

The Scientific Approach to Getting
Healthier as You Get Older

HOW



TO



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NEW YORK TIMES BESTSELLING AUTHOR OF *HOW NOT TO DIE*
AND *HOW NOT TO DIET*

FEATURING DR. GREGER'S ANTI-AGING EIGHT
FOR LONGEVITY AND VITALITY

HOW NOT TO AGE

THE SCIENTIFIC APPROACH TO GETTING
HEALTHIER AS YOU GET OLDER

MICHAEL GREGER, M.D.



[Begin Reading](#)

[Table of Contents](#)

[About the Author](#)

[Copyright Page](#)

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*For my great-aunt Pearl
(1911–2015)*

Preface

I turned fifty in the process of writing this book, so the subject has a certain salience lacking from my last nutrition book, *How Not to Diet*, which covered weight loss. There is, however, a clear parallel between the two topics: Both are tainted with the same corrupting influence of commercial interests. The diet¹ and anti-aging² industries are both multibillion-dollar behemoths. With so much money in the mix, the temptation to promote products purporting all sorts of preposterous claims is apparently irresistible.

Even an educated layperson seeking basic, practical advice in either arena, living lighter or longer, is faced with an inscrutable barrage of pills and potions. Even as a physician with the luxury of wading neck deep through the peer-reviewed medical literature, it's been a challenge to tease out the naked truth from the emperor's clothing. But that makes the endeavor all the more important. If it took me three years to sift through all the science on aging, I'm afraid the casual observer would have little hope in separating facts from farce. A former president of the Gerontological Society of America wrote that "few subjects ... have been more misleading to the uncritical and more profitable to the unscrupulous."³

The anti-aging field is said to be a "fertile ground for cons, scams and get-rich-quick schemes,"⁴ with the popular literature on the subject harboring a "huge amount of misinformation."⁵ Marketers often target older people with quack remedies for aging.⁶ Their wares are hawked pervasively on the internet as well as brick-and-mortar "anti-aging" clinics.⁷ These schemes have been the subject of multiple Senate and congressional inquiries with names like "Swindlers, Hucksters and Snake Oil Salesmen"⁸ and "Quackery: A \$10 Billion Scandal."⁹ These days, the anti-aging industry in America may be worth more like \$88 billion,¹⁰ with the global industry valued at \$292 billion.¹¹ This encompasses everything from wrinkle creams to televangelist Pat Robertson offering "Pat's Age-

Defying Protein Pancakes.” Aging may not be good for health, one economics editorial put it, “but it certainly is good for business.”¹²

BLINDED BY SCIENCE

According to one industry group, 60 percent of Americans sixty-five and older are pursuing anti-aging interventions,¹³ yet, according to the director of the Institute for Biomedical Aging Research, in almost all instances, these interventions are not supported by science.¹⁴ They sound like they are, though. Scientific breakthroughs exploited by the sensationalist press have long been opportunistically repackaged by profiteers.

Nineteenth-century advances in magnetism led to ads asserting, “[t]here need not be a sick person in America ... if our Magneto-Conservative Underwear would become a part of the wardrobe of every lady and gentleman, as also of infants and children.” Less comically, more tragically, public interest in Marie Curie’s work led to a range of radioactive products said to “revitalize” and “energize.”¹⁵ As one *Wall Street Journal* headline read, “The Radium Water Worked Fine Until His Jaw Came Off.”¹⁶

Today, this so-called scienceploitation is evident in hundreds of rogue “stem cell” clinics concentrated in California and Florida,¹⁷ using the language of science to give a veneer of legitimacy to their unproven therapies.¹⁸ In their *Scientific American* feature “No Truth to the Fountain of Youth,” three noted aging researchers concluded that the “public is bombarded by hype and lies.”¹⁹

