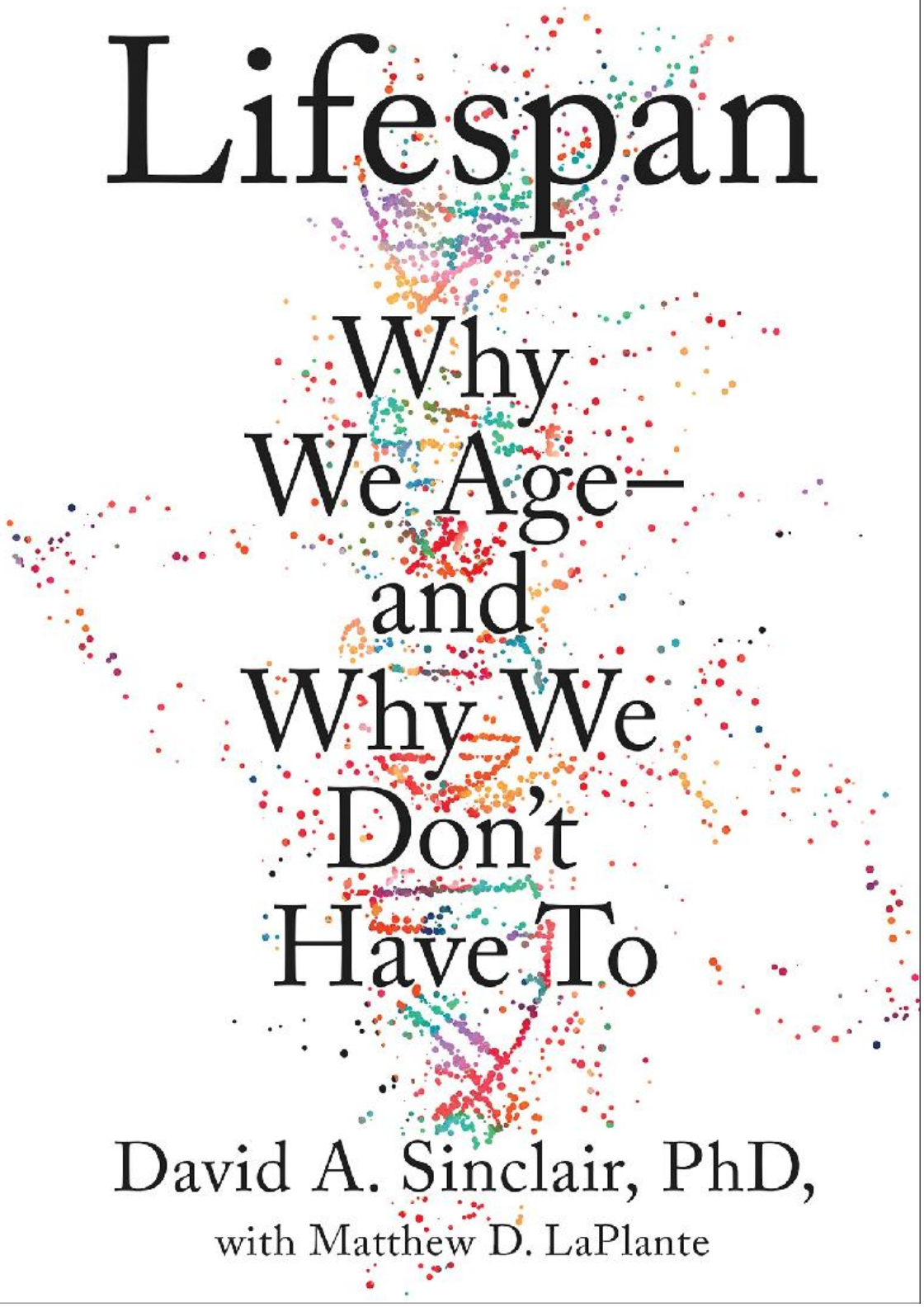
"An elegant and exciting book that deserves to be read broadly and deeply."
—**Siddhartha Mukherjee,** Pulitzer Prize–winning and #1 *New York Times* bestselling author

Lifespan

Why We Age—and Why We Don't Have To



David A. Sinclair, PhD,
with Matthew D. LaPlante

Praise for LIFESPAN

“In this insightful and provocative book that asks questions about how we age,

and whether humans can overcome decay and degeneration, Sinclair grapples

with some of the most fundamental questions around the science of aging. The

result is an elegant and exciting book that deserves to be read broadly and deeply.”

—Siddhartha Mukherjee, Pulitzer Prize–winning and #1 *New York Times*

bestsel ing author

“If you ever wondered how we age, if we can slow or even reverse aging, and if we

can live a healthy 100-plus years, then David Sinclair’s new book, *Lifespan* . . . wil

guide you through the science and the practical strategies to make your health

span equal your lifespan, and make your lifespan long and vibrant.”

—Mark Hyman, MD Director, Cleveland Clinic Center for Functional

Medicine and #1 *New York Times* bestsel ing author

“This is the most visionary book about aging I have ever read. Seize the day —and

seize this book!”

—Dean Ornish, MD, founder & president, Preventive Medicine Research

Institute, and *New York Times* bestsel ing author of *UnDo It!*

“In *Lifespan*, David Sinclair eloquently tel s us the secret everyone wants to know:

how to live longer and age slower. Sinclair convinces us that it is not only possible

to live beyond one hundred years, it is inevitable that we wil be able to one day do

so. If you are someone who wants to know how to beat aging, *Lifespan* is a must-

read.”

—Wil iam W. Li, MD, *New York Times* bestsel ing author of *Eat to Beat*

Disease

“[I]nsightful, inspiring, and informative. [Sinclair] has translated a wealth of

molecular detail into a program that we can al use to live longer and healthier. For

anyone interested in understanding the aging process, living longer, and avoiding

the diseases of aging, this is *the* book to read.”

—Dale Bredesen, MD, *New York Times* bestsel ing author of *The End of*

Alzheimer’s

“A visionary book from one of the most masterful longevity scientists of our time.

Lifespan empowers us to change our health today while revealing a potential

future when we live younger for longer.”

—Sara Gottfried, MD, *New York Times* bestsel ing author of *The Hormone*

Cure

“Prepare to have your mind blown. You are holding in your hands the precious

results of decades of work, as shared by Dr. David Sinclair, the rock star of aging

and human longevity.”

—Dave Asprey, founder and CEO of Bul etproof and *New York Times*

bestsel ing author of *The Bulletproof Diet*

“Imagine a world in which we can live long enough to meet not just our

grandchildren, but our great-grandchildren. This is Sinclair’s vision for the future

of humankind, a vision that looks to science, nature, history, and even politics to

make the case that it is possible to live wel into our hundreds. *Lifespan* is boldly

leading the way.”

