. These nutrients included Vitamins A, C, B12, and E, folate, selenium, magnesium, dietary fiber, and isoflavones.

Table 2. Scoring Rubric for the ENI as Based on the Dietary Reference Intakes^a

Nutrient	Criteria for 0 points (minimum score)	Criteria for 1 point	Criteria for 2 points (maximum score)
Vitamin A (total activity in retinol equivalents), µg/d ^b	<EAR (500)	$EAR \leq x < RDA$	$\geq RDA$ (700)
Vitamin C (total ascorbic acid), mg/d	<EAR (60)	$EAR \leq x < RDA$	$\geq RDA$ (75)
Vitamin E (total α-tocopherol), mg/d	<EAR (12)	$EAR \leq x < RDA$	$\geq RDA$ (15)
Folate (total folate), µg/d ^c	<EAR (320)	$EAR \leq x < RDA$	$\geq RDA$ (400)
Vitamin B ₁₂ (total cobalamin), µg/d	<EAR (2)	$EAR \leq x < RDA$	$\geq RDA$ (2.4)
Zinc, mg/d	<EAR (6.8)	$EAR \leq x < RDA$	$\geq RDA$ (8)
Selenium, µg/d	<EAR (45)	$EAR \leq x < RDA$	$\geq RDA$ (55)
Magnesium, mg/d	<EAR (265)	$EAR \leq x < RDA$	$\geq RDA$ (320)
Dietary fiber (total dietary fiber), g/d	<AI/1.2	$AI/1.2 \leq x < AI$ (25)	$\geq AI$ (25)
MUFA:SFA (as calories from MUFA:calories from SFA)	<Median _{as}	$Median_{as} \leq x < 1.2 \times median_{as}$	$\geq 1.2 \times Median_{as}$
Isoflavones (sum of daidzein, genistein, glycitein, biochanin A, and formononetin), mg/d	<Median _{as}	$Median_{as} \leq x < 1.2 \times median_{as}$	$\geq 1.2 \times Median_{as}$
Total sugar, g/d	$\geq 1.2 \times 90$ g	$90 < x < 1.2 \times 90$	≤ 90
Sum each component's score to obtain the total ENI score	0	NA	24

Abbreviations: AI, adequate intake; EAR, estimated average requirement; ENI, Epigenetic Nutrient Index; median_{as}, median of the analytic sample; MUFA, monounsaturated fatty acids; NA, not applicable; RDA, recommended dietary allowance; SFA, saturated fatty acids.

^a Values corresponding to the EAR, RDA, and AI for each nutrient component are noted (in parentheses) as based on age- and sex-based intake estimates put forth by the Food

and Nutrition Board of the US Institute of Medicine and the National Health Service of the United Kingdom (here, values correspond to those for women aged 36-43 years).³⁴

^b Not accounting for differences in vitamin A activity of carotenoids.³⁵

^c Not accounting for differences in folate absorption between natural and synthetic forms.³⁵

Scoring Rubric for the ENI as Based on the Dietary Reference Intakes (CREDIT: Jama Network)© The Brighter Side of News

Adherence to any of these diets was significantly associated with lower epigenetic age, with the Mediterranean diet showing the strongest association. Even when considering healthy diets, foods with added sugar were still linked to accelerated biological aging.

“Given that epigenetic patterns appear to be reversible, it may be that eliminating 10 grams of added sugar per day is akin to turning back the biological clock by 2.4 months, if sustained over time,” said co-senior author Barbara Laraia, PhD, RD, a UC Berkeley professor in the Food, Nutrition and Population Health program. “Focusing on foods that are [high in key nutrients](#) and low in added sugars may be a new way to help motivate people to eat well for longevity.”

These findings emphasize the importance of reducing added sugar intake and following a nutrient-rich diet to promote healthier aging at the cellular level. By making mindful dietary choices, you can potentially improve your health and longevity.

How Much Sugar is Too Much?

The [American Heart Association](#) recommends that women consume no more than 6 teaspoons (25 grams) of added sugar per day, and men should limit themselves to 9 teaspoons (38 grams). Unfortunately, many people consume far more than this, often without realizing it.

Short-Term Effects of Excessive Sugar Intake **Energy Spikes and Crashes:** When you consume [sugary foods or drinks](#), your blood sugar levels spike quickly. This can give you a temporary boost of energy. However, this is often followed by a rapid drop in blood sugar, leading to feelings of fatigue and irritability. **Dental Problems:** Sugar is a major cause of [tooth decay](#). Bacteria in your mouth feed on sugar and produce acid that can erode tooth enamel, leading to cavities. **Long-Term Health Risks** **Weight Gain and Obesity:** Consuming high amounts of sugar can lead to weight gain. [Sugary foods](#) and drinks are high in calories but low in nutritional value, which can contribute to obesity. Obesity is a significant risk factor for many health problems, including heart disease and diabetes. **Type 2 Diabetes:** A diet high in sugary foods and drinks can increase your risk of developing type 2 diabetes. Excessive sugar consumption can lead to insulin resistance, where your body's cells become less responsive to insulin, causing higher blood sugar levels. **Heart Disease:** High sugar intake is linked to an increased risk of heart disease. [Diets rich in sugar](#) can raise blood pressure, increase inflammation, and lead to higher levels of triglycerides (a type of fat found in the blood), all of which are risk factors for heart disease. **Non-Alcoholic Fatty Liver Disease (NAFLD):** Consuming too much sugar, especially fructose, can lead to fat buildup in the liver, resulting in NAFLD. This condition can progress to liver damage if left unchecked. **Mental Health Issues:** Some studies suggest that high sugar consumption may be linked to an increased risk of depression and anxiety. The exact relationship is still being studied, but it's believed that sugar can affect mood and stress levels. **How to Reduce Sugar Intake** **Read Labels:** Pay attention to food labels and ingredient lists. Look for hidden sugars, which can be listed under various names such as [high fructose corn syrup](#), sucrose, and dextrose. **Choose Whole Foods:** Opt for whole, unprocessed foods like fruits, vegetables, whole grains, and lean proteins. These foods are naturally lower in sugar and provide essential nutrients. **Limit Sugary Drinks:** Beverages like soda, fruit juices, and sports drinks are often high in added sugars. Choose water, unsweetened tea, or sparkling water instead. **Watch Out for Snacks:** Many snacks, such as granola bars and [flavored yogurt](#), can contain high amounts of added sugar. Choose healthier options like nuts, seeds, and fresh fruit. **Cook at Home:**

Preparing meals at home allows you to control the ingredients and reduce the amount of added sugar in your diet.

Being mindful of your sugar intake can help you [maintain a healthy weight](#), reduce your risk of chronic diseases, and improve your overall well-being. Making small changes, such as choosing whole foods and reading labels, can make a big difference in your health over time.

Can Your Biological Age Be Reversed? AI Aging Clocks Reveal New Insights



AI-driven metabolomic aging clocks can predict health and lifespan, offering insights into biological ageing and enabling preventative health strategies based on blood metabolite data. (Artist's concept.) Credit: SciTechDaily.com

King's College London researchers found that AI-based aging clocks using blood metabolite data can predict health and lifespan, with accelerated aging linked to

higher health risks. Non-linear machine learning algorithms, especially Cubist regression, were most effective.

Researchers at the Institute of Psychiatry, Psychology & Neuroscience (IoPPN) at [King's College London](#) have conducted a detailed study to assess artificial intelligence-based aging clocks, which estimate health and lifespan by analyzing blood data.

The study involved training and testing 17 machine learning algorithms using data on blood markers from over 225,000 participants in the UK Biobank, who were aged 40 to 69 at the time of recruitment. The researchers evaluated how accurately these metabolomic aging clocks predict lifespan and how strongly they correlate with various measures of health and aging.

Metabolomic age, referred to as “MileAge,” reflects a person’s internal biological age based on blood metabolites—small molecules generated during metabolism, such as those produced when food is converted into energy. The difference between a person’s metabolite-predicted age (MileAge) and their actual chronological age, called the MileAge delta, indicates whether their biological aging is accelerated or decelerated.

Study Insights and Key Findings

The study was published in *Science Advances* and is the first to comprehensively compare different machine learning algorithms on their ability to develop biological aging clocks using metabolite data, leveraging one of the largest datasets globally. It was funded by the National Institute for Health and Care Research (NIHR) Maudsley Biomedical Research Centre (BRC) and used data from the UK Biobank.

Individuals with accelerated aging (i.e., with a metabolite-predicted age older than their chronological age) were, on average, frailer, more likely to have a chronic illness, rated their health worse, and had a higher mortality risk. They also had shorter telomeres (‘caps’ at the end of chromosomes), which are a marker of cellular aging and linked with age-related diseases such as atherosclerosis. However, decelerated biological aging (with a metabolite-predicted age younger than chronological age) was only weakly linked with good health.

Aging clocks could help spot early signs of declining health, enabling preventative strategies and interventions before disease onset. They may also allow people to proactively track their health, make better lifestyle choices, and take steps to stay healthy for longer.

Expert Perspectives on Aging Clocks

Dr. Julian Mutz, King’s Prize Research Fellow at the IoPPN and lead author of the study, said: “Metabolomic aging clocks have the potential to provide insights into who might be at

greater risk of developing health problems later in life. Unlike chronological age, which cannot be changed, our biological age is potentially modifiable. These clocks provide a proxy measure of biological age for biomedical and health research, which could help shape lifestyle choices taken by individuals and inform preventative strategies implemented by health services. Our study evaluated a broad range of machine learning approaches for developing aging clocks, showing that non-linear algorithms perform best at capturing aging signals.”

Professor Cathryn Lewis, Professor of Genetic Epidemiology & Statistics, Co-Deputy Lead of the Trials, Genomics and Prediction theme at the NIHR Maudsley BRC, and senior author of the study, said: “There is substantial interest in developing aging clocks that accurately assess our biological age. Powerful big data analytics can play a critical role in advancing these tools. This study is an important milestone in establishing the potential of biological aging clocks and their ability to inform health choices.”

The researchers found that a metabolomic clock developed using a specific machine learning algorithm, called Cubist rule-based regression, was most strongly associated with most health and aging markers. They also found that algorithms which can model non-linear relationships between metabolites and age generally performed best at capturing biological signal informative of health and lifespan.

Reference: “Metabolomic age (MileAge) predicts health and life span: A comparison of multiple machine learning algorithms” by Julian Mutz, Raquel Iniesta and Cathryn M. Lewis, 18 December 2024, *Science Advances*.

DOI: [10.1126/sciadv.adp3743](https://doi.org/10.1126/sciadv.adp3743)

Artificial Intelligence Unlocks New Possibilities in Anti-Aging Medicine



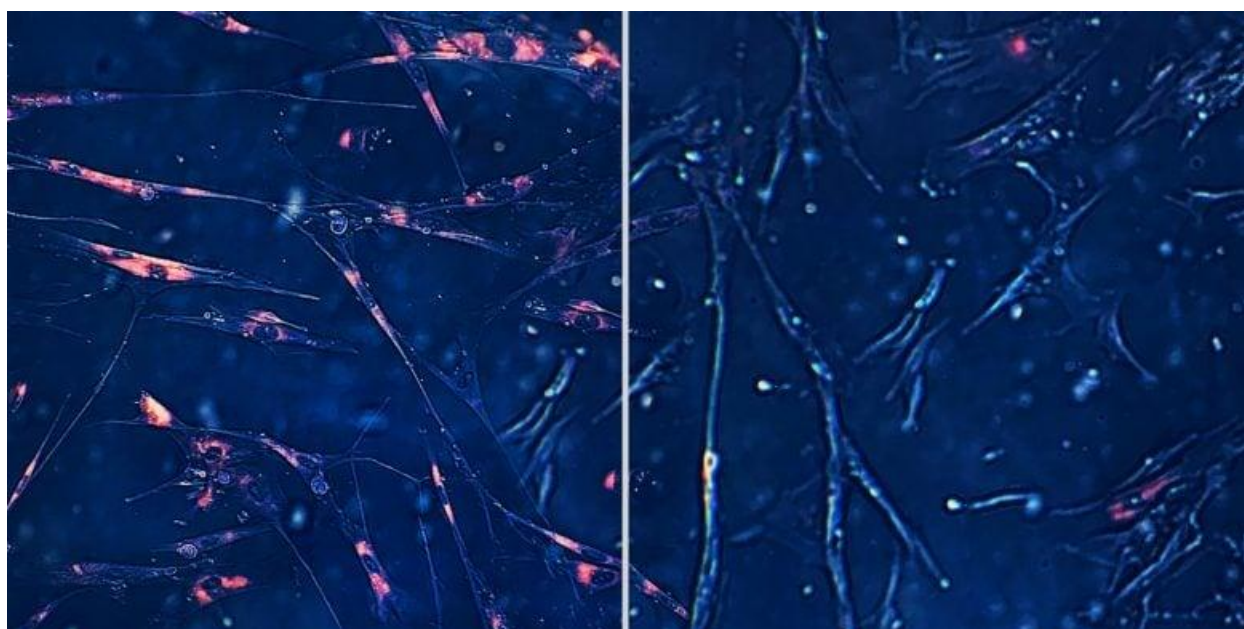
Researchers have utilized AI to discover new senolytic compounds that can suppress age-related processes, such as cancer and inflammation. By training deep neural networks on experimental data, they were able to identify three potent drug candidates from a chemical pool of over 800,000 molecules, promising superior clinical properties to existing senolytics.

New platform holds the promise to drive progress in the development of senolytic anti-aging compounds and research on longevity.

A recent paper published in *Nature Aging* by researchers from Integrated Biosciences, a biotechnology company combining synthetic biology and machine learning to combat aging. The paper demonstrates how artificial intelligence (AI) can be utilized to identify new senolytic compounds. These are a class of small molecules receiving significant attention due to their potential to inhibit aging-related processes like fibrosis, inflammation, and cancer.

The research paper is the result of a collaborative effort involving researchers from the [Massachusetts Institute of Technology \(MIT\)](#) and the Broad Institute of MIT and [Harvard](#). The publication outlines the AI-led analysis of over 800,000 compounds, which successfully identified three potential drugs with comparable efficacy and superior medicinal chemistry properties to those of senolytics currently under investigation.

“This research result is a significant milestone for both longevity research and the application of artificial intelligence to drug discovery,” said Felix Wong, Ph.D., co-founder of Integrated Biosciences and first author of the publication. “These data demonstrate that we can explore chemical space *in silico* and emerge with multiple candidate anti-aging compounds that are more likely to succeed in the clinic, compared to even the most promising examples of their kind being studied today.”



Senolytics are an emerging class of investigational drug compounds that selectively kill aging-associated senescent cells (left, with red stain) without affecting other cells (right). Using artificial intelligence, researchers from Integrated Biosciences have, for the first time, identified three senolytics with comparable efficacy and superior drug-like properties relative to leading investigational compounds. Credit: Integrated Biosciences

Senolytics are compounds that selectively induce apoptosis, or programmed cell death, in senescent cells that are no longer dividing. A hallmark of aging, senescent cells have been implicated in a broad spectrum of age-related diseases and conditions including cancer, diabetes, cardiovascular disease, and Alzheimer’s disease.

Despite promising clinical results, most senolytic compounds identified to date have been hampered by poor bioavailability and adverse side effects. Integrated Biosciences was founded in 2022 to overcome these obstacles, target other neglected hallmarks of aging, and advance anti-aging drug development more generally using artificial intelligence, synthetic biology, and other next-generation tools.

“One of the most promising routes to treat age-related diseases is to identify therapeutic interventions that selectively remove these cells from the body similarly to how antibiotics kill bacteria without harming host cells. The compounds we discovered display high selectivity, as well as the favorable medicinal chemistry properties needed to yield a successful drug,” said Satotaka Omori, Ph.D., Head of Aging Biology at Integrated Biosciences and joint first author of the publication. “We believe that the compounds discovered using our platform will have improved prospects in clinical trials and will eventually help restore health to aging individuals.”

In their new study, Integrated Biosciences researchers trained deep neural networks on experimentally generated data to predict the senolytic activity of any molecule. Using this AI model, they discovered three highly selective and potent senolytic compounds from a chemical space of over 800,000 molecules.

All three displayed chemical properties suggestive of high oral bioavailability and were found to have favorable toxicity profiles in hemolysis and genotoxicity tests. Structural and biochemical analyses indicate that all three compounds bind Bcl-2, a protein that regulates apoptosis and is also a chemotherapy target. Experiments testing one of the compounds in 80-week-old mice, roughly corresponding to 80-year-old humans, found that it cleared senescent cells and reduced the expression of senescence-associated genes in the kidneys.

“This work illustrates how AI can be used to bring medicine a step closer to therapies that address aging, one of the fundamental challenges in biology,” said James J. Collins, Ph.D., Termeer Professor of Medical Engineering and Science at MIT and founding chair of the Integrated Biosciences Scientific Advisory Board. “Integrated Biosciences is building on the basic research that my academic lab has done for the last decade or so, showing that we can target cellular stress responses using systems and synthetic biology. This experimental tour de force and the stellar platform that produced it make this work stand out in the field of drug discovery and will drive substantial progress in longevity research.”

Reference: “Discovering small-molecule senolytics with deep neural networks” by Felix Wong, Satotaka Omori, Nina M. Donghia, Erica J. Zheng and James J. Collins, 4 May 2023, *Nature Aging*.

DOI: [10.1038/s43587-023-00415-z](https://doi.org/10.1038/s43587-023-00415-z)

Dr. Collins, who is senior author on the *Nature Aging* paper, led the team which discovered the first antibiotic identified by machine learning in 2020.

Anti-Aging Breakthrough: Cellular Rejuvenation Therapy Safely Reverses the Aging Process in Mice



Anti-aging artist's concept.

Salk researchers treated mice with anti-aging regimen beginning in middle age and found no increase in cancer or other health problems later on.

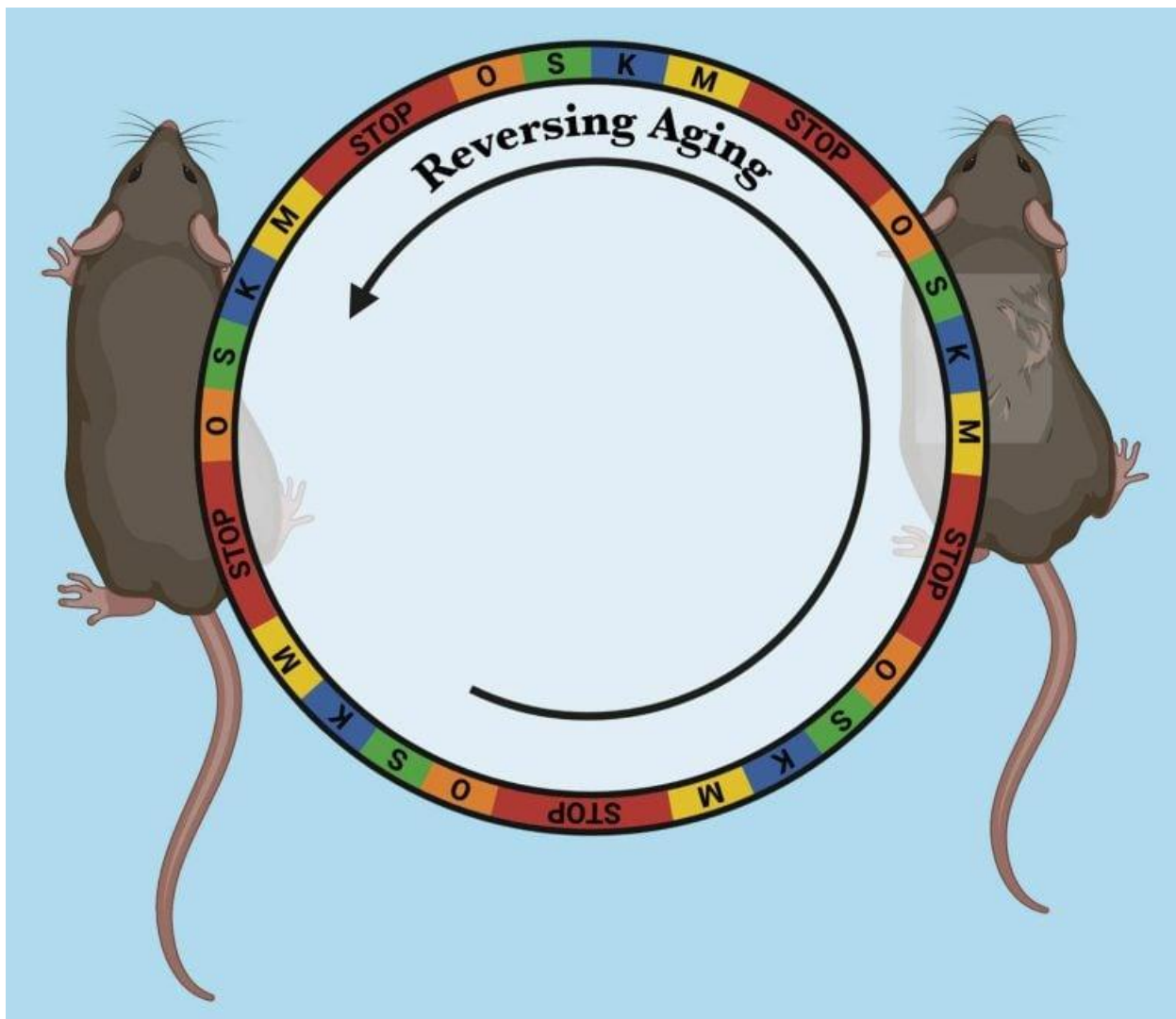
Age may be just a number, but it's a number that often carries unwanted side effects, from brittle bones and weaker muscles to increased risks of cardiovascular disease and cancer. Now, scientists at the Salk Institute, in collaboration with Genentech, a member of the Roche group, have shown that they can safely and effectively reverse the aging process in middle-aged and elderly mice by partially resetting their cells to more youthful states.

"We are elated that we can use this approach across the life span to slow down aging in normal animals. The technique is both safe and effective in mice," says co-corresponding author Juan Carlos Izpisua Belmonte, professor in Salk's Gene Expression Laboratory and holder of the Roger Guillemin Chair. "In addition to tackling age-related diseases, this approach may provide the biomedical community with a new tool to restore tissue and

organismal health by improving cell function and resilience in different disease situations, such as neurodegenerative diseases.”

Yamanaka Factors in Cellular Rejuvenation

As organisms age, it is not just their outward appearances and health that change; every cell in their bodies carries a molecular clock that records the passage of time. Cells isolated from older people or animals have different patterns of chemicals along their DNA—called epigenetic markers—compared to younger people or animals. Scientists know that adding a mixture of four reprogramming molecules—Oct4, Sox2, Klf4, and cMyc, also known as “Yamanaka factors”—to cells can reset these epigenetic marks to their original patterns. This approach is how researchers can dial back adult cells, developmentally speaking, into stem cells.