One of those researchers was sued for more than \$200 million by the cofounders of the American Academy of Anti-Aging Medicine²⁰ for presenting the organization with a Silver Fleece Award, a mock prize shaming “the most ridiculous, outrageous, scientifically unsupported or exaggerated assertions about intervening in ageing or age-related diseases.”²¹ The American Academy of Anti-Aging Medicine countered that it “does not promote or endorse any specific treatment nor does it sell or endorse any commercial product.”²² However, looking back at its website, it has actively solicited and displayed a whole catalog of advertisements in its “Find an Anti-Aging Product or Service” directory whose development, it justifies, was “prompted by the numerous inquiries received each day.”^{23,24}

The “gerontological establishment” has been accused of trying to wantonly sabotage upstarts like the American Academy of Anti-Aging

Medicine,²⁵ whose cofounder claims to be fighting the “old-line philosophy” that “aging is inevitable, nothing can be done, get used to it, grow old and die.”²⁶ I see merit on both sides of this culture clash, with the field of gerontology (the study of old age) struggling to retain hard-fought gains in public funding for basic aging research versus the more ambitious anti-aging crusaders who appear to more fundamentally question underlying assumptions. “Simply put,” the American Academy of Anti-Aging Medicine’s official response to the criticism read, “the death cult of gerontology desperately labors to sustain an arcane, outmoded stance that aging is natural and inevitable.”²⁷

The anti-aging medicine movement would have more credibility had it been started by those steeped in the research rather than “entrepreneurial businessmen responding to market opportunities,”²⁸ but the backlash against the anti-aging new wave may have pushed the pendulum too far in the other direction. Yes, as noted by the founding editor in chief of *Biogerontology*, the history of anti-aging research is undoubtedly “replete with fraud, pseudoscience, quackery and charlatanism,”²⁹ but the (admirable!) crusade against any whiff of impropriety seems to have led to a knee-jerk “all hype, no hope” position that belies the genuine scientific advances that have been made in the feasibility of intervening in the aging process.³⁰

I know in some circles today, “science” is a dirty word. After years of COVID craziness, colleagues I once respected for their intellect seemed to have abandoned their critical thinking skills. If you have been similarly sucked down some rabbit hole of cabalistic conspiracies, this may not be the book for you. It is true that the pandemic revealed glaring institutional flaws that even encroached on the scholarly literature. Two of the most prestigious medical journals were forced to retract papers over concerns of data integrity.^{31,32} But scientific journals remain the gold standard for establishing the best approximation of truth about our shared reality. To paraphrase Winston Churchill’s quote about democracy as a form of governance, the peer-reviewed medical literature is the worst way to establish facts about our health—except for all the others.

SHOWING MY WORK

An editor in chief of a leading gerontology journal claims that most anti-aging scientists “widely known to the public are unscrupulous purveyors of useless nostrums.”³³ It is easy to be swayed by charismatic gurus, but

when it comes to something as life-and-death important as the health and well-being of ourselves and our families, we should rely not on anecdote but on evidence. That's why I cite everything to the teeth. *How Not to Die* had about 2,000 citations. *How Not to Diet*, 5,000. This book ended up with more than 13,000, which turned out to be a problem.

I promised the publisher a book with no more than about 600 pages, but when all was said and done, my manuscript was closer to 2,150 pages. Yikes. I didn't want to lose any content, so my first stab at trimming was to put the 995 pages of citations online. [here](#), there's a web address (see.nf/citations) and QR code for the full list of searchable citations referenced throughout this book.

Over the last three years, my team and I read more than 20,000 papers on aging so you don't have to—but you're certainly welcome to! The advantage of presenting the citations online is that it allows me to hyperlink each one to take you directly to the source. That way, you can download the PDFs and access the original research yourself.

Nevertheless, that still left me with a manuscript with a quadruple-digit page count. I needed to figure out how to essentially halve the book to meet the publisher's printing specifications. The problem is there wasn't any chaff to chop. Too many popular physician authors recycle rehashed content from their prior works to cash in on another publication. I try to do the opposite, featuring all-new material, which is why, throughout the text, I refer you to sections in my previous books where I covered relevant concepts. (Search worldcat.org to find print copies, e-books, or audiobooks of all my works at your local public library.) So, the only way I could think of to meet the target page count was to turn *How Not to Age* into a full audiovisual experience.

