

Michael Specter Decoding Iceland*

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The next big medical breakthroughs may result from one scientist's battle to map the Viking gene pool.

If not for a single genetic peculiarity, passed invisibly through the generations, it is unlikely that we would know a thing about a sixteenth-century Icelandic cleric named Einar. That's no surprise; on the surface, at least, he does not appear to have been unusual. Genealogies suggest that he was one of about four hundred men named Einar living at the time, each of them struggling among the high moors and dwarf birches on the edge of the habitable world. Einar's ancestors had managed to survive the black plague in the early fifteenth century, which killed as many as forty thousand people—two-thirds of the population—and some of his descendants lived through the next epidemic, smallpox, which struck in 1707, just as the livestock and the settlers were beginning to flourish again on the farmsteads of the countryside. This time, more than fifteen thousand people—a third of the population—perished.

Not only did each of these disasters kill many people but there was an equally dramatic, Darwinian effect: they cut back sharply on the genetic diversity of the island as if a giant tree had been pruned again and again until only its trunk and a few of the sturdiest branches remained. The entire population had descended from a small band of ninth- and tenth-century Norse settlers mixed with a few early Irish slaves. The island had almost no immigration from then until the Second World War, so for more than a thousand years Icelanders bred among themselves. In the middle of the eighteenth century, the population stood at fewer than fifty thousand, no more than it had been five hundred years before.

The greatest calamity was still to come, however. In 1783, Lakagigar, a volcano in southern Iceland, erupted. By the time the lava stopped, eight months later, it had produced the largest flow in recorded times, more than two hundred square miles of fire and ash. In a remarkable diary, which was eventually published under the title "Fires of the Earth," the Reverend Jon Steingrimsson wrote:

"The flood of fire flowed with the speed of a great river swollen with meltwater on a spring day. In the middle of the flood of fire great cliffs and slabs of rock were swept along, tumbling about like large whales swimming, red-hot and glowing."

The eruption itself killed few people, but the sulfur dioxide it released caused one of the deadliest events in the history of Iceland. It blanketed the earth with a dusty poison, and twenty-five per cent of the population died in the resulting famine, as did almost all the horses and sheep. A toxic cloud smothered the nation. Tales of crop damage, drought, asthma, headaches, and a widespread fear of damnation were common throughout Europe. "Those terrors that fell over and upon us I can hardly describe," Steingrimsson wrote. "It will be for all eternity a source of the greatest wonder that any living thing should have survived."

Many did survive, of course—the descendants of Einar among them. We know this now because it turns out that there was something special about that sixteenth-century cleric after all: one of his genes was missing five units of DNA—a mistake on the scale of having mistyped one letter in a volume that holds all the plays of Shakespeare. Such mutations—

permanent changes in the order of genetic information—are not rare. Everyone is born with them. They are almost always harmless.

Einar's was not. The mutation he carried, in which a few of the basic units of DNA had accidentally been deleted from a gene that is now known as BRCA2, is responsible for virtually every case of hereditary breast cancer in Iceland today. Both women and men with this mutation have an extremely high risk of developing cancer, because one function of that gene is to make a protein that repairs DNA when things go wrong. BRCA2 and BRCA1 (the latter is the first gene that was shown to cause breast cancer, and to do so in even greater numbers) are thought to suppress tumors, when they are working normally. Mutations like the one that was traced to Einar through his descendants lie dormant in the cells unless—or until—the remaining good copy of the gene is lost or damaged. That begins the mysterious chain of events that, in ways still not fully understood, ultimately lead to cancer. Researchers at the Icelandic Cancer Society were able to discover Einar's mutation because they worked on a remote island where nearly every genetic possibility could be examined with the kind of detail that would be impossible anywhere else. Many mutations of these genes exist, and so far more than a hundred are associated with BRCA1. But after examining five hundred and seventy-five Icelandic breast-cancer patients, including thirty-four men who had been found since the Second World War to have the disease, researchers discovered only one BRCA2 mutation in Iceland: Einar's. That means scientists don't have to guess what caused cancer in those people; they know. And knowing the root of a disease is the first step along the difficult road toward curing it.