—Jason Fung, MD, author of *The Diabetes Code* and *The Obesity Code*

“In *Lifespan*, Dr. David Sinclair . . . provides us with the everyday tools that we

can al use to stop what he now cal s ‘the disease of aging.’. . . You owe it to

yourself and your loved ones to read and fol ow his advice, as I have for the last 15

years!”

—Steven R. Gundry, MD, *New York Times* bestsel ing author of *The Longevity Paradox* and medical director of the International Heart and Lung Institute

“*Lifespan* . . . transcends everything we know about aging and longevity—a combination of bril iant scientific work, a pioneering mind, and the dream for a longer, healthier and happier life. *Lifespan* provides a vision for our future and the road map on how to get there, merging scientific breakthroughs and simple lifestyle changes to not only help us feel younger, but actual y become younger.”

—Naomi Whittel, *New York Times* bestsel ing author of *Glow15*

“David Sinclair masterful y presents a bold vision of the future in which humanity is able to slow or reverse the aging process and live younger, healthier lives for longer.”

—Victor J. Dzau, MD, president of the US National Academy of Medicine and CEO of Duke University Medical Center

“There are few books that have ever made me think about science in a fundamental y new way. David Sinclair’s book did that for me on aging. This is a book that anyone who ages must read.”

—Leroy Hood, PhD, professor at the California Institute of Technology, inventor, entrepreneur, member of al three US National Academies, and coauthor of *Code of Codes*

"In *Lifespan*, the ful force of [Sinclair's] optimism, humor, and soft-spoken eloquence as a storytel er-scientist come through. I'm hoping we have David Sinclair with us and doing his science and writing books for another 500 years, give or take a century."

—David Ewing Duncan, award-winning journalist, bestsel ing author, and curator of *Arc Fusion*

"*Lifespan* gives us hope for an extraordinary life. As the bril iant Dr. David Sinclair explains, aging is a disease, and that disease is treatable. This eye-opening book takes you to front lines of incredible breakthroughs. Enjoy this must-read masterpiece!"

—Peter H. Diamandis, MD, *New York Times* bestsel ing author of *Abundance* and *Bold*

"[D]escribes real science that wil question the foundation of everything we assume about our life and society."

—Salman Khan, founder of Khan Academy

“David is a pioneer poised to change how we think about and understand aging.”

—Stephanie Lederman, CEO of the American Federation for Aging Research (AFAR), New York

“The most important message and priority of our time. For years to come, humanity wil reflect on this book with awe and respect. Read it. . . . Your life depends on it.”

—Marc Hodosh, former owner & cocreator of TEDMED

“A tour de force. Sinclair’s book, and his life’s work, ranks with humanity’s greatest contributions to helping enhance the joy and happiness of life, ranking with the works of Jenner, Pasteur, Salk, Locke, Gandhi, and Edison. A masterpiece.”

—Martine Rothblatt, founder, Chairwoman of the Board, and CEO of United Therapeutics and creator of SiriusXM Satel ite Radio

“Stepping on the moon changed humanity. In *Lifespan*, Sinclair takes the ultimate step for humanity that wil transform our lives beyond anything we could ever have imagined. The author is bold, the science is profound, and our future is here.”

—Henry Markram, PhD, professor at EPFL, Switzerland, director of the Blue Brain Project, and founder of Frontiers open-access journals

“An intel ectual y fascinating book with tantalizing insights on the most

important issue about yours and everyone’s future.”

—Andrew Scott, PhD, professor of economics at the London Business

School and author of *The 100-Year Life*

LIFESPAN

WHY WE AGE—

AND

WHY WE DON'T HAVE TO

David A. Sinclair, PhD, AO,

with Matthew D. LaPlante

Illustrations by Catherine L. Delphia

ATRIA BOOKS

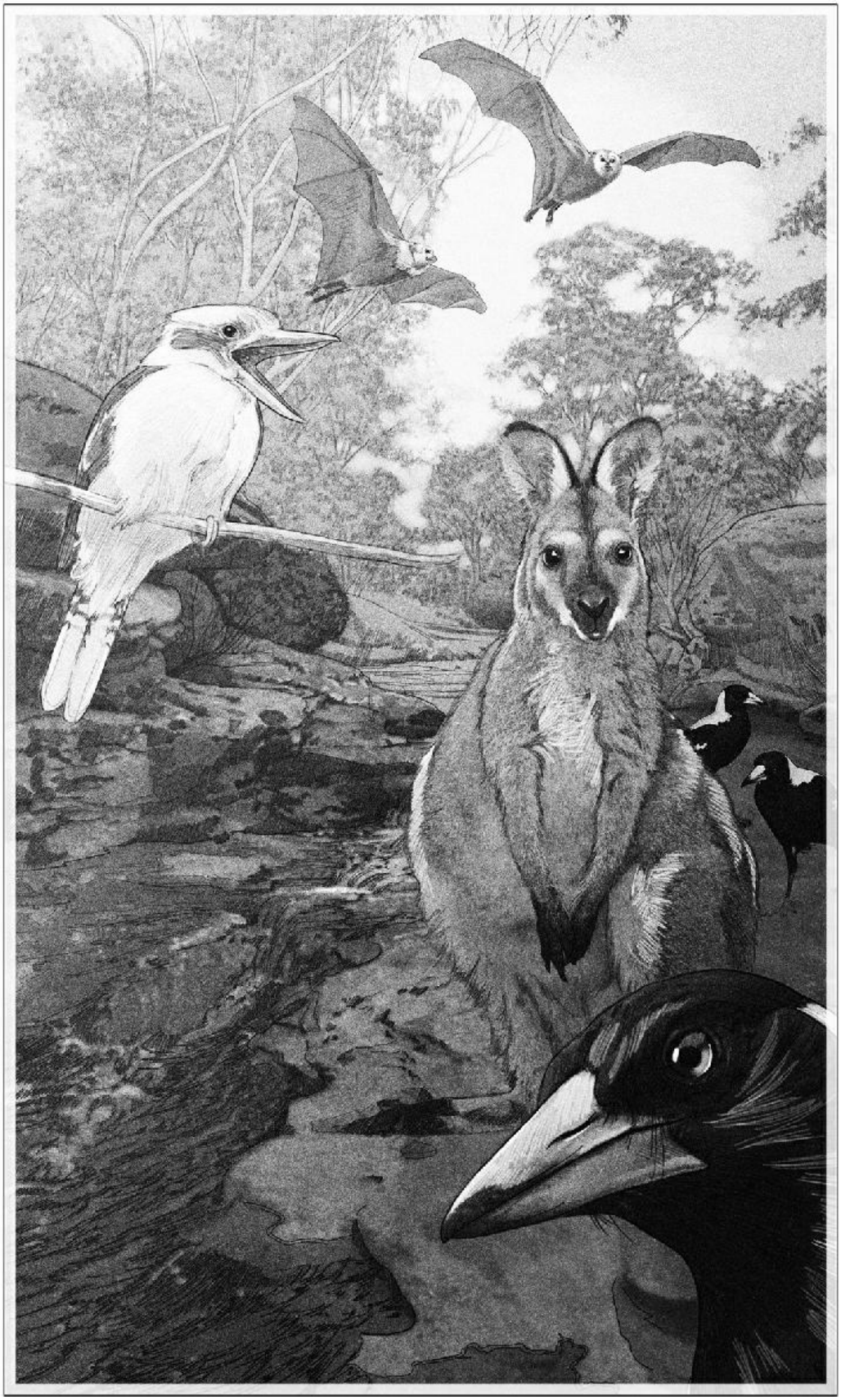
NEW YORK LONDON TORONTO SYDNEY NEW DELHI

To my grandmother Vera, who taught me to see the world the way it could be.