Cellular rejuvenation therapy safely reverses signs of aging in mice. Credit: Salk Institute

In 2016, Izpisua Belmonte's lab reported for the first time that they could use the Yamanaka factors to [counter the signs of aging and increase life span](#) in mice with a premature aging disease. More recently, the team found that, even in young mice, the Yamanaka factors can [accelerate muscle regeneration](#). Following these initial observations, other scientists have used the same approach to improve the function of other tissues like the heart, brain, and optic nerve, which is involved in vision.

In the new study, Izpisua Belmonte and his colleagues tested variations of the cellular rejuvenation approach in healthy animals as they aged. One group of mice received regular doses of the Yamanaka factors from the time they were 15 months old until 22 months, approximately equivalent to age 50 through 70 in humans. Another group was treated from 12 through 22 months, approximately age 35 to 70 in humans. A third group was treated for just one month at age 25 months, similar to age 80 in humans.

"What we really wanted to establish was that using this approach for a longer time span is safe," says Pradeep Reddy, a Salk staff scientist and co-first author of the new paper. "Indeed, we did not see any negative effects on the health, behavior, or body weight of these animals."

From left: Juan Carlos Izpisua Belmonte and Pradeep Reddy. Credit: Salk Institute

Compared to control animals, there were no blood cell alterations or neurological changes in the mice that had received the Yamanaka factors. Moreover, the team found no cancers in any of the groups of animals.

Youthfulness Restored

When the researchers looked at normal signs of aging in the animals that had undergone the treatment, they found that the mice, in many ways, resembled younger animals. In both the kidneys and skin, the epigenetics of treated animals more closely resembled epigenetic patterns seen in younger animals. When injured, the skin cells of treated animals had a greater ability to proliferate and were less likely to form permanent scars—older animals usually show less skin cell proliferation and more scarring. Moreover, metabolic molecules in the blood of treated animals did not show normal age-related changes.

This youthfulness was observed in the animals treated for seven or 10 months with the Yamanaka factors, but not the animals treated for just one month. What's more, when the treated animals were analyzed midway through their treatment, the effects were not yet as evident. This suggests that the treatment is not simply pausing aging, but actively turning it backwards—although more research is needed to differentiate between the two.

The team is now planning future research to analyze how specific molecules and genes are changed by long-term treatment with the Yamanaka factors. They are also developing new ways of delivering the factors.

“At the end of the day, we want to bring resilience and function back to older cells so that they are more resistant to stress, injury, and disease,” says Reddy. “This study shows that, at least in mice, there’s a path forward to achieving that.”

Reference: “In vivo partial reprogramming alters age-associated molecular changes during physiological aging in mice” by Kristen C. Browder, Pradeep Reddy, Mako Yamamoto, Amin Haghani, Isabel Guillen Guillen, Sanjeeb Sahu, Chao Wang, Yosu Luque, Javier Prieto, Lei Shi, Kensaku Shojima, Tomoaki Hishida, Zijuan Lai, Qingling Li, Feroza K. Choudhury, Weng R. Wong, Yuxin Liang, Dewakar Sangaraju, Wendy Sandoval, Concepcion Rodriguez Esteban, Estrella Nuñez Delicado, Pedro Guillen Garcia, Michal Pawlak, Jason A. Vander Heiden, Steve Horvath, Heinrich Jasper and Juan Carlos Izpisua Belmonte, 7 March 2022, *Nature Aging*.

[DOI: 10.1038/s43587-022-00183-2](https://doi.org/10.1038/s43587-022-00183-2)

Belmonte is currently an Institute Director at Altos Labs, Inc., in addition to being a professor at the Salk Institute.

Other authors included Mako Yamamoto, Isabel Guillen Guillen, Sanjeeb Sahu, Chao Wang, Yosu Luque, Javier Prieto, Lei Shi, Kensaku Shojima, Tomoaki Hishida and Concepcion Rodriguez Esteban of Salk; Kristen Browder, Zijuan Lai, Qingling Li, Feroza Choudhury, Weng Wong, Yuxin Liang, Dewakar Sangaraju, Wendy Sandoval, Michal Pawlak, Jason Vander Heiden and Heinrich Jasper of Genentech, Inc.; Amin Haghani and Steve Horvath of UCLA; Estrella Nuñez Delicado of Universidad Católica San Antonio de Murcia; and Pedro Guillen Garcia of Clínica CEMTRO.

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Scientists Develop New Gene Therapy Strategy to Delay Aging and Extend Lifespan



Researchers have pinpointed new senescence-promoting genes in humans using a genome-wide CRISPR/Cas9 screening system. This discovery offers a fresh therapeutic approach for addressing aging and related pathologies.

Cellular senescence, a state of permanent growth arrest, has emerged as a hallmark and fundamental driver of organismal aging. It is regulated by both genetic and epigenetic factors. Despite a few previously reported aging-associated genes, the identity and roles of additional genes involved in the regulation of human cellular aging remain to be elucidated. Yet, there is a lack of systematic investigation on the intervention of these genes to treat aging and aging-related diseases.

How many aging-promoting genes are there in the human genome? What are the molecular mechanisms by which these genes regulate aging? Can gene therapy alleviate individual

aging? Recently, researchers from the Chinese Academy of Sciences have shed new light on the regulation of aging.

Recently, researchers from the Institute of Zoology of the Chinese Academy of Sciences (CAS), Peking University, and Beijing Institute of Genomics of CAS have collaborated to identify new human senescence-promoting genes by using a genome-wide CRISPR/Cas9 screening system and provide a new therapeutic approach for treating aging and aging-related pathologies.

In this study, the researchers conducted genome-wide CRISPR/Cas9-based screens in human premature aging stem cells and identified more than 100 candidate senescence-promoting genes. They further verified the effectiveness of inactivating each of the top 50 candidate genes in promoting cellular rejuvenation using targeted sgRNAs.

Among them, *KAT7* encoding a histone acetyltransferase was identified as one of the top targets in alleviating cellular senescence. It increased in human mesenchymal precursor cells during physiological and pathological aging. *KAT7* depletion attenuated cellular senescence whereas *KAT7* overexpression accelerated cellular senescence.

Mechanistically, inactivation of *KAT7* decreased histone H3 lysine 14 acetylation, repressed *p15^{INK4b}* transcription, and rejuvenated senescent human stem cells.

Cumulative studies have described that age-associated accumulation of senescent cells and proinflammatory cells in tissues and organs contribute to the development and progression of aging as well as aging-related disorders. Prophylactic ablation of senescent cells mitigates tissue degeneration and extends the health span in mice.

In this study, the researchers found that intravenous injection of a lentiviral vector encoding Cas9/sg-*KAT7* reduced the proportions of senescent cells and proinflammatory cells in the liver, diminished circulatory senescence-associated secretory phenotype (SASP) factors in the serum, and extended healthspan and lifespan of aged mice.

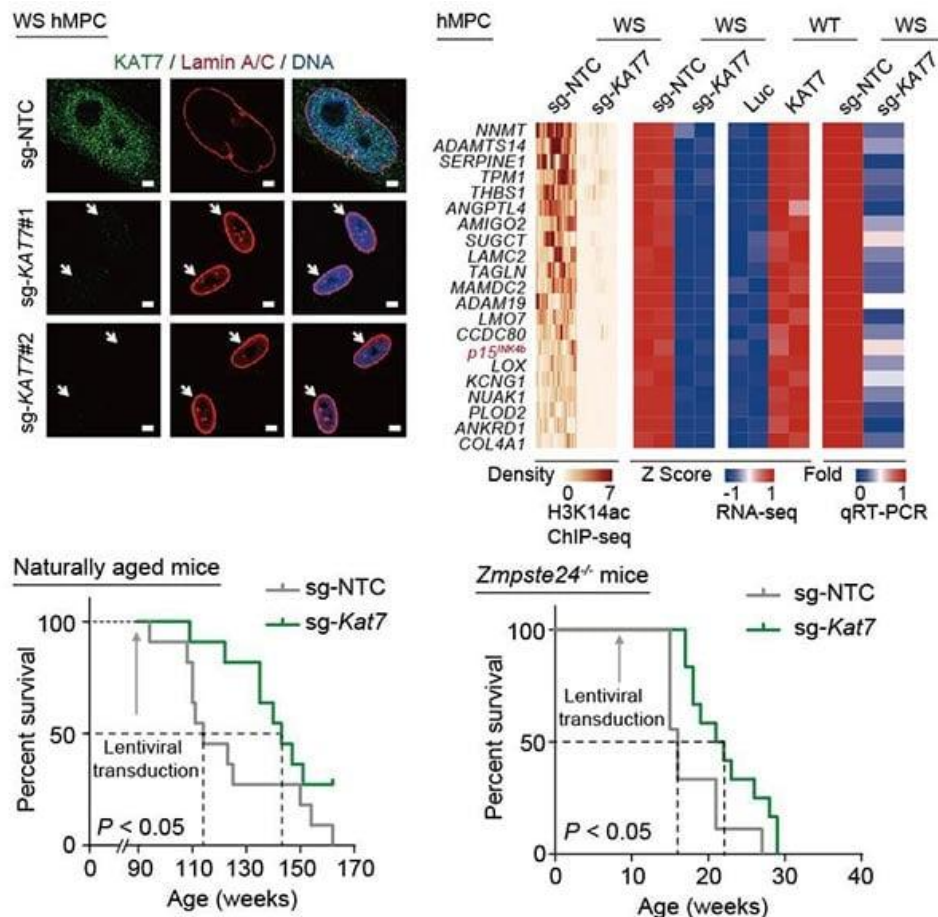


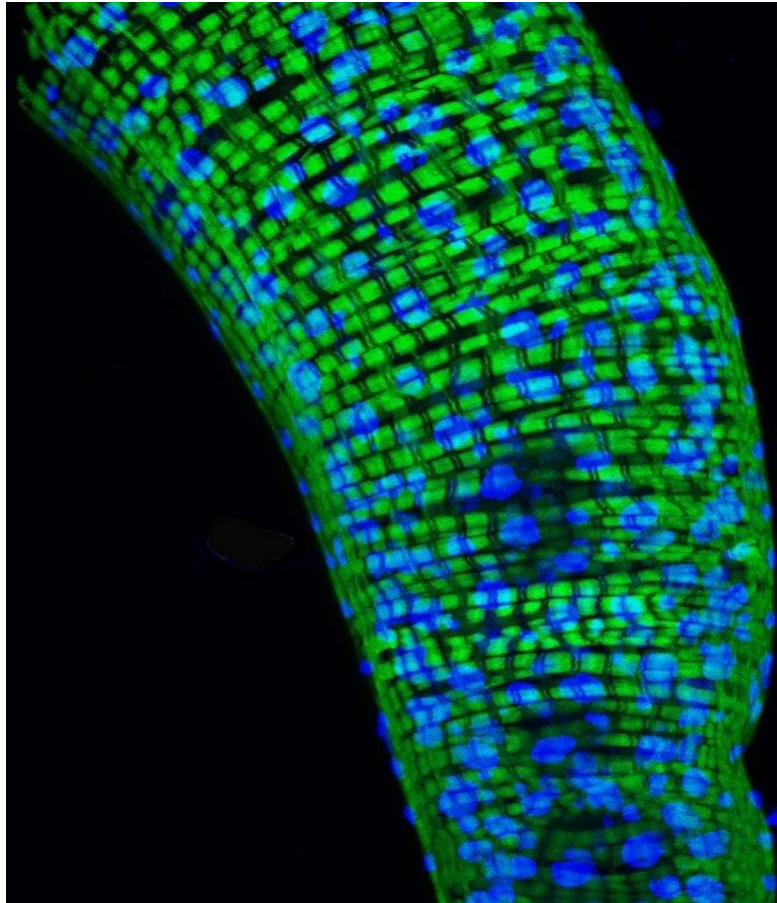
Figure. Gene therapy targeting Kat7 extends lifespan in naturally aged and progeria mice.
Credit: IOZ

These results suggest that gene therapy based on single-factor inactivation may be sufficient to extend mouse lifespan. The researchers also found that the treatment with the lentiviral vector encoding Cas9/sg-KAT7 or a KAT7 inhibitor WM-3835 alleviated human hepatocyte senescence and reduced the expression of SASP genes, suggesting the possibility of applying these interventions in clinical settings.

Altogether, this study has successfully expanded the list of human senescence-promoting genes using CRISPR/Cas9 genome-wide screen and conceptually demonstrated that gene therapy based on single-factor inactivation is able to delay individual aging. This study not only deepens our understanding of aging mechanism but also provides new potential targets for aging interventions.

Reference: "A genome-wide CRISPR-based screen identifies KAT7 as a driver of cellular senescence" by Wei Wang, Yuxuan Zheng, Shuhui Sun, Wei Li, Moshi Song, Qianzhao Ji, Zeming Wu, Zunpeng Liu, Yanling Fan, Feifei Liu, Jingyi Li, Concepcion Rodriguez Esteban, Si Wang, Qi Zhou, Juan Carlos Izpisua Belmonte, Weiqi Zhang, Jing Qu, Fuchou Tang and

Surprise Discovery Suggests Scientists May Need To Rethink Which Genes Control Aging



In a study of *Drosophila* fruit flies, NIH scientists found that only about 30% of the genes that are hallmarks for aging may set an animal's internal clock. The rest may reflect the body's response to bacteria. Above is a picture of a *Drosophila* gut, a key source of bacteria. Credit: Courtesy of the Giniger lab NIH/NINDS

NIH scientists discover that bacteria may drive activity of many hallmark aging genes in flies.

To better understand the role of bacteria in health and disease, National Institutes of Health researchers fed fruit flies antibiotics and monitored the lifetime activity of hundreds of genes that scientists have traditionally thought control aging. To their surprise, the antibiotics not only extended the lives of the flies but also dramatically changed the activity

of many of these genes. Their results suggested that only about 30% of the genes traditionally associated with aging set an animal's internal clock while the rest reflect the body's response to bacteria.

"For decades scientists have been developing a hit list of common aging genes. These genes are thought to control the aging process throughout the animal kingdom, from worms to mice to humans," said Edward Giniger, Ph.D., senior investigator, at the NIH's National Institute of Neurological Disorders and Stroke (NINDS) and the senior author of the study published in *iScience*. "We were shocked to find that only about 30% of these genes may be directly involved in the aging process. We hope that these results will help medical researchers better understand the forces that underlie several age-related disorders."

The results happened by accident. Dr. Giniger's team studies the genetics of aging in a type of fruit fly called *Drosophila*. Previously, the team showed how a hyperactive immune system may play a critical role in the neural damage that underlies several aging brain disorders. However, that study did not examine the role that bacteria may have in this process.

To test this idea, they raised newborn male flies on antibiotics to prevent bacteria growth. At first, they thought that the antibiotics would have little or no effect. But, when they looked at the results, they saw something interesting. The antibiotics lengthened the fly's lives by about six days, from 57 days for control flies to 63 for the treated ones.

"This is a big jump in age for flies. In humans, it would be the equivalent of gaining about 20 years of life," said Arvind Kumar Shukla, Ph.D., a post-doctoral fellow on Dr. Giniger's team and the lead author of the study. "We were totally caught off guard and it made us wonder why these flies took so long to die."

Dr. Shukla and his colleagues looked for clues in the genes of the flies. Specially, they used advanced genetic techniques to monitor gene activity in the heads of 10, 30, and 45-day old flies. In a previous study, the team discovered links between the age of a fly and the activity of several genes. In this study, they found that raising the flies on antibiotics broke many of these links.

Overall, the gene activity of the flies fed antibiotics changed very little with age. Regardless of their actual age, the treated flies genetically looked like 30-day old control flies. This appeared to be due to a flat line in the activity of about 70% of the genes the researchers surveyed, many of which are thought to control aging.

"At first, we had a hard time believing the results. Many of these genes are classical hallmarks of aging and yet our results suggested that their activity is more a function of the presence of bacteria rather than the aging process," said Dr. Shukla.

Notably, this included genes that control stress and immunity. The researchers tested the impact that the antibiotics had on these genes by starving some flies or infecting others with harmful bacteria and found no clear trend. At some ages, the antibiotics helped flies survive starvation or infection longer than normal whereas at other ages the drugs either had no effect or reduced the chances of survival.

Further experiments supported the results. For instance, the researchers saw similar results on gene activity when they prevented the growth of bacteria by raising the flies in a completely sterile environment without the antibiotics. They also saw a similar trend when they reanalyzed the data from another study that had raised flies on antibiotics. Again, the antibiotics severed many of the links between aging and hallmark gene activity.

Finally, the team found an explanation for why antibiotics extended the lives of flies in the remaining 30% of the genes they analyzed. In short, the rate at which the activity of these genes changed with age was slower than normal in flies that were fed antibiotics.

Interestingly, many of these genes are known to control sleep-wake cycles, the detection of odorants, and the maintenance of exoskeletons, or the crunchy shells that encase flies. Experiments on sleep-wake cycles supported the link between these genes and aging. The activity of awake flies decreased with age and this trend was enhanced by treating the flies with antibiotics.

“We found that there are some genes that are in fact setting the body’s internal clock,” said Dr. Giniger. “In the future, we plan to locate which genes are truly linked to the aging process. If we want to combat aging, then we need to know precisely which genes are setting the clock.”

Reference: “Common features of aging fail to occur in *Drosophila* raised without a bacterial microbiome” by Arvind Kumar Shukla, Kory Johnson and Edward Giniger, 24 June 2021, *iScience*.

DOI: [10.1016/j.isci.2021.102703](https://doi.org/10.1016/j.isci.2021.102703)

This study was supported by the NIH Intramural Research Program at the NINDS.

Synergistic Cellular Pathways Identified That Extend Lifespan by 500%

Jarod A. Rollins of the MDI Biological Laboratory in Bar Harbor, Maine, is a lead author of a recent scientific paper that identifies synergistic cellular pathways for longevity that amplify lifespan fivefold in *C. elegans*, a nematode worm used as a model in aging research. The increase in lifespan would be the equivalent of a human living for 400 or 500 years. The discovery of the synergistic effect opens the door to new, more effective anti-aging therapies. Credit: MDI Biological Laboratory

Discovery of cellular mechanisms could open door to more effective anti-aging therapies.

Scientists at the MDI Biological Laboratory, in collaboration with scientists from the Buck Institute for Research on Aging in Novato, California, and Nanjing University in China, have identified synergistic cellular pathways for longevity that amplify lifespan fivefold in *C. elegans*, a nematode worm used as a model in aging research.

The increase in lifespan would be the equivalent of a human living for 400 or 500 years, according to one of the scientists.

The research draws on the discovery of two major pathways governing aging in *C. elegans*, which is a popular model in aging research because it shares many of its genes with humans and because its short lifespan of only three to four weeks allows scientists to quickly assess the effects of genetic and environmental interventions to extend healthy lifespan.

Because these pathways are “conserved,” meaning that they have been passed down to humans through evolution, they have been the subject of intensive research. A number of drugs that extend healthy lifespan by altering these pathways are now under development. The discovery of the synergistic effect opens the door to even more effective anti-aging therapies.

“The synergistic extension is really wild. The effect isn’t one plus one equals two, it’s one plus one equals five.” Jarod A. Rollins, Ph.D.

The new research uses a double mutant in which the insulin signaling (IIS) and TOR pathways have been genetically altered. Because alteration of the IIS pathways yields a 100 percent increase in lifespan and alteration of the TOR pathway yields a 30 percent increase, the double mutant would be expected to live 130 percent longer. But instead, its lifespan was amplified by 500 percent.

“Despite the discovery in *C. elegans* of cellular pathways that govern aging, it hasn’t been clear how these pathways interact,” said Hermann Haller, M.D., president of the MDI

Biological Laboratory. “By helping to characterize these interactions, our scientists are paving the way for much-needed therapies to increase healthy lifespan for a rapidly aging population.”

The elucidation of the cellular mechanisms controlling the synergistic response is the subject of a [recent paper](#) in the online journal *Cell Reports* entitled “Translational Regulation of Non-autonomous Mitochondrial Stress Response Promotes Longevity.” The authors include Jarod A. Rollins, Ph.D., and Aric N. Rogers, Ph.D., of the MDI Biological Laboratory.

“The synergistic extension is really wild,” said Rollins, who is the lead author with Jianfeng Lan, Ph.D., of Nanjing University. “The effect isn’t one plus one equals two, it’s one plus one equals five. Our findings demonstrate that nothing in nature exists in a vacuum; in order to develop the most effective anti-aging treatments we have to look at longevity networks rather than individual pathways.”

The discovery of the synergistic interaction could lead to the use of combination therapies, each affecting a different pathway, to extend healthy human lifespan in the same way that combination therapies are used to treat cancer and HIV, Pankaj Kapahi, Ph.D., of the Buck Institute, has said. Kapahi is a corresponding author of the paper with Rogers and Di Chen, Ph.D., of Nanjing University.

The synergistic interaction may also may explain why scientists have been unable to identify a single gene responsible for the ability of some people to live to extraordinary old ages free of major age-related diseases until shortly before their deaths.

The paper focuses on how longevity is regulated in the mitochondria, which are the organelles in the cell responsible for energy homeostasis. Over the last decade, accumulating evidence has suggested a causative link between mitochondrial dysregulation and aging. Rollins’ future research will focus on the further elucidation of the role of mitochondria in aging, he said.

Reference: “Translational Regulation of Non-autonomous Mitochondrial Stress Response Promotes Longevity” by Jianfeng Lan, Jarod A. Rollins, Xiao Zang, Di Wu, Lina Zou, Zi Wang, Chang Ye, Zixing Wu, Pankaj Kapahi, Aric N. Rogers and Di Chen, 23 July 2019, *Cell Reports*. DOI: [10.1016/j.celrep.2019.06.078](https://doi.org/10.1016/j.celrep.2019.06.078)

The research was conducted at the MDI Biological Laboratory and Nanjing University using information from double mutants developed by Kapahi. Rollins’ and Rogers’ work was supported by the National Institutes of Health (AG056743), the Morris Scientific Discovery Fund and the National Institute of General Medical Sciences (P20GM103423 and P20GM104318).

Newly Discovered Gene Could Be the Secret to Longevity



Researchers from the University of Copenhagen have identified a protein, OSER1, that plays a significant role in regulating longevity across multiple species, including humans. This discovery could lead to new treatments for age-related diseases. Credit: SciTechDaily.com

A study reveals that the OSER1 protein significantly impacts longevity, suggesting new treatment possibilities for aging.