It's a cliché, but the first thing a visitor to Iceland notices, after the volcanic landscape that lies beneath the approach to Keflavik International Airport, is just how closely Icelanders resemble each other. From Geysir, which has become the generic name for half the spouting hot springs on earth, to the Levittown-like suburbs that threaten to overwhelm the rustic, port-side ambience of Reykjavik, Iceland sometimes seems to be inhabited by one enormous family, not one of whose members ever leaves the neighborhood where he was born.

It is the unique nature of this extended family that made Einar's genetic flaw so easy to find: the hereditary instructions for blue eyes and blond hair, which are so prevalent in Iceland, have been passed undiluted through a small gene pool for fifty generations. After a thousand years of plagues, epidemics, earthquakes, and volcanoes finished weeding out the population, what remains in the middle of the turbulent fishing grounds of the North Atlantic is a nation of two hundred and seventy thousand of the most genetically similar people on earth—a place where phone numbers are organized by first names. It takes an amateur genealogist with a five-hundred-dollar computer about three minutes to show how any two Icelanders are related.

No hobby could be more useful to molecular biologists. Prospecting for genetic flaws has become the age's great Klondike: researchers from Newfoundland to Papua New Guinea are sifting through the world's genetic heritage looking for the causes of common diseases by comparing the DNA of sick people with that of their healthy relatives. You can't do that easily in a racially and ethnically diverse place like America; if people's backgrounds, habits, genetic composition, and environments are all different, then so, almost certainly, are the causes of their illnesses. But many scientists believe that Iceland, with a history of isolation and of the repeated catastrophes that have kept the population small, is the richest natural genetics laboratory on earth.

Recent cancer research helps show why. Most breast cancer is not inherited; when it is, the genetic component is almost always complex. If five women in New York City (or in Bombay, Moscow, or Tokyo) each had an inherited form of breast cancer, the causes, the actual genetic mutations, would vary. Some would have one mutation; others another; the cancer of still others might be a result of subtle interaction among several seemingly unrelated genes. But if those women were from Iceland such differences wouldn't exist; each almost certainly would have an identical genetic flaw, inherited from that same clergyman—Einar.

"This is the absolute essence of human genetics," Mary-Claire King told me on the telephone one day from the University of Washington, where she is a professor in the Department of Medicine and Genetics. King, who is among the world's most prominent geneticists, spent nearly two decades searching for the first breast-cancer gene. "To be able to trace the genealogy of an entire nation for a thousand years, and then to have the ability to obtain samples of blood and tissue from healthy living people and to compare the DNA with the tissue of those who have died, and to actually see the differences," King said with obvious excitement, "that information could become one of the treasures of modern medicine." She went on to say, "The first breast-cancer gene took me seventeen years just to map. Comparable work on the second gene was done in about two years. A lot of that credit goes to vastly improved technology. But it is also true that the single, ancient BRCA2 mutation was a golden key. Iceland is just an amazing place to do genetics. The population there is like a gift from heaven."

It was impossibly dreary in Reykjavik at eight on the November morning that Kari Stefansson arrived to show me how he plans to turn Iceland into the Athens of genetic research. The mountain basin that rings the city was covered with what looked like ash. The day was sleeting and dark, and remained that way for at least two hours—until the sun began vaguely to skirt the horizon. By noon, waiters were putting candles on the tables in the city's lunch spots. Shortly after that, complete darkness returned. "You get used to it," said Stefansson, who is forty-nine and is unquestionably the most controversial man in a country usually more occupied with fishing rights and the quality of sheepskin. Stefansson, a neurologist, is the founder of Iceland's first biotechnology firm, Decode Genetics and he developed a plan to take all the research gifts that the country offers and create a giant electronic database, which will allow his firm to hunt for the causes of dozens of common diseases. Most genetic researchers agree that such a database could become a scientific instrument of unparalleled power, but the proposal has also set off one of the most rancorous debates in the long history of Iceland.

