Change Your Genes, Change Your Life

Creating Optimal Health with the

New Science of Epigenetics

SAMPLE CHAPTER

Dr. Kenneth R. Pelletier

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Praise for Change Your Genes, Change Your Life

"An integrative medicine pioneer shares cutting-edge insights into the power of epigenetics to upgrade the genetic cards of life you have been dealt."

Mehmet Oz, MD
Professor, New York Presbyterian Columbia
Emmy Award Winning Host, The Dr Oz Show

"The future of healthcare will be preventable, personalized, predictable, and participatory. Read this book to find out how."

—Deepak Chopra, MD
Founder of the Chopra Center; Clinical Professor of Medicine, University of California School of Medicine at San Diego

"If you have ever worried that the genetic hand you have been dealt determines your destiny, worry no more. Dr. Pelletier's book redefines your genes from something you are stuck with to something you have profound influence over by the choices you make every day. If you want to be empowered to be the full expression of yourself, read this book."

—Mark Hyman, MD, New York Times bestselling author of Food: What the Heck Should I Eat?; Director of the Cleveland Clinic Center for Functional Medicine.

"In a health literate and innovative way, Dr. Pelletier unravels the mystery of your genes and the epigenetic inputs throughout life that continue to program your genes. Reading this book is an essential epigenetic input that will help you optimize your gene expression."

—Richard Carmona, MD, MPH, FACS
Seventeenth Surgeon General of The United States
Distinguished Professor, University of Arizona

"Not only does this book provide a scientific basis for our ability to shape our health trajectories through belief and lifestyle choices, but it also outlines the emerging power of personalized medicine. It's must-read for everybody interested in integrative medicine!"

—Emeran A. Mayer, MD, PhD
Executive Director, Oppenheimer Center for Neurobiology of Stress & Resilience;
Professor of Medicine at UCLA; author of The Mind-Gut Connection

"So you think health is all in your genes? Think again. It in your epigenes! Dr. Pelletier once again show he is a master translator of this complex science into the simple and useable. Read it. Use it."

—Wayne Jonas, MD
Executive Director, Samueli Integrative Health Programs; Former Director, Office of Alternative Medicine at the NIH; author of How Healing Works

"I found genetics to be the most complex subject in medical school. Now, fifty years later, the field is one hundred times more complicated. But leave it to Kenneth Pelletier to once again not only tackle the importance of this rapidly evolving field but, as with his other timely books, to make the practical application of these breakthroughs easy to understand for most readers. No one does it better."

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Associate Clinical Professor of Psychiatry at Harvard Medical School; Chief Medical Officer, iHope Network

"Dr. Pelletier continues in his visionary streak of anticipating and informing people about critical emerging trends in health promotion. In this newest book, he turns his sights on understanding the potential of lifestyle choices on changing the expression of the genes that shape our health. It is refreshing to see precision medicine focused on lifestyle change as an underappreciated complement to the development of pharmaceuticals. The book distills the complexities of genetics and metabolism into easy-to-understand concepts, metaphors, and examples that make these often arcane topics accessible and applicable to practical health improvement solutions."

—David S. Sobel, MD, MPH
Adjunct Lecturer, Stanford University School of Medicine; Former Director of Patient Education and Health Promotion, Kaiser Permanente Northern California; author of The Mind & Body Health Handbook

"Dr. Pelletier has been a trusted colleague for many years as well as an inspiration on the journey for health and wellness. In this book he has tackled the difficult subject of genomics and given us all hope that we still have control over our destinies as they relate to health. The introduction of any new technology requires the science to mature in order to provide a more complete understanding of its relevance and appropriate use. Dr. Pelletier has taken this information and broken it down into an interesting, informative read complete with advice on optimizing our own health. I am confident readers will walk away from this ground-breaking book reassured that lifestyle and environmental changes can make a big difference in each of our lives."

—K. Andrew Crighton, MD
Past Chairman of the Health Enhancement Research Organization

"The mapping of the human genome was truly one of the greatest scientific undertakings of the past century, detailing with incredible accuracy the blueprint of our species. It also paved the way for the field of epigenetics, which has shown that when it comes to our genes, nurture is inextricably linked with nature. In his new book, Dr. Pelletier, a true pioneer in mind-body medicine and integrative health research, makes a compelling case for why understanding our own unique genetic make-up can allow us to each make lifestyle and medical choices that can truly alter the trajectory of our lives. Scientifically based, informative, and thought-provoking, this book is for anyone interested in optimizing their health."

—Tieraona Low Dog, MD
Professor of Medicine, Universty of New Mexico School of Medicine; Author National Geographic's Fortify Your Life

"This extraordinary guidebook distills cutting-edge science and is beautifully written with practical tools for achieving optimal health. A must read for consumers and clinicians."

—Woodson Merrell, MD
Assistant Professor of Medicine, Mt. Sinai School of Medicine; Chairperson, Integrative Healthcare Symposium

"Healthy aging has been my passion for over 40 years. During that time I have always found the pioneering research and writings of my longtime friend Ken Pelletier to be invaluable. Now with Change Your Genes, he leads the way again into the realm of the emerging science of epigenetics with practical insights for all of us to attain optimal health and longevity. I highly recommend this book to anyone hoping to lead a healthy long life."

—Ken Dychtwald, PhD
Author of A New Purpose: Redefining Money, Family, Work, Retirement, and Success

"Dr. Pelletier's new book is practically giving away Ferraris—when it comes to sitting in the driver's seat of your own vehicle and steering an enjoyable journey to vibrant health. He has integrated decades of experience and research on how our genes truly respond to our lifestyle, including the role of stress, consciousness, and gut health. And, he offers us our own dashboard of markers, guidance systems, and practices to fulfill our potential as radiant, thriving beings."

—Foster Gamble
Co-creator, THRIVE Movie and Movement

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Foreword

By Dr. Andrew Weill

Over the past four decades, my friend Dr. Kenneth R. Pelletier has devoted his professional life to the study of what constitutes health and wellness. His entire body of work, including over a dozen books, has been a series of signposts pointing the way to a well-lived or "healthy" life. From diet and exercise to alternative medicine, and from acupuncture and meditation to the Fortune 500 corporate health programs that he was among the first to develop, Ken has always tried to show how our personal choices, when they are based in the latest research science, can lead to a healthier and hopefully longer life.

