

The art of medicine Life writing in the genomic age

When Francis Collins announced the publication of a draft of the human genome in 2000, he compared the genome to a book: “It’s a history book—a narrative of the journey of our species through time. It’s a shop manual, with an incredibly detailed blueprint for building every human cell. And it’s a transformative textbook of medicine, with insights that will give health care providers immense new powers to treat, prevent and cure disease.” Craig Venter, who simultaneously published the draft of the first human genome sequence, also compared the genome to a book, although he emphasised the special challenges this book poses for its readers because of uncertainty about what the entire code means: “Imagine the genome as a book written without capitalization or punctuation, without breaks between words, sentences, or paragraphs, and with strings of nonsense letters scattered between and even within sentences.” Collins and Venter chose the same analogy, but their visions of the genome as a book are strikingly different. For Collins, the text clarifies history, biology, and the future of medicine; for Venter, its message is vexingly encrypted.

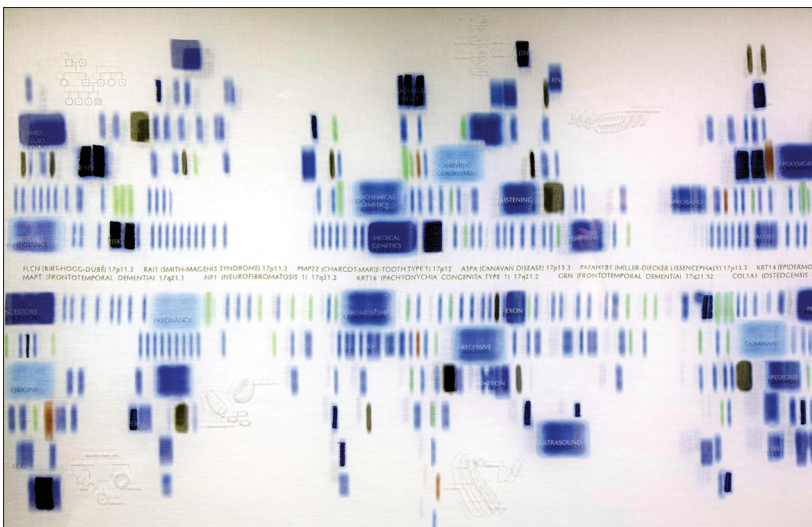
In the next decade some people began to have their personal genomes sequenced, and a new textual analogy emerged: the genome as autobiography. For example, cognitive psychologist Steven Pinker wrote “My Genome, My Self”, geneticist Misha Angrist published *Here is a Human Being*, and novelist Richard Powers penned “The Book of Me”. In fact, when Powers was deciding whether to have just 600 000 of his single-nucleotide polymorphisms (SNPs) scanned or to get his whole genome sequenced, he rejected the “thumbnail synopsis”, which seemed to be only

“an index of a book no one really knows how to read”, in favour of the unabridged “book of me”.

The analogy of the genome and autobiography raises various questions. How will the stories we tell about our lives evolve as our understanding of humanity is transformed by personal genomics? Can we resist simplistic tales of genetic determinism? What will genomic and genetic life narratives reveal about the challenges posed by DNA to our understanding of health, illness, and risk, as well as self?

We can get a better sense of the changes that lie ahead by considering how previous scientific studies of human inheritance and evolution transformed the stories that we tell about ourselves. The first edition of Charles Darwin’s *On the Origin of Species* in 1859 threatened to erase both divine and human will from the history of life in favour of a story about natural laws. In the final paragraph of this book, Darwin emphasised how completely his theory redefined our understanding of life on Earth. “It is interesting to contemplate an entangled bank”, he wrote, “clothed with many plants of many kinds, with birds singing on the bushes, with various insects flitting about, and with worms crawling through the damp earth, and to reflect that these elaborately constructed forms, so different from each other, and dependent on each other in so complex a manner, have all been produced by laws acting around us”. While Darwin muted the radicalism of his ideas in later editions by suggesting that these laws may have been set in motion “by the Creator”, in his first version, the idea that natural selection alone led to “the production of the higher animals” was sufficient to inspire in him a sense of life’s grandeur. Even after the insertion of “the Creator”, Darwin’s account of life’s evolution was a startlingly new narrative about chance, variation, interdependence, and the agentless activity of natural laws.

