# 1 Your Personal Genome: Googling Your DNA

Not many homeowners can boast having a garage that changed the world. But Susan Wojcicki can. She can look back at her decision in 1998 to rent out her garage at 232 Santa Margarita Avenue in Menlo Park, California, as a world-changing event. Her renters, two graduate students in computer science at nearby Stanford University, needed space to develop a new company around their revolutionary approach to searching the web. Sergey Brin and Larry Page would not occupy her garage for long; they soon needed more spacious headquarters for the company that would launch their combined net worth into the stratospheric level occupied by the likes of Bill Gates and Warren Buffett.

But before they launched Google, Brin and Page devised something they called PageRank, a method to rank a webpage according to how many other pages have links to it, and the number of links each of those other pages in turn has to yet other pages. PageRank provided a much more effective means of searching the Web than that offered by then-available search engines such as AltaVista or Excite. Capitalizing on its vast ability to organize and serve up information on the Web and provide a host of other services—Google Earth, Google Image, Google News, Google Maps, Google Groups, Google Books, and more—Google quickly went beyond PageRank as its instrument for dominating the lucrative search market.

Susan Wojcicki must have realized that her young tenants were on to something: she became one of Google's first employees, going on to develop its online advertising business. But in addition to connecting people to information, Wojcicki also introduced Sergey Brin to her younger sister Anne. That introduction culminated in the May 2007 wedding of Brin and Anne Wojcicki, then both thirty-three, on a private island in the

Bahamas. The wedding couple wore bathing suits, and some of the guests joined them in swimming to the ceremony.

Like her husband, Anne Wojcicki is one half of a business duo that launched a start-up company. But the company founded by Wojcicki and her partner Linda Avey—23andMe—does not deal in Internet search results, digital images, or city maps. Instead, it serves up genetic information. Despite Google's investment of $3.9 million in 23andMe, this start-up, and other similar ventures such as Navigenics, deCODEme, Knome, and Sciona, leverage no recent insight from computer science. They rely on a principle known for over seventy years: the more closely related two individuals are to each other, the more similar are their personal DNA codes. This is the principle that allows geneticists to figure out whether a particular version of a gene makes an individual who carries it more prone to a disease such as diabetes, Parkinson's disease, or cancer than does another version. This is also the guiding principle of our book, as we lead you to an understanding of what DNA is, how its four-letter alphabet spells out the genes that determine the traits of human beings with all our complexity, and how the way those four letters line up six billion times in our personal DNA code influences how we look, how we behave, how we get sick, and how we respond to treatment.

Named after the 23 pairs of chromosomes we carry in every one of our cells, 23andMe has as its mission "to take the genetic revolution to a new level by offering a secure, web-based service where individuals can explore, share and better understand their own genetic information." It can't provide an individual with her complete DNA code, but for $999 it can reveal enough of it (about 1/6000th) to give her a glimpse of her risk for a few diseases. The web-based service the company provides allows you, in effect, to Google your own DNA: instead off typing words into a search engine to scan the world's web pages, you type the DNA letters of a gene to scan the world of your own DNA, searching for the relevant text stored therein.

Today their service is at the cutting edge; in a few years it will seem primitive. This mere glimpse of a customer's DNA will soon be replaced by a complete reading of how the four letters of its alphabet are used 6 billion times to spell out his DNA code. So far, the DNA code of only a few people has been read, at a cost of over $1 million each, prohibitive for all but the wealthiest. But new technologies are rapidly reducing the cost, bringing

this brave new world into view. An added bonus to the acclaim and profits that will accrue to those who solve the issues of cost and speed is the Archon X Prize of $10 million, which will be awarded to the first team that reads the DNA code of one hundred people in ten days at a cost of ten thousand dollars each. It is possible, maybe even likely, that that reward will have been claimed by the time you read these words.

While a reading of our complete DNA code may be still out of reach for you and for us, it was realized recently by James D. Watson. More than half a century ago, on February 28, 1953, Watson and his colleague, Francis Crick, launched an age of genetic discovery with their announcement to the lunchtime patrons of the Eagle Pub in Cambridge, England, that they had "found the secret of life." Their discovery of the structure of DNA—the most important molecule of life, which specifies the form and function of every living thing—made clear how traits are passed down through the generations. Watson and Crick's breakthrough paved the way for an age of discovery that culminated in the announcement on June 25, 2000—not in a pub but at the White House—that the human DNA code had been determined. A few years later Watson himself became one of the first two people to read his own personal DNA code.