In concert with my own work over these decades, all of Ken's books and research and his many keynote talks given all over the world have encouraged us to consider not only the influence the mind has on health but also to explore our own consciousness for its own sake. He has urged us to ask ourselves who we are and what more is possible for all of us in terms of health, happiness, and longevity. He has always endeavored to show how our minds and bodies are an expression of a greater consciousness at work.

Epigenetics, the subject of this book, is but another marker buoy in the maritime channel that validates the importance of these previous considerations and perspectives, especially as they

Ken's intent has always been to lead us to seek for discover what more each of us can do to make healthier choices. Epigenetics now offers us the promise of far more specific health choices tailored to the special needs of each individual according to the unique characteristics of their genome. In Ken's hands, this revolutionary new science provides yet another luminous signpost pointing to the untapped potential of the human mind. It confirms once again what we have long suspected, that what we believe and how we think and behave has a literal impact on matter—that is, on the body's highly complex biochemical processes. While the right equation may not be "mind over matter," it is profoundly true, as Ken likes to say, that our mind matters! That's why in this book he asks this crucial question: "What does epigenesis tell us about our own untapped potentials and our self-limiting beliefs?" Answering it, and coming up with health-optimizing practices based on that answer, is a central purpose of this effort.

Epigenetics is now at the forefront of modern medicine, with new studies and findings pouring out almost daily. According to Dr. Pelletier, the real upshot of the epigenetic revolution for healthcare is that it opens the door to what futurists call personalized medicine. For perhaps the first time in an introductory trade book, he explains in layperson's language the genetic biomarkers that will become the standard reference for measuring which specific lifestyle changes are required to optimize your health. In the very near future, he explains, a state-of-

Acknowledgments

There have been many individuals who have had a direct and indirect role in the writing of this book over several years. First of all, my deepest gratitude to my editor Byron Belitsos for his insights, perseverance, research skills, and writing ability to make this esoteric subject into a personal odyssey for the reader. Also a respectful thank you to my agent James Levine for his patience and guidance in finding the right publisher for this manuscript. Of course I need to extend a heartfelt thank you my girlfriend Ms. Kathrin E. Nikolussi for her unwavering support and encouragement to see my way through the long and winding road leading to this book.

Among the many colleagues who have influenced my thinking and made invaluable contributions to the research and knowledge in this book, I wish to thank Paula Nenn, Richard Carmona, David Sobel, Steve Locke, Rachel Naomi Remen, Eric Topol, Tieroana Low Dog, Mehmet Oz, Brian and Sue Berman, Deepak Chopra, Mark Hyman, Michael McGinnis, Regina Herzlinger, Jeff Bland, C. Norman Shealy, Joan Schleicher, Brent Bauer, Victoria Maizes, Joe Helms, Emeran Mayer, Steve Schroeder, John Weeks, James Dalen, Bruce Lipton, Roger Morrison, Ken Dychtwald, Patrick Hanaway, Wayne Jonas, Jeff Davis, Larry and Barbara Dossey, Elizabeth Blackburn, Alain Enthoven, Mark Liponis, Michael O'Donnell, Don Berwick, Margaret Chesney, Barrie Cassileth, Mimi Guarneri, Tracy Gaudet, Michael Lerner, Cathy Baase, Jon Kabat-Zinn, Michael Schmidt, Andy Crighton, Robert Rountree, Dexter Shurney, Dave Thom, Ron Goetzel, Justine Greene, Seth Serxner, Tony Elite, Foster Gamble, Margaret Chesney, David Peters, Michael Finkelstein, Doug Metz, MJ Osmick, George and Jan DeVries, Jonathan Fielding, Woody Merrell, Marty Rossman, Jack Farquhar, Bill Haskell, John Sailer, Ben Kligler, Dean Ornish, Heather Tick, Jim Gordon, Arya Neilsen, Jim Fries, Denise Herzing, Jeri Ryan, Brent Bauer, Daniel Kraft, Robert Bonakdar, and of course Elizabeth A. Pelletier. Together these pioneering individuals have and are creating a true health care system for all of the people they influence and touch as well as for the entire planet.

Dedication

To my Parents:

Roger N. Pelletier and Lucy B. Pelletier

Who gave me their gifts of compassion,

honesty, charity, hard work, love. . .

and life itself.

INTRODUCTION

In early 2001, I can vividly remember my excitement, and the enthusiasm of my medical colleagues, when the leaders of the Human Genome Project announced that they had achieved the "sequencing" of the complete human genome, thereby providing us with the first detailed map of the genetic code that resides in the nucleus of every cell.

Scientists and doctors are not known for expressing lofty sentiments, but a distinct feeling of celebration was in the air—and for good reason. To this day, this effort remains one of humankind's greatest feats of scientific exploration. Hundreds of researchers in numerous countries had collaborated with a single purpose. They had finally succeeded in identifying and precisely mapping the "language of life"—that is, the entirety of the genetic material of the human organism, or the actual chemical sequence of the more than 20,000 genes that comprise the famed "double helix," the two twisted strands that make up each DNA molecule. Most of us believed at that time that acquiring this knowledge would be a boon to medicine—and ultimately to every person's prospect for health and longevity—because our genes contain the biochemical instructions that direct every aspect of our biological function at each moment of our lives.

As a result, we were told, a great revolution had arrived that would change the way my colleagues and I would practice. An "era of personalized medicine" would unfold before our eyes. Soon, the detailed knowledge of each person's genome would become an intricate part of our treatment plans. This virtual instruction manual would tell us doctors just what medications our patients should take, which diseases they were likely to get, and even how long they might live.

Along with this promise of the detailed understanding of the genetic origin of diseases came the new hope that, over time, our leading medical researchers would find ways to remedy the negative genetic inheritance or even harmful random mutations that might be found in a given individual's genome. In the first few years that desirable prospect seemed like a distant vision. But new technologies for the massive, parallel-processing of genomes had become a reality by 2005. It suddenly seemed like the future was already here.

Yet, more than a decade has passed since those heady days, and we have not seen the widespread application of advanced genetic technology in the ways that were promised. As new treatments trickled out, we slowly realized that only a tiny percentage of diseases could be directly treated with genetic interventions. Had something gone wrong with the glowing prognosis we were given for the future of medicine? Was our celebratory mood in 2001 premature or perhaps in vain?

