18 Your Personal DNA Code: Summing Up

If you've made the journey with us to this point, you've learned some little-known facts about an eclectic collection of characters, some obscure—Patricia Stallings, Mike O'Brien, and Andrew Jackson Mattingly—others world-famous—Pearl Buck, Rita Hayworth, and Katie Couric. All of them confronted the heart-breaking consequences of a small change in their DNA code or in that of a loved one. You saw that the prognosis of people who are dealing with a lethal infectious disease, like Isaac Asimov and Arthur Ashe, is affected by their genetic endowments. And you have come to know some renowned biologists—Karl Link, Frederick Banting, and Seymour Benzer—who were driven to discover the principles of life's processes, and who were subject to the same inspiration, competition, determination, trepidation, and exhilaration that drive all of us.

But the personal stories were just appetizers. Our main dish consisted of answers to the basic questions that we all have about genetics, questions we confront daily in reports of discoveries of how genes influence our lives. If you digested the meal we set before you, the following will sound familiar to you.

Each of us inherits two sets of chromosomes, one from each of our parents, which are very long strands of A, C, G, and T, the chemical units of DNA that twist around each other in a double helix. Long is truly long: one hundred million or more DNA base-pairs can be present in a single chromosome; six billion base-pairs are crammed into each one of the trillions of cells in our bodies.

The critical feature of our DNA is the order—the sequence—of its A, C, G, and T letters. That sequence of A's, C's, G's, and T's is unique to each of us (unless we're an identical twin)—it's our personal DNA code. It's what makes everyone different from the other six and a half billion people on our planet.

Our chromosomes are partitioned into about twenty thousand segments called genes, each of which provides the information to manufacture a protein. Proteins, composed of unique sequences of twenty different chemical units called amino acids, do the work in the body's cells: breaking down food, making energy, signaling the state of affairs, protecting us from invaders such as bacteria and viruses, and much more. We each look different from everyone else on the planet, and our cells carry out their affairs slightly differently than everyone else's cells, because the exact sequences of amino acids in our proteins are slightly different from everyone else's. That's because a small fraction, about 0.1 percent, of each individual's DNA code is slightly different from everyone else's.

The distinct types of cells in the human body—blood, nerve, muscle, skin, and the rest—look and behave differently because they contain distinct subsets of the twenty thousand proteins encoded in our DNA. Some specialized cells are the only ones that produce a particular protein; for example pancreatic "beta" cells are the only cells that produce insulin. All cells contain many common proteins that carry out necessary functions, such as metabolism. The kinds of proteins a cell makes is determined by which of its genes are turned "on," a decision made by a special type of protein called a transcription factor. These are important decisions indeed: beginning with a fertilized egg, each cell division brings new corps of transcription factors to orchestrate the relentless specialization of cells that results in the birth of a complete and utterly unique human being.

The precise collection of proteins in each of us is determined by the specific versions of the genes we inherit from our parents. Our proteins are more similar to theirs than to those of any other pair of parents, making us resemble our own mom and dad more than we resemble others' moms and dads. And because our siblings inherit many of the same versions of genes as we do, our resemblance to them is also usually obvious. Proteins affect more than just our looks: they are involved in learning and memory, mood and behavior, addiction and desire. Each of these traits is influenced, to varying degrees, by our personal DNA codes.

Because the process of copying DNA during each cell division is imperfect, mutations—changes in the sequence of the DNA letters—continuously occur. Some of the mistakes are replacements of one letter for another; others are insertions or deletions of letters, sometimes thousands or even millions of them. Mutations can add to the diversity of life; by changing the sequence of letters in the DNA they can change a gene, thereby altering the action or the amount or some other property of a protein. In consequence, we look or act a little bit different than we would have if no DNA copying mistake had been made. Mutations contribute to our individuality.

Although most mutations are inert in their effects, some mutations eliminate the ability of an important protein to do its job. Usually that's not a problem, because most of these mutations are recessive, meaning that with two sets of chromosomes we have a backup copy of every gene, and the backup is sufficient. These recessive mutations make mayhem only when they are in a double dose, one coming from each parent. The consequence can be a terrible disease if the missing protein is needed to carry out an essential task. Occasionally a mutation creates an altered protein that all by itself becomes a wrench in the gears of our cells. A single copy of such a dominant mutation is sufficient to lead to disease. When one of Mom's or Dad's chromosomes carries a mutation, what determines whether we get the good copy of a gene or the bad one? Only blind luck: the decision is determined by which of Dad's millions of sperm cells fertilizes which of Mom's egg cells. It's an important decision, but one over which we have absolutely no control.

The chromosomes in those sperm cells and egg cells are not the exact same ones our mom and dad inherited from their parents. Bits and pieces of each one exchanged places while making their way into a sperm or egg cell, so that all of our chromosomes are mosaics of those present in previous generations, all the way back to our ancestors who lived in Africa fifty thousand years ago.

Variation in a single gene is sufficient to cause rare diseases such as phenylketonuria or Huntington's disease. Furthermore, variations in many genes contribute to our risk for common diseases such as cancer, heart disease, diabetes, Alzheimer's disease, Parkinson's disease, and many others. Tracking down the variants responsible for disease risk is now a major focus of medical research, and the pace of progress picks up every day. By the time you read this book, some people will know their own personal DNA code; we expect that you will know your own code sooner rather than later. When that happens you'll likely have a lot of questions.

We hope the basic concepts we've provided in this book will help you answer them.

We have tried to convey a few more ideas than those just summarized, notions about gene therapy, stem cells, pharmacogenomics, evolution, and race. But those were the dessert, and you may have taken in more calories than you need. If you're too full, remember that the concepts of genetics are simple, and they explain how small changes in your personal DNA code affect your health and happiness.

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