To my mother, Diana, who cared more about her children than herself.

To my wife, Sandra, my bedrock.

And to my great-great-grandchildren; I am looking forward to meeting you.



THE BUSH. In the wild and wonderful world of the Garigal clan, waterfal s and saltwater estuaries wind

through ancient sandstone escarpments, under shadowy canopies of charred bloodwoods, angophoras, and

scribbly gums that kookaburras, currawongs, and wal abies cal home.

INTRODUCTION

A GRANDMOTHER'S PRAYER

I GREW UP ON THE edge of the bush. In figurative terms, my backyard was a hundred-

acre wood. In literal terms, it was much bigger than that. It went on as far as my

young eyes could see, and I never grew tired of exploring it. I would hike and hike,

stopping to study the birds, the insects, the reptiles. I pul ed things apart. I rubbed

the dirt between my fingers. I listened to the sounds of the wild and tried to

connect them to their sources.

And I played. I made swords from sticks and forts from rocks. I climbed trees

and swung on branches and dangled my legs over steep precipices and jumped off

of things that I probably shouldn't have jumped off. I imagined myself as an

astronaut on a distant planet. I pretended to be a hunter on safari. I lifted my

voice for the animals as though they were an audience at the opera house.

“Coooeey!” I would hol er, which means “Come here” in the language of the Garigal people, the original inhabitants.

I wasn’t unique in any of this, of course. There were lots of kids in the northern suburbs of Sydney who shared my love of adventure and exploration and imagination. We expect this of children. We *want* them to play this way.

Until, of course, they’re “too old” for that sort of thing. Then we want them to go to school. Then we want them to go to work. To find a partner. To save up.

To buy a house.

Because, you know, the clock is ticking.

My grandmother was the first person to tel me that it didn’t have to be that way. Or, I guess, she didn’t tel me so much as show me.

She had grown up in Hungary, where she spent Bohemian summers swimming in the cool waters of Lake Balaton and hiking in the mountains of its northern shore at a holiday resort that catered to actors, painters, and poets. In the winter months, she helped run a hotel in the Buda Hil s before the Nazis took it over and converted it to the central command of the Schutzstaffel, or “SS.”

A decade after the war, in the early days of the Soviet occupation, the

Communists began to shut down the borders. When her mother tried to cross

il egal y into Austria, she was caught, arrested, and sentenced to two years in jail

and died shortly after. During the Hungarian Uprising in 1956, my grandmother

wrote and distributed anti-Communist newsletters in the streets of Budapest.

After the revolution was crushed, the Soviets began arresting tens of thousands of

dissidents, and she fled to Australia with her son, my father, reasoning that it was

the furthest they could get from Europe.

She never set foot in Europe again, but she brought every bit of Bohemia with

her. She was, I have been told, one of the first women to sport a bikini in Australia

and got chased off Bondi Beach because of it. She spent years living in New

Guinea—which even today is one of the most intensely rugged places on our

planet—al by herself.

Though her bloodline was Ashkenazi Jew and she had been raised a Lutheran,

my grandmother was a very secular person. Our equivalent of the Lord's Prayer

was the English author Alan Alexander Milne's poem "Now We Are Six," which

ends:

But now I am six,

I'm as clever as clever.

So I think I'll be six now

for ever and ever.

She read that poem to my brother and me again and again. Six, she told us, was

the very best age, and she did her damnedest to live life with the spirit and awe of a

child of that age.

Even when we were very young, my grandmother didn't want us to cal her

"grandmother." Nor did she like the Hungarian term, "nagymama," or any of the

other warm terms of endearment such as "bubbie," "grandma," and "nana."

To us boys, and everyone else, she was simply Vera.

Vera taught me to drive, swerving and swaying across al of the lanes,

"dancing" to whatever music was on the car's radio. She told me to enjoy my

youth, to savor the feeling of being young. Adults, she said, always ruined things.

Don't grow up, she said. Never grow up.

Wel into her 60s and 70s, she was stil what we cal "young at heart," drinking

wine with friends and family, eating good food, tel ing great stories, helping the

poor, sick, and less fortunate, pretending to conduct symphonies, laughing late

into the night. By just about anyone's standard, that's the mark of a "life wel

lived."

But yes, the clock was ticking.

By her mid-80s, Vera was a shel of her former self, and the final decade of her

life was hard to watch. She was frail and sick. She stil had enough wisdom left to

insist that I marry my fiancée, Sandra, but by then music gave her no joy and she

hardly got out of her chair; the vibrancy that had defined her was gone.

Toward the end, she gave up hope. "This is just the way it goes," she told me.

She died at the age of 92. And, in the way we've been taught to think about

these things, she'd had a good, long life. But the more I have thought about it, the

more I have come to believe that the person she *truly* was had been dead many

years at that point.

Growing old may seem a distant event, but every one of us wil experience the

end of life. After we draw our last breath, our cel s wil scream for oxygen, toxins

wil accumulate, chemical energy wil be exhausted, and cel ular structures wil

disintegrate. A few minutes later, al of the education, wisdom, and memories that

we cherished, and al of our future potential, wil be irreversibly erased.

I learned this firsthand when my mother, Diana, passed away. My father, my

brother, and I were there. It was a quick death, thankful y, caused by a buildup of

liquid in her remaining lung. We had just been laughing together about the eulogy

I'd written on the trip from the United States to Australia, and then suddenly she

was writhing on the bed, sucking for air that couldn't satisfy her body's demand

for oxygen, staring at us with desperation in her eyes.

I leaned in and whispered into her ear that she was the best mom I could have

wished for. Within a few minutes, her neurons were dying, erasing not just the

memory of my final words to her but al of her memories. I know some people die

peaceful y. But that's not what happened to my mother. In those moments she

was transformed from the person who had raised me into a twitching, choking

mass of cel s, al fighting over the last residues of energy being created at the

atomic level of her being.