In actual fact, the science of genetics was now poised to take a surprising and even more profound new turn. Gradually, an exhilarating new reality began to reveal itself, one that is now culminating in a new paradigm for human genetics and for the genetics of all living things. The successful mapping of the human genome was only a first big step, it turns out, one that would become the foundation for yet another quantum leap in biology. More advanced research, especially in the last decade, points to the advent of a new field called epigenetics, which studies the human epigenome.

One reigning assumption of genomic researchers had long been that our genes are deterministic in their expression. But the new epigenetic research demonstrated that this premise is largely false. Instead, we have come to see that our genes respond, or more specifically our epigenome responds, to how we interact with our world.

In other words, our lifestyle choices and our life conditions play a large part in how our epigenome functions, which in turn determines the function of the underlying genome. What we eat, what we drink and breathe, our stress levels, our use of pharmaceuticals, our interaction with the immediate physical and social environment—these are the essential factors in genetic expression. Most notably, studies in identical twins have conclusively shown that while each twin's genome remains identical throughout their lives, their individual epigenomes can vary significantly over time. And this variability can only be explained by the differing ways each twin lives out his or her life on a daily basis, as well as their environmental exposures.

Today we know that surrounding every gene is a complex set of switches that determine what property of that gene will or will not be expressed. These switches interact with—and are directly affected by—all of our lifestyle choices. As I will explain in this book, this new concept represents a major breakthrough in understanding the direct influence each of us can have on our inherited genes. Whereas we once thought our genes rigidly determine our biological reality, we now know that it is largely the other way around!

What can all these dramatic developments in the world of science mean for your life and your health? Actually, the answer to this question is almost stark. The upshot is that that our diet, exercise, stress management, and other lifestyle and environmental choices matter even more than before. In other worlds, if we change our lives, we can change our genetic expression.

And, you may wonder, are there real-world applications of this knowledge that you and your doctor can use today? Indeed there are. I will introduce to you specific medical protocols for applying the epigenetic approach to our biology right now, today, to improve your life and your health. They largely involve "reading" the results of state of-the-art biological assays that involve at least three key components:

1) A genetic profile of the key genes that govern all of the major chronic diseases.

2) A comprehensive blood draw that will depict the hundreds of biomarkers in your blood that predict your state of health or illness with precision.

3) A "biomic" or intestinal tract assessment that tells you how well your body is actually using the nutrients you are ingesting as well as the impact of stress, exercise, and pharmaceuticals.

Together, these three sets of data—along with other indicators—provide an unprecedented, accurate, and even self-administered means of tracking the subtle impact of lifestyle changes that can move you toward optimal health and longevity. Because they set the stage for these advances, we should be grateful to the pioneers in genetics whose heroic work presaged this revolutionary new approach to health and medicine.

This book is laid out in six chapters that bring these and many other important lessons home.

In Chapter 1, "New Reasons to Hope," I survey the new era of medicine that is arising because of what we've learned about the human epigenome. It is true that certain rare and unpreventable diseases are caused by a single defective gene; but aside from these unusual cases, we now understand that scientists can only predict genetic probabilities, not certainties, and that our lifestyle choices are the crucial factor in shaping these probabilities into outcomes. Generally, we can identify inherited genetic proclivities for specific conditions like heart disease or type 2 diabetes, but the success of such predictions remains limited and contingent. Just as important, we have discovered that genes don't work alone. We sometimes have effective treatments for conditions governed by a single gene, but the more common disorders are the result of complex interactions between many genes and numerous lifestyle and environmental factors, as these are mediated by the individual's ever-changing epigenome. The complexities involved are catalyzing a new world of "big data" approaches to medicine that are sometimes called bioinformatics or computational biology.

These things are all important, but my most essential message is our ability to create our own biological reality and to determine by our actions our own heath and longevity. Ultimately, the new knowledge that we are active participants in determining our own prognosis for health is a profoundly spiritual message of hope.

In Chapter 2, "Keys to Wellness," I introduce the biomarkers that provide clues to our health prospects. We are beginning to list the markers that are the most essential indicators of health and disease. As noted, we will soon have accurate and inexpensive tests for these biomarkers that can help us determine how particular health practices and medical interventions are affecting our genetic expression. The good news is that an emerging panel of essential biomarkers, along with other criteria such as a "biomic" (intestinal tract) assay and a complete blood test, is becoming available now at a reasonable price. What's more, we may soon get the key list of markers down to only a few dozen in number. In other words, doctors of the future will not need to analyze your entire genome; they will only need to examine a handful of genetic and biological markers with the most influence.

With your profile in hand, doctors will soon be able to design a highly personalized health plan that covers all the bases: diet, drugs, exercise, meditation, stress management, psychosocial and environmental influences, as well as other lifestyle recommendations. Then, at the end of a ten to twelve-week period of carrying out these recommendations, we can expect that the genetic markers we are measuring should improve. We simply need to retest them again, and continue to make adjustments at regular intervals in light of the findings of the most recent test. With the advent of this personalized medicine approach that is based on epigenetics, we can focus on very specific, individualized behaviors, practices, products, and services that optimize your health.

In Chapter 3, "Epigenesis," I explicate seven crucial biological pathways in the body that my colleagues and I have identified, and then I explain in brief how to facilitate optimal wellness along each pathway. Inflammation is one of these key pathways; and we now know, for example, that extreme psychological states—such as trauma, depression, and even job stress—can switch on an inflammatory response in certain genes. Plus, certain high-fat diets can switch on the expression of these same genes, which in turn increases inflammation in the arteries, a major risk factor for heart disease. In Chapter 3 and the chapters that follow, I detail specific changes in lifestyle that correspond with each of the pathways. In brief, these seven gateways to health include:

1. Oxidative Stress, which occurs when the body is unable to eliminate the damaging by-products of excessive oxygenation.

2. Inflammation, which is a major risk factor for virtually every chronic disease, but fortunately is easily influenced through nutrition and stress management.

3. Immunity, a crucial pathway that protects us from infection caused by external agents.

4. Detoxification, which is critical in every cell throughout our bodies.

5. Lipid Metabolism, a form of fat metabolism, which is a pathway that responds well to proper dietary changes.

6. Mineral Metabolism, which concerns biomarkers that help us identify how well our bodies are metabolizing minerals.

7. Methylation, the best known of the epigenetic switching processes that control DNA expression.

With the essential knowledge of the seven biochemical pathways in hand, we can identify patterns that point to more specific steps you can take to influence these passageways. I present what we know about these patterns in the final three chapters.