A new study from the [University of Copenhagen](#) reveals that a specific gene plays a significant role in determining longevity, potentially opening the door to new treatments.

Sleep, fasting, exercise, green porridge, black coffee, a healthy social life...

There is an abundance of advice out there on how to live a good, long life. Researchers are working hard to determine why some people live longer than others, and how we get the most out of our increasingly long lives.

Now researchers from the Center for Healthy Aging, Department of Cellular and Molecular Medicine at the University of Copenhagen have made a breakthrough. They have discovered that a particular protein known as OSER1 has a great influence on longevity.

"We identified this protein that can extend longevity (long duration of life, red.). It is a novel pro-longevity factor, and it is a protein that exists in various animals, such as fruit flies, nematodes, silkworms, and in humans," says Professor Lene Juel Rasmussen, senior author behind the new study.

Because the protein is present in various animals, the researchers conclude that new results also apply to humans:

"We identified a protein commonly present in different animal models and humans. We screened the proteins and linked the data from the animals to the human cohort also used in the study. This allows us to understand whether it is translatable into humans or not," says Zhiquan Li, who is a first author behind the new study and adds:

"If the gene only exists in animal models, it can be hard to translate to human health, which is why we, in the beginning, screened the potential longevity proteins that exist in many organisms, including humans. Because at the end of the day, we are interested in identifying human longevity genes for possible interventions and drug discoveries."

Paves the way for new treatment

The researchers discovered OSER1 when they studied a larger group of proteins regulated by the major transcription factor FOXO, known as a longevity regulatory hub.

"We found 10 genes that, when – we manipulated their expression – longevity changed. We decided to focus on one of these genes that affected longevity most, called the OSER1 gene," says Zhiquan Li.

When a gene is associated with shorter a life span, the risk of premature aging and age-associated diseases increases. Therefore, knowledge of how OSER1 functions in the cells and preclinical animal models is vital to our overall knowledge of human aging and human health in general.

"We are currently focused on uncovering the role of OSER1 in humans, but the lack of existing literature presents a challenge, as very little has been published on this topic to date. This study is the first to demonstrate that OSER1 is a significant regulator of aging and longevity. In the future, we hope to provide insights into the specific age-related diseases and aging processes that OSER1 influences," says Zhiquan Li.

The researchers also hope that the identification and characterization of OSER1 will provide new drug targets for age-related diseases such as metabolic diseases, cardiovascular and neurodegenerative diseases.

"Thus, the discovery of this new pro-longevity factor allows us to understand longevity in humans better," says Zhiquan Li.

Reference: "FOXO-regulated OSER1 reduces oxidative stress and extends lifespan in multiple species" by Jiangbo Song, Zhiquan Li, Lei Zhou, Xin Chen, Wei Qi Guinevere Sew, Héctor Herranz, Zilu Ye, Jesper Velgaard Olsen, Yuan Li, Marianne Nygaard, Kaare Christensen, Xiaoling Tong, Vilhelm A. Bohr, Lene Juel Rasmussen and Fangyin Dai, 21 August 2024, *Nature Communications*.

DOI: [10.1038/s41467-024-51542-z](https://doi.org/10.1038/s41467-024-51542-z)

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Unlocking Immortality: T Cells as the New Fountain of Youth

Researchers at Cold Spring Harbor Laboratory, have discovered that T cells can be genetically modified to target and eliminate senescent cells, which contribute to aging and related diseases. Their findings in mice show that a single treatment with CAR T cells can lead to improved health outcomes, including reduced body weight and enhanced metabolism, with the potential for lifelong benefits.

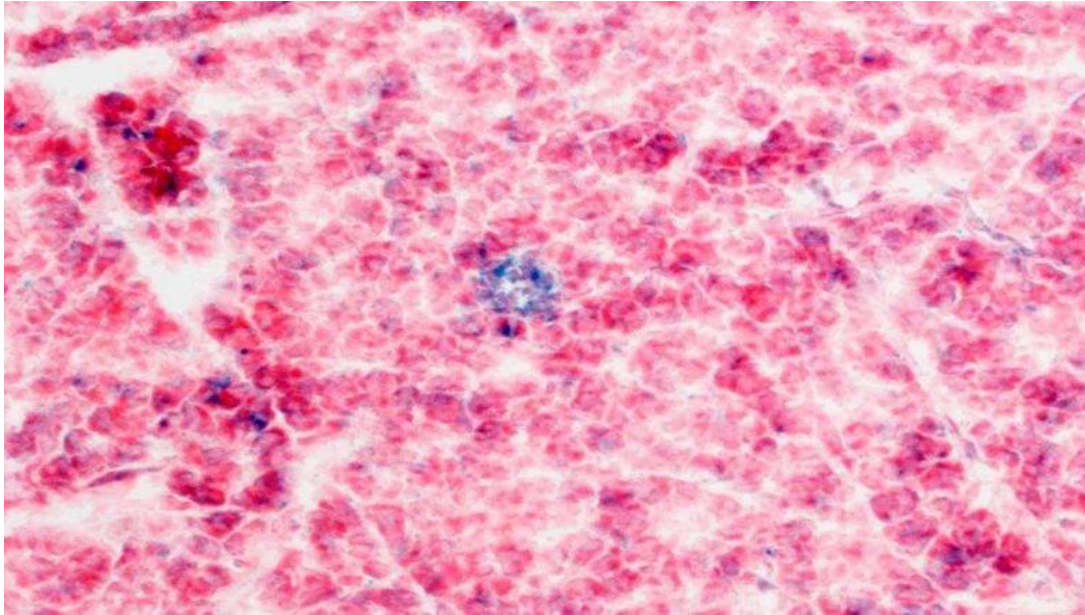
Scientists have discovered that CAR T cells, traditionally used in cancer treatment, can be engineered to fight aging by eliminating senescent cells, offering a promising single-dose, lifelong treatment against aging-related diseases.

The fountain of youth has eluded explorers for ages. It turns out the magic anti-aging elixir might have been inside us all along.

Cold Spring Harbor Laboratory (CSHL) Assistant Professor Corina Amor Vegas and colleagues have discovered that T cells can be reprogrammed to fight aging, so to speak. Given the right set of genetic modifications, these white blood cells can attack another group of cells known as senescent cells. These cells are thought to be responsible for many of the diseases we grapple with later in life.

“If we give it to aged mice, they rejuvenate. If we give it to young mice, they age slower. No other therapy right now can do this.” Amor Vegas
Senescent cells are those that stop replicating. As we age, they build up in our bodies, resulting in harmful inflammation. While several drugs currently exist that can eliminate these cells, many must be taken repeatedly over time.

As an alternative, Amor Vegas and colleagues turned to a “living” drug called CAR (chimeric antigen receptor) T cells. They discovered CAR T cells could be manipulated to eliminate senescent cells in mice. As a result, the mice ended up living healthier lives. They had lower body weight, improved metabolism and glucose tolerance, and increased physical activity. All benefits came without any tissue damage or toxicity.

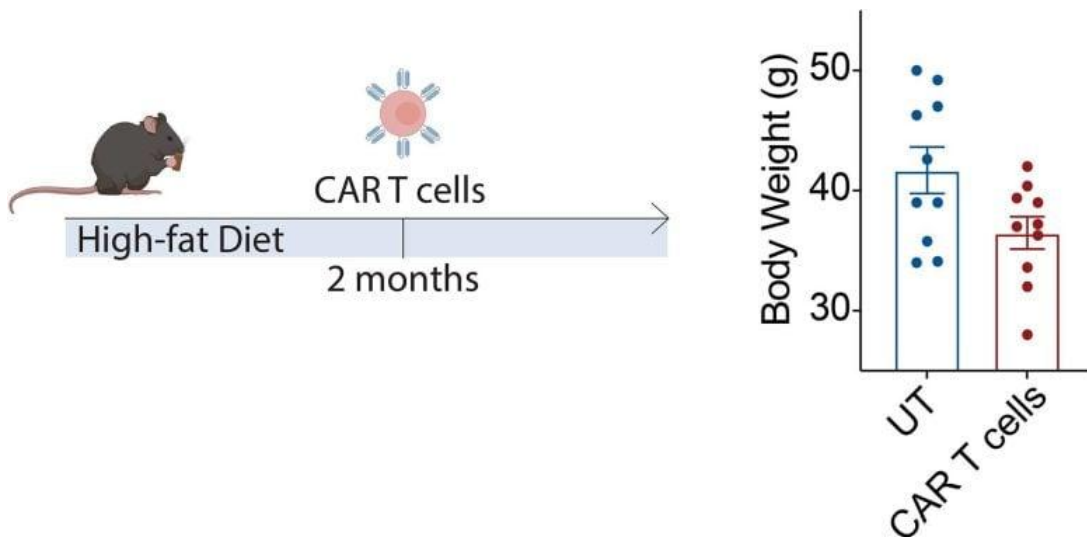


Senescent

cells (blue) accumulate as we age. CAR T cells can be programmed to seek them out and destroy them. The image above shows healthy pancreatic tissue samples from an old mouse treated with CAR T cells as a young pup. Credit: Amor Vegas lab/Cold Spring Harbor Laboratory

“If we give it to aged mice, they rejuvenate. If we give it to young mice, they age slower. No other therapy right now can do this,” says Amor Vegas.

Perhaps the greatest power of CAR T cells is their longevity. The team found that just one dose at a young age can have lifelong effects. That single treatment can protect against conditions that commonly occur later in life, like obesity and diabetes.



Young mice

treated with CAR T cells age slower and have protection from natural aging-associated conditions like obesity and diabetes. The cartoon above shows a young mouse, treated with CAR T cells, who ate a high-fat diet for two months. The charts show that compared to

untreated mice on the same diet, the treated mouse had lower body weight. Credit: Amor Vegas lab/Cold Spring Harbor Laboratory

“T cells have the ability to develop memory and persist in your body for really long periods, which is very different from a chemical drug,” explains Amor Vegas. “With CAR T cells, you have the potential of getting this one treatment, and then that’s it. For chronic pathologies, that’s a huge advantage. Think about patients who need treatment multiple times per day versus you get an infusion, and then you’re good to go for multiple years.”

CAR T cells have been used to treat a variety of blood cancers, receiving FDA approval for this purpose in 2017. But Amor Vegas is one of the first scientists to show that CAR T cells’ medical potential goes even further than cancer.

Amor Vegas’ lab is now investigating whether CAR T cells let mice live not only healthier but also longer. If so, society will be one mouse step closer to the coveted fountain of youth.

Reference: “Prophylactic and long-lasting efficacy of senolytic CAR T cells against age-related metabolic dysfunction” by Corina Amor, Inés Fernández-Maestre, Saria Chowdhury, Yu-Jui Ho, Sandeep Nadella, Courtenay Graham, Sebastian E. Carrasco, Emmanuella Nnuji-John, Judith Feucht, Clemens Hinterleitner, Valentin J. A. Barthet, Jacob A. Boyer, Riccardo Mezzadra, Matthew G. Wereski, David A. Tuveson, Ross L. Levine, Lee W. Jones, Michel Sadelain and Scott W. Lowe, 24 January 2024, *Nature Aging*.

DOI: [10.1038/s43587-023-00560-5](https://doi.org/10.1038/s43587-023-00560-5)

Turning Back the Clock: Genetic Engineers Rewire Cells for an 82% Increase in Lifespan

A team of researchers has developed a biosynthetic genetic ‘clock’ that significantly extends cellular lifespan, as reported in the journal *Science*. The study involved genetically rewiring the gene regulatory circuit that controls cell aging, transforming it from a toggle switch to a clock-like device or gene oscillator. This oscillator periodically switches the cell between two detrimental aged states, thereby preventing prolonged commitment to either and slowing cell degeneration. The team used yeast cells in their study and achieved an 82% increase in lifespan compared to control cells. This ground-breaking research, underpinned

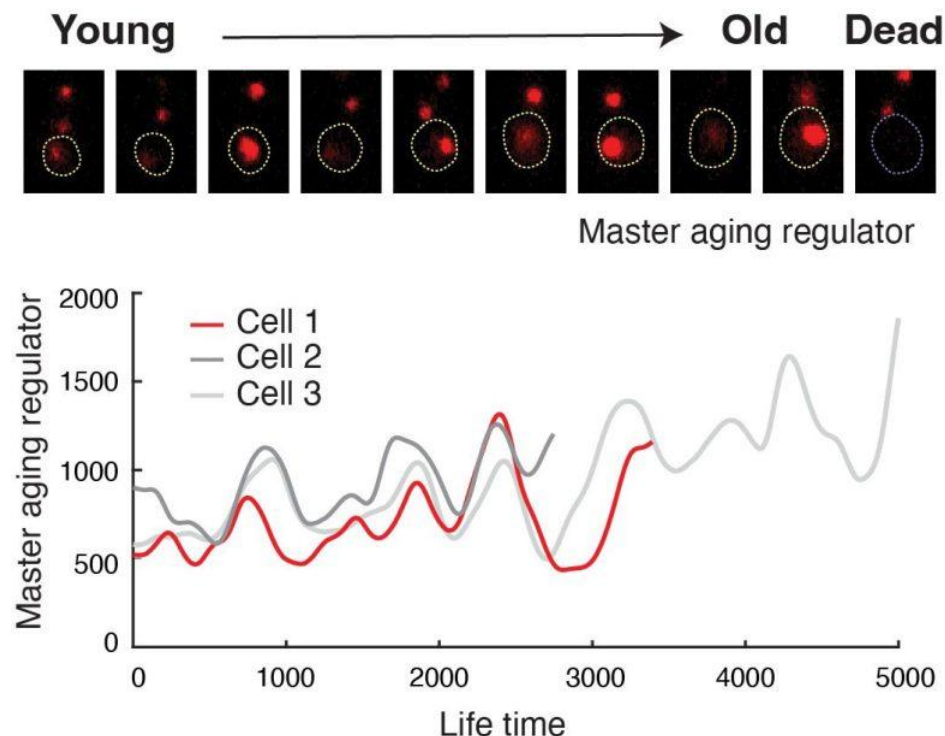
by computational simulations and synthetic biology, could revolutionize scientific approaches to age delay, going beyond attempts to artificially revert cells to a state of 'youth'. The team is now expanding its research to human cell types.

Studying yeast cells, researchers build a biosynthetic genetic 'clock' to extend lifespan.

Researchers have created a synthetic genetic 'clock' that significantly extends cellular lifespan. By reprogramming the gene regulatory circuit that controls aging, cells periodically switch between two detrimental states, slowing their degeneration. This innovative approach, tested on yeast cells, led to an 82% lifespan increase and could revolutionize age-delay strategies.

Human lifespan is related to the aging of our individual cells. Three years ago a group of University of California San Diego (UCSD) researchers deciphered [essential mechanisms behind the aging process](#). After identifying two distinct directions that cells follow during aging, the researchers genetically manipulated these processes to extend the lifespan of cells. As described on April 27, 2023, in the journal *Science*, they have now extended this research using synthetic biology to engineer a solution that keeps cells from reaching their normal levels of deterioration associated with aging. Cells, including those of yeast, plants, animals, and humans, all contain gene regulatory circuits that are responsible for many physiological functions, including aging.

"These gene circuits can operate like our home electric circuits that control devices like appliances and automobiles," said Professor Nan Hao of the School of Biological Sciences' Department of Molecular Biology, the senior author of the study and co-director of UC San Diego's Synthetic Biology Institute.



Engineered cells show oscillating abundance of a master aging regulator. Credit: Hao Lab, UC San Diego

However, the UC San Diego group uncovered that, under the control of a central gene regulatory circuit, cells don't necessarily age the same way. Imagine a car that ages either as the engine deteriorates or as the transmission wears out, but not both at the same time. The UC San Diego team envisioned a "smart aging process" that extends cellular longevity by cycling deterioration from one aging mechanism to another.

In the new study, the researchers genetically rewired the circuit that controls cell aging. From its normal role functioning like a toggle switch, they engineered a negative feedback loop to stall the aging process. The rewired circuit operates as a clock-like device, called a gene oscillator, that drives the cell to periodically switch between two detrimental "aged" states, avoiding prolonged commitment to either, and thereby slowing the cell's degeneration.

These advances resulted in a dramatically extended cellular lifespan, setting a new record for life extension through genetic and chemical interventions.

As electrical engineers often do, the researchers in this study first used computer simulations of how the core aging circuit operates. This helped them design and test ideas before building or modifying the circuit in the cell. This approach has advantages in saving time and resources to identify effective pro-longevity strategies, compared to more traditional genetic strategies.

"This is the first time computationally guided synthetic biology and engineering principles were used to rationally redesign gene circuits and reprogram the aging process to effectively promote longevity," said Hao.

Several years ago the multidisciplinary UC San Diego research team began studying the mechanisms behind cell aging, a complex biological process that underlies human longevity and many diseases. They discovered that cells follow a cascade of molecular changes through their entire lifespan until they eventually degenerate and die. But they noticed that cells of the same genetic material and within the same environment can travel along distinct aging routes. About half of the cells age through a gradual decline in the stability of DNA, where genetic information is stored. The other half ages along a path tied to the decline of mitochondria, the energy production units of cells.

The new synthetic biology achievement has the potential to reconfigure scientific approaches to age delay. Distinct from numerous chemical and genetic attempts to force cells into artificial states of "youth," the new research provides evidence that slowing the

ticks of the aging clock is possible by actively preventing cells from committing to a pre-destined path of decline and death, and the clock-like gene oscillators could be a universal system to achieve that.

“Our results establish a connection between gene network architecture and cellular longevity that could lead to rationally-designed gene circuits that slow aging,” the researchers note in their study.

During their research, the team studied *Saccharomyces cerevisiae* yeast cells as a model for the aging of human cells. They developed and employed microfluidics and time-lapse microscopy to track the aging processes across the cell’s lifespan.

In the current study, yeast cells that were synthetically rewired and aged under the direction of the synthetic oscillator device resulted in an 82% increase in lifespan compared with control cells that aged under normal circumstances. The results revealed “the most pronounced lifespan extension in yeast that we have observed with genetic perturbations,” they noted.

“Our oscillator cells live longer than any of the longest-lived strains previously identified by unbiased genetic screens,” said Hao.

“Our work represents a proof-of-concept example, demonstrating the successful application of synthetic biology to reprogram the cellular aging process,” the authors wrote, “and may lay the foundation for designing synthetic gene circuits to effectively promote longevity in more complex organisms.”

The team is currently expanding its research to the aging of diverse human cell types, including stem cells and neurons.

Reference: “Engineering longevity—design of a synthetic gene oscillator to slow cellular aging” by Zhen Zhou, Yuting Liu, Yushen Feng, Stephen Klepin, Lev S. Tsimring, Lorraine Pillus, Jeff Hasty and Nan Hao, 27 April 2023, *Science*.

DOI: [10.1126/science.add7631](https://doi.org/10.1126/science.add7631)

The research team, Zhen Zhou, Yuting Liu, Yushen Feng, Stephen Klepin, Lev Tsimring, Lorraine Pillus, Jeff Hasty and Nan Hao, are based across UC San Diego, including the Department of Molecular Biology (School of Biological Sciences), Synthetic Biology Institute, Moores Cancer Center (UC San Diego Health) and Shu Chien-Gene Lay Department of Bioengineering (Jacobs School of Engineering).

Telomerase Gene Therapy Extends Mouse Lifespan by 24%

Researchers have extended the lifespan of mice by 24% with a single treatment by inducing cells to express telomerase.

Inducing cells to express telomerase, the enzyme which is supposed to slow down the metabolic clock, has enabled researchers boost the lifespan of mouse by 24% with a single treatment.

The scientists published their findings in the journal *EMBO Molecular Medicine*. The gene therapy acts on specific genes and is applied in adult life, not from the embryonic stage. Researchers at the Spanish National Cancer Research Center (CNIO) have demonstrated that the mouse lifespan can be extended by the application of one treatment acting directly on the animal's genes in adult life. The therapy has been found to be safe and effective in mice.

Adult and aged mice were treated with the gene therapy, delivering a rejuvenating effect. On average, the mice lived 24% longer. The older mice lived 13% longer. The therapy produces an appreciable improvement on the animal's health and delayed the onset of age-related diseases.

The genes were treated with a DNA-modified virus. The viral genes were replaced by those of the telomerase enzyme, which plays a key role in aging. Telomerase repairs the extreme ends of chromosomes, and slows the cells and therefore the body's biological clock.

There is a potential to develop a telomerase-based anti-aging gene therapy that won't increase the risk of cancer. Telomeres are the caps that protect the end of chromosomes, but each time the cell divides, the telomeres get shorter until they lose all functionality. The cell then stops dividing or dies. Telomerase prevents telomeres from shortening or even rebuilding them.

In most cells, telomerase is only active before birth. The cells of adult organisms contain no telomerase. There are some exceptions such as adult stem cells and cancer cells, which divide limitlessly and could be immortal.

The risk of cancer tumor promotion is a risk that has set back telomerase-based anti-aging therapies. The kind of virus employed to carry the telomerase gene to the cells is very important. The viruses used in this study have been successfully used in gene therapy treatment of hemophilia and eye disease. They are non-replicating viruses derived from others that are non-pathogenic in humans.

Reference: “Telomerase gene therapy in adult and old mice delays aging and increases longevity without increasing cancer” by Bruno Bernardes de Jesus, Elsa Vera, Kerstin Schneeberger, Agueda M. Tejera, Eduard Ayuso, Fatima Bosch and Maria A. Blasco, 15 May 2012, *EMBO Molecular Medicine*.

DOI: [10.1002/emmm.201200245](https://doi.org/10.1002/emmm.201200245)

Is Immortality in Our Reach? Unveiling Sea Anemone Secrets



Scientists have found stem cells in sea anemones that could explain their seemingly eternal life, a discovery that might also impact our understanding of human aging and disease. (A single *Nematostella* polyp.) Credit: Yulia Kraus

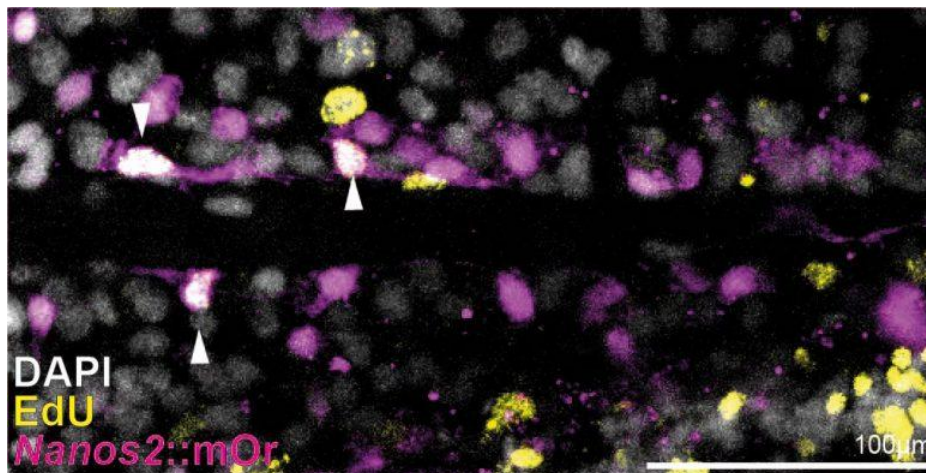
Researchers have discovered cells in a sea anemone that might explain its potential immortality. These cells, regulated by ancient genes, offer insights into regeneration and aging processes that could illuminate human health and longevity.