You'll see I've sprinkled video links throughout the book. My team and I produced hundreds of bite-sized videos, each about five minutes long, to cover the hundreds of thousands of words of additional information I had to cut from this manuscript. Don't worry, all the actionable takeaways are self-contained within this text. I just never want anyone to take my word for anything. I always strive to justify exactly how I arrive at each recommendation. Unfortunately, space limitations didn't always allow me to do that in this book, so even though I still relay the bottom-line conclusions, you may want to follow the links to take a deeper dive into the supporting evidence.

AGING IS THE ACTUAL LEADING CAUSE

There may be no such thing as dying from old age. From a study of more than 42,000 consecutive autopsies, centenarians—those who lived at least to one hundred—were found to have succumbed to diseases in 100 percent of the cases examined. Though most were perceived, even by their physicians, to have been healthy just prior to death, not one “died of old age.” They died from disease, most commonly heart attacks.³⁴ Similar results were found from other autopsy series of centenarians³⁵ and those over eighty-five, an age bracket referred to in the medical literature as the “oldest old.”^{36,37,38}

If aging kills via diseases,³⁹ why wasn't my *How Not to Die* the only longevity book anyone needs? In it, I ran through what we can do to prevent, arrest, and reverse each of our fifteen leading causes of death, starting with heart disease, not only the number one killer of centenarians but of people in general.⁴⁰ In the United States, heart disease has been the leading cause of death every year since 1900, with the exception of 1918 when pandemic flu ruled the roost.⁴¹ (In contrast, as I detail in *How to Survive a Pandemic*, COVID only made it to number three.⁴²) Heart disease has been the leading cause of death and disability around the world for most of this century⁴³ and is projected to remain that way in the decades to come.⁴⁴ But is it *really*?

Because old age is the greatest risk factor for most of our killer diseases,⁴⁵ one could argue that the leading cause of death is actually aging.⁴⁶ The rate of death increases exponentially for age-related diseases, such as heart disease, cancer, stroke, and dementia.⁴⁷ So, yes, in the same age bracket, having high cholesterol can increase your risk of heart disease as much as twentyfold,⁴⁸ but an eighty-year-old may have *five hundred* times the risk of having a heart attack⁴⁹ compared to someone in their twenties.⁵⁰ Eating a plant-based diet may reduce the risk of dementia as much as threefold,⁵¹ but the difference in dementia rates between those older than eighty-five compared to younger than sixty-five is *three hundredfold*.⁵² The reason we focus on things like cholesterol is that it is a *modifiable* risk factor, but what if the rate of aging was modifiable, too?

Instead of our current, piecemeal approach of focusing on individual degenerative diseases, what about slowing down the aging process itself? I remember as a nerdy kid I wanted to cure cancer when I grew up. Even if all forms of cancer were eliminated, the average life expectancy in the United States would only go up about three years.⁵³ Why? Because

dodging cancer would just mean delaying death from something like a heart attack or stroke. If one age-related ailment doesn't get us, another will. Rather than playing "whack-a-mole" by tackling each disease separately, progress in decelerating aging could address all these issues simultaneously.⁵⁴

Imagine if there was an intervention that didn't just reduce your risk of the leading killers but also arthritis, dementia, osteoporosis, Parkinson's disease, and sensory impairments. Because such risks tend to double every seven years, even just slowing aging, such that the average sixty-five-year-old, for example, would have the health profile and disease risk of today's fifty-eight-year-old, would be expected to cut *in half* everyone's risk of death, frailty, and disability.⁵⁵

This is why I wrote *How Not to Age*.

Is Aging Itself a Disease?