Chapter 4, "Nutrigenomics," hones in on the growing number of studies that have shown that there are vital nutrients or plant compounds that can "talk" to our genes, turning genetic messages on or off. In this chapter, you will especially learn how to maximize your health by eliminating metabolic syndrome—that cluster of conditions that increases the risk of heart disease, stroke, and diabetes.

We all wonder which diet optimizes our health in the face of a confusing flurry of often contradictory options. Fortunately, more advanced studies, often based on genetic analysis, will remove a much of this speculation. It will provide a more objective, scientific basis for the optimal diet for each person. This chapter will make specific dietary recommendations, describing their genetic impact on the key pathways and biomarkers. It also covers today's increasingly important research into the gut microbiome, which is looming large as a major factor in health and disease—and even in epigenetic regulation.

Chapter 5, "Mind Matters," explains how to turn off our genetic vulnerabilities both by reducing stress and by developing emotional well-being. My first book back in 1977 provided scientific proof of the link between stress and the major types of disease, and offered compelling evidence that the mind holds a profound influence over the body. That insight has remained as a theme throughout my research, clinical practice, and writing ever since.

Conclusive evidence makes it clear that our beliefs, attitudes, and emotions—be they positive or negative—have a direct, causal, and enduring impact on the DNA core of every cell in our bodies. For example, we have compelling evidence that the experience of childhood trauma negatively influences a young person's capacity to respond to ordinary stress as they reach adulthood. Epigenetic influences literally burn trauma into the brain cells of a child. However, just as difficult events can affect our genes, so is it possible to have a positive impact on the expression of our genetic code in childhood as well as adulthood.

The concluding section, Chapter 6, "The Era of Personalized Medicine," provides a broad look into what the future holds for self-care, medical care, and national healthcare. Our goal should be to embrace the new world described in this book and dramatically accelerate biomedical progress in the light of the epigenetics revolution and the allied advances in computational biology.

Even today we have the advanced technology and know-how that is required to get started in earnest with truly personalized medicine. It is now only a matter of making the techniques discussed in this book more readily available in laboratories across the country, then educating both patients and doctors to apply it to their everyday lives. We are at a point when literally anyone can self-administer a simple, inexpensive set of assays to determine exactly what is needed for optimal heath and longevity. Once this data is analyzed, sometimes with the use of artificial intelligence software, there will be much less guessing about the "right" diet, or which supplements or herbs to take or not, or whether a particular exercise is beneficial, or how effective your stress management practice or your medication is—or any other health question or issue. Read outs, some of them in real time, will tell you almost immediately what the effect a given health practice or protocol will have on your body-mind system.

The futuristic methodologies I present in the closing chapter are already proving to be more effective than the current reactive, episodic, fragmented, and impersonal treatment of disease episodes. That's why I argue in this book that it is time for a seismic shift in the way we deliver medicine.

Ultimately, the same tools that are introducing us to personalized medicine will lead to new approaches in prevention, so we can eliminate more conditions that lead to disease before they start. But when early preventive measures or when later lifestyle changes are not adequate, we can justifiably turn to our physicians to come up with the right drug treatment at the right dose at the right time, with minimum side effects, and maximum effectiveness—thanks to the epigenetic tools they will have in hand.

At the center of this brave new world of health care will stand you—your commitment to be educated and engaged in your own health in a way that is both cost-effective and a sustainable boost to our national health and economy. Most importantly, the advent of personalized medicine based on the new findings of epigenetics heralds an age of optimal health that is unparalleled in human history. Because of these advances in science and technology, a hopeful future is just up ahead—as you will see in the coming chapters. This truly is cause for celebration.

NEW REASONS TO HOPE

What We Have Learned About Our Genes

In May of 2013, celebrity actress Angelina Jolie suddenly made headlines—not because she was starring in a new movie—but because she has made a drastic medical decision. She announced to the world in a New York Times op-ed that she had undergone a preventive double mastectomy. Her decision to submit to such invasive surgery was, she wrote, the result of genetic tests that indicated she had an 87 percent likelihood of developing breast cancer. Jolie also shared that she had lost both her mother and grandmother to ovarian cancer, which is closely tied to breast cancer. As the mother of six young children, Jolie decided on their behalf "to be proactive and to minimize the risk as much as I could."

Jolie's dramatic story had worldwide impact. The New York Times later reported on how awareness of the breast cancer issue had exploded in Israel as a result of Jolie's announcement. Jolie is of Ashkenazi Jewish descent, and it is known that about half the Ashkenazi women in Israel and the majority of them in the United States are likely to have the same mutation Jolie has. As these susceptible women learned of their increased genetic risk, the Times noted they face the same¬¬¬ crisis that Jolie did before them.

Was the famed actress misguided in making such a drastic choice? Or is preventive mastectomy the only ethical and reasonable medical choice for women with Jolie's mutation? If the answer to the latter question is "yes," should insurers cover this procedure for all women with this mutation?

Giving informed answers to questions like these requires a short course in the revolutionary new understanding of human biology that we examine in this book. The discovery early in this century of the significance of epigenetics—and more recently of the genetic role of our body's symbiotic cousin, the gut microbiome—was the tip-off to researchers that something far more complex was going on than had ever been imagined in twentieth-century medicine. Because of these developments, we can now safely say that Angelia Jolie had unwittingly based her decision on a model of genetic determinism that is on the brink of extinction—as you will soon learn.

The End Game for Genetic Determinism

Advances in genetics of the last few decades have been nothing short of astonishing. Scientists can now locate and map (or "sequence") every single gene in the human genome at an increasingly lower cost. The relative ease and precision of today's gene-sequencing technology now makes it commercially feasible to identify the biochemical make up of every one of the over 20,000 genes in each person's DNA, as well as every other molecular feature of the DNA strand on their inherited genome.

The first effort at comprehensive gene sequencing in 2001, the Human Genome Project, cost about $100 million. Since then, the cost had dropped 15 years later to about $500, and continues to fall from there. Impressively, these techniques allow us to zero in on the tiniest molecular units of our DNA, known as base pairs. Geneticists designate these biochemical units by a simple series of four letters. Sequencing techniques allow them to locate those genes that carry potentially harmful mutations—rogue base pairs in whose letters are out of proper order. These unique variations in a standard base pair are also known as gene variants.

