ONE

Introduction: "As deep as life itself"

"Aylmer," resumed Georgiana, solemnly, "I know not what may be the cost to both of us to rid me of this fatal birthmark. Perhaps its removal may cause cureless deformity . . ."

"If there be the remotest possibility of it," continued Georgiana, "let the attempt be made at whatever risk . . . You have deep science . . . Cannot you remove this little, little, mark, which I cover with the tips of two small fingers? . . ."

"Noblest, dearest, tenderest wife," cried Aylmer, rapturously, "doubt not my power. . . . I feel myself fully competent to render this dear cheek as faultless as its fellow; and then, most beloved, what will be my triumph when I shall have corrected what Nature left imperfect in her fairest work!"

Nathaniel Hawthorne, *The Birthmark*, 1843

The great dry fog and deCODE genetics

In 1783, a massive volcanic eruption took place in the Lakagígar area in southeast Iceland. Not only did the ash from the eruption settle on pastures throughout Iceland, it was also carried over great distances, covering the Northern Hemisphere like a large veil. The summer of 1783 was characterized by a phenomenon described by contemporaries as the "great dry fog," in areas as far apart as many countries in Europe, Alaska, Labrador,

Newfoundland, Tunisia, Asia Minor, and possibly China (Demarée and Ogilvie 2001). Icelanders carefully observed the eruption and could hardly fail to see where the ash came from. Meanwhile, continental Europeans remained puzzled, eagerly commenting upon the causes of the fog as well as its implications. For some, it signified the end of the world. In Europe the cause of the great fog remained unknown for months. Scholars and the public at large observed that it correlated with a series of other natural events, including earthquakes, fireballs, climate change, and epidemics, but it was unclear how, if at all, these events were causally related. Later, however, when Danish merchant ships arrived in Copenhagen with the news from Iceland, the larger world learned about the actual nature and origin of the "fog." The local geological events of the Lakagígar had widespread and complex global consequences, climatic and social. Roughly two centuries later, another great dry fog began to spin around Iceland. In 1998, the Icelandic government planned to construct, along with a private company, a national Health Sector Database for the purpose of biomedical research, as part of a larger project combining three kinds of "dry" data (see Gulcher and Stefánsson 2000) – genealogical records since the Middle Ages, medical documents since 1915, and genetic information on modern Icelanders.

Almost overnight, the international press got focused on the story of a tiny nation selling (or giving away) their "Viking" genes to a multinational corporation, deCODE genetics, and its Icelandic subsidiary *Íslensk erfðagreining*. An entourage of observers from all over the world flew in to cover the story – journalists, bioethicists, and scientists of all kinds (see, for instance, Specter 1999, Fortun 2000, Rose 2003). And a whole army of commentators stayed behind, constructing their narrative on the basis of second-hand information, puzzled by this new mysterious fog and upset if not outraged by its potential implications (Chadwick 1999, Lewontin 1999, Greely 2000). This time the news erupted first on Euro-American shores, although Icelandic scholars soon joined the debate (see, for instance, Andersen, Arnason, and Sigurdsson 1999,

Palsson and Thorgeirsson 1999). During the following months and years, a whole series of somewhat similar "biobank" projects were conceived and planned in different parts of the world although they received far less attention. While some of them have collapsed, many others are on course. Winickoff rightly observes that the Icelandic Health Sector Database became an experimental site for geonomics and genomic governance in the sense that it "helped produce the technological, political, and normative terrain of all large-scale genomics initiatives today, not just Iceland's" (2006: 97).

In 1996 deCODE genetics was established by two physicians, the Icelander Kári Stefánsson, a professor at Harvard University, and his collaborator and former student Jeff Gulcher. In company lore, the deCODE idea was conceived over coffee at Starbucks in Boston. The plan was to exploit the relatively homogeneous Icelandic genome and the wealth of local historical records for the purpose of biomedical research. Investors received the idea warmly and soon the company began operations on the outskirts of Reykjavík. While the company operates in Iceland, it was funded by venture-capital funds co-ordinated in the United States. deCODE genetics soon strengthened its financial position through a business arrangement with the pharmaceutical giant Hoffmann-LaRoche. At that time, the company had outlined plans for a national Health Sector Database on Icelanders. The central idea of the database project, and the source of much of the controversy around it, was the assembly of medical records for the entire population. After nine months of national debate, in December 1998 the Icelandic Parliament passed a bill authorizing the construction of the database. The company grew spectacularly during its first six years or so, hiring more and more staff (employing 600 people in 2002). Then came an economic backlash, triggered partly by general trends in biomedicine on the global scene, as a result of which the company was forced to make about one-third of its personnel redundant. In an attempt to make ends meet, the company streamlined its research on patient groups and increasingly moved into drug

discovery and development. At the same time, work on the database project slowed down. In 2004, most of the people involved seemed to assume that the project had collapsed, although accounts of the reasons differed. According to some narratives, the "shelving" of the database was due to legal developments (Abbot 2004), but in reality the reasons seem more complex. Despite the apparent collapse of the database project, deCODE genetics has made important advances in genetic research. A recent somewhat generous article in *Time* magazine suggests the "Iceland experiment" has "captured the lead in the genetic revolution" (Lemonick 2006: 50).