For decades, one of the most contested questions in gerontology has been whether or not aging itself should be considered a disease.⁵⁶ Aging is natural, yes, but so is getting an infection and we call that a disease. Aging is universal. Yes, but everybody gets the common cold, too.⁵⁷ If you're interested, I dive deeper into the discussion in my video see.nf/agingdisease. What does it matter what we call it? A rose by any other name wilts just as fast. The hope is that disease classification would lead to greater resource allocation for aging research, just as the recent declaration of obesity as a disease did for obesity research.⁵⁸

You'd think Big Pharma would invest in what would certainly be a blockbuster drug. But why spend the money on research when it can be spent on marketing all the unproven anti-aging products they already sell? Many of the leading lines of dietary supplements are owned by drug companies.^{59,60} They're the ones selling "cosmeceuticals"⁶¹ and "age reverse" skin creams.⁶² Drug maker Sanofi even partnered with Coca-Cola to come up with a "beauty drink."⁶³ They're already making money hand over fist

preying on the public's gullibility and desperation for anti-aging products.⁶⁴ Why waste money on proving anything actually works?

ALIVE AND WELL

When asked, *How long do you wish to live?* and offered the choice of 85, 120, or 150 years, or indefinitely, about two-thirds said they'd prefer to live to be eighty-five. But, when the question was reframed as *How long do you wish to live in guaranteed mental and physical health?*, the most popular answer switched to an unlimited lifespan.⁶⁵ It's not just how long we live, but how well, embodied in the Greek myth of Tithonus, to whom Zeus granted eternal life, but not eternal youth, so he shriveled with age and began to babble continuously (before eventually transforming into a cicada).⁶⁶

Longevity is indeed a Pyrrhic victory if those additional years are characterized by inexorable decline.⁶⁷ Only about 18 percent of people can be described as undergoing "successful aging."⁶⁸ Studies have found the prevalence of multimorbidity, the coexistence of multiple chronic diseases, ranges between 55 percent and 98 percent among older individuals.⁶⁹ By age eighty-five, more than 90 percent may have at least one disease and, on average, about four diseases.⁷⁰ And just like 85 percent of cancer patients tend to overestimate their survival,⁷¹ so, too, do those with other chronic diseases. Those suffering from heart failure or chronic obstructive lung diseases like emphysema are about three times more likely to die within the subsequent year than they predicted. Ninety-six percent of outpatient dialysis patients thought the odds were in their favor that they'd be alive five years later, but nearly half were dead in fewer than two years.⁷²

This raises the concept of healthspan, the period of life spent in good health, free from chronic disease and disability.⁷³ No wonder people are skeptical about longevity interventions as we see our lifespans expand but our healthspans contract. "Everyone wants to live forever," to paraphrase Jonathan Swift, "but no one wants to grow old."

In the United States, for example, we're living longer in sickness, not in health. A twenty-year-old in 1998 could expect to live about fifty-eight more years, while a twenty-year-old in 2006 could look forward to fifty-nine more years. However, the twenty-year-old from the 1990s might live

ten of those years with chronic disease, whereas now it's more like thirteen years. So it feels like one step forward, three steps back. The researchers also noted that we're living two fewer *functional* years—that is, years we're no longer able to perform basic life activities, such as walking a quarter of a mile, standing or sitting for two hours without having to lie down, or standing without special equipment.⁷⁴ In other words, we're living longer, but we're living *sicker*.

That is why this book addresses both lifespan and healthspan. What's the point of living longer if you can't enjoy it vibrantly? It is my sincere hope this book adds not just years to your life but life to your years.

Introduction

My earlier book, *How Not to Die*, was not about living forever. It was not *How to Not Die*. Instead, it was how not to die prematurely, in pain after a long, chronic, disabling illness. The good news I shared is that we have tremendous power over our health destiny, in that the vast majority of premature death and disability is preventable with a healthy enough diet and lifestyle. *How Not to Age* has a similar premise. This book is not about immortality but rather how to age with grace and vitality rather than suffering from the ravages of infirmity and decrepitude. But why can't we stop aging and go on forever?