Is there a practical import for your health? Yes, indeed there is, because gene variants can often be correlated with some degree of risk for a specific disease. Such a statistical association of a variant with a particular disease makes you vulnerable to it; only rarely is it a certainty. The new science of epigenetics shows that many other crucial influences are at work in creating disease conditions in the body that may or may not activate this genetic predisposition. Plus, some variants can actually be beneficial adaptations—though again, rarely.

Because advances in gene-sequencing now make it easy to locate variants, a giant new industry for gene mapping is beginning to have wide influence in clinical medicine. And while it is a wonderful gift to become aware of our inherited genetic traits and possible disease vulnerabilities, putting such information in the wrong hands can also be dangerous and misleading.

According to the National Institutes of Health, the genetic testing industry will grow to about $20 billion by 2020. Most of these billions will be spent on promises to predict your risk of major diseases. But what the public doesn't know is that such genetic tests can only predict with certainty a few percent of all known diseases. All other cases of disease occurrence depend at least in part on factors outside of your inherited genome, most notably your lifestyle and your particular life conditions.

Nevertheless, because of the persistence of the mechanistic paradigm of genetics inherited from the last two centuries, massive resources are being spent on predicting genetic diseases and matching drugs to such conditions. This can be a blessing to those millions of Americans who suffer from the inexorable expression of one of roughly 5,000 rare genetic diseases that afflict about ten percent of the population. But what about vast majority of us who don't have such defective genes? An even greater blessing would be to refocus genetic research on optimizing the expression of our good genes! This book reveals the state-of-the-art of this more expansive and proactive approach to human biology.

The difficult case of Angelina Jolie illustrates the transitional state of the genetics industry, as we wait for clinical practice to catch up with the new biology. Jolie has a well-understood mutation in genes known as BRCA1 and BRCA2, which work as tumor suppressors. This relatively common mutation can make these genes incapable of performing their important function, giving women with these variants a high risk of both breast and ovarian cancer.

Brace yourself, because what follows is a graphic description the aggressive intervention necessitated by Jolie's decision. Once she knew her test results, Ms. Jolie opted for a complex form of preventive surgery that requires three consecutive operations over several months. First she underwent a procedure designed to spare the nipple and surrounding areola. Next, surgeons removed all the breast tissue while saving the skin that contains the breasts. In a third procedure, her breasts were reconstructed with implants. This procedure only targeted her breasts because, as she wrote, "my risk of breast cancer is higher than my risk of ovarian cancer." Jolie still has to face a decision about preventive surgery on her ovaries as well—yet another drastic and expensive intervention.

The Better Choice: Change Your Gene Expression

Without a doubt, Jolie faced a big risk for breast cancer and made a tough decision. But we can only wonder to what extent she was made aware of the valid alternate approaches for women who face this dilemma, even within the old paradigm of medicine. For example, a far less invasive approach would have been to take tamoxifen, an estrogen-blocking drug. Or, she could have opted for preventive medical monitoring in an effort to catch breast cancer early. The best approach of all would have been to combine these two treatments with what we in California

call a "reframe—that is, to simply leave behind the outmoded concept of genetic determinism and embrace the science of epigenetic modification. This would entail that she consciously change her patterns of gene expression in ways that compensate for her inherited BRCA1 and BRCA2 mutation. We now know that the most powerful option for Jolie—or anyone with a known genetic predisposition to any disease—is to change their environment and their lifestyle in the ways we will discuss in future chapters. Such an approach can reduce or may even eliminate every type of inherited genetic risk, with the exception of those rare genetic diseases that are virtually irreversible.

And you and I can go even further with this new understanding: We can engage in practices that optimize gene expression for a lifetime of sustained wellness.

We sometimes designate this new approach to human biology by the term epigenesis, which conveys the sense that our genes and DNA are dynamic and fluid in their expression. Evidence for epigenesis is now very well-established in the leading medical journals. Hundreds of studies show that our genes are responsive to the biochemical and energetic environment we create in and around our cells through our daily choices. As a result, a thrilling new picture is emerging: the discovery that our biology is consciously modifiable. Scientists are discovering that our bodies—and our gene expressions—quickly adapt to new conditions, and they are also learning that these adaptations can be traced to specific biomarkers (covered in the next chapter) that you and I can target to boost our health prospects. The general academic discipline concerned with this approach is systems biology, and its clinical application has been called functional medicine.

Yet, the mindsets of many geneticists and doctors are out of step with these newly discovered realities, too often because of biases in favor of the old paradigm based on previous training—or sadly, because they are driven by the momentum of commercial considerations. As a result, today's biomedical science is riddled by at least two very divergent approaches. Genetic researchers and medical clinicians are diverging into two general types:

- The mechanistic approach: Those who focus on using whole-genome mapping to identify mutations that have a probability of resulting in disease, with the aim of developing drugs or surgical procedures that either treat these genetic predispositions preventively or after the associated genetic disease appears.
- The systems approach: Those who search for modifiable biomarkers—including gene variants, epigenetic modifiers, and biomic markers in the gut—and who use this information to design a set of lifestyle and environmental changes that create measurable health improvements in the targeted biomarkers.

Clearly, the first approach above is of course the one chosen by Ms. Jolie. This reductionistic understanding of the genome has given rise to a host of companies that exploit the fear that our genes dictate our destiny. Again, it is true that inheriting certain gene variants guarantees you will get a rare disease; but the overemphasis on that isolated fact has gone so far that, as we'll see, government regulators have had to step in powerfully to protect the public.

This lesson especially applies to all of us concerned with optimal health, especially if we work in the healthcare industry. All of us will need to modify our business practices and our health practices in light of the research that conclusively proves that our genes respond—or more specifically our epigenome and our gut biome respond—to how we interact with ourselves, with each other, and with our world.

Introducing the New Science of Epigenetics

We've noted that when the map of the human genome was first revealed, it was believed that geneticists would soon be able to make solid predictions about which diseases each of us would get as we age. But the immediate aftermath of the mapping of the human genome has led in a radically different direction as we begin to understand the human epigenome. We now know that environmental and psychosocial factors as well as lifestyle choices play the largest part in how our epigenome functions, which in turn determines the expression of the genes that govern our health and longevity.