The study reveals how these genes, active in humans for forming reproductive cells, also confer regenerative abilities on cnidarians, a group of animals including sea anemones.

Discovering Immortality in Sea Anemones

The sea anemone *Nematostella vectensis* is potentially immortal. Using molecular genetic methods, developmental biologists led by Ulrich Technau from the University of Vienna have now identified possible candidates for multipotent stem cells in the sea anemone for the first time. These stem cells are regulated by evolutionary highly conserved genes, which in humans are usually only active in the formation of egg and sperm cells, but give ancient animal phyla such as cnidarians a high degree of regenerative capacity to even escape aging. The results are currently being published in Science Advances and could also provide insights into the human aging process in the future.

“We live as long as our stem cells” is a somewhat bold but essentially accurate statement. Stem cells contribute to the constant renewal of various cells and tissues in humans, e.g. blood cells, skin, or hair. If stem cells lose this ability or their number decreases in the course of life, the body ages or develops diseases. Stem cells are therefore of great interest for biomedical research.



Laser scanning microscope picture of the body of the sea anemone *Nematostella vectensis*. The red fluorescence (Nanos2) marks the transgenic putative stem cells, white (DAPI) are all cell nuclei and yellow (EdU) those cells that are actively engaged in DNA-synthesis, hence in the cell cycle like some of the stem cells. Credit: Andreas Denner and Ulrich Technau

Regeneration in the Animal Kingdom

While humans and most vertebrates can only regenerate parts of certain organs or limbs, other animal groups have far stronger regeneration mechanisms. This ability is made possible by pluripotent or multipotent stem cells, which can form (differentiate) almost all cell types of the body. The sea anemone *Nematostella vectensis* is also highly regenerative: it can reproduce asexually by budding and also shows no signs of aging, which makes it an interesting subject for stem cell research. However, researchers have not yet been able to identify any stem cells in these animals.

Using the new “Single Cell Genomics” method, Technau and his team could identify cells of a complex organism based on their specific transcriptome profiles and

determine from which stem cells they have developed. “By combining single-cell gene expression analyses and transgenesis, we have now been able to identify a large population of cells in the sea anemone that form differentiated cells such as nerve cells and glandular cells and are therefore candidates for multipotent stem cells,” explains first author Andreas Denner from the University of Vienna. They have remained undiscovered until now due to their tiny size.

Gene Conservation Across Species

These potential stem cells express the evolutionarily highly conserved genes *nanos* and *piwi*, which enable the development of germ cells (sperm and egg cells) in all animals, including humans. By specifically mutating the *nanos2* gene using the CRISPR gene scissors, the scientists were also able to prove that the gene is necessary for the formation of germ cells in sea anemones. It has also been shown in other animals that this gene is essential for the production of gametes.

This proves that this gene function emerged around 600 million years ago and has been preserved to this day. In future studies, Ulrich Technau and his team now want to investigate which special properties of the sea anemone’s stem cells are responsible for its potential immortality.

Reference: “*Nanos2* marks precursors of somatic lineages and is required for germline formation in the sea anemone *Nematostella vectensis*” by Andreas Denner, Julia Steger, Alexander Ries, Elizaveta Morozova-Link, Josefine Ritter, Franziska Haas, Alison G. Cole and Ulrich Technau, 16 August 2024, *Science Advances*.

DOI: [10.1126/sciadv.ado0424](https://doi.org/10.1126/sciadv.ado0424)

Slowing the Aging Process: Two Blood Proteins Could Be Key to a Long and Healthy Life

Researchers identified two proteins with significant negative effects on various aging measures. People with DNA causing higher levels of these proteins were frailer, had poorer self-rated health, and were less likely to live exceptionally long lives.

Research has identified two blood proteins, LPA and VCAM1, that significantly impact aging and longevity.

By targeting these proteins, new drugs could potentially slow aging and improve life quality, echoing genetic advantages seen in individuals naturally possessing lower levels of these proteins.

Key Proteins Identified in Aging Study

Two blood proteins have been shown by scientists to influence how long and healthy a life we live, research suggests.

Developing drugs that target these proteins could be one way of slowing the aging process, according to the largest genetic study of aging.

As we age, our bodies begin to decline after we reach adulthood, which results in age-related diseases and death. This latest research investigates which proteins could influence the aging process.

Many complex and related factors determine the rate at which we age and die, and these include genetics, lifestyle, environment, and chance. The study sheds light on the part proteins play in this process.

The Role of DNA in Protein Levels

Some people naturally have higher or lower levels of certain proteins because of the DNA they inherit from their parents. These protein levels can, in turn, affect a person's health.

University of Edinburgh researchers combined the results of six large genetic studies into human aging – each containing genetic information on hundreds of thousands of people,

Among 857 proteins studied, researchers identified two that had significant negative effects across various aging measures.

People who inherited DNA that causes raised levels of these proteins were frailer, had poorer self-rated health, and were less likely to live an exceptionally long life than those who did not.

The first protein, called apolipoprotein(a) (LPA), is made in the liver and thought to play a role in clotting. High levels of LPA can increase the risk of atherosclerosis – a condition in which arteries become clogged with fatty substances. Heart disease and stroke is a possible outcome.

The second protein, vascular cell adhesion molecule 1 (VCAM1), is primarily found on the surfaces of endothelial cells – a single-cell layer that lines blood vessels. The protein controls vessels' expansion and retraction – and function in blood clotting and the immune response.

Potential for Drug Development

Levels of VCAM1 increase when the body sends signals to indicate it has detected an infection, VCAM1 then allows immune cells to cross the endothelial layer, as seen for people who have naturally low levels of these proteins.

The researchers say that drugs used to treat diseases by reducing levels of LPA and VCAM1 could have the added benefit of improving quality and length of life.

One such example is a clinical trial that is testing a drug to lower LPA as a way of reducing the risk of heart disease.

There are currently no clinical trials involving VCAM1, but studies in mice have shown how antibodies lowering this protein's level improved cognition during old age.

The findings have been published in the journal *Nature Aging*.

Dr. Paul Timmers, lead researcher at the MRC Human Genetics Unit at University of Edinburgh, said: "The identification of these two key proteins could help extend the healthy years of life. Drugs that lower these protein levels in our blood could allow the average person to live as healthy and as long as individuals who have won the genetic lottery and are born with genetically low LPA and VCAM1 levels."

Professor Jim Wilson, Chair of Human Genetics at the University of Edinburgh's Usher Institute, said: "This study showcases the power of modern genetics to identify two potential targets for future drugs to extend lifespan."

Reference: "Mendelian randomization of genetically independent aging phenotypes identifies LPA and VCAM1 as biological targets for human aging" by Paul R. H. J. Timmers, Evgeny S. Tiys, Saori Sakaue, Masato Akiyama, Tuomo T. J. Kiiskinen, Wei Zhou, Shih-Jen Hwang, Chen Yao, Biobank Japan Project, FinnGen, Joris Deelen, Daniel Levy, Andrea Ganna, Yoichiro Kamatani, Yukinori Okada, Peter K. Joshi, James F. Wilson and Yakov A. Tsepilov, 20 January 2022, *Nature Aging*.

DOI: [10.1038/s43587-021-00159-8](https://doi.org/10.1038/s43587-021-00159-8)

Immune System “Clock” Developed That Accurately Predicts Illness and Mortality

Not all humans age biologically at the same rate, with differences largely attributed to varying rates of immune system decline. You’re as old as your immune system. Investigators at the Stanford University School of Medicine and the Buck Institute for Research on Aging have built an inflammatory-aging clock that’s more accurate than the number of candles on your birthday cake in predicting how strong your immune system is, how soon you’ll become frail or whether you have unseen cardiovascular problems that could become clinical headaches a few years down the road.

In the process, the scientists fingered a bloodborne substance whose abundance may accelerate cardiovascular aging.

The story of the clock’s creation will be published today (July 12, 2021) in *Nature Aging*.

“Every year, the calendar tells us we’re a year older,” said David Furman, PhD, the study’s senior author. “But not all humans age biologically at the same rate. You see this in the clinic — some older people are extremely disease-prone, while others are the picture of health.”

This divergence, Furman said, traces in large part to differing rates at which people’s immune systems decline. The immune system — a carefully coordinated collection of cells, substances, and strategies with which evolution has equipped us to deal with threats such as injuries or invasions by microbial pathogens — excels at mounting a quick, intense, localized, short-term, resist-and-repair response called acute inflammation. This “good inflammation” typically does its job, then wanes within days. (An example is that red, swollen finger you see when you have a splinter, and the rapid healing that follows.)

As we grow older, a low-grade, constant, bodywide “bad inflammation” begins to kick in. This systemic and chronic inflammation causes organ damage and promotes vulnerability to a who’s who of diseases spanning virtually every organ system in the body and including cancer, heart attacks, strokes, neurodegeneration, and autoimmunity.

To date, there have been no metrics for accurately assessing individuals’ inflammatory status in a way that could predict these clinical problems and point to ways of addressing them or staving them off, Furman said. But now, he said, the study has produced a single-number quantitative measure that appears to do just that.

Furman directs the Stanford 1000 Immunomes Project and is a visiting scholar at Stanford’s Institute for Immunity, Transplantation and Infection. In addition, he’s an associate professor at the Novato, California-based Buck Institute for Research on Aging and director of the Artificial Intelligence Platform at the same institute.

Lead authors of the study are Nazish Sayed, MD, PhD, assistant professor of vascular surgery at Stanford, and Yingxiang Huang, PhD, senior data scientist at the Buck Institute.

1,001 blood samples

For the 1000 Immunomes Project, blood samples were drawn from 1,001 healthy people ages 8-96 between 2009 and 2016. The samples were subjected to a barrage of analytical procedures determining levels of immune-signaling proteins called cytokines, the activation status of numerous immune-cell types in responses to various stimuli, and the overall activity levels of thousands of genes in each of those cells.

The new study employed artificial intelligence to boil all this data down to a composite the researchers refer to as an inflammatory clock. The strongest predictors of inflammatory age, they found, were a set of about 50 immune-signaling proteins called cytokines. Levels of those, massaged by a complex algorithm, were sufficient to generate a single-number inflammatory score that tracked well with a person's immunological response and the likelihood of incurring any of a variety of aging-related diseases.

In 2017, the scientists assessed nearly 30 1000 Immunomes Project participants ages 65 or older whose blood had been drawn in 2010. They measured the participants' speed at getting up from a chair and walking a fixed distance and, through a questionnaire, their ability to live independently ("Can you walk by yourself?" "Do you need help getting dressed?"). Inflammatory age proved superior to chronological age in predicting frailty seven years later.

Next, Furman and his colleagues obtained blood samples from an ongoing study of exceptionally long-lived people in Bologna, Italy, and compared the inflammatory ages of 29 such people (all but one a centenarian) with those of 18 50- to 79-year-olds. The older people had inflammatory ages averaging 40 years less than their calendar age. One, a 105-year-old man, had an inflammatory age of 25, Furman said.

To further assess inflammatory age's effect on mortality, Furman's team turned to the Framingham Study, which has been tracking health outcomes in thousands of individuals since 1948. The Framingham study lacked sufficient data on bloodborne-protein levels, but the genes whose activity levels largely dictate the production of the inflammatory clock's cytokines are well known. The researchers measured those cytokine-encoding genes' activity levels in Framingham subjects' cells. This proxy for cytokine levels significantly correlated with all-cause mortality among the Framingham participants.

A key substance

The scientists observed that blood levels of one substance, CXCL9, contributed more powerfully than any other clock component to the inflammatory-age score. They found that levels of CXCL9, a cytokine secreted by certain immune cells to attract other immune cells to a site of an infection, begin to rise precipitously after age 60, on average.

Among a new cohort of 97 25- to 90-year-old individuals selected from the 1000 Immunomes Project for their apparently excellent health, with no signs of any disease, the investigators looked for subtle signs of cardiovascular deterioration. Using a sensitive test of arterial stiffness, which conveys heightened risk for strokes, heart attacks and kidney failure, they tied high inflammatory-age scores — and high CXCL9 levels — to unexpected arterial stiffness and another portent of untoward cardiac consequences: excessive thickness of the wall of the heart’s main pumping station, the left ventricle.

CXCL9 has been implicated in cardiovascular disease. A series of experiments in laboratory dishware showed that CXCL9 is secreted not only by immune cells but by endothelial cells — the main components of blood-vessel walls. The researchers showed that advanced age both correlates with a significant increase in endothelial cells’ CXCL9 levels and diminishes endothelial cells’ ability to form microvascular networks, to dilate, and to contract.

But in laboratory experiments conducted on tissue from mice and on human cells, reducing CXCL9 levels restored youthful endothelial-cell function, suggesting that CXCL9 directly contributes to those cells’ dysfunction and that inhibiting it could prove effective in reducing susceptible individuals’ risk of cardiovascular disease.

“Our inflammatory aging clock’s ability to detect subclinical accelerated cardiovascular aging hints at its potential clinical impact,” Furman said. “All disorders are treated best when they’re treated early.”

Reference: “An inflammatory aging clock (iAge) based on deep learning tracks multimorbidity, immunosenescence, frailty and cardiovascular aging” by Nazish Sayed, Yingxiang Huang, Khiem Nguyen, Zuzana Krejciova-Rajaniemi, Anissa P. Grawe, Tianxiang Gao, Robert Tibshirani, Trevor Hastie, Ayelet Alpert, Lu Cui, Tatiana Kuznetsova, Yael Rosenberg-Hasson, Rita Ostan, Daniela Monti, Benoit Lehallier, Shai S. Shen-Orr, Holden T. Maecker, Cornelia L. Dekker, Tony Wyss-Coray, Claudio Franceschi, Vladimir Jojic, François Haddad, José G. Montoya, Joseph C. Wu, Mark M. Davis and David Furman, 12 July 2021, *Nature Aging*.

DOI: [10.1038/s43587-021-00082-y](https://doi.org/10.1038/s43587-021-00082-y)

Other Stanford study co-authors are Robert Tibshirani, PhD, professor of biomedical data science and of statistics; Trevor Hastie, PhD, professor of statistics and of biomedical data; senior research scientist Lu Cui, PhD; Human Immune Monitoring Center Immunoassays director Yael Rosenberg-Hasson, PhD; former neurology instructor Benoit Lehallier, PhD; former postdoctoral scholar Shai Shen-Orr, PhD; Holden Maecker, PhD, professor of microbiology and immunology; Cornelia Dekker, MD, professor of pediatric infectious diseases, emeritus; Tony Wyss-Coray, PhD, professor of neurology and neurological sciences; Francois Haddad, MD, clinical professor of cardiovascular medicine; Jose Montoya, MD, former professor of infectious diseases; Joseph Wu, MD, professor of radiology and director of the Stanford Cardiovascular Institute; and Mark Davis, PhD,

professor of microbiology and immunology and director of the Institute for Immunity, Transplantation and Infection.

Researchers from the Buck Institute, Edifice Health, the University of North Carolina, Technion-Israel Institute of Technology, the University of Leuven, the University of Bologna, the University of Florence and the Institute of Neurological Sciences of Bologna also contributed to the work.

The work was funded by the Stanford Alzheimer's Disease Research Center, the Buck Institute for Research on Aging, the Ellison Foundation, the National Institutes of Health (grants U19 AI057229, U19 AI090019, UL1 RR025744, K01 HL135455 and P50 AG047366) and the Paul F. Glenn Foundation.

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Simple & Free: Scientists Find What Enhances Your Immune System and Helps You Live Longer

New study that provides the most detailed report to date of the cellular effects of a calorie-restricted diet in rats concludes that eating less food will enhance your immune system, reduce levels of inflammation throughout your body, delay the onset of age-related diseases, and help you live longer.

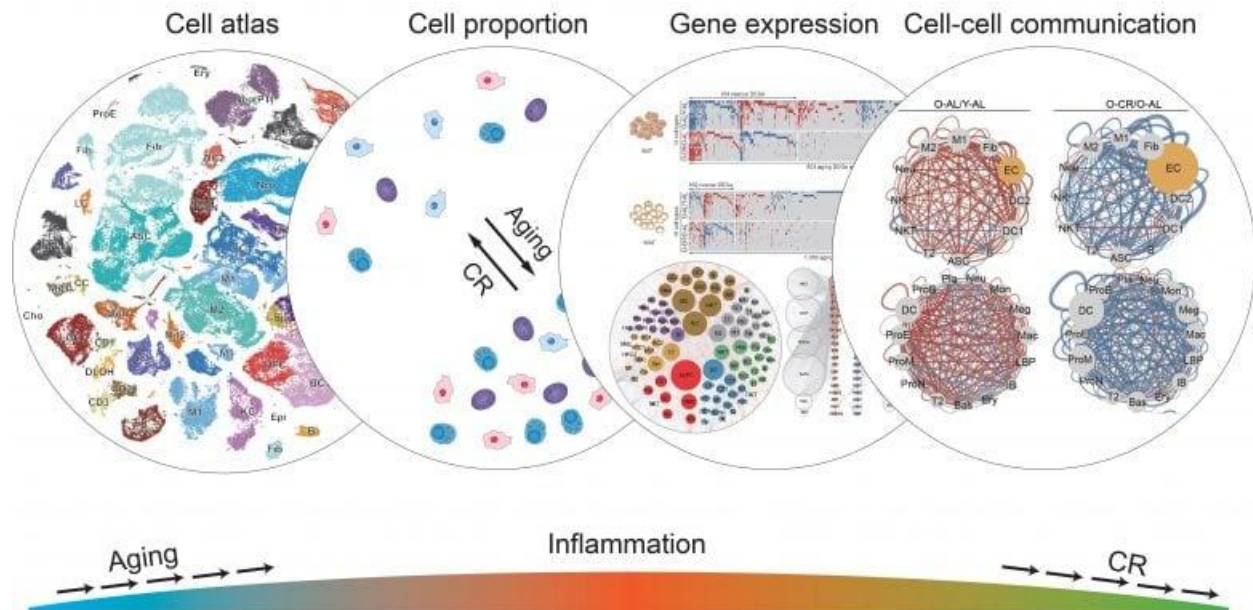
If you want to enhance your immune system, reduce levels of inflammation throughout your body, delay the onset of age-related diseases, and live longer — eat less food. That's the conclusion of a new study by scientists from the US and China that provides the most detailed report to date of the cellular effects of a calorie-restricted diet in rats. While the benefits of caloric restriction have long been known, the new results show how this restriction can protect against aging in cellular pathways, as detailed in *Cell* on February 27, 2020.

"We already knew that calorie restriction increases life span, but now we've shown all the changes that occur at a single-cell level to cause that," says Juan Carlos Izpisua Belmonte, a senior author of the new paper, professor in Salk's Gene Expression Laboratory and holder of the Roger Guillemin Chair. "This gives us targets that we may eventually be able to act on with drugs to treat aging in humans."

Aging is the highest risk factor for many human diseases, including cancer, dementia, diabetes, and metabolic syndrome. Caloric restriction has been shown in animal models to be one of the most effective interventions against these age-related diseases. And although

researchers know that individual cells undergo many changes as an organism ages, they have not known how caloric restriction might influence these changes.

In the new paper, Belmonte and his collaborators — including three alumni of his Salk lab who are now professors running their own research programs in China — compared rats who ate 30 percent fewer calories with rats on normal diets. The animals' diets were controlled from age 18 months through 27 months. (In humans, this would be roughly equivalent to someone following a calorie-restricted diet from age 50 through 70.)



The illustration represents the ways in which caloric restriction affects various aspects of cellular function, with the overall result of reducing inflammation and the activity of many aging-related genes. Credit: Salk Institute

At both the start and the conclusion of the diet, Belmonte's team isolated and analyzed a total of 168,703 cells from 40 cell types in the 56 rats. The cells came from fat tissues, liver, kidney, aorta, skin, bone marrow, brain, and muscle. In each isolated cell, the researchers used single-cell genetic-sequencing technology to measure the activity levels of genes. They also looked at the overall composition of cell types within any given tissue. Then, they compared old and young mice on each diet.

Many of the changes that occurred as rats on the normal diet grew older didn't occur in rats on a restricted diet; even in old age, many of the tissues and cells of animals on the diet closely resembled those of young rats. Overall, 57 percent of the age-related changes in cell composition seen in the tissues of rats on a normal diet were not present in the rats on the calorie-restricted diet.

"This approach not only told us the effect of calorie restriction on these cell types, but also provided the most complete and detailed study of what happens at a single-cell level during aging," says co-corresponding author Guang-Hui Liu, a professor at the Chinese Academy of Sciences.

From left: Concepcion Rodriguez Esteban and Juan Carlos Izpisua Belmonte. Credit: Salk Institute

Some of the cells and genes most affected by the diet are related to immunity, inflammation, and lipid metabolism. The number of immune cells in nearly every tissue studied dramatically increased as control rats aged but were not affected by age in rats with restricted calories. In brown adipose tissue — one type of fat tissue — a calorie-restricted diet reverted the expression levels of many anti-inflammatory genes to those seen in young animals.

“The primary discovery in the current study is that the increase in the inflammatory response during aging could be systematically repressed by caloric restriction,” says co-corresponding author Jing Qu, also a professor at the Chinese Academy of Sciences.

When the researchers homed in on transcription factors — essentially master switches that can broadly alter the activity of many other genes — that were altered by caloric restriction, one stood out. Levels of the transcription factor Ybx1 were altered by the diet in 23 different cell types. The scientists believe Ybx1 may be an age-related transcription factor and are planning more research into its effects.

“People say that ‘you are what you eat,’ and we’re finding that to be true in lots of ways,” says Concepcion Rodriguez Esteban, another of the paper’s authors and a staff researcher at Salk. “The state of your cells as you age clearly depends on your interactions with your environment, which includes what and how much you eat.”

The team is now trying to utilize this information in an effort to discover aging drug targets and implement strategies toward increasing life and health span.