After 1953, Watson went on to a celebrated career, directing a laboratory at Harvard University, then a storied scientific institution at Cold Spring Harbor on Long Island, and ultimately the Human Genome Project, which deciphered the human DNA code. But shortly before his own DNA code was determined, Watson's professional life ended amid charges of racism. He was quoted in the October 14, 2007 edition of The Sunday Times that he was "inherently gloomy about the prospect of Africa" because "all our social policies are based on the fact that their intelligence is the same as ours—whereas all the testing says not really." He also said, "There is no firm reason to anticipate that the intellectual capacities of peoples geographically separated in their evolution should prove to have evolved identically. Our wanting to reserve equal powers of reason as some universal heritage of humanity will not be enough to make it so."

As his comments rapidly circled the globe, drawing condemnation from his fellow scientists, the 1962 Nobel Laureate quickly apologized for them. Speaking at a meeting of the Royal Society in London on October 18, 2007, he said, "To all those who have drawn the inference from my words that

Africa, as a continent, is somehow genetically inferior, I can only apologize unreservedly. . . . That is not what I meant. More importantly, there is no scientific basis for such a belief."

But the damage was done, and so was Watson's job. The board of trustees of Cold Spring Harbor Laboratory relieved Watson of his position as chancellor. They wrote, "The comments attributed to Dr. James Watson that first appeared in . . . *The Sunday Times* U.K. are his own personal statements and in no way reflect the mission, goals, or principles of Cold Spring Harbor Laboratory's Board, administration or faculty. . . . The Board of Trustees, administration and faculty vehemently disagree with these statements and are bewildered and saddened if he indeed made such comments."

Watson had steered into the always-dangerous shoals of the genetics of race, and he should not have been surprised that his words sank him. In our penultimate chapter we, too, venture into these treacherous waters. We will show you that there are many more genetic differences *within* racially defined populations such as Africans and Caucasians than *between* these populations. You can see the close resemblance of the DNA codes of these races if you compare the few available sequences. Or, you can wait a few years and see it when you read your entire DNA code.

Just as Google's computers read a digital code composed of 1s and 0s, living creatures read a chemical code of four different units, abbreviated as A, C, G and T. We'll see how strings of these four chemicals get decoded in the production of proteins, the workhorses of the body that enable us to move, see, breathe, think, and reproduce. These four chemical units are strung together 6 billion times (6 followed by 9 zeros, or 6 thousand thousand thousand)—but this number is infinitesimal compared to a "googol"—1 followed by a hundred zeros, or ten thousand trillion trillion trillion trillion trillion trillion trillion trillion. Yet even a googol is barely a speck in comparison to a "googolplex," which is 10 raised to the power of one googol, or 1 followed by $10^{100}$ zeros. (It would take much more space than the pages in this book to write that number.)

The algorithm Larry Page developed to search the Web originally went by the unbusinesslike name of BackRub. But in late 1997, as he and Sergey Brin contemplated starting a company to exploit their search engine, BackRub had to go in favor of a more fashionable term that would connote

the vastness of what they were trying to organize. Unfortunately, the names they first came up with had already been claimed by other people. Page's officemate Sean Anderson made a number of suggestions, but Page nixed all of them. Anderson eventually offered "Googolplex," a name that suggested the vast amount of information the new search engine could scan. Page liked it, but preferred the shorter "Googol." Computational brilliance they may have possessed, but world-class spelling was not their forte. When Anderson used the new search engine to see if the name was available, he typed in "Google" and found that it was unclaimed. That evening Page registered the domain name Google.com. Only the next day did they learn they had misspelled the term, and discovered that the domain name "Googol.com" had in fact been claimed.

As Google rapidly expanded, Brin and Page focused on maintaining its spirit of adventure and cohesiveness. Employee number 56, who arrived in November 1999, was Charlie Ayers, their executive chef. Ayers provided free, wholesome food to the young Google workforce, maintaining their energy for the ambitious tasks they were tackling. He later recalled to David A. Vise and Mark Malseed, authors of *The Google Story*, "I could feel the energy. They had it. Everyone was so focused and into it, and they all had one goal: to make this company successful. It was 'Look at what we did,' not 'Look at me.'"