The fog persists. Somewhat similar biomedical projects (usually with less comprehensive records but on a far larger scale) have been reported in many other countries, including Australia, Canada, China, Denmark, Estonia, Japan, Newfoundland, Norway, Quebec, Singapore, South Africa, Sweden, Tonga, and the United Kingdom. Despite all the accounts, popular and scholarly, the unfolding events are poorly understood, along with similar events in biomedicine and bioinformatics. Just as the Lakagígar eruption during the *annus mirabilis* of 1783 has potential implications for the understanding of current environmental change – it probably had climatological, oceanographic, and geophysical implications throughout the Northern Hemisphere – the Icelandic Health Sector Database may be seen as an empirical site with potential implications for genomic and medical research elsewhere. Iceland is neither more nor less unique than other database contexts, but it happens to be the site of influential innovations in biomedicine and bioinformatics.

This book seeks, among other things, to ground the debates and developments surrounding the Icelandic database and similar genome projects elsewhere, emphasizing their global connections and the contribution of anthropology to the understanding of contemporary biomedical debates and issues. More generally, the book presents anthropological perspectives on the so-called new genetics, focusing on the development and implications of scientific practices that have enabled the visualizing and

mapping of genetic material, in particular the social imaginaries they have both fashioned and been fashioned by. It explores its themes by looking at a diversity of projects associated with research on the human genome, genetic diversity, and biomedicine, emphasizing some of their wider social implications for human relatedness. By necessity, a range of other kinds of ongoing projects that truly deserve no less attention have to be only mentioned in passing or practically ignored. This includes explorations of therepeutic cloning, stem-cell research, new reproductive technologies, and reproductive medicine. Among the projects discussed are biomedical studies of particular patient groups, regional and national biogenetic projects, the human genome projects, and the plan to chart the diversity and history of the species (the Human Genome Diversity Project). All of these projects, and many more, illustrate a growing fascination with the potentials of molecular biology and the complex coupling of biotechnology, informatics, medicine, and the market. And most, if not all, are hotly debated among researchers, a variety of interest groups, and the general public. The key issues discussed here, in fact, have been widely discussed for some years throughout the world. Public interest in them is unlikely to wane, given the growing importance of biotechnology and biomedicine and the social and ethical concerns often associated with the new genetics.

Based on my research for the last decade or so, the book draws upon my reading of pertinent literature in anthropology, the social sciences, science studies, the humanities, and human genetics, domestic and international media material, as well as my ethnographic fieldwork in Iceland. While recognizing the successes of the new genetics and its potential contributions to human well-being and our understanding of the history of the species, it is argued, the larger implications of human genetics and the gene centrism on which it is based need to be thoroughly explored. In order to understand "epigenetic" interactions in the constitution of life – the unity of genes, organism, and environment – students of human development, relatedness, history, and diversity need to move beyond

both the dualism of nature and society and the languages of genetic codes, family trees, and insular populations.

The new genetics

A few basic observations on the development and conceptual framework of the new genetics are in order to give the newcomer an absolutely minimal idea of an extremely complex terrain and development. At the same time they serve to provide a background for the following discussion of gene hunting, biogenetic projects, and the study of human genetic variation (for detailed introductions to molecular biology and its manifold uses, see, for instance, Krude 2004, Watson 2004). This is necessary, moreover, to appreciate theoretical attempts to move beyond the simple language and determinism of genetic codes. To underline more complex mutual interactions in the constitution of life, a growing number of scholars representing a variety of disciplines are operating with the notion of epigenetics (Neumann-Held and Rehmann-Sutter 2006). Given such a perspective, development and evolution are co-operative projects rather than the monologues of genetic codes and adaptive pressures. The tension between this theoretical perspective, I suggest, and the successes of reductionist molecular biological methods deserves particular scrutiny.