Al I could think was “No one tel s you what it is like to die. Why doesn’t

anyone tel you?”

There are few people who have studied death as intimately as the Holocaust

documentary filmmaker Claude Lanzmann. And his assessment—indeed, his

warning—is chil ing. “Every death is violent,” he said in 2010. “There is no

natural death, unlike the picture we like to paint of the father who dies quietly in

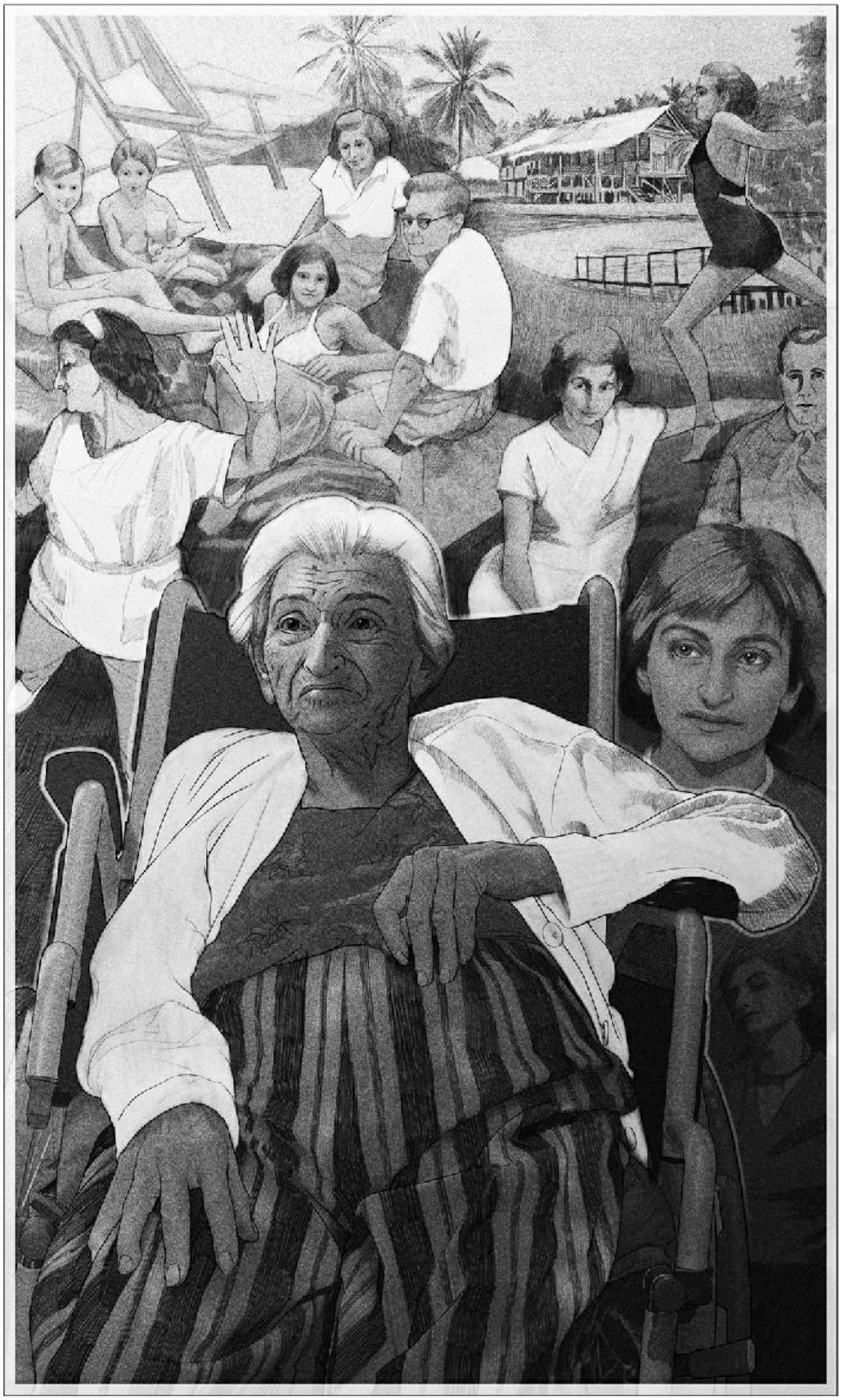
his sleep, surrounded by his loved ones. I don’t believe in that.” 1

Even if they don’t recognize its violence, children come to understand the

tragedy of death surprisingly early in their lives. By the age of four or five, they

know that death occurs and is irreversible. 2 It is a shocking thought for them, a

nightmare that is real.



A “GOOD, LONG LIFE.” My grandmother “Vera” sheltered Jews in World War II, lived in primitive New

Guinea, and was removed from Bondi Beach for wearing a bikini. The end of her life was hard to watch.

“This is just the way it goes,” she said. But the person she truly was had been dead many years at that point.

At first, because it’s calming, most children prefer to think that there are

certain groups of people who are protected from death: parents, teachers, and

themselves. Between 5 and 7, however, al children come to understand the

universality of death. Every family member wil die. Every pet. Every plant.

Everything they love. Themselves, too. I can remember first learning this. I can

also very wel remember our oldest child, Alex, learning it.

“Dad, you won’t *always* be around?”

“Sadly, no,” I said.

Alex cried on and off for a few days, then stopped, and never asked me about it

again. And I’ve never again mentioned it, either.

It doesn’t take long for the tragic thought to be buried deep in the recesses of

our subconscious. When asked if they worry about death, children tend to say

that they don’t think about it. If asked what they do think about it, they say it is

not a concern because it wil occur only in the remote future, when they get old.

That's a view most of us maintain until wel into our fifties. Death is simply

too sad and paralyzing to dwel on each day. Often, we realize it too late. When it

comes knocking, and we are not prepared, it can be devastating.

For Robin Marantz Henig, a columnist at the *New York Times*, the "bitter

truth" about mortality came late in life, after she became a grandparent. "Beneath

al the wonderful moments you may be lucky enough to share in and enjoy," she

wrote, "your grandchild's life wil be a long string of birthdays you wil not live to

see. "3

It takes courage to consciously think about your loved ones' mortality before it

actual y happens. It takes even more courage to deeply ponder your own.

It was the comedian and actor Robin Wil iams who first demanded this

courage from me through his portrayal of John Keating, the teacher and hero in

the film *Dead Poets Society*, who chal enges his teenage students to stare into the

faces of the long-dead boys in a fading photo.4

“They are not that different from you, are they?” Keating says. “Invincible, just

like you feel. . . . Their eyes are ful of hope . . . But you see, gentlemen, these boys

are now fertilizing daffodils.”

Keating encourages the boys to lean in closer to listen for a message from the

grave. Standing behind them, in a quiet, ghostly voice, he whispers, “*Carpe. Carpe*

diem. Seize the day, boys. Make your lives extraordinary.”