An equivalent organizational spirit exists within every one of the trillions of cells in your body. DNA provides the corporate vision and hiring plan, but it's the roughly twenty thousand varieties of proteins that carry out all the necessary activities of the cell. Like Google employees, proteins engage in a team effort that is much greater than the sum of their parts. You'll see as you read on how proteins read the DNA code in the single cell that is the fertilized egg and tell it to divide into two, then four, then eight and so on. Successive generations of cells take on new functions, specializing as heart and blood, brain and nerves, bone and teeth and all the other tissues of the body. The result, a living human being, is more magnificent than any company, no matter how much revenue it generates.

Sergey Brin was born in the Soviet Union in 1973 to two mathematicians. His father, Michael, is now a professor at the University of Maryland, and his mother, Eugenia, works at NASA's Goddard Space Flight Center, in

Washington, D.C. Anti-Semitism in the Soviet Union in the 1970s prevented his parents from advancing very far in their academic careers, so they decided to apply for exit visas, even though doing that meant running the risk of becoming unemployed and ostracized by colleagues. They were fortunate to be some of the last Jews allowed to leave the Soviet Union before it broke up a decade later. Michael and Eugenia Brin left with their young son in 1979, and settled into a new life in Maryland.

Larry Page, born just a few months earlier than Brin, is the son of the late Carl Victor Page, a professor of computer science at Michigan State University who was one of the first to receive a doctorate in this field of study. His mother, Gloria, earned a master's degree in computer science and taught programming at Michigan State. Page benefited from a rich exposure to computers long before most Americans had ever seen one.

Brin and Page seem to have a knack for science and technology, like their parents. They are bright, inquisitive, and creative, like their parents. They have a risk-taking, adventuresome attitude, like their parents. Humans have recognized for thousands of years that offspring resemble their parents, knowledge that they applied early in the course of human civilization to the selective breeding of plants and animals. Yet if you could compare the strings of DNA units in Brin's or Page's personal DNA code to the strings in your own DNA code, you would find that they are 99.9 percent identical. If you lined up your DNA code with that of Tiger Woods, or Madonna, or Barack Obama, George W. Bush, Hillary Rodham Clinton, or Paris Hilton—you would find that these, too, are 99.9 percent identical. Since all these people look and act differently from each other and from you, that 0.1 percent difference between any of these people must play a big role in personal appearance and behavior. And as we'll discuss in subsequent chapters, that 0.1 percent difference also results in some of us getting cancer, or Alzheimer's disease, or having the good fortune to escape these diseases altogether.

We expect that within the next ten years the parents of a newborn will be presented with the code that is written in the strings of letters of her DNA, in addition to their child's footprints and thumbprints and APGAR score. They will be able to Google that code and predict their child's risk for some diseases and behaviors. They will know what to watch for, and in some cases they will be able to intervene to minimize unwanted consequences and maximize desirable outcomes. The child born ten years from

now will have unprecedented self-awareness (genetically speaking), and unheard of self-control (medically speaking).

Clearly, we are on the cusp of a genetic revolution, one that will affect all of us in a personal way, every day. To benefit from this revolution and manage the consequences, everyone needs to understand what is meant by "personal DNA code" and how the small fraction of differences between individuals' long lists of DNA letters makes each of us unique. How does that code determine who we are, what diseases we may get, how we feel, and what we're capable of? How much control does our personal DNA code exert over our fate?

In this book we provide some answers to the questions: What is a "personal DNA code" and what will it tell us about ourselves? How do the genes specified in the human DNA code get assigned to specific cellular functions? How do individuals' differences in this code result in differences in disease risk? The answers require us first to explain what DNA and genes are, how they are inherited, and how they collaborate to allow a fertilized egg to turn into a creature of amazing complexity in nine short months. From there, we can begin to show you why each person's DNA code is a little bit different from everyone else's, and how these variations influence our lives.

# Genetic Twists of Fate

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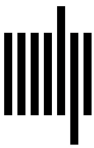

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