In return for conceiving, creating, and paying for this database, which Stefansson says will cost his company at least a hundred and fifty million dollars, the government will grant Decode exclusive rights to market it abroad for twelve years. The plan has stimulated great excitement among researchers throughout the world. No other country—and certainly no other private company—has ever tried to collect, store, package, and sell a nation's genetic heritage.

The proposal also frightens many people, in part because the relationship between genetics and commerce often seems somewhat threatening. But there is more than that: under a bill that has come before Iceland's parliament, the Althing, Decode would become the sole manager of this vast collection of information. Many critics say that Iceland, by becoming the first nation to catalogue its gene pool completely and then make it available to a private company, risks yielding control of the fundamental mystery of its existence.

At six feet five, Stefansson is tall even for a Viking, and he speaks in a toned-down brogue that makes him sound a bit like a scholarly Sean Connery. On the day we met, he picked me up in his car, a blue Saab, and I found him hunched over the wheel, muttering to himself, darkly. After a minute or two, I saw the wire dangling from his ear: he was talking—rather forcefully—on a cell phone, something he did at least once during nearly every conversation we had.

"I'm so sorry," he said, sheepishly, as he hung up. "If I seem preoccupied today that is because my enemies have deposited the usual lies and half-truths in the newspapers again. They are saying that if we go forward with genetic research in this country, if I am allowed to prepare the database that will help solve so many medical mysteries and make heroes of the people here, then Iceland will be stigmatized and the people will become pariahs in the world. What a horrendous crock of shit."

Stefansson is a flamboyant man in a very gray land; yet he is charming and well-read enough to salt most conversations with apposite lines from Auden, Yeats, or Iceland's great novelist, Halldor Laxness. Like many medical entrepreneurs, he is often accused of being more interested in deals than in research, but, in our discussions, he sometimes seemed interested in neither. When I asked him what kind of scientist he considered himself to be, he said he didn't really see himself as a scientist at all.

"I look at myself as a failed writer," he said, without any of the grim self-consciousness that usually accompanies such comments. "A successful man is a great writer. But as a writer and as a journalist, if you are any good at all, you watch. You are outside events. You can never really participate, and I am afraid that my personality does not allow me to stand on the outside." Stefansson's eloquence is one of the reasons he has become so controversial in Iceland: he is an unusually effective advocate for his ideas.

But if Stefansson is incisive and determined, he also seems incapable of humility, and he treats his intellectual combatants with contempt. "When the newspapers say that I am the most popular person in Iceland, and when they say that I am the most intelligent man in Iceland, I don't even want to respond to that," he remarked one day, although I had not asked him about any such thing. "But when they say that I could be elected to any office I desire I can assure you that is true." At the moment, however, he is not seeking elective office; his ambitions are much greater. "I want to cure major diseases," he told me matter-of-factly. "I want to use this tool to generate unbelievable amounts of vital knowledge."

"This tool" is Stefansson's ambitious plan to create a central health database; it will include nearly every significant medical and genetic fact about every citizen of Iceland. But the country has far more than raw data to offer scientists: Iceland has a national system of medical insurance which keeps immaculate records concerning almost every major illness since 1915; it has an immense and well-documented tissue bank that can be used as a modern history of the nation's DNA; it has a reservoir of patients who trust their doctors and are far more willing to participate in medical research than people in many other countries. And what is perhaps most important is that Iceland has such a profound passion for recording its ancestry that Decode has already compiled a database with the family histories of nearly seventy-five per cent of the eight hundred thousand Icelanders who have ever lived.