That scene had an enormous impact on me. It is likely that I would not have

had the motivation to become a Harvard professor if it hadn’t been for that

movie. At the age of 20, I had final y heard someone else say what my

grandmother had taught me at an early age: Do your part to make humanity be

the best it can be. Don’t waste a moment. Embrace your youth; hold on to it for

as long as you can. Fight for it. Fight for it. Never stop fighting for it.

But instead of fighting for youth, we fight for life. Or, more specifical y, we

fight against death.

As a species, we are living much longer than ever. But not much better. Not at

al . Over the past century we have gained additional years, but not additional life

—not life worth living anyway. 5

And so most of us, when we think about living to 100, stil think “God

forbid,” because we’ve seen what those final decades look like, and for most

people, most of the time, they don’t look appealing at al . Ventilators and drug

cocktails. Broken hips and diapers. Chemotherapy and radiation. Surgery after

surgery after surgery. And hospital bil s; my God, the hospital bil s.

We’re dying slowly and painful y. People in rich countries often spend a

decade or more suffering through il ness after il ness at the ends of their lives. We

think this is normal. As lifespans continue to increase in poorer nations, this wil

become the fate of bil ions of additional people. Our successes in extending life,

the surgeon and doctor Atul Gawande has noted, have had the effect of “making

mortality a medical experience. ”6

But what if it didn’t have to be that way? What if we could be younger longer?

Not years longer but decades longer. What if those final years didn’t look so

terribly different from the years that came before them? And what if, by saving

ourselves, we could also save the world?

Maybe we can never be six again—but how about twenty-six or thirty-six?

What if we could play as children do, deeper into our lives, without worrying

about moving on to the things adults *have to do* so soon? What if al of the things

we need to compress into our teenage years didn't need to be so compressed after

al ? What if we weren't so stressed in our 20s? What if we weren't feeling middle-

aged in our 30s and 40s? What if, in our 50s, we wanted to reinvent ourselves and

couldn't think of a single reason why we shouldn't? What if, in our 60s, we

weren't fretting about leaving a legacy but *beginning* one?

What if we didn't have to worry that the clock was ticking? And what if I told

you that soon—very soon, in fact—we won't?

Wel , that's what I'm tel ing you.

I'm fortunate that after thirty years of searching for truths about human

biology, I find myself in a unique position. If you were to visit me in Boston,

you'd most likely find me hanging out in my lab at Harvard Medical School,

where I'm a professor in the Department of Genetics and codirector of the Paul F.

Glenn Center for the Biological Mechanisms of Aging. I also run a sister lab at my

alma mater, the University of New South Wales in Sydney. In my labs, teams of

bril iant students and PhDs have both accelerated and reversed aging in model

organisms and have been responsible for some of the most cited research in the

field, published in some of the world's top scientific journals. I am also a

cofounder of a journal, *Aging*, that provides space to other scientists to publish

their research on one of the most chal enging and exciting questions of our time,

and a cofounder of the Academy for Health and Lifespan Research, a group of

the top twenty researchers in aging worldwide.

In trying to make practical use of my discoveries, I've helped start a number of

biotechnology companies and sit as a chair of the scientific boards of advisers of

several others. These companies work with hundreds of leading academics in

scientific areas ranging from the origin of life to genomics to pharmaceuticals. 7 I

am, of course, aware of my own labs' discoveries years before they are made

public, but through these associations, I'm also aware of many other

transformational discoveries ahead of time, sometimes a decade ahead. The

coming pages wil serve as your backstage pass and your front-row seat.

Having received the equivalent of a knighthood in Australia and taken on the

role of an ambassador, I've been spending quite a bit of my time briefing political

and business leaders around the world about the ways our understanding of aging

is changing—and what that means for humanity going forward. 8

I've applied many of my scientific findings to my own life, as have many of my

family members, friends, and col eagues. The results—which, it should be noted,

are completely anecdotal—are encouraging. I'm now 50, and I feel like a kid. My

wife and kids wil tel you I act like one, too.

That includes being a *stickybeak*, the Australian term for someone who is

overly inquisitive, perhaps derived from the currawong crows that used to punch

through the foil lids of the milk bottles delivered to our homes and drink the milk

out of them. My old high school friends stil like to tease me about how, whenever

they came over to my parents' house, they would find me pul ing something

apart: a pet moth's cocoon, a spider's curled-up leaf shelter, an old computer, my

father’s tools, a car. I became quite good at it. I just wasn’t very good at putting

these things back together.

I couldn’t bear *not* knowing how something worked or where it came from. I

stil can’t—but at least now I get paid for it.

My childhood home is perched on a rocky mountainside. Below is a river that

runs into Sydney Harbor. Arthur Phil ip, the first governor of New South Wales,

explored these val eys in April 1788, only a few months after he and his First Fleet

of marines, prisoners, and their families established a colony on the shores of what

he cal ed the “finest and most extensive harbor in the universe.” The person most

responsible for him being there was the botanist Sir Joseph Banks, who eighteen

years earlier had sailed up the Australian coastline with Captain James Cook on

his “voyage round the world.” 9

After returning to London with hundreds of plant specimens to impress his

col eagues, Banks lobbied King George III to start a British penal colony on the

continent, the best site for which, he argued, not coincidental y, would be a bay

cal ed “Botany” on “Cape Banks.” 10 The First Fleet settlers soon discovered that

Botany Bay, despite its most excel ent name, had no source of water, so they sailed

up to Sydney Harbor and found one of the world’s largest “rias,” a highly

branched, deep waterway that formed when the Hawkesbury River system had

been flooded by rising sea levels after the last ice age.

At the age of 10, I had already discovered through exploration that the river in

my backyard flowed down into Middle Harbor, a branch of Sydney Harbor. But I

could no longer stand not knowing where the river originated. I needed to know

what the *beginning* of a river looked like.

I fol owed it upstream, left the first time it forked and right the time after that,

wending into and out of several suburbs. By nightfal I was miles from home,

beyond the last mountain on the horizon. I had to ask a stranger to let me cal my

mother to beg her to come pick me up. A few times after that I tried searching

upstream, but never did get anywhere close to the fount. Like Juan Ponce de

León, the Spanish explorer of Florida known for his apocryphal quest to find the

Fountain of Youth, I failed. 11

Ever since I can remember, I have wanted to understand why we grow old. But

finding the source of a complex biological process is like searching for the spring at

the source of a river: it's not easy.

On my quest, I've wound my way left and right and had days when I wanted

to give up. But I've persevered. Along the way, I have seen a lot of tributaries, but

I've also found what may be the spring. In the coming pages, I wil present a new

idea about why aging evolved and how it fits into what I cal the Information

Theory of Aging. I wil also tel you why I have come to see aging as a disease—the

most common disease—one that not only can but *should* be aggressively treated.