Epigenomics, the new scientific discipline of research into the epigenome, is the study of the chemical tags that park themselves on the genome that literally control the activities of our genes. In a sense, these markers appear "above" the genes—and is thus signified by the Greek prefix "epi," which means "above" or "upon." It is almost as if there are two languages being "spoken" by our DNA: the original "script" of our genome, and a secondary and more powerful linguistic control system that sits on top of each gene. This system determines, more than 95 percent of the time, whether, when, and how much a given gene (or some other portion of the DNA strand) is permitted to express itself as it does its routine work of "coding" for a myriad of biochemical activities in the cell.

The analogy of a theatrical script helps illustrate how epigenetic regulation works. Perhaps you have seen different movie versions of William Shakespeare's Hamlet—for example, those featuring Richard Burton (1964), Kenneth Branagh (1995), or more recently Benedict Cumberbatch (2015). These films differ greatly from one another, but of course the words on the page in Shakespeare's underlying script never change. Shakespeare's original theatrical script can be compared to our genetic code, and the differing performances of Hamlet are analogous to the function of epigenetic regulation. Once we inherit our unique genome, how it appears "on the printed page" remains stable throughout our lives; what is critical is our expression of these "lines" of the DNA script in and by the way we live our lives. In that sense, we are like actors who are "directing" the "performance" of our genetic script in ways that are unique to us, but in a manner that is also conditioned by the "theatrical set"—our immediate environment.

Allow me to extend the metaphor a bit more. If we could read our epigenome, it would look like a director's "notes" that we have been written above the lines or in the margins of our genetic "screenplay"; this "shooting script" provides the epigenetic modifications that are made possible by our directorial choices. In essence, we direct our biological lives in the same sense that a movie director determines the expression of the underlying script by the actors (not to mention set designers, lighting and camera crew, etc.).

Bear in mind, however, that the variations in gene expression that comprise our epigenome do not govern every biological trait or function. Certain physical characteristics, such as eye color or height, are one hundred percent predetermined by the inherited genes. This characteristic of gene expression is known as gene penetrance. For example, in identical twins, the penetrance of their genes for physical appearance is one hundred percent guaranteed. Plus, as noted, gene mutations that program for certain rare diseases also have this level of predictability—they can't be modified epigenetically. But again, complete penetrance is the exception, and not the rule—as we will soon observe in living color when we examine the genetic studies of identical twins.

Penetrant genes comprise only about five percent of the human genome. In all other cases, genes for thousands of functions must be either activated, suppressed, or modified by epigenetic mechanisms. That's the bottom line for this discussion, but there's one more feature of the epigenome to ponder later on. The epigenetic alterations that you may acquire don't just change your biology during your lifetime; some of these modifications can be passed on to future generations that follow you. This surprising phenomenon is known as transgenerational epigenetic inheritance.

If I may use yet another analogy, we can compare epigenetic regulation to switching on or off a light in your bedroom. Much like our genetic code, the light switch on your wall and the light bulbs and their fixtures that are connected by wires to this switch are a stable presence—they are the infrastructure that always remains in place. But you are the determining factor in this simple equation. You must decide whether or not you want the light to shine, or whether this light should be turned up or down in intensity.

Our growth from the time of our conception and our daily health practices and habits—along with the routine moment-to-moment shifts in the functions of the tissues and organs of our bodies through a variety of biochemical pathways—all these factors constitute a galaxy of biological changes that determine our well-being in this life. All of these elements are orchestrated by the biochemical switches that comprise the epigenomic superstructure that sits on top of our inherited genetic infrastructure. Specific chemical reactions are able to switch the relevant parts of our genome on and off or up and down at strategic times and locations on a given gene or on the vast regions of the DNA strand that were once known as "junk DNA." Epigenomics is the study of the biochemistry that regulates those switches—for humans as well as for all organisms.

By way of illustrating this vital principle of gene switching, let's briefly consider one of many determining factors that have been closely studied: the impact of nutrition on the epigenetic modification. What you eat, whether that consists of healthy nutrients or processed chemicals, provides the chemical environment in which your cells are sustained and in which they bathe. We now know that eating a nutritious diet high in fresh vegetables can add a layer of protection to your epigenome; that's because certain compounds the body uses to switch off harmful genes are uniquely found in your veggies. In this case, it's a matter of providing your body with the basic chemical building blocks of the epigenetic switches themselves. If these chemicals are present, they can insure that all the switches are turned off that actually need to be off in order to ensure healthy functioning. For example, if your diet is low in folate (a component of the B-vitamin complex), some harmful genes may be left on because there wasn't enough "off factor" to go around.

In other words, your genetic expression is determined, in part, from what you decide to eat—which in turn programs the function of biochemical regulators in your epigenome. As yet, not many hard and fast studies detail exactly what foods or supplements, or the lack thereof, will lead in a straight line to a specific disease or health improvement. But there is a large amount of evidence that what you are eating does indeed condition your genetic expression in innumerable ways. Details of the known dietary influences will be spelled out in Chapter 4.

But again, always bear in mind that this example of our diet's impact on our genes also holds true for exercise, environmental toxins, stress, emotional states, smoking, radiation exposure, pharmaceuticals, and many other influences that we are now beginning to map and understand. And if this sounds like we have come a long way from the deterministic paradigm that led to Angelina Jolie's decision, you would be correct.

One of the many discoveries that led the way to the epigenetic revolution were studies in identical twins, the results of which have conclusively shown that while each twin's underlying genome remains identical throughout their lives, their individual epigenomes can vary significantly over time. And this variability can only be explained by the differing ways each twin lives out his or her life on a daily basis. Perhaps the most important study of identical twins was carried out at Johns Hopkins University, which we now examine.

Game Changer: Studies of Identical Twins

Identical twins have identical genomes—a marvellous fact of nature. But we now know that twins vary greatly in their incidence of disease and other life changes. To get to this weighty finding, genetic researchers have asked one key question: If one twin gets a disease, what are the chances that the other twin contracts this same disease, say, in a fifteen-year period? The results are eye-popping. Studies have shown that, for example, their chance of getting Parkinson's disease is only five percent; this means that if one twin comes down with it, the other twin's lifestyle and environment plays a 95 percent role in determining whether they too will contract Parkinson's. With respect to coronary heart disease, the likelihood is 50 percent—no more than random chance. For most cancers, the chance the other twin will suffer from this disease is less than 50 percent. You can see that a remarkable statistical trend shows up in these studies.