While Darwin transformed the story of how life developed, *On the Origin of Species* offered little insight into individual lives. Theories of Mendelian inheritance and natural selection supplied few answers to questions about a life’s progress, meaning, or purpose. Will personal genomics change that story? In “The Book of Me”, Powers argues that it will, and that the human experience of biological existence is about to change for the better. “Once upon a time”, he writes, “we were dealt a hand by Fate, God, or the Unreliable Narrator, and the task of life was to deal with that hand. Now the task is to improve the deal.” Powers recognises that his DNA will never change, but he also sees that “what that story means—the live links to the growing online literature, the changing interpretations of these variations, and the response I choose to take to them—is changing by the moment”. Powers



Chromosome 17 (2011) by Geraldine Ondrizek
Dyed and embroidered silk and cotton, 36 x 108 in.

evokes the ending of Darwin's *On the Origin of Species*, with the tangled bank of "elaborately constructed forms produced by laws acting around us", when he closes his essay. As his plane lands in Chicago after a trip to Boston to learn about his genome, he looks down at the "tangled, incalculable network of Chicago". He makes his way through O'Hare's "mobbed concourse" with the report about his genome in his bag, contemplating human evolution and how, "for a very long time, we have been moving from scripted characters to the co-authors of our own lives". "The personal genome", he then adds, "is one more tentative step from fate to agency, from fatalism to risk management. We are determined not to be determined." Powers believes that he—and we along with him—are living in a new era between agentless evolution, as Darwin conceived it, and previously unimaginable choice and responsibility.

As genetic testing has become more widely available, a broader array of stories is emerging that reveals some surprises about the choices people are making in the territory between accepting their genetically determined fate and the not-yet-realised promises of genomic medicine. A new anthology, *The Story Within: Personal Essays on Genetics and Identity*, begins with a cluster of essays about "Finding Out: Genetics and Ideas of Self". Five writers with family histories of disease contemplate their choices—two are at risk for Huntington's disease (Kelly Cupo and Alice Wexler), two for Alzheimer's disease (Charlie Pierce and Kate Preskenis), and one for breast and ovarian cancer (Amy Boesky). Given what Powers has written about the dream of coauthorship, one would expect that all or most of them would have chosen to have genetic testing, but only one out of five did so. Neither writer at risk for Huntington's disease chose to be tested, for example, because the genetic test would have revealed either that they had escaped the disease or that they would certainly develop it, and both preferred living with uncertainty (as do many other adults at risk for this disease). When the one writer who did choose to have genetic testing, Charlie Pierce, learned that he did not have a particular risk variant for Alzheimer's disease, the information was not as significant as he expected. After all, he had been tested for one variant, not for all of the as-yet-unknown genetic paths to the disease, and he possessed a long family history of early-onset Alzheimer's disease.

The problem with genetic information, writes Amy Boesky, the author of an essay on breast and ovarian cancer and the editor of *The Story Within*, is not only how little scientists know at this point, but that "what we mean by knowledge is, in itself, so limited, so laden". Choosing to find out whether one has a particular genetic variant is one way to coauthor one's life, but choosing not to find out serves a different kind of self-authorship. Boesky did not get tested for an identified genetic mutation; she did, however, decide to have prophylactic surgery on the basis of her family history. In her experience, as in the experience

of many of the other essayists in this remarkable collection, the personal value and meaning of genetic information depends on circumstances, culture, financial resources, family history, and whether medical intervention is possible. The significance of the information is also, quite reasonably, diminished by awareness that so much remains unknown about genetics, genomics, and health.

The tension between "The Book of Me" and the narratives in *The Story Within* suggests that the analogy of the genome and the book needs greater scrutiny. Perhaps more complex, informed, and meaningful genomic narratives are needed to understand more fully how genome sequences aren't like stories. Although it seems that personal genomics offers a record of our own particular origins and a map of our body's life course, those who try to find personal meaning in their DNA face an extraordinary challenge. There are about 22 000 genes encoded among the 3 billion base pairs of the human genome; science knows only an infinitesimal amount about them and their unimaginably complex interactions. Any individual genomic sequence points to billions of possibilities and probabilities. With the exception of single-gene disorders, such as Huntington's disease or Tay-Sachs disease, there is no way to predict with certainty what will happen with and to the body and mind over the course of a life, and, even in single-gene disorders, environmental and epigenetic factors can contribute to radically different experiences. A person's genome is not a script or a blueprint or an oracle, and there is a profound difference between genetic data and a story that seeks to define a life's meaning.

Even if we reject the idea that the genome is a "book of life", we will no doubt still be compelled to narrate stories about our experiences with genomics and genetics. We compose narratives to explore contingency, uncertainty, and the unknown, to preserve memory, and to construct understanding. Narrative, in other words, is a tool human beings have long used to grapple with vast and complex issues, including the effects of unprecedented technological and social change, and the limits and possibilities of human lives. It might be that we're genetically predisposed to narrate and thus that we cannot help but narrate the genome now that it is a presence in our lives. But we need not let it narrate us. Figuring out how to tell the stories of our interaction with genetic information and probabilities, however, will require experimentation with new literary forms. Rather than turning inward and focusing only on the codes in our cells, we need to invent new ways to compose the story of the self in connection with the whole entangled bank of earth in which we live.

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Further reading

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