That's part I.

In part II, I wil introduce you to the steps that can be taken right now—and

new therapies in development—that may slow, stop, or reverse aging, bringing an

end to aging as we know it.

And yes, I ful y recognize the implications of the words "bringing an end to

aging as we know it," so, in part III, I wil acknowledge the many possible futures

these actions could create and propose a path to a future that we can look forward

to, a world in which the way we can get to an increased lifespan is through an ever-

rising *healthspan*, the portion of our lives spent without disease or disability.

There are plenty of people who wil tel you that's a fairy tale—closer to the

works of H. G. Wel s than those of C. R. Darwin. Some of them are very smart. A

few are even people who understand human biology quite wel and whom I

respect.

Those people wil tel you that our modern lifestyles have cursed us with

shortening lifespans. They'l say you're unlikely to see 100 years of age and that

your children aren't likely to get to the century mark, either. They'l say they've

looked at the science of it al and done the projections, and it sure doesn't seem

likely that your grandchildren wil get to their 100th birthdays, either. And they'l

say that if you *do* get to 100, you probably won't get there healthy and you

definitely won't be there for long. And if they grant you that people wil live

longer, they'l tel you that it's the worst thing for this planet. Humans are the

enemy!

They've got good evidence for al of this—the entire history of humanity, in

fact.Sure, little by little, milennia by milennia, we've been adding years to the

average human life, they wil say. Most of us didn't get to 40, and then we did.

Most of us didn't get to 50, and then we did. Most of us didn't get to 60, and then

we did.12 By and large, these increases in life expectancy came as more of us gained

access to stable food sources and clean water. And largely the average was pushed

upward from the bottom; deaths during infancy and childhood fel , and life

expectancy rose. This is the simple math of human mortality.

But although the *average* kept moving up, the *limit* did not. As long as we've

been recording history, we have known of people who have reached their 100th

year and who might have lived a few years beyond that mark. But very few reach

110. Almost no one reaches 115.

Our planet has been home to more than 100 bil ion humans so far. We know

of just one, Jeanne Calment of France, who ostensibly lived past the age of 120.

Most scientists believe she died in 1997 at the age of 122, although it's also

possible that her daughter replaced her to avoid paying taxes. 13 Whether or not

she actual y made it to that age real y doesn't matter; others have come within a

few years of that age but most of us, 95 percent to be precise, are dead before 100.

So it certainly makes sense when people say that we might continue to chip

away at the average, but we're not likely to move the limit. They say it's easy to

extend the maximum lifespan of mice or of dogs, but we humans are different.

We simply live too long already.

They are wrong.

There's also a difference between extending life and prolonging vitality. We're

capable of both, but simply keeping people alive—decades after their lives have

become defined by pain, disease, frailty, and immobility—is no virtue.

Prolonged vitality—meaning not just more years of life but more active,

healthy, and happy ones—is coming. It is coming sooner than most people expect.

By the time the children who are born today have reached middle age, Jeanne

Calment may not even be on the list of the top 100 oldest people of al time. And

by the turn of the next century, a person who is 122 on the day of his or her death

may be said to have lived a ful , though not particularly long, life. One hundred

and twenty years might be not an outlier but an expectation, so much so that we

won't even cal it longevity; we wil simply cal it "life," and we wil look back with

sadness on the time in our history in which it was not so.

What's the upward limit? I don't think there is one. Many of my col eagues

agree. 14 There is no biological law that says we must age. 15 Those who say there is

don't know what they're talking about. We're probably stil a long way off from a

world in which death is a rarity, but we're not far from pushing it ever farther into

the future.

Al of this, in fact, is inevitable. Prolonged healthy lifespans are in sight. Yes,

the entire history of humanity suggests otherwise. But the science of lifespan

extension in this particular century says that the previous dead ends are poor

guides.

It takes radical thinking to even begin to approach what this wil mean for our

species. Nothing in our bil ions of years of evolution has prepared us for this,

which is why it's so easy, and even al uring, to believe that it simply cannot be

done.

But that's what people thought about human flight, too—up until the moment someone did it.

Today the Wright brothers are back in their workshop, having successful y flown their gliders down the sand dunes of Kitty Hawk. The world is about to change.

And just as was the case in the days leading up to December 17, 1903, the majority of humanity is oblivious. There was simply no context with which to construct the idea of control ed, powered flight back then, so the idea was fanciful, magical, the stuff of speculative fiction.16

Then: liftoff. And nothing was ever the same again.

We are at another point of historical inflection. What hitherto seemed magical wil become real. It is a time in which humanity wil redefine what is possible; a time of ending the inevitable.

Indeed, it is a time in which we wil redefine what it means to be human, for this is not just the start of a revolution, it is the start of an evolution.

PART I

WHAT WE KNOW

(THE PAST)

ONE

VIVA PRIMORDIUM

IMAGINE A PLANET ABOUT THE size of our own, about as far from its star, rotating

around its axis a bit faster, such that a day lasts about twenty hours. It is covered

with a shal ow ocean of salty water and has no continents to speak of—just some

sporadic chains of basaltic black islands peeking up above the waterline. Its

atmosphere does not have the same mix of gases as ours. It is a humid, toxic

blanket of nitrogen, methane, and carbon dioxide.

There is no oxygen. There is no life.

Because this planet, our planet as it was 4 bil ion years ago, is a ruthlessly

unforgiving place. Hot and volcanic. Electric. Tumultuous.

But that is about to change. Water is pooling next to warm thermal vents that

litter one of the larger islands. Organic molecules cover al surfaces, having ridden

in on the backs of meteorites and comets. Sitting on dry, volcanic rock, these

molecules wil remain just molecules, but when dissolved in pools of warm water,

through cycles of wetting and drying at the pools' edges, a special chemistry takes

place.[1] As the nucleic acids concentrate, they grow into polymers, the way salt

crystals form when a seaside puddle evaporates. These are the world's first RNA

molecules, the predecessors to DNA. When the pond refil s, the primitive genetic

material becomes encapsulated by fatty acids to form microscopic soap bubbles—

the first cel membranes. 2

It doesn't take long, a week perhaps, before the shal ow ponds are covered with

a yel ow froth of tril ions of tiny precursor cel s fil ed with short strands of nucleic

acids, which today we cal genes.

Most of the protocel s are recycled, but some survive and begin to evolve

primitive metabolic pathways, until final y the RNA begins to copy itself. That

point marks the origin of life. Now that life has formed—as fatty-acid soap

bubbles fil ed with genetic material—they begin to compete for dominance.

There simply aren't enough resources to go around. May the best scum win.

Day in and day out, the microscopic, fragile life-forms begin to evolve into

more advanced forms, spreading into rivers and lakes.