In 2012, Dr. Bert Vogelstein of Johns Hopkins University Medical School announced the results of perhaps the most comprehensive genetic study of twins ever done. He and his team compared the genomes of thousands of identical twins and confirmed—this time by referencing a very large dataset—that disease cannot be predicted by genes alone other than in exceptional cases. They also concluded that the medical use of whole-genome sequencing to determine our genetic susceptibility to specific diseases can not only lack significance but can even be misleading.

In this breakthrough project, the Johns Hopkins team focused on 24 major diseases. Their complex analysis showed that genetic tests could alert most individuals to an increased risk of only one disease on average, which means that such tests are a rather poor predictor. In other words, a profile of a given twin's whole genome in comparison to that of their twin would give a negative test outcome for the vast majority of diseases known to humankind. But such a finding does not mean anything like "free pass," points out Vogelstein and his team. This individual will still have the same risk for all other diseases as the general population. Indeed, each member of a set identical twins will get all sorts of diseases according to the general statistical risk—just not the same diseases as the other twin!

The genetic study of identical twins proves once again that, with some exceptions, our genes do not inexorably determine our fate, but instead adapt to how we direct our daily lives. And when you consider that evolution favors adaptation, this finding makes perfect sense. From the very beginning, our survival as a species has depended on our ability to adjust biologically to relentless change. Studies of twins make it clear that directing our lives in such a way that we adapt to changing life conditions is built right into our genetic makeup, showing up there as the director's ever-changing "shooting script," the epigenome.

More Basics of Today's Genetics

Genetic sequencing has come a very long way, but the basic technology that researchers currently use to map the genome has been in place for over thirty years. The method for sequencing was invented in the mid-1970s by Dr. Frederick Sanger of the Medical Research Council in Cambridge, England. His first step was to isolate the long strings of double-stranded DNA from cells. Sanger and his successors soon discovered that attached to each string are millions and millions of tiny chemicals that we noted before now are called bases, of which there are four types. These four fundamental chemical units go by the names of adenine, thymine, guanine, and cytosine, and researchers refer to these bases by their initials, A, T, G, and C. Different permutations of these letters form the millions of rungs on the ladder of the DNA helix, and in each rung we find that an A is always linked with a T, and a G is always paired with a C—which is why they are known as base pairs. This little sketch of our DNA's structure may sound simple, but what complicates the work of sequencing the entire human genome is that each gene is made up of more than 3 billion pairs of these bases from each of your parents. When such base pairs are linked to either side of that living ladder—the double helix that comprises a DNA strand—that molecular unit is known as a nucleotide; in other words, each nucleotide is joined "at the hip" to the each side of the helix. Large sets of these DNA strands are, in turn, lumped together into the 46 chromosomes found in each cell that you learned about in high school biology.

We should note here that a very tiny percentage of our inherited 3 billion base pairs, roughly 3 million of them, are the pesky gene variants I introduced earlier. These are mutant nucleotides. They are the culprits that can sometimes guarantee a certain disease. Far more often they simply make you susceptible to the expression of a certain disease or may predispose you to a certain behavior or personality trait.

Each gene is a basic functional unit of the language of the genome. Genes spell out a code—much like letters in the alphabet spell out words—and the basic unit of this genetic alphabet is the four-letter base. But how do mutations actually occur in this alphabet? Due to a wide variety of biochemical factors, single letters can get deleted, added, or rearranged, resulting in a mutation or variation. We noted that you may inherit your parent's gene mispellings as part of your genome, but you also generate unique mutations in the course the biological spelling bee of your own life. However it may occur, these altered genes may continue functioning normally if the mutation is minor, because the epigenome has built-in safeguards that can repair mutated genes. But sometimes even this "back up" system breaks down. In theory at least, a disease like cancer can be the result of such a double failure.

Gene expressions are almost always mediated by our epigenome. You may inherit a strange gene or generate a mutant nucleotide that codes for a specific disease, but again, if this unit of your DNA stays in the off position, the change it codes for will never express itself; on the other hand, environmental or lifestyle factors may turn this gene on. In practice, however, bear in mind that gene regulation is actually far more complex than a simple binary difference. Many genes work on what might be called a sliding scale, more like the rheostat switch you use to turn your dining room light up or down in intensity. In addition, genes communicate fluidly with one another. Some genetically determined characteristics require only a single gene (and thus are penetrant), but the vast number of genetic influences are created by a dance or symphony of genes delivering dynamic input to the whole system, along with the many epigenetic influences we have identified.

Ultimately, the lessons of epigenetics mean that control is being given back to you and me. We are no longer puppets of our DNA. Our human genome is like the theatrical stage for the future steps in evolution that we ourselves direct, making the power of choice an integral part of genetics. Unless our personal decisions about lifestyle and environment are all taken into consideration, a full picture of the mysteries of our DNA can never be attained.

Genes Don't Work Alone

Because of today's revolution in our understanding of DNA, complexity is now the rule in biology and medicine. Geneticists have learned that even specific physical traits are not determined by single genes. For example, no one gene exists for height; more than 20 genes have been identified so far, and we know little about how their interactions might contribute toward determining how tall we will grow up to be. And while single gene mutations can explain some rare diseases, some of the more complex diseases such as breast cancer, heart disease, and the even the majority of Parkinson's cases can be traced to unfortunate combinations of a set of normal genes.

We understand very well how a single gene codes the instructions (through its associated RNA, to be discussed later) to create a particular protein—which then turns on a certain trait or bodily process. But we know far less about the operation of systems of genes, including how the genome, epigenome, and gut biome ultimately work together as a whole to regulate the human organism, thereby enabling clinicians like myself to guide patients in the right direction. Some call this great systemic collaboration the supergenome.

Because of their training under the old paradigm, most doctors prefer to think in terms of simple cause and effect: symptom "X" can be traced to cause "Y." But the emerging story of the complexity of our biology points to a very different picture. We've noted that the cutting edge of academic biological research is now known as systems biology, which has led geneticists to think in terms of a "cloud" of influences leading to outcomes—good, bad, or ugly. Fortunately, most of these factors are potentially under our control, provided that we embrace the lessons of the epigenetic revolution and continue along the lines of research recommended in this book.

Like a real cloud, the "biological cloud" changes almost moment to moment. That's because our bodies are designed to flexibly adapt to inputs of every kind, including the biological impact of our thoughts and feelings. Because of the more inclusive perspective of mind-body medicine that I have championed for my whole career, the mind itself—and even the impulses of the human soul and spirit—are influences that add complexity to the genomic equation.