Genealogy is the national obsession. When somebody dies, the local newspapers always carry an obituary, listing in great detail a family tree, with names and dates of birth that can go back for a hundred years or more. At a dinner party in Reykjavik I asked a biologist to translate an

obituary—one I had selected pretty much at random from that day's paper. He dutifully began, and by the time he had gone through the parents and the children, the brothers and the cousins, and back to a great-grandmother on the maternal side of the dead man's family, he looked up with a grin and said, "Hey, I think she was my wife's great-grandmother, too." The University of Iceland has a professor of genealogy; there is a daily column on the subject in one of the newspapers; it is against the law for anyone to change his or her last name, which is a patronymic; and the government exempts most genealogical data from basic privacy laws. Newspaper profiles often include a detailed account of that person's family tree.

"Why all this genealogy?" Stefansson said over dinner one night. "Look around this barren land. There are no remains. No sculptures. No cathedrals from hundreds of years ago. The country was too poor for any of that. There was a culture here for eleven hundred years, but try to find it. There were books that survive and they are the only way we have to convince ourselves that we fit into the context of human history. Write it all down," he said, referring to the single lasting legacy of ancient Iceland, the sagas—the most complete profile of any Western medieval society. The sagas present a vast literary and historical portrait of the feuds, battles, seductions, and triumphs of early Icelandic society. They almost always begin with long lists of genealogical information and they are alive for Iceland today because, unlike Old English, Swedish, or Norwegian, all of which have changed dramatically, Icelandic has remained essentially the same. If you can read an Icelandic magazine article today, you can read the saga about the warrior Egill Skallagrimsson, written in the thirteenth century.

"This was our means of survival," Stefansson said. "People were huddled on mountains in the howling wind. For eleven hundred years, everything in Iceland has always been about the lists of names. It's what we all have in common. Without those links we really have no heritage."

Geneticists have been relying on family histories to explore the roots of human disease at least since the mid-nineteenth century when Darwin's cousin Francis Galton coined the term "eugenics", one of the most heavily freighted words in the history of science. Galton was convinced that such characteristics as intelligence were inherited and that a society could breed for them the way you breed an Irish setter or a Vidalia onion. For years, Icelandic researchers have recognized the special characteristics of the country's segregated DNA, but it was Kari Stefansson who first seems to have understood what Iceland could contribute to the current frenzied hunt for the genetic causes of human illness. The idea of a computerized database that would incorporate all of the country's essential health and genetic information has the unwavering support of, among others, Prime Minister David Oddsson, and it has met with strong approval in polls. One obvious reason for that support is the potential payoff: pharmaceutical companies are expected to spend enormous sums—billions of dollars—if Decode is able to identify genes that contribute to major diseases. More than one Icelandic politician has expressed the hope that the Decode database might do for Iceland what North Sea oil did for Norway.

Yet scientists in Iceland, and many abroad, have become enraged by the notion that such a treasure could simply be handed over to Decode. They argue, often bitterly, that surrendering such a resource to a private company will jeopardize patients' privacy, violate long-established standards of medical ethics and prevent other researchers from taking advantage of this invaluable new tool. There is also a widely-shared belief that if a bonanza is to be made from the DNA of the Icelandic people most of the profits should go to the nation, and not to Decode.

"This is what colonial treasure hunters have done for hundreds of years," I was told by the geneticist Mary-Claire King. Like many of her colleagues, she sees the promise of the research but also worries about the potential for harm in such a vast arsenal of biological data. "It is not that it wasn't important to find gold, diamonds, and minerals in Africa or Mexico," she said. "It was taking the treasures away and the absolute evisceration of the societies that were there which were wrong.

This is the twenty-first-century version of that. It is an elegant approach, which could yield much information—nobody disputes that. But there is a price. And if the price is the destruction of the field of genetics in Iceland—or the loss of the trust patients put in their doctors—then perhaps elegance isn't all that matters."

Stefansson concedes he was not prepared for opposition of that sort, and he acknowledges that early versions of the database plan were badly flawed in their naiveté. But he dismisses current criticism mostly as the prejudice of competing scientists and partly as a reaction to anything far-reaching and new. "Now it has become like the Sturla period in Iceland again," he said one day, referring to a famous saga of the thirteenth century, when warriors dismantled their commonwealth and splattered each other's brains against stone walls. "I am besieged by little people. This is a fascinating controversy and I understand it well. But these few people, opponents"—he spat the word out as if it were a rusty nail—"are scared of change and unwilling to lose their standing in the scientific community. But remember one thing while you are ingesting their propaganda: those who are opposed to what we are trying to do are a small group. They are not important. And they will lose."