“MAN WILL NEVER BE CONTENTED UNTIL HE CONQUERS DEATH.” —BERNARD STREHLER

From the Epic of Gilgamesh more than 4,000 years ago⁷⁵ to the recent quincentennial of Ponce de León's pursuit for the fountain of youth, humankind has yearned for the mythical elixir of life that would remedy the scourges of aging.⁷⁶ And why not? It's not like aging is some immutable constant in nature. Evolution has produced lifespans in animals that vary more than a millionfold, from mayflies whose adult lives may last only a few minutes to clams clocking in at over five hundred years.⁷⁷ Just like the Wright brothers may have taken inspiration from birds, we can take inspiration from animals that age slowly, if at all.⁷⁸

Why can't we live forever? Some animals do, and I'm not talking about a two-hundred-year-old whale or even a thousand-year-old tree. There are actually species (with names like the immortal jellyfish) who apparently do not age and could technically go on forever.⁷⁹ In a sense, humans are immortal, in that a few of our cells live on—the sperm or egg cells lucky enough to find each other. Each of our kids grows out of one of our cells, and that alone—I mean, the fact that a single cell can grow into a

person—should make, in comparison, the notion of keeping our body going indefinitely seem biologically trivial. One little fertilized microscopic blob can turn into perhaps the most complex object in the known universe, the human brain, with its 100,000 miles⁸⁰ of 86 billion neurons⁸¹ making 150 trillion connections.⁸² If that’s possible in biology, then what isn’t?

Still, there is much skepticism in the scientific community, where many believe aging is an irreversible process.⁸³ “Anti-aging” is compared to “anti-gravity.”⁸⁴ Vocal critics in the gerontology community have accused those suggesting the possibility of greatly extended human lifespans as being “contemptible ... for duping the public” and claim that “anything past 130 [years of age] is ridiculous.”⁸⁵ Such doubts are reliably countered by proponents who quote preeminent scientists of yore making similarly absolutist claims that did not age well.⁸⁶ Nobel Prize–winning physicists spoke of the prospect of nuclear power as “talking moonshine,” a “completely unscientific Utopian dream, a childish bug-a-boo.”⁸⁷ Lord Kelvin, considered one of the greatest scientists of his time, notoriously asserted, “Heavier-than-air flying machines are impossible,”⁸⁸ doubling down on their impracticality in 1902, just one year before the first flight at Kitty Hawk.⁸⁹

Already in the laboratory, genetic mutations can affect a tenfold increase in lifespan, at least in a species of tiny worm.⁹⁰ In mice, dietary and genetic manipulation yields more like a 70 percent increase.⁹¹ Single tweaks, such as methionine restriction, incorporated into one of my Anti-Aging Eight (see [here](#)), can extend the average and maximum lifespans of rats by about 40 percent,⁹² which could translate to boosting human lifespan to an average of about 110, with the rare “centenarian” hitting 140 years of age.⁹³ These results have yet to be replicated in people, but if we discovered interventions not only to slow aging but to actively repair the accumulated damage, the sky could be the limit.

Starry-eyed scientists in the field imagine that time could be effectively melted away, like that surrealist painting of drooping clocks,⁹⁴ a “rejuvenation of your body leading ultimately to an endless summer of literally perpetual youth.”⁹⁵ A “longevity escape velocity” is envisaged in which we would just have to live long enough for innovations to add more time than is passing, the tipping point at which each year we can add at least one extra year of life expectancy.⁹⁶ This could theoretically enable humanity to have an essentially unlimited lifespan. Imagine dying the year

before the critical juncture! I remain agnostic as to whether such a breakthrough is possible, but I hope this book will help regardless, whether you're striving to live long enough to live forever⁹⁷ or just trying to die young as old as possible.

FOUR BOOKS IN ONE

When I sat down to write (or rather stood up and started walking, typing at my treadmill desk), I needed to make a decision. What should I focus on? The more superficial signs of aging that everybody wants to know about, like wrinkles and graying hair, or the clinical aspects, like declining cognition? Or should I address how we might slow the aging process itself? I decided, as you can probably guess by the heft if you're reading a printed copy old-school style, all of the above.