Reference: “Caloric Restriction Reprograms the Single-Cell Transcriptional Landscape of *Rattus Norvegicus* Aging” by Shuai Ma, Shuhui Sun, Lingling Geng, Moshi Song, Wei Wang, Yanxia Ye, Qianzhao Ji, Zhiran Zou, Si Wang, Xiaojuan He, Wei Li, Concepcion Rodriguez Esteban, Xiao Long, Guoji Guo, Piu Chan, Qi Zhou, Juan Carlos Izpisua Belmonte, Weiqi Zhang, Jing Qu and Guang-Hui Liu, 27 February 2020, *Cell*.

DOI: [10.1016/j.cell.2020.02.008](https://doi.org/10.1016/j.cell.2020.02.008)

Other researchers on the study were Shuai Ma, Shuhui Sun, Lingling Geng, Moshi Song, Wei Wang, Yanxia Ye, Qianzhao Ji, Zhiran Zou, Si Wang, and Qi Zhou of the Chinese Academy of Sciences; Xiaojuan He, Wei Li, Piu Chan and Weiqi Zhang of Xuanwu Hospital Capital Medical University; Xiao Long of Peking Union Medical College Hospital; and Guoji Guo of Zhejiang University School of Medicine.

The work and researchers involved were supported by grants from the National Key Research and Development Program of China, the Strategic Priority Research Program of the Chinese Academy of Sciences, the National Natural Science Foundation of China, Beijing Natural Science Foundation, Beijing Municipal Commission of Health and Family Planning,

Advanced Innovation Center for Human Brain Protection, the State Key Laboratory of Membrane Biology, the Moxie Foundation, and the Glenn Foundation.

Scientists Have Discovered a Dietary Compound That Increases Longevity



Researchers from the University of Seville and the University of Kent have shown that the carotenoid phytoene extends the lifespan of the nematode *Caenorhabditis elegans* and reduces paralysis linked to Alzheimer's disease. Their studies observed a lifespan increase of 10-18.6% and a reduction in amyloid plaque effects by 30-40%.

A study found that phytoene, a carotenoid, extends the lifespan of *Caenorhabditis elegans* and reduces Alzheimer's-related plaque effects. Researchers are exploring its broader potential in disease prevention.

Researchers from the Color and Food Quality group at the Faculty of Pharmacy, University of Seville, in partnership with Dr. Marina Ezcurra's team at the University of Kent (UK),

have demonstrated that the carotenoid phytoene extends the lifespan of the nematode *Caenorhabditis elegans*. Additionally, it delays the onset of paralysis linked to amyloid plaque formation in an Alzheimer's disease model.

Specifically, increases in longevity of between 10 and 18.6% and decreases in the proteotoxic effect of plaques of between 30 and 40% were observed. The studies, which form part of Ángeles Morón Ortiz's doctoral thesis, tested pure phytoene and extracts rich in this carotenoid obtained from microalgae.

According to Dr. Paula Mapelli Brahm, "These are very exciting preliminary results, so we are looking for funding to continue this line of research and to find out by what mechanisms these effects are produced."

The Importance of *Caenorhabditis elegans* in Biomedical Research

Caenorhabditis elegans is a widely used animal model in biomedicine. In fact, it has been instrumental in important discoveries that have been recognized with the Nobel Prize, such as programmed cell death, RNA interference, and applications of the GFP protein.

Professor Antonio Jesús Meléndez Martínez's team has spent 15 years studying phytoene, which is found in foods such as tomatoes, carrots, apricots, red peppers, oranges, mandarins and passion fruit, among others. It is a compound that is efficiently absorbed and found in many tissues, including the skin, where studies indicate that it can protect against ultraviolet radiation.

The team works on the sustainable production of healthy foods to reduce the risk of disease, with an emphasis on the applications of carotenoids in agri-food, nutrition, and cosmetics. In this area, they have coordinated international networks in which researchers from more than 50 countries have participated.

Reference: "Phytoene and Phytoene-Rich Microalgae Extracts Extend Lifespan in *C. elegans* and Protect against Amyloid- β Toxicity in an Alzheimer's Disease Model" by Ángeles Morón-Ortiz, Antonis A. Karamalegkos, Paula Mapelli-Brahm, Marina Ezcurra and Antonio J. Meléndez-Martínez, 30 July 2024, *Antioxidants*.

DOI: [10.3390/antiox13080931](https://doi.org/10.3390/antiox13080931)

The researchers have received funding from the Ministry of Science and Innovation – State Research Agency/10.13039/501100011033, specifically from the NEWCARFOODS-PID2019-110438RB-C21 project and the Spanish Carotenoid Network (CaRed-RED2022-134577-T). NEWCARFOODS has been developed in coordination with the group of Professor Rosa León (University of Huelva) who provided the microalgae used in the study.

The Secret to a Longer Life Might Be in Your Next Meal

A comprehensive mouse study shows that eating fewer calories rather than fasting extends lifespan more effectively, with genetic resilience to stress playing a crucial role in longevity, suggesting a need to rethink aging markers in human studies.

Researchers conduct pivotal study into aging and lifespan to uncover new details about how diets might make people live longer — but also their negative side effects.

Recent research involving nearly one thousand genetically distinct mice examined the impact of various diets on lifespan, uncovering that lower caloric intake significantly enhances longevity compared to periodic fasting. The study's pivotal findings suggest that genetic resilience and maintaining health during caloric restriction are crucial, potentially challenging existing theories on the biological markers of aging and longevity.

Groundbreaking Longevity Research

For nearly a century, laboratory studies have consistently shown that animals live longer when they eat less food or eat less frequently. However, scientists have struggled to understand why these restrictive diets extend lifespan and how they can be effectively applied to humans. Now, in a pivotal study published in the October 9 issue of *Nature*, researchers at The Jackson Laboratory (JAX) and their collaborators tracked the health of nearly one thousand mice on various diets to explore these questions further.

The study was meticulously designed to ensure each mouse was genetically unique, better mirroring the genetic diversity of humans. This approach enhances the clinical relevance of the findings, marking the study as one of the most significant contributions to the research on aging and lifespan to date.

Key Findings on Caloric Restriction and Lifespan

The study concluded that eating fewer calories had a greater impact on lifespan than periodic fasting, revealing that very-low-calorie diets generally extended the mice's lifespan regardless of their body fat or glucose levels — both typically seen as markers of metabolic health and aging. Surprisingly, the mice that lived the longest on the restrictive diets were those that lost the least weight despite eating less. Animals that lost the most weight on these diets tended to have low energy, compromised immune and reproductive systems, and shorter lives.

“Our study really points to the importance of resilience,” said Gary Churchill, Karl Gunnar Johansson Chair and professor at JAX who led the study. “The most robust animals keep their weight on even in the face of stress and caloric restriction, and they

are the ones that live the longest. It also suggests that a more moderate level of calorie restriction might be the way to balance long-term health and lifespan.”

Churchill and his colleagues assigned female mice to any of five different diets: one in which the animals could freely eat any amount of food at any time, two in which the animals were provided only 60% or 80% of their baseline calories each day, and two in which the animals were not given any food for either one or two consecutive days each week but could eat as much as they wanted on the other days. Then, the mice were studied for the rest of their lives with periodic blood tests and extensive evaluation of their overall health.

Genetic Factors and Lifespan Variability

Overall, mice on unrestricted diets lived for an average of 25 months, those on the intermittent fasting diets lived for an average of 28 months, those eating 80% of baseline lived for an average of 30 months, and those eating 60% of baseline lived for 34 months. But within each group, the range of lifespans was wide; mice eating the fewest calories, for example, had lifespans ranging from a few months to four and a half years.

A graphic representing the power of genetic diversity in mice to study longevity and healthspan. Credit: The Jackson Laboratory

Surprising Insights into Longevity and Diet

When the researchers analyzed the rest of their data to try to explain this wide range, they found that genetic factors had a far greater impact on lifespan than diets, highlighting how underlying genetic features, yet to be identified, play a major role in how these diets would affect an individual person’s health trajectory. Moreover, they pinpointed genetically-encoded resilience as a critical factor in lifespan; mice that naturally maintained their body weight, body fat percentage and immune cell health during periods of stress or low food intake, as well as those that did not lose body fat late in life, survived the longest.

“If you want to live a long time, there are things you can control within your lifetime such as diet, but really what you want is a very old grandmother,” Churchill said.

Reevaluating the Markers of Aging

The study also cast doubt on traditional ideas about why certain diets can extend life in the first place. For example, factors like weight, body fat percentages, blood glucose levels and body temperature did not explain the link between cutting calories and living a longer life. Instead, the study found that immune system health and traits related to red blood cells were more clearly connected to lifespan. Importantly, those findings mean that human studies of longevity – which often use metabolic measurements as markers for aging or youthfulness – may be overlooking more important aspects of healthy aging.

“While caloric restriction is generally good for lifespan, our data show that losing weight on caloric restriction is actually bad for lifespan,” Churchill explained. “So when we look at human trials of longevity drugs and see that people are losing weight and have better metabolic profiles, it turns out that might not be a good marker of their future lifespan at all.”

Reference: “Dietary restriction impacts health and lifespan of genetically diverse mice” by Andrea Di Francesco, Andrew G. Deighan, Lev Litichevskiy, Zhenghao Chen, Alison Luciano, Laura Robinson, Gaven Garland, Hannah Donato, Matthew Vincent, Will Schott, Kevin M. Wright, Anil Raj, G. V. Prateek, Martin Mullis, Warren G. Hill, Mark L. Zeidel, Luanne L. Peters, Fiona Harding, David Botstein, Ron Korstanje, Christoph A. Thaiss, Adam Freund and Gary A. Churchill, 9 October 2024, *Nature*.
[DOI: 10.1038/s41586-024-08026-3](https://doi.org/10.1038/s41586-024-08026-3)

Higher Levels of Omega-3 in the Blood Increase Life Expectancy by Almost Five Years

A 1% increase in this substance in the blood is associated with a change in mortality risk similar to that of quitting smoking.

Levels of omega-3 fatty acids in the blood are as good a predictor of mortality from any cause as smoking, according to a study involving the Hospital del Mar Medical Research Institute (IMIM), in collaboration with *The Fatty Acid Research Institute* in the United States and several universities in the United States and Canada. The study, published in *The American Journal of Clinical Nutrition*, used data from a long-term study group, the *Framingham Offspring Cohort*, which has been monitoring residents of this Massachusetts town, in the United States, since 1971.

Researchers have found that omega-3 levels in blood erythrocytes (the so-called red blood cells) are very good mortality risk predictors. The study concludes that “Having higher levels of these acids in the blood, as a result of regularly including oily fish in the diet, increases life expectancy by almost five years,” as Dr. Aleix Sala-Vila, a postdoctoral researcher in the IMIM’s Cardiovascular Risk and Nutrition Research Group and author of the study, points out. In contrast, “Being a regular smoker takes 4.7 years off your life expectancy, the same as you gain if you have high levels of omega-3 acids in your blood,” he adds.

2,200 people monitored over eleven years

The study analyzed data on blood fatty acid levels in 2,240 people over the age of 65, who were monitored for an average of eleven years. The aim was to validate which fatty acids function as good predictors of mortality, beyond the already known factors. The results

indicate that four types of fatty acids, including omega-3, fulfill this role. It is interesting that two of them are saturated fatty acids, traditionally associated with cardiovascular risk, but which, in this case, indicate longer life expectancy. “This reaffirms what we have been seeing lately,” says Dr. Sala-Vila, “not all saturated fatty acids are necessarily bad.” Indeed, their levels in the blood cannot be modified by diet, as happens with omega-3 fatty acids.

These results may contribute to the personalization of dietary recommendations for food intake, based on the blood concentrations of the different types of fatty acids. “What we have found is not insignificant. It reinforces the idea that small changes in diet in the right direction can have a much more powerful effect than we think, and it is never too late or too early to make these changes,” remarks Dr. Sala-Vila.

The researchers will now try to analyze the same indicators in similar population groups, but of European origin, to find out if the results obtained can also be applied outside the United States. The *American Heart Association* recommends eating oily fish such as salmon, anchovies or sardines twice a week because of the health benefits of omega-3 acids.

Reference: “Using an erythrocyte fatty acid fingerprint to predict risk of all-cause mortality: the Framingham Offspring Cohort” by Michael I McBurney, Nathan L Tintle, Ramachandran S Vasan, Aleix Sala-Vila and William S Harris, 16 June 2021, *The American Journal of Clinical Nutrition*.

DOI: [10.1093/ajcn/nqab195](https://doi.org/10.1093/ajcn/nqab195)

Fountain of Youth: Cutting Calories and Eating at the Right Time of Day Leads to a Longer Life

Eating only during your most active time of day, while following a reduced-calorie diet, may lead to a substantially longer life, according to new research conducted on mice.

Many of us wish for a fountain of youth, filled with magical water that could restore our youth and vitality. It is so simple and easy but unfortunately doesn't exist.

A real key to longevity that is simple, but not easy for most of us, is to eat less. Numerous studies on various animals have shown that a restricted-calorie diet can lead to a longer and healthier lifespan.

In new research on mice, scientists found that a reduced-calorie diet led to a 10% longer life. However, their big discovery was that by combining the reduced-calorie diet with a time-restricted diet (only feeding during their most active time of day, which for mice is at night), the animals lived 35% longer.

One recipe for longevity is simple, if not easy to follow: eat less. Restricting calories can lead to a longer, healthier life, as studies have shown in a variety of animals.

Now, new research suggests that the body's daily rhythms play a significant role in this longevity effect. Eating only during their most active time of day substantially extended the lifespan of mice on a reduced-calorie diet, Howard Hughes Medical Institute (HHMI) Investigator Joseph Takahashi and colleagues reported in the journal *Science* on May 5, 2022.

In his team's study of hundreds of mice over four years, a reduced-calorie diet alone extended the animals' lives by 10 percent. But feeding mice the diet only at nighttime, when mice are most active, extended life by 35 percent. That combo – a reduced-calorie diet plus a nighttime eating schedule – tacked on an extra nine months to the animals' typical two-year median lifespan. For people, an equivalent plan would limit eating to daytime hours.

Experiments that tested various diet plans in mice found that the animals live longest on a low-calorie diet with daily fasting periods. Credit: Fernando Augusto/<http://made-for.studio>

The research helps disentangle the controversy around diet plans that emphasize eating only at certain times of day, says Takahashi, a molecular biologist at the University of Texas Southwestern Medical Center. Such plans may not [speed weight loss in humans](#), as a recent study in the *New England Journal of Medicine* reported, but they could prompt health benefits that add up to a longer lifespan.

Takahashi's team's findings highlight the crucial role of metabolism in aging, says Sai Krupa Das, a nutrition scientist at the Jean Mayer USDA Human Nutrition Research Center on Aging who was not involved with the work. "This is a very promising and landmark study," she says.

Fountain of Youth

Decades of research has found that calorie restriction extends the lifespan of animals ranging from worms and flies to mice, rats, and primates. Those experiments report weight loss, improved glucose regulation, lower blood pressure, and reduced inflammation.

But it has been difficult to systematically study calorie restriction in people, who can't live in a laboratory and eat measured food portions for their entire lives, Das says. She was part of the research team that conducted the first controlled study of calorie restriction in humans, called the Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy, or CALERIE. In that study, even a modest reduction in calories "was remarkably beneficial" for reducing signs of aging, Das says.

HHMI Investigator Joseph Takahashi's team has discovered that eating a calorie-restricted diet at the right time of day can extend lifespan in mice. Credit: Brandon Wade/AP Images for HHMI

Scientists are just beginning to understand how calorie restriction slows aging at the cellular and genetic level. As an animal ages, genes linked to inflammation tend to become more active, while genes that help regulate metabolism become less active. Takahashi's new study found that calorie restriction, especially when timed to the mice's active period at night, helped offset these genetic changes as mice aged.

Question of Time

Recent years have seen the rise of many popular diet plans that focus on what's known as intermittent fasting, such as fasting on alternate days or eating only during a period of six to eight hours per day. To unravel the effects of calories, fasting, and daily, or circadian, rhythms on longevity, Takahashi's team undertook an extensive four-year experiment. The team housed hundreds of mice with automated feeders to control when and how much each mouse ate for its entire lifespan.

Some of the mice could eat as much as they wanted, while others had their calories restricted by 30 to 40 percent. And those on calorie-restricted diets ate on different schedules. Mice fed the low-calorie diet at night, over either a two-hour or 12-hour period, lived the longest, the team discovered.

The results suggest that time-restricted eating has positive effects on the body, even if it doesn't promote weight loss, as the *New England Journal of Medicine* study suggested. Takahashi points out that his study likewise found no differences in body weight among mice on different eating schedules — “however, we found profound differences in lifespan,” he says.

Rafael de Cabo, a gerontology researcher at the National Institute on Aging in Baltimore says that the *Science* paper “is a very elegant demonstration that even if you are restricting your calories but you are not [eating at the right times], you do not get the full benefits of caloric restriction.”

Takahashi hopes that learning how calorie restriction affects the body's internal clocks as we age will help scientists find new ways to extend the healthy lifespan of humans. That could come through calorie-restricted diets, or through drugs that mimic those diets' effects.

In the meantime, Takahashi is taking a lesson from his mice – he restricts his own eating to a 12-hour period. But, he says, “if we find a drug that can boost your clock, we can then test that in the laboratory and see if that extends lifespan.”

Reference: “Circadian alignment of early onset caloric restriction promotes longevity in male C57BL/6J mice” by Victoria Acosta-Rodríguez, Filipa Rijo-Ferreira, Mariko Izumo, Pin Xu, Mary Wight-Carter, Carla B. Green and Joseph S. Takahashi, 5 May 2022, *Science*.

DOI: [10.1126/science.abk0297](https://doi.org/10.1126/science.abk0297)

How Intermittent Fasting Extends Life Spans – Time-Restricted Eating Reshapes Gene Expression Throughout the Body

Time-restricted eating reshapes gene expression throughout the body. In this illustration, the Ferris wheel displays the interconnected organ systems working smoothly during time-restricted eating, which is represented by the clock in the middle. Credit: Salk Institute **Salk researchers find that timing calorie intake synchronizes circadian rhythms across multiple systems in mice.**

Numerous studies have shown health benefits of time-restricted eating including increase in life span in laboratory studies. This has made practices like intermittent fasting a hot topic in the wellness industry. However, exactly how it affects the body on the molecular level, and how those changes interact across multiple organ systems, has not been well understood. Now, [Salk](#) scientists show in mice how time-restricted eating influences gene expression across more than 22 regions of the body and brain. Gene expression is the process through which genes are activated and respond to their environment by creating proteins.

The findings, published in *Cell Metabolism* on January 3, 2023, have implications for a wide range of health conditions where time-restricted eating has shown potential benefits, including diabetes, heart disease, hypertension, and cancer.

Satchidananda Panda. Credit: Salk Institute

“We found that there is a system-wide, molecular impact of time-restricted eating in mice,” says Professor Satchidananda Panda, senior author and holder of the Rita and Richard Atkinson Chair at Salk. “Our results open the door for looking more closely at how this nutritional intervention activates genes involved in specific diseases, such as cancer.”

For the study, two groups of mice were fed the same high-calorie diet. One group was given free access to the food. The other group was restricted to eating within a feeding window of nine hours each day. After seven weeks, tissue samples were collected from 22 organ groups and the brain at different times of the day or night and analyzed for genetic changes. Samples included tissues from the liver, stomach, lungs, heart, adrenal gland, hypothalamus, different parts of the kidney and intestine, and different areas of the brain.

Genes and Hormonal Regulation

The authors found that 70 percent of mouse genes respond to time-restricted eating.

“By changing the timing of food, we were able to change the gene expression not just in the gut or in the liver, but also in thousands of genes in the brain,” says Panda.

Nearly 40 percent of genes in the adrenal gland, hypothalamus, and pancreas were affected by time-restricted eating. These organs are important for hormonal regulation. Hormones coordinate functions in different parts of the body and brain, and hormonal imbalance is implicated in many diseases from diabetes to stress disorders. The results offer guidance to how time-restricted eating may help manage these diseases.

Interestingly, not all sections of the digestive tract were affected equally. While genes involved in the upper two portions of the small intestine—the duodenum and jejunum—were activated by time-restricted eating, the ileum, at the lower end of the small intestine, was not. This finding could open a new line of research to study how jobs with shiftwork, which disrupts our 24-hour biological clock (called the circadian rhythm) impact digestive diseases and cancers. [Previous research](#) by Panda’s team showed that time-restricted eating improved the health of firefighters, who are typically shift workers.

The researchers also found that time-restricted eating aligned the circadian rhythms of multiple organs of the body.

Synchronizing Circadian Rhythms with Eating Patterns

“Circadian rhythms are everywhere in every cell,” says Panda. “We found that time-restricted eating synchronized the circadian rhythms to have two major waves: one during fasting, and another just after eating. We suspect this allows the body to coordinate different processes.”

Next, Panda’s team will take a closer look at the effects of time-restricted eating on specific conditions or systems implicated in the study, such as atherosclerosis, which is a hardening of the arteries that is often a precursor to heart disease and stroke, as well as chronic kidney disease.

Reference: “Diurnal transcriptome landscape of a multi-tissue response to time-restricted feeding in mammals” by Shaunak Deota, Terry Lin, Amandine Chaix, April Williams, Hiep Le, Hugo Calligaro, Ramesh Ramasamy, Ling Huang and Satchidananda Panda, 3 January 2023, *Cell Metabolism*.

DOI: [10.1016/j.cmet.2022.12.006](https://doi.org/10.1016/j.cmet.2022.12.006)

Other authors include Shaunak Deota, Terry Lin, April Williams, Hiep Le, Hugo Calligaro, Ramesh Ramasamy, and Ling Huang of Salk; and Amandine Chaix of the University of Utah.

The research was supported by the National Institutes of Health (grants CA258221, DK115214, CA014195, and AG065993) and the Wu Tsai Human Performance Alliance.

Why Sleep Is the Key to Living Longer

One of the most important (and least appreciated) keys to extending your healthspan is a great night's sleep. It rejuvenates the body, boosts cognitive function, and powers your immune system. It's the foundation for your health and longevity.

Sleep expert Matthew Walker, director of the Center for Human Sleep Science at the University of California, Berkeley and author of the excellent book *Why We Sleep*, says that sleep is the single most effective thing we can do to reset our mental and physical health each day. There is a direct relationship between how well you sleep and how long you live, and almost nobody can get away with fewer than six hours of sleep a night without harming their health.

For most people, regularly getting eight hours of sleep boosts memory retention, enhances concentration, augments creativity, stabilizes emotions, strengthens the immune system, enhances athletic performance, and staves off deadly ailments like cancers and heart disease.

1. The difference between getting a good night's sleep and a bad one is a decrease from 100% to 60% in the brain's ability to retain new facts. That's the difference, as Walker puts it, between "acing an exam and failing it miserably."