Biological understanding of the nature of inheritance seems to take a great leap forward every half a century or so. In 1900, three men, Carl Correns, Erich von Tschermak, and Hugo De Vries, rediscovered Mendel's laws of inheritance, thereby paving the way for modern genetics (the term "genetics" was coined by William Bateson in 1906 and three years later the term "gene" was introduced by Wilhelm Johannsen). Then by the middle of the twentieth century, a series of critical insights, experiments, and measurements developed by Francis Crick, Rosalind Franklin, James Watson, and Maurice Wilkins and some others mainly at King's College London and the Cavendish Laboratory in Cambridge led to the discovery

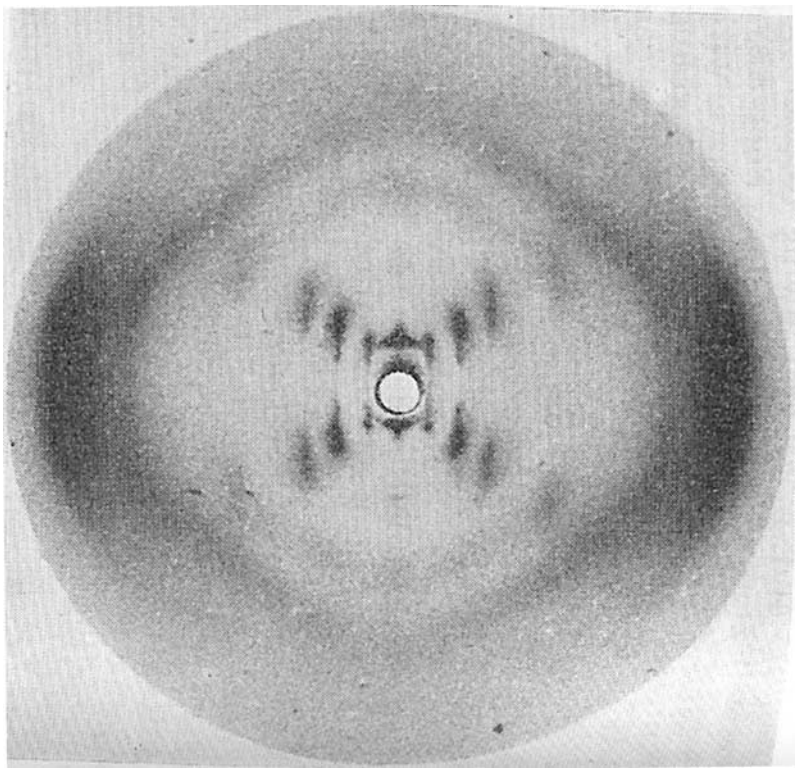

FIGURE 1.1 Rosalind Franklin's Photograph 51 of the B form of DNA

in the spring of 1953 of the double helix of DNA, revealing at last the mechanisms of inheritance, the "secret of life." Key developments were Franklin's calculations and X-ray images, including Photograph 51 of the B form of DNA taken between 1 and 2 March 1952 (see Figure 1.1). Franklin's photograph had a strong impact on its own as it was the clearest picture ever taken of a DNA molecule, with a stark x radiating from the middle and blank spaces between the arms of the x. To some of the key players in the discovery of the structure of DNA it immediately suggested the molecule was a helix (see, for example, Maddox 2002). In Watson's own words (2004: 50): "The X-ray pattern of this B form was a distinct

cross . . . DNA had to be a helix!" Gradually, the image has achieved an iconic status along with that of the three-dimensional helix itself (Nelkin and Lindee 1995, Keller 1996, Klug 2004).

Finally, in 2000, the first draft of a map of the human genome was announced. On that occasion, the journal *Nature* triumphantly published a poster, "The geography of our genome" (see Figure 1.2). *Nature* underlined its cartographic language by inviting its readers on a tour into the "universe within" with the following grand statement:

> Since ancient times we have drawn charts of the sky, of the world, and of our anatomy. Today, a new chart is added to the collection: The map of our genome. Its purpose is to synthesize the insights and meaning gained from the sequence of the human genome. We invite you on a tour of the geography of the genome, exploring the chromosomes, the sequence, and the differences between individuals and populations. The integration of these exciting new findings ushers in a new era of scientific and medical progress.

Intensive research over the past decades has revealed what practitioners of the new genetics would take as the elementary structures of the universe within and the geography of the genome. Each organism, in their language, possesses a *genome* that contains instructions necessary for constructing and maintaining a living example of that organism. Most genomes, including that of humans, are made of *DNA*, polymeric molecules (deoxyribonucleic acid) made up of chains of subunits called *nucleotides*. The iconic double helix of DNA is built up of four kinds of subunits, the chemical bases of A, G, C, T – adenine, guanine, cytosine, and thymine. The human genome, a copy of which is contained in practically every cell in the adult human body, has two parts: the *nuclear genome* encompassing approximately 3.2 billion nucleotides, divided into 24 linear molecules (chromosomes), and the *mitochondrial genome* (mtDNA), a circular DNA molecule of 16,569 nucleotides. *Genes* are seen as the most important part of the genome thanks to the biological information they contain. In humans, genes are unevenly distributed