Stefansson has white hair and a white beard that are short but fashionably messy, and his usual choice of clothing—muted earth tones blended with black and gray—makes him look rather like the carefully dishevelled director of an experimental theatre group instead of what he is: a physician, an entrepreneur, and a professor. He is intensely competitive; he plays basketball regularly, and "with an extreme and sometimes ugly need to win," according to one of his colleagues. Lately, he has lost so much weight (from the basketball and a lot of worrying) that his secretary provides him with a daily bright-pink protein milkshake and makes sure he drinks it all.

Stefansson's father was Iceland's most famous radio personality and a frequently published writer; his wife raised their five children. Stefansson was evidently audacious from the start. When he was twelve, his father made him an offer: if he learned to type he could transcribe all his father's book manuscripts. For several years, Kari had a great summer job; then one day his father happened to read through one of his published books. "He found that I had changed a few sentences," Stefansson told me. "The changes were not big, but they were absolutely necessary. That wasn't the way he saw it, of course, and my career as a typist ended that minute."

Stefansson spent fifteen years at the University of Chicago, where he became a tenured professor of neurology. He returned to Iceland very briefly, to run the Institute of Pathology, then the country's most distinguished scientific research organization, and afterward spent five years as a professor of neurology and pathology at the Harvard Medical School.

In the early nineties, after travelling to Iceland to do research on his special area of interest, which is related to multiple sclerosis, Stefansson realized that the island was an ideal place to pursue the origins of almost any common disease in which a genetic component played an important role. Although genetic diseases such as cystic fibrosis or sickle-cell anemia are

caused by the mutations of individual genes which can best be traced in families, the most common illnesses, among them cancer, heart disease, and many psychiatric disorders, can be fully examined only by studying a much larger population. Those diseases almost certainly have an environmental component as well as a genetic one, and such complexity makes them incredibly difficult to understand. There are three billion pairs of chemical bases—the building blocks of DNA—in each person's body and as many as a hundred thousand genes in the human genome. The process of deducing the causes of a common illness is one of the most daunting ever faced by medicine.

Geneticists recognized long ago that the people of Iceland, despite their relative seclusion, developed serious modern conditions, like cancer and heart disease, in roughly the same proportion that people do in other industrialized countries. Iceland is not a bizarre offshoot of humanity—such as, for instance, the tiny Atlantic island of Tristan da Cunha, where nearly a third of its three hundred residents have asthma. "Iceland reflects the gene pool of Northern Europe in about 800 A.D.," I was told by Jeff Gulcher, an American former doctoral student of Stefansson's, who is now Decode's chief of research and development. "This is not a rare, special twig of evolution. It is a central branch. When you look at disease here, it ought to be able to tell you much about the cause of human illness in general."

That is what Decode is counting on. In 1996, Stefansson set out to raise capital at a time when investors had become skeptical about the many unfulfilled promises made by companies claiming that genetic research would solve the ills of humanity. He was a forceful salesman, however, and raised twelve million dollars in three months, at which point he left his job at Harvard, returned home, and began working with physicians and their patients, trying to discover disease-prone genes.

Decode soon managed to provide two hundred and fifty well-paid research jobs in a country that earns nearly three-quarters of its income from fishing and has struggled to build a broader base for its economy. (Iceland's entire federal research budget—sixty-five million dollars in 1997—is less than the amount dispensed for research so far by Decode.) "Kari was treated like a god when he returned," I was told by Jorunn Erla Eyfjord, who is the head of molecular genetics for the Icelandic Cancer Society. Eyfjord, who carried out essential work that helped locate the second breast-cancer gene, is a strong critic of Stefansson's plan for a comprehensive database. "People just acted like he had discovered medicine and brought it to Iceland."