2. Going twenty-four hours without sleep is like having a blood alcohol concentration of 0.10%, above the legal limit for driving in most places.

3. A sleepless night with only four hours of sleep resulted in a 70% reduction in the activity of your natural killer cells (which combat infections and cancer). Remarkably, the activity of natural killer cells returns to baseline levels after one night of normal sleep.

Sleep doesn't get the respect it deserves. It's often the first thing people sacrifice to make time for almost anything else, whether leisure or work. But the popular belief that "you can sleep when you're dead" is fundamentally damaging to your health, happiness, and longevity.

For example, regularly getting fewer than six or seven hours of sleep each night [doubles your risk of cancer and can increase the likelihood that you'll develop Alzheimer's disease](#). Insufficient sleep can also [contribute to major psychiatric conditions](#) such as anxiety and depression.

One key lesson from Walker is if humans had been able to evolve with the ability to get along with less sleep, then we would have. We are most vulnerable to predation and least productive while we sleep. Yet evolutionarily our bodies retained the need for eight hours.

Read More: [How to Stop Checking Your Phone Every 10 Seconds](#)

Insufficient sleep can have serious [metabolic](#) and [hormonal](#) consequences. When individuals are sleep-deprived, the body essentially enters a state of malnutrition. "If you take the mentality of 'I'll sleep when I'm dead,' ironically, you will have both a shorter life and the quality of that life will be significantly worse as a consequence," Walker said onstage at our longevity conference this year. He then highlighted a study where young, healthy men were restricted to five hours of sleep for five nights. The result? Their [testosterone levels dropped](#) to the equivalent of someone 10 years older. "Five hours a night for five nights will age a man by a decade," Walker emphasized, noting that this also affects female reproductive hormones such as estrogen and progesterone.

Sleep deprivation also leads to cognitive and metabolic impairments. A study that restricted people to four hours of sleep for four nights found that these individuals, previously with normal blood sugar, became classified as prediabetic by the end of the trial. This underscores the profound metabolic toll that insufficient sleep can take in a very short time.

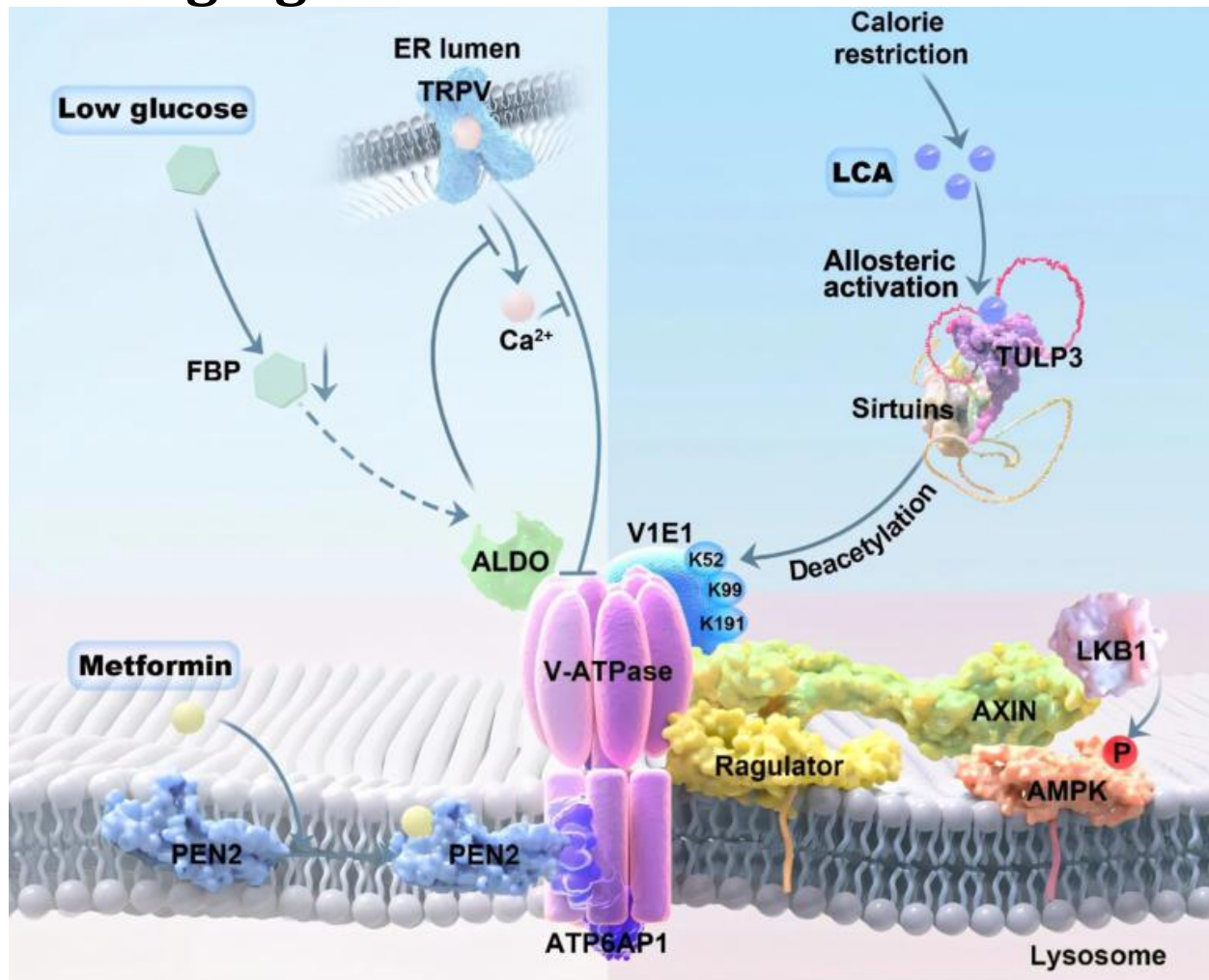
Convinced yet? Here are 9 tips for optimizing your sleep.

1. **Aim for 7-9 hours:** Anything less than 7 hours of sleep can lead to significant metabolic, cognitive, and cardiovascular impairments.
2. **Improve sleep efficiency:** Walker emphasizes that efficiency is crucial. You can get a sense of yours through sleep trackers like Oura or WHOOP. Anything less than 85% (time spent in bed sleeping versus awake) needs attention.

3. **Maintain regular sleep patterns:** Regularity is more important than quantity when it comes to long-term health benefits. Walker recommends going to bed and waking up at the same time every day, with only a +/- 25-minute variance.
4. **Align your sleep with your chronotype:** Everyone has a chronotype—whether they're a morning person or a night owl. Your goal should be to gradually adjust to a healthy sleep schedule that respects your natural tendencies. For example, if you're a night owl, start with a bedtime close to when you feel naturally drowsy, like 11:30 PM, and gradually shift it earlier by 15-30 minutes every few nights.
5. **Time your exercise right:** For optimal sleep quality, it's best to finish exercise 90 minutes before bed, allowing your body enough time to cool down.
6. **Eat at the right times, too:** It's best to finish eating at least two hours before bed, giving your body time to digest and reducing indigestion during sleep.
7. **Manage stress before sleep:** To avoid "tired and wired" syndrome before bed, consider journaling, taking a hot shower, meditation, or catching up with a friend.
8. **Practice good sleep hygiene:** An hour before bedtime, lower the lights in your room by 70%. If you need to use your phone, do it only while standing, and put it away when you lie down. Remove clocks from view to avoid watching the time pass.
9. **Monitor yourself for sleep apnea:** Sleep apnea, a condition where breathing repeatedly stops and starts during sleep, reduces oxygen levels and can lead to increased risks of heart disease, diabetes, and cognitive decline. Your doctor can order a sleep study, or you can use tools like the SnoreLab app to track signs like loud snoring or gasping for air. If symptoms appear, seek professional evaluation.

Excerpted from [Longevity Guidebook: How to Slow, Stop, and Reverse Aging — and NOT Die from Something Stupid](#)

Research reveals a molecule that may help slow aging while on a restricted diet



Schematic diagram showing that the v-ATPase serves as a common entry into the lysosomal AMPK pathway. Credit: Nature (2024). DOI: 10.1038/s41586-024-08348-2

A multi-institutional team from China and the U.S. has identified a molecule that may play a role in slowing the aging process in some animals consuming a restricted diet. The team has published [two papers](#) on their work in the journal *Nature*.

David Sinclair with Harvard Medical School has published a [News & Views piece](#) in the same journal issue giving a short history of the search for factors involved in health promotion associated with restricted diets and the work by the team on this new effort.

Prior research has shown that adhering to a low-calorie diet can promote health. Other research has also suggested restricted feeding can extend the lifespan of some animals, such as fruit flies and nematodes. Testing for such an effect in humans has proven to be too difficult, however, due to the long average human lifespan, leading medical researchers to look elsewhere for evidence.

One such avenue of research has been the study of molecules in the gut. For this new study, the team focused their efforts on lithocholic acid (LCA), a bile acid created by bacteria in the gut.

Prior research had suggested that LCA was a toxin, but more recently, researchers have found that in low doses, it can provide health benefits. Mice given LCA in low doses, for example, were found to produce more of a protein called AMPK, which has been linked to slowing muscle atrophy.

The work involved tracking changing levels of metabolites in the mouse gut when the mouse is put on a restricted diet. The researchers found hundreds of them. They then fed mouse cells the metabolites and found that LCA was a main driver of activation. That, the researchers suggest, hints at the possibility that LCA is the acid behind some of the health benefits seen by mice on restricted diets—but not their lifespan. They found no evidence of that in their testing.

That led them to conduct a second study to learn more about how LCA activates AMPK. They found that activation was dependent on signaling from certain members of the enzyme family called sirtuins. But that was as far as they got. The team plans to continue their research, hoping to pin down the benefits of LCA to humans, if there are any, or to find other metabolites that might be involved.

More information: Qi Qu et al, Lithocholic acid binds TULP3 to activate sirtuins and AMPK to slow down ageing, *Nature* (2024). DOI: [10.1038/s41586-024-08348-2](https://doi.org/10.1038/s41586-024-08348-2)

Qi Qu et al, Lithocholic acid phenocopies anti-ageing effects of calorie restriction, *Nature* (2024). DOI: [10.1038/s41586-024-08329-5](https://doi.org/10.1038/s41586-024-08329-5)

David A. Sinclair, A bile acid could explain how calorie restriction slows ageing, *Nature* (2024). DOI: [10.1038/d41586-024-04062-1](https://doi.org/10.1038/d41586-024-04062-1)

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Scientists Discover “Mortality Timer” Inside Our Cells

Cornell researchers found that smaller nucleoli in cells could slow aging and extend lifespan, a principle evident in yeast but applicable to humans, offering a potential pathway for new longevity therapies.

Smaller nucleoli slow aging, acting as a “mortality timer,” while larger nucleoli lead to cell death by destabilizing rDNA.

The secret to cellular youth may lie in maintaining a small nucleolus—a dense structure within the cell nucleus—according to investigators at [Weill Cornell Medicine](#). These findings were uncovered in yeast, a model organism renowned for its role in making bread and beer, yet surprisingly similar to humans at the cellular level.

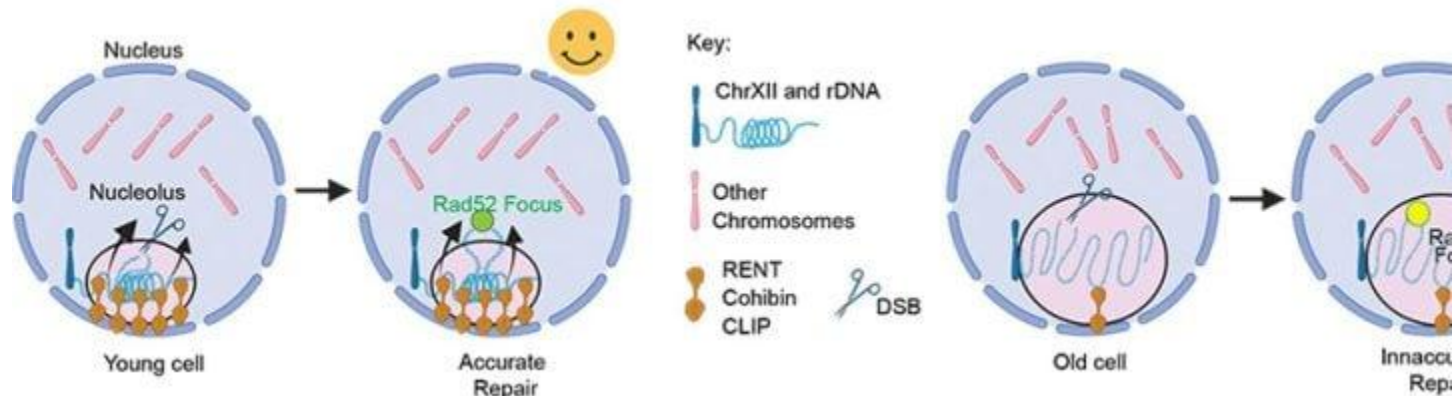
The study, published Nov. 25 in *Nature Aging*, may lead to new longevity treatments that could extend human lifespan. It also establishes a mortality timer that reveals how long a cell has left before it dies.

As people get older, they are more likely to develop health conditions, such as cancer, cardiovascular disease and neurodegenerative diseases.

“Aging is the highest risk factor for these diseases,” said Dr. Jessica Tyler, professor of pathology and laboratory medicine at Weill Cornell Medicine. “Rather than treating each disease separately, a better approach would be to develop a therapeutic or supplement that will delay the onset of diseases by preventing the underlying molecular defects that cause them.” The nucleolus may hold the key.

Small Packages

The nucleus holds the cell’s chromosomes and the nucleolus where the ribosomal DNA (rDNA) is housed. The nucleolus isolates the rDNA which encodes the RNA portions of the ribosomes, the protein-building machinery. The rDNA is one of the most fragile parts of the genome, due to its repetitive nature making it more difficult to maintain and fix if damaged. If damage in the rDNA is not accurately repaired, it can lead to chromosomal rearrangements and cell death.



This model of the nucleus with nucleolus (pink) shows how ribosomal DNA is correctly repaired in young cells. In old cells with enlarged nucleolus, however, DNA repair is inaccurate leading to faster cell death. Credit: Tyler Lab

In organisms from yeast to worms to humans, nucleoli expand during aging. On the flip side, anti-aging strategies like calorie restriction, or eating less, result in smaller nucleoli. “Calorie restriction does so many different things, and no one knows the precise way that it is extending lifespan,” Dr. Tyler said.

Dr. Tyler and postdoctoral fellow Dr. J. Ignacio Gutierrez, the first author of the paper, suspected that keeping nucleoli small could delay aging. To test this idea, they engineered an artificial way to secure rDNA to the membrane surrounding the nucleus of yeast cells so they could control when it was anchored and when it was not. “The advantage of our system is that we could isolate the nucleolus size from all of the other effects of anti-aging strategies,” Dr. Gutierrez said.

The researchers discovered that tethering the nucleolus was enough to keep it compact, and small nucleoli delayed aging to about the same extent as calorie restriction.

Final Moments

Interestingly, nucleoli did not expand at the same rate during the entire lifespan as cells aged. They remained small for most of the yeast’s life, but at a nucleolar size threshold, the nucleoli suddenly began to grow quickly and expand to a much larger size. Cells only survived for an average of about five more cell divisions after hitting this threshold.

“When we saw it wasn’t a linear size increase, we knew something really important was happening,” said Dr. Gutierrez. Passing the threshold appears to serve as a mortality timer, ticking down the final moments of a cell’s life.

During aging, DNA accumulates damage, some of which can be devastating to the cell. In tests, the team found that large nucleoli had less stable rDNA than smaller ones. Also, when the structure is large, proteins and other factors that are usually excluded

from the nucleolus are no longer kept out. It's as if the nucleolus becomes leaky, letting in molecules that can wreak havoc on the fragile rDNA.

"The whole point of condensates is to separate biological reactions to help them work efficiently, but now when you have other proteins coming into the nucleolus, it leads to genome instability, which triggers the end of the lifespan," Dr. Tyler said. These proteins can cause catastrophic problems, such as chromosomal rearrangements, to build up.

Next, the researchers plan to study nucleolar effects on aging in human stem cells. Stem cells are special because they have the potential to replace other cell types as they die. But eventually, the stem cells stop dividing, so the researchers hope to use the knowledge gained from this project to make them last longer.

"I was excited that we could connect the structure of the nucleolus with the repair process in a way that could be conserved from yeast to humans," said Dr. Gutierrez.

Reference: "A mortality timer based on nucleolar size triggers nucleolar integrity loss and catastrophic genomic instability" by J. Ignacio Gutierrez, and Jessica K. Tyler, 25 November 2024, *Nature Aging*.

DOI: [10.1038/s43587-024-00754-5](https://doi.org/10.1038/s43587-024-00754-5)

Stem Cell Technology Rejuvenates Old Human Cells by Wiping Their DNA Clean

Old human cells return to a more youthful and vigorous state after being induced to briefly express a panel of proteins involved in embryonic development, according to a new study by researchers at the Stanford University School of Medicine.

The researchers also found that elderly mice regained youthful strength after their existing muscle stem cells were subjected to the rejuvenating protein treatment and transplanted back into their bodies.

The proteins, known as Yamanaka factors, are commonly used to transform an adult cell into what are known as induced pluripotent stem cells, or iPS cells. Induced pluripotent stem cells can become nearly any type of cell in the body, regardless of the cell from which they originated. They've become important in regenerative medicine and drug discovery.

The study found that inducing old human cells in a lab dish to briefly express these proteins rewinds many of the molecular hallmarks of aging and renders the treated cells nearly indistinguishable from their younger counterparts.

"When iPS cells are made from adult cells, they become both youthful and pluripotent," said Vittorio Sebastiano, Ph.D., assistant professor of obstetrics and gynecology and

the Woods Family Faculty Scholar in Pediatric Translational Medicine. “We’ve wondered for some time if it might be possible to simply rewind the aging clock without inducing pluripotency. Now we’ve found that, by tightly controlling the duration of the exposure to these protein factors, we can promote rejuvenation in multiple human cell types.”

Sebastiano is the senior author of the study, which will be published online today (March 24, 2020) in *Nature Communications*. Former graduate student Tapash Sarkar, Ph.D., is the lead author of the article.

“We are very excited about these findings,” said study co-author Thomas Rando, MD, Ph.D., professor of neurology and neurological sciences and the director of Stanford’s Glenn Center for the Biology of Aging. “My colleagues and I have been pursuing the rejuvenation of tissues since our studies in the early 2000s revealed that systemic factors can make old tissues younger. In 2012, Howard Chang and I proposed the concept of using reprogramming factors to rejuvenate cells and tissues, and it is gratifying to see evidence of success with this approach.” Chang, MD, Ph.D., is a professor of dermatology and of genetics at Stanford.

Exposure to proteins

Researchers in Sebastiano’s laboratory make iPS cells from adult cells, such as those that compose skin, by repeatedly exposing them over a period of about two weeks to a panel of proteins important to early embryonic development. They do so by introducing daily, short-lived RNA messages into the adult cells. The RNA messages encode the instructions for making the Yamanaka proteins. Over time, these proteins rewind the cells’ fate — pushing them backward along the developmental timeline until they resemble the young, embryonic-like pluripotent cells from which they originated.

During this process the cells not only shed any memories of their previous identities, but they revert to a younger state. They accomplish this transformation by wiping their DNA clean of the molecular tags that not only differentiate, say, a skin cell from a heart muscle cell, but of other tags that accumulate as a cell ages.

Recently researchers have begun to wonder whether exposing the adult cells to Yamanaka proteins for days rather than weeks could trigger this youthful reversion without inducing full-on pluripotency. In fact, researchers at the Salk Institute for Biological Studies found in 2016 that briefly expressing the four Yamanaka factors in mice with a form of premature aging extended the animals’ life span by about 20%. But it wasn’t clear whether this approach would work in humans.

Sarkar and Sebastiano wondered whether old human cells would respond in a similar fashion, and whether the response would be limited to just a few cell types or generalizable for many tissues. They devised a way to use genetic material called

messenger RNA to temporarily express six reprogramming factors — the four Yamanaka factors plus two additional proteins — in human skin and blood vessel cells. Messenger RNA rapidly degrades in cells, allowing the researchers to tightly control the duration of the signal.

The researchers then compared the gene-expression patterns of treated cells and control cells, both obtained from elderly adults, with those of untreated cells from younger people. They found that cells from elderly people exhibited signs of aging reversal after just four days of exposure to the reprogramming factors. Whereas untreated elderly cells expressed higher levels of genes associated with known aging pathways, treated elderly cells more closely resembled younger cells in their patterns of gene expression.

When the researchers studied the patterns of aging-associated chemical tags called methyl groups, which serve as an indicator of a cell's chronological age, they found that the treated cells appeared to be about 1½ to 3½ years younger on average than untreated cells from elderly people, with peaks of 3½ years (in skin cells) and 7½ years (in cells that line blood vessels).

Comparing hallmarks of aging

Next they compared several hallmarks of aging — including how cells sense nutrients, metabolize compounds to create energy, and dispose of cellular trash — among cells from young people, treated cells from old people and untreated cells from old people.

“We saw a dramatic rejuvenation across all hallmarks but one in all the cell types tested,” Sebastiano said. “But our last and most important experiment was done on muscle stem cells. Although they are naturally endowed with the ability to self-renew, this capacity wanes with age. We wondered, Can we also rejuvenate stem cells and have a long-term effect?”

When the researchers transplanted old mouse muscle stem cells that had been treated back into elderly mice, the animals regained the muscle strength of younger mice, they found.

Finally, the researchers isolated cells from the cartilage of people with and without osteoarthritis. They found that the temporary exposure of the osteoarthritic cells to the reprogramming factors reduced the secretion of inflammatory molecules and improved the cells' ability to divide and function.

The researchers are now optimizing the panel of reprogramming proteins needed to rejuvenate human cells and are exploring the possibility of treating cells or tissues without removing them from the body.

“Although much more work needs to be done, we are hopeful that we may one day have the opportunity to reboot entire tissues,” Sebastiano said. “But first we want to make sure that this is rigorously tested in the lab and found to be safe.”