My inspiration for writing *How Not to Age* was a consensus document titled “Interventions to Slow Aging in Humans” that was compiled by the top researchers in anti-aging medicine, the likes of Drs. Fontana, Longo, Sinclair, and dozens of others—nearly everyone who's anyone in the field. Brought together to identify the most promising strategies for developing drugs to combat aging, they identified a list of “essential pathways,” for example, the pharmacological inhibition of the hormone IGF-1 or drugs to block the enzyme mTOR. As I looked through the list, I realized: *Every single one of these pathways could be regulated through diet.* That became the opening section of this book.

PART I: SLOWING ELEVEN PATHWAYS OF AGING

The science of aging has been called “the most dynamic and provocative in modern biology.”⁹⁸ An attempt to classify the theories of aging published more than thirty years ago identified more than three hundred such theories, and the number has only grown since then.⁹⁹ In Part I, I identify the eleven most promising pathways for slowing the sands of time, ending each with practical proposals for targeting them naturally with diet and lifestyle changes. Part I is the nerdy section, and it contains critical concepts and terms that will be used throughout the book.

PART II: THE OPTIMAL ANTI-AGING REGIMEN

The odds of living to age one hundred have risen from approximately one

in twenty million to as high as one in fifty.¹⁰⁰ Why do some make it to their hundredth birthday but others don't? It's not just a matter of picking better parents. Studies following identical twins suggest that no more than 20 to 30 percent of the variance in lifespan is explained by gene inheritance.¹⁰¹ The media loves stories about hard-living centenarians who attribute their longevity to some combination of lard, vodka, and their favorite brand of cigarette, but how do centenarians and supercentenarians (those older than 110) really eat and live?

In Part II, I delve deep into the behaviors that those in the five longevity hot spot “blue zones” around the world share in common. In constructing the optimal anti-aging regimen, I explore the best and worst foods and beverages. Is red wine deserving of its symbolic status for longevity? What about coffee? I cover the “longevity vitamin” ergothioneine, the vegetarian's Achilles' heel, and the best exercise and sleep routine for the longest, healthiest life.

PART III: PRESERVING FUNCTION

Then, in Part III, I get to the nitty-gritty. What can you do to preserve your bones, bowels, and circulation? Your hair, hearing, and hormone balance? Your immune function and joint health? Your mind and your muscles? Your sex life and skin? Your teeth, your vision, and, finally, your dignity in death? There are chapters on each. Sneak peeks can be had at see.nf/trailer.

PART IV: DR. GREGER'S ANTI-AGING EIGHT

My Anti-Aging Eight is the final section of the book, an actionable checklist to complement the Daily Dozen I established in my earlier book *How Not to Die*. In addition to the wealth of recommendations throughout *How Not to Age*, this last part highlights specific foods, supplements, or behaviors that have the potential to offer some of the best opportunities to slow aging or improve longevity. My aim is to cover every possible angle for developing the optimal diet and lifestyle for the longest, healthiest lifespan based on the best available balance of evidence.

I. Slowing Eleven Pathways of Aging

INTRODUCTION

It has long been said that the best hope for a long life is to choose your parents wisely.¹⁰² Doesn't longevity just run in the family? Siblings of centenarians, people who live to be at least one hundred, are certainly more likely to become centenarians themselves, and their parents are more likely to have lived to be at least ninety.¹⁰³ On the other hand, the lifespans of spouses sometimes correlate as much as—or even more than—those of genetic relatives.¹⁰⁴ Your partner may have as much of an impact as your parent. After all, we don't only pass down genes. Perhaps Grandma's healthy recipes or even a lifelong love of running runs in the family, too.

HOW IMPORTANT ARE YOUR GENES?

To tease out the role of genetics, researchers often turn to twin studies, comparing differences between identical twins and fraternal twins.¹⁰⁵ Check out [see.nf/genes](#) to understand exactly how this ingenious method works to estimate heritability and what this and other methods have found. In short, only about 15 to 30 percent¹⁰⁶ or less¹⁰⁷ of our lifespan appears determined by our genes, which means *how* we live our lives may determine the bulk of our destiny.