Along comes a new threat: a prolonged dry season. The level of the scum-

covered lakes has dropped by a few feet during the dry season, but the lakes have

always fil ed up again as the rains returned. But this year, thanks to unusual y

intense volcanic activity on the other side of the planet, the annual rains don't fal

as they usual y do and the clouds pass on by. The lakes dry up completely.

What remains is a thick, yel ow crust covering the lake beds. It is an ecosystem

defined not by the annual waxing and waning of the waters but by a brutal

struggle for survival. And more than that: it is a fight for the future—because the

organisms that survive wil be the progenitors of every living thing to come:

archaea, bacteria, fungi, plants, and animals.

Within this dying mass of cel s, each scrapping for and scraping by on the

merest minimums of nutrients and moisture, each one doing whatever it can to

answer the primal cal to reproduce, there is a unique species. Let's cal it *Magna*

superstes. That's Latin for "great survivor."

It does not look very different from the other organisms of the day, but *M.*

superstes has a distinct advantage: it has evolved a genetic survival mechanism.

There wil be far more complicated evolutionary steps in the eons to come,

changes so extreme that entire branches of life wil emerge. These changes—the

products of mutations, insertions, gene rearrangements, and the horizontal

transfer of genes from one species to another—wil create organisms with bilateral

symmetry, stereoscopic vision, and even consciousness.

By comparison, this early evolutionary step looks, at first, to be rather simple.

It is a circuit. A gene circuit.

The circuit begins with gene A, a caretaker that stops cel s from reproducing

when times are tough. This is key, because on early planet Earth, *most* times are

tough. The circuit also has a gene B, which encodes for a "silencing" protein. This

silencing protein shuts gene A off when times are good, so the cel can make

copies of itself when, and only when, it and its offspring wil likely survive.

The genes themselves aren't novel. Al life in the lake has these two genes. But

what makes *M. superstes* unique is that the gene B silencer has mutated to give it a

second function: it helps repair DNA. When the cel 's DNA breaks, the silencing

protein encoded by gene B moves from gene A to help with DNA repair, which

turns on gene A. This temporarily stops al sex and reproduction until the DNA

repair is complete.

This makes sense, because while DNA is broken, sex and reproduction are the

last things an organism should be doing. In future multicel ular organisms, for

instance, cel s that fail to pause while fixing a DNA break wil almost certainly lose

genetic material. This is because DNA is pul ed apart prior to cel division from

only one attachment site on the DNA, dragging the rest of the DNA with it. If

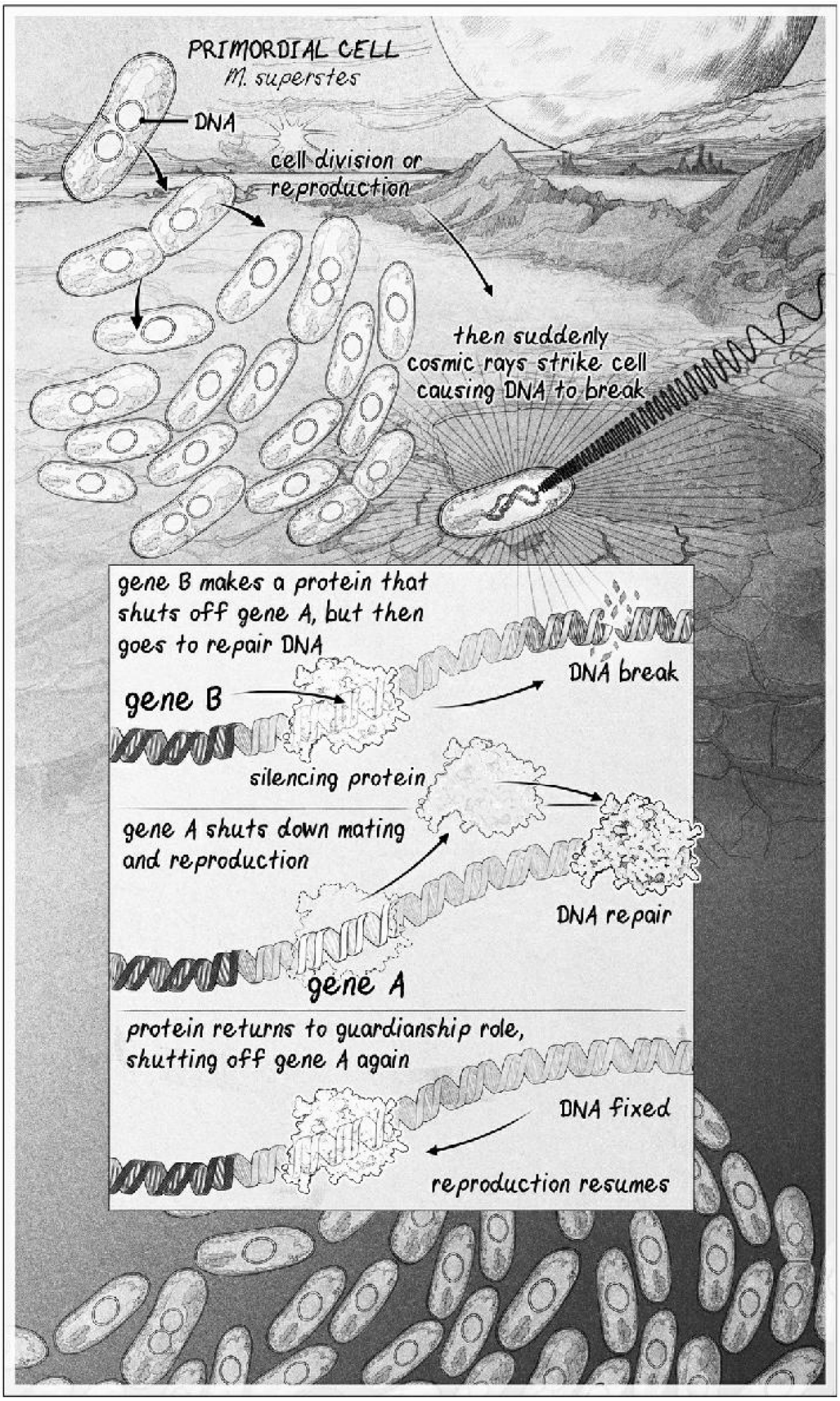
DNA is broken, part of a chromosome wil be lost or duplicated. The cel s wil

likely die or multiply uncontrol ably into a tumor.

With a new type of gene silencer that repairs DNA, too, *M. superstes* has an

edge. It hunkers down when its DNA is damaged, then revives. It is superprimed

for survival.