Reference: “Transient non-integrative expression of nuclear reprogramming factors promotes multifaceted amelioration of aging in human cells” by Tapash Jay Sarkar, Marco Quarta, Shravani Mukherjee, Alex Colville, Patrick Paine, Linda Doan, Christopher M. Tran, Constance R. Chu, Steve Horvath, Lei S. Qi, Nidhi Bhutani, Thomas A. Rando and Vittorio Sebastiano, 24 March 2020, *Nature Communications*. DOI: [10.1038/s41467-020-15174-3](https://doi.org/10.1038/s41467-020-15174-3)

Other Stanford co-authors are former postdoctoral scholar Marco Quarta, Ph.D.; postdoctoral scholar Shravani Mukherjee, Ph.D.; graduate student Alex Colville; research assistants Patrick Paine, Linda Doan and Christopher Tran; Constance Chu, MD, professor of orthopedic surgery; Stanley Qi, Ph.D., assistant professor of bioengineering and of chemical and systems biology; and Nidhi Bhutani, Ph.D., associate professor of orthopedic surgery.

Researchers from the Veterans Affairs Palo Alto Health Care System, the University of California-Los Angeles and the Molecular Medicine Research Institute in Sunnyvale, California, also contributed to the study.

The research was supported by the National Institutes of Health (grants R01 AR070865, R01 AR070864, P01 AG036695, R01 AG23806, R01 AG057433 and R01 AG047820), the Glenn Foundation for Medical Research, the American Federation for Aging Research and the Department of Veterans Affairs.

Sarkar, Quarta and Sebastiano are co-founders of the startup Turn Biotechnologies, a company that is applying the technology described in the paper to treat aging-associated conditions. Rando is a member of the scientific advisory board.

Telomeropathies: here is a cause of accelerated aging 🕒

Published by Adrien, November 14, 2024 at 08:00 AM

The ends of chromosomes, called telomeres, shorten with age. They function like a molecular clock for the cell. Premature shortening of these DNA sequences is the cause of genetic diseases: telomeropathies, the cause of which remains undetermined in many cases.

In an article published in *Genes and Development*, scientists have identified a new gene responsible for these diseases and partially reveal its function.



Telomeres are repeated DNA sequences located at the ends of chromosomes and play an essential role in genome stability. They naturally shorten over time and are therefore involved in many biological processes such as aging and tumorigenesis.

Premature shortening of these sequences is also the cause of genetic diseases (or telomeropathies) such as Dyskeratosis Congenita, bone marrow failure, idiopathic pulmonary fibrosis... In approximately 40% of cases, the genetic cause of these diseases remains uncharacterized.

RPA2, a new gene associated with telomeropathies

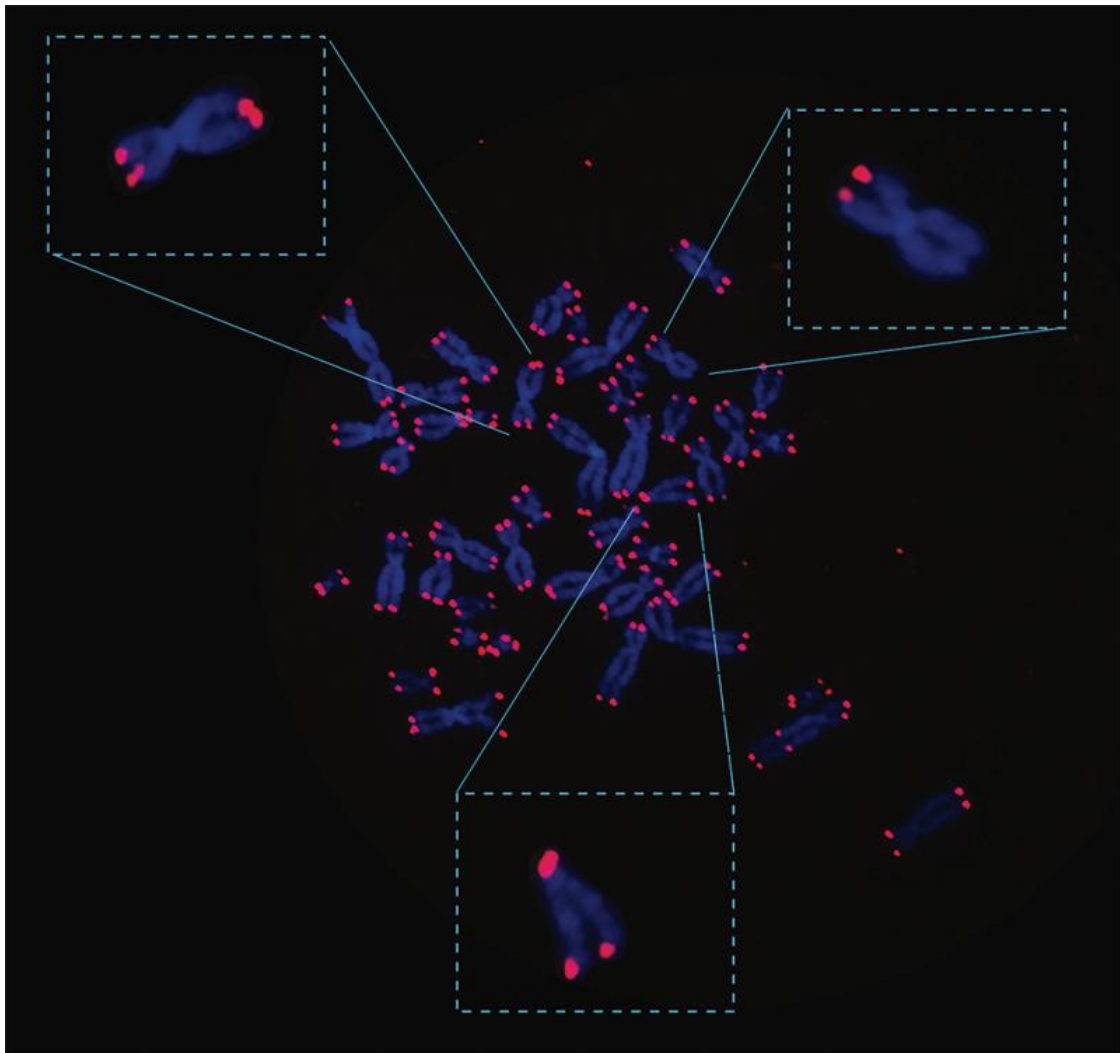
In an article published in the journal *Genes and Development*, scientists identified in two patients with pulmonary fibrosis a rare heterozygous variation in the RPA2 gene, which codes for one of the subunits of the RPA (Replication Protein A) complex.

RPA is a heterotrimeric protein complex (RPA1/2/3) that binds to DNA and is involved in genome replication and repair, and potentially in telomere replication. These patients also showed abnormally short telomeres and signs of premature aging.

Understanding its function for better disease management

The scientists then studied the impact of this mutation on telomere stability using human cell lines genetically modified with molecular scissors (CrispRCas9). They demonstrated that the mutation in the RPA2 gene is indeed responsible for the disease and the shortening of telomeres in these patients. Moreover, they managed to highlight the role of RPA in telomere replication in humans.

This work indicates that variations in the *RPA* genes should be carefully considered in the presence of symptoms associated with telomeropathies, in order to anticipate the potential development of pulmonary fibrosis, progressive bone marrow failure, liver



disease, or other conditions linked to premature aging.

Metaphase spread of a nucleus from a genetically modified cell. This cell carries the same mutation in its genome as that identified in the RPA2 gene in patients with telomeropathies. The arms of the chromosomes are stained blue and the telomeres red. Under normal conditions, a telomeric signal is detected at the end of each chromosome arm. Cells with a mutation in the RPA2 gene show a high proportion of telomeric abnormalities such as fusions, losses, and multi-telomeric signals.
© Rima Kochman and Stéphane Coulon

Reference:

Kochman R, Ba I, Yates M, et al. Heterozygous RPA2 variant as a novel genetic cause of telomere biology disorders. *Genes Dev.* 2024;38(15-16):755-771. Published 2024 Sep 19. doi:[10.1101/gad.352032.124](https://doi.org/10.1101/gad.352032.124)

Tardigrade proteins found to slow human cell metabolism

Tardigrade proteins found to slow human cell metabolism© Provided by Interesting Engineering

Scientists have been baffled by tardigrades' capacity to withstand drying out since they exhibit a behavior that seems distinct from that of several other organisms that can enter biostasis or suspended animation.

A new study has suggested that proteins discovered in resilient tardigrades, known for their remarkable indestructibility, might hold promise as a crucial component in slowing down the [aging](#) process in humans.

Tardigrades, also called water bears, are tiny animals less than half a millimeter long. They can withstand extreme temperatures and even the vacuum of space.

Researchers from the University of Wyoming (UW) have deepened their understanding of how tardigrades endure harsh environments. They have demonstrated that proteins from these [microscopic](#) creatures can decelerate molecular processes when introduced into human cells.

The details of the [study](#) were published in the journal *Protein Science*.

Focus on tardigrade proteins

Tardigrades are tiny organisms capable of enduring harsh conditions by morphing into dehydrated balls and nearly halting their metabolisms. Researchers say they rely on naturally disordered CAHS proteins for survival when dried out. These proteins enable their survival and prevent drying-induced disruptions in laboratory settings and other organisms.

The organisms can also withstand being completely dried out, frozen to a temperature just above absolute zero (minus 458 degrees Fahrenheit, when all molecular motion ceases), heated to a temperature higher than 300 degrees Fahrenheit, and exposed to radiation thousands of times higher than humans could tolerate.

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The study looks at the processes tardigrades utilize to go into and out of suspended animation in response to environmental stress. Scientists specifically examined CAHS D, a tardigrade [protein](#) that adopts a gel-like form when introduced to human cells.

The team noticed that CAHS D creates networks of fibers in living organisms when there's osmotic stress. These fiber networks help cells survive when they're shocked by changes in their environment. Two important things happen with these fibers: they stop cells from changing size and slow down how fast cells use energy during the shock.

"Amazingly, when we introduce these proteins into human cells, they gel and slow down metabolism, just like in tardigrades. Furthermore, just like tardigrades, when you put human cells that have these proteins into biostasis, they become more resistant to stresses, conferring some of the tardigrades' abilities to the human cells," said Sanchez-Martinez, a member of UW lab and the lead author of the study, in a [statement](#).

A reversible process

In more crucial findings, the team could also demonstrate that the entire process is reversible. Once the stress is alleviated, the gels formed by the tardigrades dissolve, and human cells revert to their regular metabolism.

"Our findings provide an avenue for pursuing technologies centered on the induction of biostasis in cells and even whole organisms to slow aging and enhance storage and stability," said the team in the study.

Previous research by the team suggests that an essential medication for patients with hemophilia and other disorders can be preserved using natural and synthetic tardigrade proteins. Remarkably, refrigeration is not required for stabilization.

Researchers claim that the study adds to the body of evidence suggesting that tardigrade proteins may one day be employed to improve the preservation of cell-based therapies like stem cells and enable access to life-saving medications for patients in areas without refrigeration.

Study Abstract

Tardigrades are microscopic animals that survive desiccation by inducing biostasis. To survive drying, tardigrades rely on intrinsically disordered CAHS proteins, which also function to prevent perturbations induced by drying in vitro and in heterologous systems. CAHS proteins have been shown to form gels both in vitro and in vivo, which has been speculated to be linked to their protective capacity. However, the sequence features and mechanisms underlying gel formation and the necessity of gelation for protection have not been demonstrated. Here, we report a mechanism of fibrillization and gelation for CAHS D that is similar to that of intermediate filament assembly. We show that in

vitro gelation restricts molecular motion, immobilizing and protecting labile material from the harmful effects of drying. In vivo, we observe that CAHS D forms fibrillar networks during osmotic stress. Fibrillar networking of CAHS D improves the survival of osmotically shocked cells. We observe two emergent properties associated with fibrillization: (i) prevention of cell volume change and (ii) reduction of metabolic activity during osmotic shock. We find that there is no significant correlation between maintenance of cell volume and survival, while there is a significant correlation between reduced metabolism and survival. Importantly, CAHS D's fibrillar network formation is reversible, and metabolic rates return to control levels after CAHS fibers are resolved. This work provides insights into how tardigrades induce reversible biostasis through the self-assembly of labile CAHS gels.

The strange reason why your body ages most rapidly between 44 and 60—and how to combat it

[Aging](#) is not a slow, linear process, according to new research from Stanford researchers.

In fact, [aging](#), particularly metabolism slowing and skin wrinkling, may happen in what scientists describe as “[age-related waves](#)” versus a steady climb. The study published in the *Nature Aging* journal found that the body's molecules and the microbes and bacteria that make up the gut microbiome experience rapid change at two key intervals: Age 44 and 60.

“We’re not just changing gradually over time; there are some really dramatic changes,” Michael Snyder, PhD, professor of genetics at Stanford University and one of the study's researchers, said in the [university's press coverage](#). “It turns out the mid-40s is a time of dramatic change, as is the early 60s. And that's true no matter what class of molecules you look at.”

Molecular change, when the molecules and microbes increase or decrease the most, impacts the body's risk of chronic disease, the ability to fight off disease, and the pace of aging, per the study. The changes in people's 40s were closely tied to heart disease, skin and muscle function, and how people metabolize caffeine, fat, and alcohol. The molecular changes in peoples' 60s play a role in

oxidative stress, immune health, heart disease, [caffeine](#) metabolism, kidney disease, and [skin](#) and muscle aging. It is in line with the [12 hallmarks of aging](#), such as [chronic inflammation](#) and cellular senescence, that happen on a molecular level as people grow older. It also explains how older adults experience a higher sensitivity to alcohol, gain weight, and experience age-related muscle loss.

Researchers studied over 100 volunteers between the ages of 25 and 75 who donated blood or provided biological samples every few months over nearly two years, assessing changes in over 135,000 molecules and microbes. The authors concluded that a vast majority of the molecules and microbes, 81%, did not change in a linear fashion as the individual aged. The most rapid changes were in the mid-40s and early 60s for both men and women.

"This suggests that while [menopause or perimenopause](#) may contribute to the changes observed in women in their mid-40s, there are likely other, more significant factors influencing these changes in both men and women," said Xiaotao Shen, PhD, an author of the study and assistant professor at Nanyang Technological University Singapore, in Stanford's news release. "Identifying and studying these factors should be a priority for future research."

While the underlying mechanisms of why rapid molecular change happens at these two key intervals is largely unknown and the study only captured data after a two-year follow up, it sends a message to pay particular attention to [prioritizing your health as you hit mid-life](#) to battle some of the molecular changes that are out of your control.

This means regular resistance training to counter muscle loss, [moving daily](#) to offset the risk of heart disease, and eating nutritious, filling whole foods to combat the metabolism dip.

Top aging expert says these 4 FDA-approved drugs hold promise for extending life

October 29, 2024

“The evidence that we're looking for is from clinical trials, not if it cured an animal and not if people who took it told me that they're doing better,” says Dr. Nir Barzilai.

There's not a cure-all drug to help us [live longer](#).

Dr. Nir Barzilai, the director of the Institute for Aging Research at the Albert Einstein College of Medicine and board member at The American Federation for Aging Research (AFAR), predicts it will take a few decades to see impactful gerotherapeutics—drugs that counter the aging process—for the average person. The key is discovering safe and effective drugs that target mechanisms, like [inflammation](#) and cellular damage, that lead to aging.

GLP-1s

Barzilai and other experts have pointed to [GLP-1s](#) (Ozempic, Wegovy), the wildly popular class of drugs targeting [diabetes](#) and obesity, as potential [longevity boosters](#).

“It was developed for diabetes, and it was shown to actually decrease obesity,” says Barzilai, who adds there is evidence of a reduced risk of heart disease, kidney disease, Parkinson's, and [Alzheimer's](#). The drugs scored a 10 out of 12 on the gerotherapeutic scale. “It actually targets the mechanisms of aging.”

Dr. Douglas Vaughan, a professor of medicine at Northwestern University and director of the Potocsnak Longevity Institute, previously

told [Fortune](#) that extensive research on animals has found [calorie restriction](#) to be the most effective way to extend life.

GLP-1s suppress appetite and have been shown to improve blood sugar levels for those with type 2 diabetes. They may also play a larger role in chronic disease mitigation and reducing inflammation, although more long-term evidence is needed to also ensure that you can lose weight but not muscle weight.

SGLT2 inhibitors

SGLT2 inhibitors, blood-sugar-lowering drugs, are the only drugs on the list scoring a perfect score on Barzilai's scale. The inhibitors are typically prescribed for those with type 2 diabetes to remove [sugar](#) from the kidneys through urine, which lowers blood sugar levels.

The drugs, while used to treat diabetes, show promise in reducing the risk of age-related diseases and kidney disease, by reducing oxidative stress and inflammation, and improving heart health and even cognition. [New research](#) also suggests the inhibitors may reduce the risk of dementia in people with type 2 diabetes after longer-term use.

Bisphosphonates

Bisphosphonates, scoring 11 out of 12, treat osteoporosis, which affects 10 million Americans. They are prescribed to those with the condition to reduce the loss of bone density.

“Since their introduction to clinical practice, bisphosphonates have transformed the clinical care of an array of skeletal disorders,” [reads](#) one paper published in the [Mayo Clinic Proceedings](#).

Observational studies also suggest the drugs reduce mortality. [One analysis](#) found people using bisphosphonates were 15% less likely to die than nonusers after a 2.8 year follow up.

Metformin

Metformin, which has been around for 60 years, is the [most prescribed type 2 diabetes drug](#). Studies also show that the drug, scoring an 11 out of 12 as a gerotherapeutic, targets hallmarks of aging like cellular senescence by protecting DNA, decreasing inflammation, and improving insulin sensitivity, according to a paper in the *Aging and Disease* journal.

However, researchers note that while metformin makes the list as a possible anti-aging drug, the results in nondiabetic patients are not as understood.

More broadly, while research suggests that any of these drugs may target mechanisms of aging, they are not approved for anti-aging alone, and eligible candidates are those who typically present with one or more preexisting conditions.

“Every drug has some contraindication or side effects,” Barzilai says. “You just have to know who’s the right patient.”

People should speak with a provider about their health status, drug interactions, and whether any of these are an appropriate remedy. And still, the main pillars of healthy aging are lifestyle changes, especially for healthy, young people, Barzilai says.

“Not every drug that’s good for old people is good for young people, but the things that are good for young and old are exercise, diet, sleep, and social connectivity,” Barzilai says. “You can always maximize that.”

Still, he says it won’t be lifestyle alone that will be able to dramatically extend human life span.

Will you live to 150? Here's what 5 geneticists and aging researchers say

October 6, 2024

"We want to spend our time treating our health, rather than spend our time treating a disease," says leading geneticist Dr. Nir Barzilai.

WESTEND61—GETTY

At the turn of the 20th Century, one could expect to live until 47 in the U.S. Now, medical advancements, like vaccines and antibiotics, and public health initiatives have increased life expectancy in the U.S. to 77 years old and 73 globally.

While health conditions and systemic barriers like socioeconomic inequities and environmental conditions play a role in [how long you live](#), researchers are finding that through individual lifestyle modifications and [precision medicine](#), there are ways to counter the [mechanisms behind aging](#) to potentially help people live even longer and healthier.

"Healthy longevity medicine is not science fiction anymore," Dr. Andrea Maier, a professor in medicine and functional aging at the National University of Singapore and the founding president of the Healthy Longevity Medicine Society, told *Fortune* at the [Longevity Investors Conference](#) in Gstaad, Switzerland last month. "We understand why we age. We understand, especially through [life interventions](#), how to intervene."

The idea that we play a role in how well we age has led to a proliferation of biohackers or [longevity optimists](#) confident they will live to 150—and even beyond—because they are willing to experiment with the latest interventions to optimize health. [Kayla Barnes](#), CEO of LYV Wellness, an LA-based longevity clinic, previously told *Fortune* she hopes to live 150 healthy years alongside her husband. At the same time, the entrepreneur

turned biohacker [Bryan Johnson](#) doesn't have a goal age but is preaching his motto "[Don't die](#)" for as long as possible.

But how long will it *really* be possible to live, according to available science?

How long can we expect to live?

Those under 50, who will have the most time to take advantage of emerging research, therapeutics, and interventions, can likely expect to live up to 100, says Dr. Evelynne Bischof, an internal medicine physician, oncologist, and vice president of the Healthy Longevity Medicine Society.

Alina Su, an aging researcher at The Conboy Laboratory at UC Berkeley and a biomedical PhD candidate at Harvard, is even more hopeful.

"Living well beyond 100—potentially up to 120 or more— isn't just a dream. It can be a reality for those who are serious about optimizing their health," says Su, cofounder of Generation Lab, a precision medicine company. "With the rapid pace of innovation in anti-aging research, we're seeing new therapies, gene editing, personalized medicine, and other things that will push the upper limits of human lifespan."

The world's leading geneticist, Dr. Nir Barzilai, who is the director of the Institute for Aging Research at the Albert Einstein College of Medicine, tells *Fortune* that while he cannot predict society's potential longevity, the maximum human life span is around 115 years today (the woman thought to be the oldest person in the world died at 122 in 1997). Barzilai says how much longer we can live depends on the efficacy of the evolving aging research coming to light in the next few decades.

"Aging drives age-related disease. Therefore, you want to stop aging, and so we want to spend our time treating our health, rather than spend our time treating a disease," says Barzilai, who also holds titles as a board member at the American Federation for Aging Research (AFAR) and

investigator of the AFAR SuperAgers Family Study. “We know we can target aging ... depends how fast funding can accelerate it.” He emphasizes that educating the public on ways to intervene will make a difference in meaningfully extending life.

To live past 100 today, Barzilai says it’s about following basic guidelines around exercise, nutrition, and managing stress while also keeping an eye on the next frontier of longevity science—which he believes to be a combination of precision medicine, [AI interventions](#), and gerotherapeutics or drugs to target the underlying processes of aging.

Still, Barzilai, Bischof, and Maier, who are working to create standards in the field of longevity medicine, say it’s much more about how well you live than how long you live.

“The question is, will they live up to 100 in good health, or will the last usually 20% see a significant decline in function?” says Bischof, who also spoke at the Longevity Investors Conference. Closing the healthspan-lifespan gap is the most imperative, she adds.

The health optimizers

Those who will substantially extend life and close the healthspan-lifespan gap will treat their body like a “[top sport](#),” Maier says. “I really think that we should not treat our body as a snapshot, but a story and the story can only be written if you have more words, which means that you should test the body continuously,” she says, touting the growing field of precision geromedicine (therapeutics to tackle aging depending on a person’s biomarkers and genetic makeup), which requires testing and tracking to influence habits. The most common types of tracking include wearing a glucose monitor, sleep tracker, and activity monitor.

Right now, partaking in the craze to extend life is reserved for those with the time and financial resources to pay out of pocket for additional testing, wearables, and subscription-based longevity clinics.