To leverage the lifespan leeway we have beyond the relatively small genetic component, we must first understand the various aging pathways. The term “anti-aging” has been much abused in popular culture, attached to all manner of unproven products and procedures. The term should probably be reserved for things that can delay or reverse aging through the targeting of one or more of the established aging mechanisms.¹⁰⁸ In a

landmark paper cited more than 7,000 times in the biomedical literature,¹⁰⁹ “The Hallmarks of Aging” identified nine common denominators of the aging process. I expound on them in [see.nf/genes](#) and address each one in this book.

There’s a Fly in My Aging Research!

There are numerous ways to try to unlock the mysteries of aging. You could study long-lived individuals like centenarians and supercentenarians (people who reached the age of 110), for instance, or particularly long-lived smokers to uncover the secrets to their resilience.¹¹⁰ Or, you could strike out in the opposite direction and study short-lived people, investigating tragic accelerated aging syndromes like progeria, where children age at eight to ten times the normal rate,¹¹¹ wrinkling, balding, and then typically dying around age thirteen of a heart attack or stroke.¹¹² Or, you could study long-lived animals. There’s a clam called the ocean quahog, whose heart can beat more than a billion times over its five-century lifespan.¹¹³

In my video [see.nf/models](#), I talk about both the opportunities and difficulties of extrapolating from the “model organisms” used in aging research, such as yeast, worms, flies, and mice,¹¹⁴ as well as citizen science initiatives in which family dogs are enrolled in noninvasive studies to investigate why some “Methuselah dogs” reach ages of twenty-five or more, but 99.9 percent of other dogs do not.¹¹⁵ Aged pooches suffer many of the same ravages of aging that we do, such as arthritis, cancer, cataracts, kidney problems, and muscle loss.¹¹⁶ Advances made in canine longevity might not only be applicable to human aging but have the intrinsic value of enhancing the quality and quantity of life for the more than seventy million canine companions with whom we share our homes in the United States alone.¹¹⁷

AMPK

In my book on everything evidence-based in weight loss, *How Not to Diet*, there is a section titled Amping AMPK. AMPK (AMP-activated protein kinase) is an enzyme that acts as a sensor for plants and animals, similar to a fuel gauge in a car. It revs up when it detects a depletion of the universal fuel, just as a light may blink on your dashboard when you're almost out of gas. AMPK flips the switch in your body from storing fat to burning it to restore energy balance. That's why AMPK is known not only as the *master energy sensor*¹¹⁸ in our body but also the *fat controller*.¹¹⁹ That's why it played a starring role in *How Not to Diet*. But it doesn't affect only weight control. It can also control aging.¹²⁰

In times of plenty, our cells can plow full steam ahead. However, when times are lean—when there isn't enough food for an animal or enough light for a plant (darkness is essentially plant starvation)¹²¹—AMPK kicks in to reorient the cell into conservation mode and start tapping into energy stores, like burning off body fat. Our cells can also institute a recycling program called autophagy.

Autophagy is a housekeeping process by which defective cellular components, such as misfolded proteins that had been allowed to build up wastefully in times of surplus, are broken down and scrapped for spare parts. As I discuss in detail in the Autophagy chapter, autophagy doubles as both salvage operation and garbage disposal unit, scavenging raw materials in scarce supply while clearing away some of the built-up damaged debris that is implicated in the aging process. This is one of the reasons AMPK is increasingly recognized as a pro-longevity factor.¹²² AMPK induces autophagy, which cleans house, sweeps away accumulated waste, and effectively institutes a sort of cellular reset.¹²³

There are three main ways longevity researchers establish an aging pathway: Does the factor worsen with age? If you amplify it, does it accelerate aging? And, if you dampen it, does it slow aging and thereby extend lifespan?¹²⁴ The loss of AMPK activity as we age fits all three criteria. As we grow older, AMPK levels drop and it gets harder to activate, harder to flip the switch to recharge our batteries.¹²⁵ When this decline is exacerbated, aging is hastened (at least in mice),¹²⁶ but when this process is reversed and AMPK activation is boosted, lifespan is extended in model organisms¹²⁷—by as much as 38 percent in *C. elegans*,¹²⁸ a roundworm I profile in see.nf/models.