PRIMORDIAL CELL
M. superstes
DNA
cell division or reproduction
then suddenly cosmic rays strike cell causing DNA to break
gene B makes a protein that shuts off gene A, but then goes to repair DNA
DNA break
gene B
silencing protein
gene A shuts down mating and reproduction
DNA repair
gene A
protein returns to guardianship role, shutting off gene A again
DNA fixed
reproduction resumes

THE EVOLUTION OF AGING. A 4-bil ion-year-old gene circuit in the first life-forms would have turned off

reproduction while DNA was being repaired, providing a survival advantage. Gene A turns off reproduction,

and gene B makes a protein that turns off gene A when it is safe to reproduce. When DNA breaks, however,

the protein made by gene B leaves to go repair DNA. As a result, gene A is turned on to halt reproduction

until repair is complete. We have inherited an advanced version of this survival circuit.

And that's good, because now comes yet another assault on life. Powerful

cosmic rays from a distant solar eruption are bathing the Earth, shredding the

DNA of al the microbes in the dying lakes. The vast majority of them carry on

dividing as if nothing has happened, unaware that their genomes have been

broken and that reproducing wil kil them. Unequal amounts of DNA are shared

between mother and daughter cel s, causing both to malfunction. Ultimately, the

endeavor is hopeless. The cel s al die, and nothing is left.

Nothing, that is, but *M. superstes*. For as the rays wreak their havoc, *M.*

superstes does something unusual: thanks to the movement of protein B away

from gene A to help repair the DNA breaks, gene A switches on and the cel s stop

almost everything else they are doing, turning their limited energy toward fixing

the DNA that has been broken. By virtue of its defiance of the ancient imperative

to reproduce, *M. superstes* has survived.

When the latest dry period ends and the lakes refil , *M. superstes* wakes up. *Now*

it can reproduce. Again and again it does so. Multiplying. Moving into new

biomes. Evolving. Creating generations upon generations of new descendants.

They are our Adam and Eve.

Like Adam and Eve, we don't know if *M. superstes* ever existed. But my

research over the past twenty-five years suggests that every living thing we see

around us today is a product of this great survivor, or at least a primitive organism

very much like it. The fossil record in our genes goes a long way to proving that

every living thing that shares this planet with us stil carries this ancient genetic

survival circuit, in more or less the same basic form. It is there in every plant. It is

there in every fungus. It is there in every animal.

It is there in us.

I propose the reason this gene circuit is conserved is that it is a rather simple

and elegant solution to the chal enges of a sometimes brutish and sometimes

bounteous world that better ensures the survival of the organisms that carry it. It

is, in essence, a primordial survival kit that diverts energy to the area of greatest

need, fixing what exists in times when the stresses of the world are conspiring to

wreak havoc on the genome, while permitting reproduction only when more

favorable times prevail.

And it is so simple and so robust that not only did it ensure life's continued

existence on the planet, it ensured that Earth's chemical survival circuit was passed

on from parent to offspring, mutating and steadily improving, helping life

continue for bil ions of years, no matter what the cosmos brought, and in many

cases al owing individuals' lives to continue for far longer than they actual y

needed to.

The human body, though far from perfect and stil evolving, carries an

advanced version of the survival circuit that al ows it to last for decades past the

age of reproduction. While it is interesting to speculate why our long lifespans

first evolved—the need for grandparents to educate the tribe is one appealing

theory—given the chaos that exists at the molecular scale, it's a wonder we survive

thirty seconds, let alone make it to our reproductive years, let alone reach 80 more

often than not.

But we do. Marvelously we do. Miraculously we do. For we are the progeny of

a very long lineage of great survivors. Ergo, we are great survivors.

But there is a trade-off. For this circuit within us, the descendant of a series of

mutations in our most distant ancestors, is also the reason we age.

And yes, that definite singular article is correct: it is *the* reason.

TO EVERYTHING THERE IS A REASON

If you are taken aback by the notion that there is a singular cause of aging, you are

not alone. If you haven't given any thought at al as to why we age, that's perfectly

normal, too. A lot of biologists haven't given it much thought, either. Even

gerontologists, doctors who specialize in aging, often don't ask why we age—they

simply seek to treat the consequences.

This isn't a myopia specific to aging. As recently as the late 1960s, for example,

the fight against cancer was a fight against its symptoms. There was no unified

explanation for why cancer happens, so doctors removed tumors as best they

could and spent a lot of time tel ing patients to get their affairs in order. Cancer

was “just the way it goes,” because that’s what we say when we can’t explain

something.

Then, in the 1970s, genes that cause cancer when mutated were discovered by

the molecular biologists Peter Vogt and Peter Duesberg. These so-cal ed

oncogenes shifted the entire paradigm of cancer research. Pharmaceutical

developers now had targets to go after: the tumor-inducing proteins encoded by

genes, such as *BRAF*, *HER2*, and *BCR-ABL*. By inventing chemicals that

specifical y block the tumor-promoting proteins, we could final y begin to move

away from using radiation and toxic chemotherapeutic agents to attack cancers at

their genetic source, while leaving normal cel s untouched. We certainly haven’t

cured al types of cancer in the decades since then, but we no longer believe it’s

impossible to do so.

Indeed, among an increasing number of cancer researchers, optimism abounds.

And that hopefulness was at the heart of what was arguably the most memorable

part of President Barack Obama's final State of the Union address in 2016.

"For the loved ones we've al lost, for the family we can stil save, let's make

America the country that cures cancer once and for al ," Obama said as he stood

in the House of Representatives chamber and cal ed for a "cancer moon shot."

When he placed then Vice President Joe Biden—whose son Beau had died of

brain cancer a year earlier—in charge of the effort, even some of the Democrats'

staunch political enemies had trouble holding back the tears.

In the days and weeks that fol owed, many cancer experts noted that it would

take far more than the year remaining to the Obama-Biden administration to end

cancer. Very few of those experts, however, said it absolutely couldn't be done.

And that's because, in the span of just a few decades, we had completely changed

the way we think about cancer. We no longer submit ourselves to its inevitability

as part of the human condition.

One of the most promising breakthroughs in the past decade has been immune

checkpoint therapy, or simply “immunotherapy.” Immune T-cel s continual y

patrol our body, looking for rogue cel s to identify and kil before they can

multiply into a tumor. If it weren’t for T-cel s, we’d al develop cancer in our

twenties. But rogue cancer cel s evolve ways to fool cancer-detecting T-cel s so

they can go on happily multiplying. The latest and most effective

immunotherapies bind to proteins on the cancer cel s’ surface. It is the equivalent

of taking the invisible cloak off cancer cel s so T-cel s can recognize and kil them.

Although fewer than 10 percent of al cancer patients currently benefit from

immunotherapy, that number should increase thanks to the hundreds of trials

currently in progress.

We continue to rail against a disease we once accepted as fate, pouring bil ions

of dol ars into research each year, and the effort is paying off. Survival rates for

once lethal cancers are increasing dramatical y. Thanks to a combination of a

BRAF inhibitor and immunotherapy, survival of melanoma brain metastases, one

of the deadliest types of cancer, has increased by 91 percent since 2011. Between