One of the pioneers in the exploration of biological complexity is Dr. Eric Schadt, Chairman of Genetics and Genomics Science at the Icahn School of Medicine at Mount Sinai. Dr. Schadt and his colleagues have concluded—like all researchers on the cutting edge of this field—that most diseases cannot be explained by the conventional mechanistic view of genetics. Instead, he believes, illnesses (and good health) are caused by a vast network of biological influences that can only be understood with advanced computer modeling.

Because he is an articulate exponent of the medical use of big data or bioinformatics, Schadt has even been featured in popular magazines such as Wired and Esquire. As the story goes, at one point in his career he headed a research lab at Merck (a large American pharmaceutical company) that was tasked with developing new drugs. Schadt's work was considered a great success by the company, but he soon became disillusioned. His team's research taught him

that the underlying premise of conventional biology was false—that is, the idea that we could understand disease one gene at a time and target drugs at defective genes. Schadt eventually told Merck that "this was a strategy doomed to fail, because disease arose not from single genes or pathways but rather out of vast networks of genes and pathways whose interactions could be understood only by supercomputers guided by abstruse algorithms."

As researchers have faced up to this complexity, they have turned to what is known as "genome-wide association studies" (GWAS). This is one form of Schadt's big data approach. In such large-scale studies, the genetic sequences of many thousands of individuals with a specific disease are mapped and studied with algorithms in order to determine if there is a statistical correlation between a particular gene or set of genes and a specific condition—across this huge sample of subjects.

As this more advanced and data-intensive research progresses, it is still essential to acknowledge the progress we have made with single-gene or monogenic maladies that are 100 percent penetrant. One instance where genetic testing is accurate and predictive is for Huntington's disease, a very unfortunate inherited condition in which nerve cells in the brain break down over time. A gene for this disease was first identified in 1993, in the world's earliest attempt to locate a single disease-causing gene by tracking variants in the human genome. A genetic test for Huntington's is now widely available, but for those individuals at risk for inheriting it, the decision as to whether to get tested or not can be excruciatingly painful since there is no known cure for this disease.

Exceptions to the rule, such as the case of Huntington's, actually prove our rule. They serve to call our attention to the role of the epigenome and ultimately to the role of human consciousness in guiding our health decisions.

Genes Are Also Governed by Our Beliefs and Choices

You may remember this oft-quoted line from Shakespeare's Hamlet, "The fault lies not in the stars but in ourselves." Allow me to paraphrase that quotation for our purposes: The fault lies not in our genes but in ourselves. The new era of epigenesis points us right back to our own habits and decisions. Our inherent power to choose our destiny is a spiritual reality that, in turn, governs our biological reality. We are not victims of genetic programming; instead, the truth is just the opposite.

If we and our doctors—and the scientists we fund with our tax dollars—believe that we are helpless pawns fated to live out our genetic code, then we will pour all of our research funds into discovering what is encrypted in our cells. However, the new knowledge that we are active participants in determining our own life directions is a profoundly spiritual message of hope and deserves at least as much scientific and medical attention.

There is a wonderful true story from John Lennon who was asked about what he thought the purpose of his life was to be. He quipped that, "When I was five years old, my mother always told me that happiness was the key to life. When I went to school, they asked me what I wanted to be when I grew up. I wrote down 'happy.' They told me I didn't understand the assignment, and I told them they didn't understand life." For individuals seeking optimal health and longevity, John Lennon's response makes a great deal of sense. Choosing to be happy may in fact have a profound impact on how our genes are expressed in our lives.

Without question, our minds and emotions directly affect gene activity. And since the

mind is the source of our lifestyle and behavior, it ultimately directs our biological destiny. Self-awareness holds the key to this process of transformation. Consciousness invisibly reaches into the biochemistry of every moment of life. In your body, as in every cell, the phenomenon of epigenetic regulation is integrative, self-generating, self-organizing, and self-directing in concert with the status of your beliefs and your commitment to conscious living. We'll turn in detail to this rich subject in Chapter 5.

Technology will also act as an ally to consciousness. Doctors are just now able to demonstrate the epigenetic effects of our conscious or unconscious daily choices with an advanced blood test, plus other assays of biomarkers. Many of these tests are already available but underutilized. Adding to this evolution is the development of wireless devices that can sense—in real time—many of our most basic biological functions, ranging from pedometers measuring our footsteps to heart monitors that relay changes in our heart rate and regularity. We can even expect "ingestible nanotechnology," a tiny microcomputer smaller than the head of a pin inside of a sugar pill. This nanocomputer will transmit signals on sleep patterns, stress hormones, blood sugar levels, and an array of basic biological functions. This data can be displayed to each individual and it can be sent to heath care providers.

In the coming chapters you will learn that these technologies exist now, but the medical infrastructure that ranges from the training of doctors to the certification of labs will need time to catch up. That day is envisioned by Dr. Francis Collins, the Director of the National Institutes of Health (NIH) and one of the original leaders of the Human Genome Project. He has observed that, "Medicine for most of human history has been one size fits all. But we're all different, and the diseases we have lumped together under one label we're finding out are actually at the molecular level quite distinct. . . . Precision medicine tries to understand what's underneath those disease layers and tries not to lump everyone together but instead think about individual differences."

That is not an idle fantasy but an evolving reality of the healthcare system of the near future. Doctors will not need to analyze your entire genome, which after all is only one factor among many. Instead, they will penetrate the "biological cloud" to discover the biomarkers with the most influence. In fact, we already know many of the markers that matter most to your health.

One day soon you will be able to see exactly how your gene expressions uniquely respond to any given choice or behavior. For reasons we don't yet full understand, some people will benefit greatly from eating a vegan diet, for instance, while others can be more flexible; or, for example, low-fat diets will be shown to be the healthiest choice by far for some people, but not for others. The biological assays of the near future will settle such mysteries. A set of markers that are modifiable by specific lifestyle practices will become evident within a span of time as short as a few days to an outside maximum of 10 to 12 weeks. Determining, changing, and monitoring our epigenetic profile for optimal health and longevity will become a widespread practice.

We may not yet have definitive studies showing the impact of every element of our lifestyles and environment, but we do have an enormous amount of evidence. In the chapters that follow, you will learn specific dietary and stress management practices that can literally change the expression of your inherited genetic code, prevent disease, and optimize your health. You don't need to wait for an imagined destiny to befall you. Your beliefs and choices are determining your wellness and longevity right now.