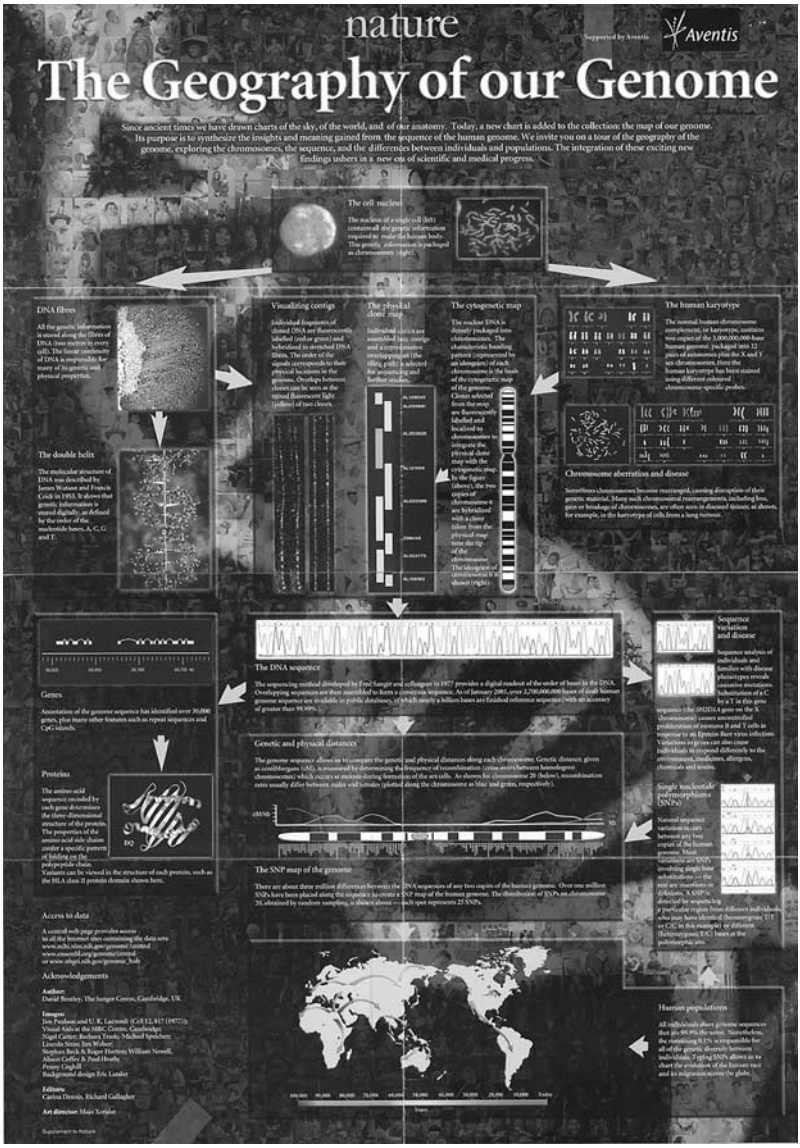

FIGURE 1.2 "The geography of our genome" (*Nature*)

on chromosomes, clustered at particular sites. Most of them encode one or more protein molecules, with RNA (ribonucleic acid, called *messenger* or *mRNA*) operating as an intermediary between genes and their protein products. Only a fraction of the genome (about 2 percent) is reported to encode for proteins; the rest is usually referred to as "junk," although such a terminology is increasingly being qualified.

Now that the structure of the human genome is being established in the wake of the human genome projects and associated advances in sequencing, computing, and bioinformatics (International Human Genome Sequencing Consortium 2004), the genes that it contains and their "functions" and activities are surveyed and studied in detail. This is more complex and ardous, however, than it may sound. The genome projects produced an enormously complex landscape of over 2.6 billion base pairs of sequence and between 30,000 and 40,000 genes, far fewer genes, though, than originally anticipated by the architects of the projects. To provide a sense of the scale of the genomic enterprise, popular and scientific accounts have often referred to geographical distances and numbers of books. The entire sequence in the "genomic alphabet," it is reckoned, would stretch thousands of kilometers and fill thousands of books.

Humans obviously differ from one another as each individual, with the possible exception of "identical" (monozygotic) twins, is biologically unique (for some recent works on twins and identity, see Prainsack and Spector 2006, Davis and Davis 2007). Any two humans, it is generally estimated, differ on average by approximately 0.1 percent of nucleotide sites or one variant per 1,000 DNA bases. Sites in the sequence where people differ at a single DNA base are referred to as single nucleotide polymorphisms or SNPs (pronounced "snips"). The exploration of genetic variation is made easier by the fact that sets of SNPs on the same chromosome are inherited in chunks, as so-called "haplotype blocks" or "DNA neighborhoods." To hunt for genes by exploring the immense expanse of SNPs in the genome would be a daunting task, working from a list of