“For today’s under-50 population, the key lies in how much they’re willing to invest in their health now. The more proactive individuals are, the more years they’re likely to add to their lives,” Su says. “In essence, we’re entering an era where personal health choices could lead to dramatically different outcomes. The decision to optimize one’s health today could mean the difference between a standard lifespan and an extended, vibrant life well past the century mark.”

Dr. Matthew Pywell, who founded the [Apex Medical Academy](#), which educates health professionals on preventative health care and healthy aging, says that while we know that it’s possible to hit that 120 mark as a species, the question will be how to deliver longevity interventions to the masses and not merely the 1%.

Those at the forefront of longevity equity are looking to put healthy aging innovations into health care systems and meet people where they are—although it’s clear there is a long way to go to ensure that longevity medicine doesn’t exacerbate existing inequalities.

“There are lots of private clinics. We now understand that we have to educate not only physicians but also all other healthcare professionals. We have to educate laymen and then really bring this new model of medicine into clinical care to really change the health trajectory [of more people],” Maier says.

How to increase your odds of becoming a ‘SuperAger’

August 11, 2024

SuperAgers have brains comparable to those 20 years their junior.

Some people have won the [longevity](#) lottery—they are among the lucky few known as [SuperAgers](#).

In a relatively new field, researchers are examining what contributes to people in their 80s and 90s having [stronger brain power](#) than their peers. Many are wondering if those findings can be distilled into a longevity routine or pill to help everyone become a SuperAger. Is it possible to increase your odds of becoming a SuperAger?

“It’s not inevitable that we will become disabled and sick as we get older. What we’re learning from these unique individuals is that it is biologically plausible for us to live long and healthy,” says Dr. Sofiya Milman, the director of the Human Longevity Studies at Einstein’s Institute for Aging Research and the lead investigator of the [SuperAgers Family Study](#), which has enrolled 550 SuperAgers since 2022. “Once we know what causes longevity, that it’s not a disease, we can then create therapies that will promote that biological longevity, and ultimately, that’s the goal of what we’re doing.”

What is a SuperAger?

There isn’t a single definition of a SuperAger.

According to the [SuperAgers Family Study](#) funded by the American Federation for Aging Research, anyone over 95 years old who has a healthy cognitive capacity and the capabilities to consent to the study is

considered a SuperAger. Researchers at the [SuperAging Research Initiative at Northwestern](#) define it as anyone in their 80s or 90s who has the brain capacity of someone in their 50s or 60s as measured by cognitive tests. The brain of SuperAgers shrinks at a slower rate than the average aging brain. Those in this category may also have the biological signs of cognitive decline but are resilient to actual cognition changes, Milman says.

However you distinguish them, Milman says the number of SuperAgers worldwide is relatively small, making it difficult to determine with confidence the lifestyle and genetic contributions to a healthy brain span.

“A lot of the research is suggesting that these people who reach these exceptional lifespans probably have a certain genetic predisposition to becoming a SuperAger, and we learned that because there’s a strong family history of longevity in these individuals,” Milman says, citing animal studies that have identified longevity genes including APoE2.

Still, what we do know is that while there is no magic pill today, lifestyle factors are the most foolproof way to extend your brain span and increase your chances of becoming a SuperAger.

How to increase your odds of becoming a SuperAger

Optimize your lifestyle with healthy habits

While there isn’t enough evidence to say that SuperAgers adhere to a set number of lifestyle habits more than their peers, there’s pre-existing research that underscores how healthy habits protect the brain from cognitive decline.

“We have enough evidence at this point that a healthy lifestyle, like getting sufficient sleep, avoiding excess alcohol intake, avoiding smoking,

and exercising, is good for you and can extend the period of time that you're disease-free and can extend somebody's lifespan," Milman says.

- Prioritize [moving your body](#) to optimize blood flow to the brain and keep your memory strong.
- [Sleep at least 7](#) hours a night to recover brain function and stay alert.
- Eat whole foods and limit highly processed [foods](#) that can lead to inflammation in the brain and harm memory.

Take on a new hobby

[Learning new things](#) to form more neural connections can keep your brain engaged and improve executive functioning. "Learning a new language or a musical instrument is so difficult that it forces your brain to change," Dr. Tara Swart, a neuroscientist, previously told *Fortune*.

In a 2016 [New York Times](#) op-ed, [Lisa Feldman Barrett](#), a SuperAgers researcher and author of *How Emotions Are Made: The Secret Life of the Brain*, said that trying new, difficult tasks can help thicken the regions of the brains responsible for emotional processing and storing memories, emulating those of SuperAgers.

So consider dedicating time weekly to cross-train your brain by trying a new game, hobby, or craft.

See the glass as half full

Preliminary research points to key personality traits of SuperAgers, including being positive and adaptable, according to Milman.

"It has been suggested that SuperAgers are more positive and have a more positive outlook on life," Milman says. "I think that may be synonymous in some ways with being more resilient and being able to overcome adversity and still have a positive outlook."

The same results have been found in Northwestern's SuperAgers study.

"We see that the SuperAgers tend to be pretty resilient and adaptable, so being open to new opportunities is a theme that seems to run through this group," Emily Rogalski, PhD, neuroscientist and director of the University of Chicago's Healthy Aging & Alzheimer's Research Care Center, previously told [Fortune](#).

[Complementary research](#) shows people who think positively about getting older tend to reduce their stress, and their risk of developing chronic conditions, including dementia.

People of any age can embrace challenges and know that change and adaptability will serve them in the future. They can also see aging as a gift, honing in on the positive traits that come with getting older, such as wisdom, self-awareness, and a broader perspective.

Foster a strong social network

The part of the brain responsible for social processing and awareness is larger in SuperAgers, according to [Northwestern Medicine](#).

"These social networks tend to protect people from cognitive decline," Milman says.

It checks out because [loneliness and a lack of strong social connections](#) are becoming an increasingly determinant factor in reducing older adults' health spans, including their brain spans. [Social isolation](#) puts people at a 50% increased risk of developing dementia.

Whether it's genetics, lifestyle, a combination of both, or a little bit of luck, SuperAgers are onto something and there is a lot we will continue learning from them in the chase for longevity.

“The rest of us can still maximize our health span, or the longevity of our good health, by implementing these healthy lifestyle choices,” Milman says.

Staying fit as you age isn’t just about exercise. Experts say to prioritize these 4 habits

August 31, 2024

A fitness regimen should incorporate mental and emotional fitness as well.

Dr. Bill Dorfman, a 64-year-old cosmetic dentist in Southern California, prides himself on looking years younger, a characteristic he attributes to good genes and a daily [workout](#) regimen.

Three days a week he focuses on abs and cardio; the other days are for lifting light weights at high reps.

Dorfman says he got serious about [exercise](#) following a lull during dental school when he found himself frequently in pain. That’s when he realized his fitness had taken a back seat following years as a high school swimmer and gymnast. “What I found was the more I exercised, the better I felt,” he says.

Outside of the gym, he credits his daily Words With Friends habit with [keeping his mind sharp](#). He also makes nightly dinner plans with various friends to [stay connected](#).

Dorfman’s wellness habits underscore that one key to a longer life is a fitness regimen—but one that incorporates mental and emotional fitness as well.

“We really need to look at the life of an older adult with a holistic lens—if they’re really [happy](#), healthy, and whole,” says Dor Skuler, cofounder and CEO of [Intuition Robotics](#) and an expert on loneliness in aging adults.

Here are four ways to focus on whole-body fitness as you age.

1. Exercise for the body and brain

Staying [physically active](#) can prevent injuries and help the body heal faster when they happen, plus it’s also strongly linked to good mental health and brain function.

Kirk Erickson, PhD, director of Translational Neuroscience at [AdventHealth](#) Central Florida, where he studies the plasticity and modifiability of brain systems, has found physical activity to be one of the best ways to keep the [brain healthy throughout its lifespan](#).

Erickson’s research shows that as we age, the [brain shrinks](#), specifically the hippocampus, which is responsible for memory formation. Exercise can help maintain this portion of the brain and, in some cases, increase the size. There’s much to be learned about how and why this is, but Erickson says the effects are better the longer you engage in these habits, so it’s good to start young.

Of course you can still reap the benefits if you start later in life, he says. You might find that with time, you can recall memories and information more easily and have [better executive function](#) and a longer attention span when your brain is at its best, he says.

He recommends moderate exercise, like [walking](#), five days a week for 30 minutes.

Aside from walking, Dr. Gary Small, chair of psychiatry at [Hackensack Meridian Health](#), says strength training helps combat age-related muscle loss and can lead to a longer lifespan. Additionally, balance exercises can help prevent slips and falls—the leading cause of injuries in adults ages 65 and older.

Jasmine Marcus, a physical therapist at Cayuga Medical Center in Ithaca, N.Y., where she works with patients of all ages and physical activity levels, recommends tiptoeing into exercise if you're new to it. She suggests starting with some kind of group fitness class like Zumba—anything that elevates your heart rate. It helps, too, if you have a partner to hold you accountable, she says.

2. Strive for mental fitness

Small also recommends doing activities that keep the brain in shape. One study showed the simple act of reading articles online and searching topics on [Google](#) offered valuable mental stimulation. Doing crossword puzzles, reading books, playing games, [practicing hobbies](#), and daydreaming all contribute to mental sharpness.

[Stress management](#) is also a critical part of maintaining mental fitness. Just 10 minutes of meditation a day can improve mood and cognitive agility, says Small, rewiring the brain and strengthening neural circuits.

“You don’t have to go to a retreat in Nepal or India to meditate, but you can learn the skills,” he says.

3. Stay social

The U.S. surgeon general [issued an advisory last year](#) warning of the nation’s loneliness epidemic, which negatively impacts health. One study equated lack of social connection to [smoking up to 15 cigarettes a day](#). Other studies show social connection reduces the risk of premature death. It’s clear that social and emotional fitness is key to aging well.

Skuler, whose company makes AI-powered social companions for aging adults aimed at keeping them active and engaged, says major life changes, such as the death of a spouse, often trigger loneliness.

“That is by far a watershed moment,” he says. Suddenly no one is asking how you slept or what you have planned for the day. A similar problem happens with

asynchronous aging, where one spouse has a decline with [dementia](#), for example. Other events such as retiring or sending the kids off to college might have similar impacts on social well-being, Skuler says.

[ElliQ](#), the robot companion Skuler's company makes, is one way to help aging adults stay connected, but he encourages all people to maintain [friendships](#) and relationships with family members. Volunteering, he says, can also add purpose and connection to your life.

4. Develop good sleep hygiene

There's a myth that seniors need less [sleep as they age](#), but Jamie Zeitzer, PhD, advisor and scientific reviewer at Rise Science, says the reality is [sleep](#) becomes more difficult with age. The result is that many seniors find themselves going to bed later and rising earlier.

"Humans are programmed to stay awake 16 [hours] and sleep eight hours," he says. "An older person's ability to do that diminishes, so they have to work a little harder at it."

The causes for poor sleep can be both social and physical. We become more sensitive to sounds and temperatures as we age, says Zeitzer. So the garbage truck that never woke you on its weekly route might now rouse you at 6 a.m., he says. Similarly, a bedroom that's too hot or cold might make it difficult to sleep.

As we age we also become more sensitive to caffeine. So if you used to be able to drink a cup of coffee in the evening, you could find you now have trouble falling asleep hours later.

There's also a major shift that happens once we retire, when the social constraints around sleep are suddenly lifted. Seniors who don't have social obligations early in the morning might find they're less inclined to sleep at typical hours. A nap during the day, for example, may "cannibalize their sleep at night," Zeitzer says.

Older adults might find that sleeping too little or having a fragmented night of sleep can lead to acute problems with cognition the following day, Zeitzer adds. Poor sleep over the long term is linked to health conditions including depression, Alzheimer's disease, and cancer.

A good routine can solve some sleep problems. To start, avoid caffeine later in the day. And be mindful that you [adjust the temperature in your sleep environment](#) to encourage rest.

And he recommends finding a way to wind down before bed. While some experts warn against the use of electronics before you grab some shut-eye, Zeitzer says watching a TV show can be helpful if it means you feel more relaxed and ready for bed afterward.

"It's always good to aspire to closing your eyes and falling asleep, but other people need more kinds of wind-down routines," he says.

The 5 best supplements for healthy aging, according to a longevity expert

April 28, 2024

If you've ever walked down the supplement aisle in a pharmacy, you've seen the overwhelming abundance of options available for your medicine cabinet. According to the 2022 Council on Responsible Nutrition Consumer Survey on Dietary Supplements, 75% of Americans use [dietary supplements](#), most on a regular basis.

It's important to remember that supplements are just that: supplemental. While they're good for giving you a bit of a leg up when you're lacking certain nutrients, the number one way to get the vitamins and minerals and antioxidants you need is through a healthy, nutritious diet.

Calcium for bone strength

Calcium does a lot for you: It plays an important role in blood clotting, it helps your muscles contract, and it regulates normal heart rhythms and nerve functions. It also builds and maintains strong bones. When you don't take in enough calcium, your body borrows it from your bones to keep things running smoothly. A daily intake of calcium helps you replace this calcium and [keep bones healthy](#).

When you reach age 50, your daily calcium requirement goes up. Prior to that, 1,200 milligrams a day will do you, but when you hit the half-century mark, it's time to bump up to 1,500 milligrams a day. Women who are past menopause are at the highest risk of getting [osteoporosis](#), a disease that makes bones weak and brittle. [Lack of calcium](#) ups these chances even more.

Burnstine says if you know you're not getting at bare minimum two servings from a calcium source each day, a calcium supplement is a good idea. But the supplement is only one piece of the puzzle.

"In addition to the calcium supplement, I'm also going to recommend that you get at least two servings of dairy or that you eat a lot of green leafy vegetables, and you do resistance training, which protects bones more than anything else," she says.

Vitamin D for immunity (and bone strength)

Speaking of healthy bones, your body can only absorb calcium when [vitamin D is present](#). In addition, [vitamin D](#) has anti-inflammatory, antioxidant, and neuroprotective properties. It supports immune health, muscle function, and [brain cell activity](#).

Your body doesn't make vitamin D, so you have to get it from outside sources. These include food, the sun, or vitamin D supplements. Before age 70, your daily requirement is 600 IU. After 70, it goes up to [800 IU](#). In your later years, your body may need a boost to meet these goals.

“As we age, most of us no longer absorb vitamin D as well,” says Burnstine. This can be especially true if you live in an area without much sun, or if you’re always wearing sunscreen.

Probiotics for gut health

Emerging studies suggest that supplements of [probiotics](#)—the “good” bacteria that live in your digestive system and helps keep “bad” bacteria in check—may help counteract age-related shifts in gut microbiota, improving your immune health and aiding [healthy digestion](#) as you age.

“We know that if our gut health is good, everything else follows, in terms of [inflammation](#), [brain fog](#), weight loss, [sleep](#), depression,” says Burnstine. “Our gut is tied to just about everything.”

As with most nutrients, it’s best to get probiotics through the foods you eat. You can load up on them through fermented foods such as yogurt, kefir, kombucha, refrigerated sauerkraut, kimchi, tempeh, and miso. But a probiotic supplement isn’t a bad idea.

Some supplements have upwards of 50 billion CFUs (colony-forming units), which may seem like a huge amount, but Burnstine says your body absorbs only 20% to 30% of that.

“Taking a supplement helps create that diversity and huge population of probiotics in the gut to help us be healthy, lose weight, and lower our cholesterol,” she says.

Magnesium for mood

Magnesium is attached to immune function, enzymatic reactions, and it plays a part in lowering inflammation. It’s also a key player in mood stabilization. Magnesium levels go down as age goes up, putting you at risk of mental health struggles.

“People who are low in magnesium tend to have higher depression,” says Burnstine. Chronically low levels can also increase your chances of having high blood pressure, heart disease, Type 2 diabetes, and osteoporosis.

Anyone over age 30 should be getting 320 to 420 milligrams a day, but Burnstine says not all magnesium supplements are the same.

“For example, you could take a magnesium carbonate, but you could also take something called magnesium glycinate, which is slightly easier on the stomach,” she says. “The combination of how it’s formulated causes sort of different responses.” Talk to your doctor about the best magnesium formulation for you.

Multivitamin to cover the bases

A daily multivitamin, while not a panacea, can give you an overall nutritive boost. At the very least, says Burnstine, it won’t hurt.

“I always say that a multivitamin is sort of like an insurance policy,” she says. “I would recommend a general multivitamin at any age.”

Most brands are the same, but for peace of mind, look for the USP symbol. This seal of approval marks brands that have consistent quality, the exact ingredients in the potency and amount you find listed on the label.

“While individual nutritional needs vary from person to person depending on age, sex, health status, and lifestyle, many multivitamin supplements provide nutrients that play crucial roles in various physiological processes to prevent deficiencies that would otherwise cause health problems,” [Jamie Lee McIntyre, RD](#) previously told *Fortune*.

Most multivitamins contain vitamins A, [D](#), E, [K](#), C, and B; calcium; [magnesium](#); iron; zinc; selenium; manganese; and chromium, says McIntyre.

The best multivitamins can help supplement those with dietary restrictions, like vegetarians, with vitamins and minerals they might be missing from just their diet. They aren’t a cure-all, though. Combining a balanced diet with exercise is the best way to fight against harmful diseases and manage weight, but adding a daily

multivitamin into the mix is not a bad idea—just do your research and consult a doctor first.

“Overall, while multivitamins can be a convenient way to support overall health, they should be used judiciously and in conjunction with a healthy lifestyle and dietary habits,” says McIntyre.

The best science-backed strategies for a strong mind as you age

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The lifelong learner is onto something.

Sixty-two-year-old founder Marie Jerusalem has never felt more able to adapt to the changing demands of the corporate world. “My body’s not as agile as it used to be, but mentally I’m stronger today than I’ve probably ever been in my entire career,” she tells *Fortune*.

At 57, Jerusalem was let go from her chief people officer role in private equity. But she [wasn’t financially, or emotionally, ready to retire](#). After working for a few years as a business consultant in HR, she pivoted to launch Rocket50, a membership community and job search platform that assists older workers. To get her business off the ground, she had to quickly acquire a host of new skills—from integrating AI to creating marketing and social media strategies.

Jerusalem rejects the notion that older people don’t want to learn new ways of doing things, and credits the demands of launching a business—gaining [new skills and engaging with others](#)—for boosting her confidence and mental resilience.

People often assume the mind does not work optimally with age. While there are some normal age-related declines in thinking speed and attention, people’s decision-making and abstract reasoning skills may

actually improve with age, according to research from the National Institute on Aging and the Columbia University Irving Medical Center (CUIMC).

It's good news, as employees age 55 and older are expected to constitute [more than a quarter of the workforce over the next decade](#), and Americans are increasingly [working past retirement age](#) either because they want to stay engaged or because finances and caregiving duties make it impossible not to. Regardless of why they're working, they all have one thing in common: They want to stay mentally sharp. Fortunately, the brain is adaptable, and experts say some daily habits can help people maintain cognitive resilience well into older age.

The basics

Sleep is critical for everyone's health, but it's especially important for the aging brain. "Sleep disturbances have been associated with cognitive impairment and decreased physical function," says Marie-Pierre St-Onge, PhD, director of the CUIMC Center of Excellence for Sleep & Circadian Research.

While seven to nine hours of shut-eye per night is the gold standard, about a third of older adults don't meet the minimum, according to a study published in BMC Public Health. Experts recommend sticking to a regular sleep and wake schedule, and developing a [nightly wind-down](#) that includes limiting screen time and engaging in a calming activity, in addition to any other doctor-recommended interventions.

Research has also long spotlighted [the role of exercise](#) in protecting vital brain function. Movement helps counter age-related shrinkage of the brain's hippocampus, which is responsible for memory.

It doesn't take much activity to see positive results: A study published in the *Journal of Epidemiology and Community Health* found that even 10 minutes daily of moderate to vigorous movement like brisk walking,

biking, or hiking can improve mental processing, such as planning and completing tasks efficiently. Exercise also helps reduce sleep problems like insomnia.

A friendly neighbor

Maintaining strong friendships and relationships can feel at odds with work and caregiving duties. However, having coffee with a colleague, volunteering in your community, or hosting a family dinner will help keep the brain stimulated.

“We live in a very fast-changing world, and we need to stay abreast of all those changes. We become irrelevant when we stop learning.”

MARIE JERUSALEM, 62-YEAR-OLD FOUNDER

“Social activity protects against a variety of negative health outcomes in older age, including cognitive decline, dementia, and even early mortality,” says Patricia Boyle, PhD, a trustee of the McKnight Brain Research Foundation and a neuropsychologist with the Rush Alzheimer’s Disease Center in Chicago. It may even maintain the brain’s resilience in the face of disease, she adds.

What's more, socializing, [especially across generations](#), expands people's perspectives, which invigorates the mind as one considers new ways of thinking, explains Dr. Tara Swart, a leading neuroscientist and author of *The Source: Open Your Mind. Change Your Life*.

Lifelong learning

The brain keeps developing well into old age. But the brain plateaus when people don't engage in attention-intensive activities, Swart says. Launching a business, like Jerusalem did, is one such activity, but you don't have to do something that intense to reap the benefits.

"Learning a new language or a musical instrument is so difficult that it forces your brain to change," Swart notes, strengthening executive functioning, and the ability to regulate emotions and solve complex problems.

Even passively enjoying the arts can serve as a brain booster. The novel field of neuroaesthetics suggests that anything from listening to an opera to watching ballet to observing a painting can improve attention and ultimately lengthen one's lifespan. "Those forms of beauty have a really beneficial impact on us," Swart says.

A fresh spin on aging

Research from Harvard T.H. Chan School of Public Health found that people who have a positive view of aging tend to live longer and have better physical and cognitive health.

Maddy Dychtwald, author of *Ageless Aging*, says there are a host of positives that come with climbing the chronological ladder, such as wisdom and self-acceptance. "We have agency that we never thought we had before," she says.

Lesley Steinman, a research scientist in the health promotion research center at the University of Washington, cautions against using outdated terms, like “silver tsunami,” that perpetuate negative stereotypes about aging.

A researcher with the Program to Encourage Active, Rewarding Lives (PEARLS), Steinman helps older adults stay engaged and play an active role in how they age. “People are often surprised that there’s quite a bit of things they can do, even though there still are systemic and structural issues making their lives difficult,” she says.

Positive thinking can also help ease mental health issues like [depression](#)—of particular concern for aging adults who may be faced with health challenges or coping with loss and grief. Habits like sleeping well, exercising, and thinking positively may help reduce stress and depression, which in turn can sharpen cognitive performance.

Jerusalem has no plans to retire anytime soon. She wakes up every day eager to learn and engage with older workers. She says the second she loses motivation, she’ll try something new. “Find your passion and stay engaged for as long as you can, because that’s what really makes you feel like you’re alive,” she says.