People grew more excited when, in February of 1998, Decode signed a contract with Hoffman-La Roche, among the largest agreements so far reached between a genomics company and a major pharmaceutical firm. Roche, which is based in Switzerland, agreed to pay Decode more than two hundred million dollars over the next five years if the company manages to identify genes involved with many of the world's most potent diseases, among them schizophrenia, Alzheimer's, stroke, heart disease, and emphysema. Roche will get the right to develop diagnostic tests and, it hopes, drugs based on any genes that Decode might discover. In return, the company has promised to provide any such tests and drugs without charge to all Icelanders who need them. It is a potentially lucrative arrangement for both sides.

Once the information from the comprehensive database becomes available (Stefansson thinks that this will not happen until at least two years after Decode gets its license), there is little question that many other companies—and possibly some nations—will pay dearly for what it could generate. In the past drugs were discovered almost by chance. Researchers would

identify the protein that seemed to be associated with a disease—it was often guesswork, intuition, or luck—and then they would try out thousands of animal and plant compounds to find something that blocked that protein without doing serious damage to the rest of the body. Cancer drugs can be especially dangerous because to kill tumor cells one often has to use chemicals that destroy many healthy cells, too. Genomics—the study of the genetic heritage of a species—is supposed to provide a sophisticated alternative to that.

In theory, at least, once it is discovered that a gene can cause or play a role in a disease, scientists should be able to understand the molecular basis for that disease—the chemical blueprints—and then design drugs to repair or even prevent the damage. That is why pharmaceutical companies are investing billions of dollars; the potential bounty for each gene will be immense. There will be many hurdles: genes come in all shapes and sizes, and while some provide obvious openings for drugs, others do not. But every time a gene is discovered to play a significant role in a disease the financial and health implications are going to be enormous.

Soon after Decode signed its deal with Roche, the company's cluttered labs filled with expensive gene-sequencing equipment and two dozen of the latest robotic PCR, or polymerase chain-reaction, machines. PCR is the workhorse of the genomic revolution, because the technique is used to amplify a tiny amount of DNA and permit researchers to catalogue and then compare it. Young Icelandic scientists began returning from M.I.T., Berkeley, and Harvard, largely because there was at last something to come home to. The cheerful, open labs at Decode, which look more like commercial kitchens than like medical-research facilities, have turned into the best place in Iceland to do advanced molecular research.

The strategy has been this: the company works with physicians across Iceland in order to study diseases ranging from diabetes to colon cancer to psoriasis. Doctors take blood from consenting patients and send it to the company with an encrypted number replacing the name of the patient. The researchers at Decode process the DNA, looking for important genetic markers for each patient. The raw genetic facts (called genotypes) are then compared to the physical condition of each patient (the phenotype). At the same time, Decode turns to its genealogical database to search for familial patterns of illness. That way, specialists are able to make highly sophisticated statistical interpretations of genetic relationships among people, and to find the best places in the incomprehensibly large universe of human DNA to look for genes that may cause illness.

Decode had some initial success by identifying the location of one of the central genes responsible for a syndrome called familial essential tremor, or F.E.T.—degenerative neurological condition that causes uncontrollable shaking of the arms and the head, and affects millions of people. That work was completed before Decode assembled its genealogical database. More recently, in its hunt for the molecular roots of multiple sclerosis, Decode managed to narrow the search to one piece of DNA with three or possibly four genes on it—a bit like scouring the earth for a grain of sand and reducing the possible locations to a single beach.

In the summer of 1998, the company, together with one of Reykjavik's most prominent physicians, began to investigate the origins of endometriosis, which is the leading cause of infertility in the United States; it occurs when cells from the lining of the uterus appear in other areas. Endometriosis has been regarded as, in Stefansson's words, "a hideous, baffling, and completely sporadic disease," because "nobody could say why some women get it, and

some do not." Now Decode is in the midst of computer-generated detective work on the subject. After replacing the names of the women in the study with secret I.D. numbers, Decode ran the numbers through its genealogy database. With one glance at the family pedigrees of the patients, even an uninitiated observer could see that many of them were related. The results would have surprised the women themselves. (Despite Iceland's sophisticated sense of family history, few people there can name their fourth or fifth cousins. The database, however, connects distant relatives in minutes.) "We take blood from the patient and scan it," Gulcher, who is the energetic floor leader of the Decode lab, told me. "We look at DNA of their healthy relatives to see if it's different. Then we can do a statistical analysis to see what they share with their cousins, for example. Do they share the same sequence more commonly than you would expect cousins to share genetic information?" Mendel's laws of inheritance tell you that cousins should share DNA one-eighth of the time. A larger proportion suggests that something may be worth investigation. "This way we winnow and winnow till we find the places they have in common which could be responsible for this disease," Gulcher said.

One day, almost as a lark, Stefansson set out to do the same sort of research on longevity. It has been generally assumed that there are at least some genetic reasons for certain people to live longer than others. But does that mean that these people are just likely enough to have none of the genetic mutations or other problems that kill people at earlier ages, or are there actually stretches of DNA that instruct genes to help people live a long life?

"Right before I left the University of Chicago, in 1993, I admitted the oldest living American to the hospital," Stefansson told me. "She was a hundred and sixteen. I was just wondering why she lived so long, and I asked her. She told me she gave up drinking when she was ninety. That was cute but obviously wasn't the reason. Still, you do always wonder what makes them different."

So Stefansson turned to the computer. He and Gulcher selected the five per cent of Icelanders among the hundreds of thousands in their genealogical database who had lived the longest—most of them over ninety. The database allowed the two scientists to seek an answer to a simple question: Are these people who live so long related to each other more often than the average in Iceland? The answer quickly became apparent. People over ninety are much more closely related to each other than people in the general population are, and their children are more likely to live longer than the children of others. That provides strong evidence that the trait is inherited.

The next step, of course, is to find out how—and that, of course, is where information from the controversial database could prove so valuable. If you could compare the actual DNA of people who live longest with the DNA of their dead relatives (and then search the genealogy for more comparisons), it would greatly enhance the possibility of finding a shared, special gene or set of genes able to influence longevity. That sort of unified theory of genetic research has always been Stefansson's ultimate goal.

When the bill to establish the Icelandic Health Care Database was introduced last spring, people were astonished by the haste with which Stefansson and his allies in the government had acted. There did not seem to be any room for discussion or disagreement. "That is when we all just got off the train," Sigmundur Gudbjarnason, a professor of biochemistry at the University of Iceland, told me. Gudbjarnason, who is often referred to in Reykjavik as the founding father of Icelandic biotechnology, helped start a movement to oppose Stefansson. "My whole life has been dedicated to promoting science in Iceland in every feasible way,"

Gudbjarnason said over coffee late one afternoon. "When Decode was started, three years ago, I was elated. The problems arose when they came up with this database. It ignores the rights of privacy, and patients' rights. It will turn Decode into a scientific monopoly. Society is now so dominated by profit. It's not about science anymore, it's about money."

From the beginning, Icelandic scientists have wondered how they will compete for research dollars with a company that has access to all the essential genetic information that the country can offer. They complain that Decode is about to receive what the highly respected population geneticist Einar Arnason described to me as "the greatest handout in the history of this supposedly competitive business of scientific research. If you forget the bad science it will encourage, you can think about this: Iceland gets a few hundred mostly technical jobs; Decode stands to earn billions of dollars, maybe more. Sound fair to you?"

Of all the questions that have surfaced since the database plan was first proposed by the government, however, none is mentioned as frequently or with as much emotion as the privacy issue. Many people fear that any such database—which will contain a staggering collection of highly personal information on every individual in Iceland—could be invaded and misused with ease. Critics also fear that as time goes on, and the map of the human genome becomes clearer, this personal information will become even more valuable—and subject to abuse—than it is today.

Stefansson dismisses these concerns as pettiness on the part of a small-minded medical community. "Our right to develop medicine does not come free," he told me. "We have a moral obligation to do what we can to move forward. There are opposing needs: to protect privacy and to push science forward. There are times when they clash. Medicine today would simply not exist if privacy was the only need, the only right that anyone ever considered important."

Stefansson has always maintained that an exclusive contract was necessary to raise enough money to do the job, and he promises that Icelandic researchers can use the data without charge as long as they are not collaborating with a competing firm. "I just don't have the money to construct this database if somebody else can wait till we are done and then come along and take the rights to it," he said, adding that the plan simply wouldn't work if all two hundred and seventy thousand Icelanders had to give consent for each experiment Decode hopes to carry out. That reverses the usual rule of informed consent; it assumes that people are research subjects unless they specifically request exemption; currently, though, in the endometriosis study and in many others, each person working with Decode has to agree in writing to do so.

By the time I arrived in Reykjavik, a month before the decisive parliamentary vote to create the healthcare database, the quarrels between Stefansson and his opponents, which had come to include most of the nation's research community, were constant, ugly, and very public. What had begun last spring as a political deal that would have passed without debate had suddenly become the most contentious issue in Iceland. After a few initial phone calls to scientists, I was deluged with E-mail from people who wanted to tell me about the poisons in Stefansson's plan—and in his soul. A Web site devoted to fighting the plan had appeared. No day passed without a depth charge being tossed into the newspapers. While I was in Reykjavik, and after I left, each side called me often to report the lies, plots, and scientific inadequacies of the other.

"Kari Stefansson shoved this bit down our throats," said Eiríkur Steingrímsson, a molecular biologist at the University of Iceland whom Stefansson described to me as the most brilliant young scientist in Iceland. "That is what we object to the most. If he had done this the correct way it would have been over with already. There would not have been any opposition." Steingrímsson said he was particularly offended by the implied notion that Decode would become the de-facto funding center for Icelandic genetics. "There is no way on this earth that I am going to Kari Stefansson to apply for my funds," he said.

Stefansson had campaigned for months on behalf of the database plan, appearing almost without pause on television and radio. In December, the week before the final vote in the Althing, he decided—"as much as it's agonizing for an impulsive man like me to keep his big mouth shut" that he would no longer defend himself even against the many personal charges being made against him. After I left Reykjavik, he told me, over the phone, "The people still support me and the doctors think I'm the Devil. So it's time to just let the future happen."

As the vote neared, the emotional nature of the debate spread along the Internet, through the world's close-knit genetics-research community. Richard Lewontin, a professor of zoology and biology at Harvard, suggested publicly that "a boycott of scientific cooperation with Iceland might be an appropriate measure if this bill is passed," but nobody rushed to support him. Many researchers, even some who believe the plan has merit, felt troubled. They say that once the database is approved it will be as if an arrow had been shot into the void: nobody can guess where the process might lead.

"We are not just talking about creating a market for Iceland's DNA," I was told by Henry T. Greely, who is a professor of law and a co-director of the Program in Genomics, Ethics and Society at Stanford. "This isn't fish or lamb's wool we are dealing with here. This particular product is the spirit of the human species, and before Iceland turns its DNA into a commodity—and one that they may not even earn their fair share of money from—I just hope they know what they are doing."

Support for the health-care database from Prime Minister Oddsson was essential. Yet, after voicing strong initial belief in its promise, Oddsson became silent. Many people began to believe he was looking for a graceful way to back out of a plan that had become politically sensitive. When I saw him in Reykjavik, however, he quickly made it clear that nothing could be less true.

Oddsson is a contemplative man who writes poetry, considers himself a conservative, and is very popular. "Obviously, this is all about trust," he told me one blustery Sunday afternoon when he was alone, working in his office. "In Iceland, trust is everything. I once saw a documentary about a famous defense attorney. He was asked, 'How do you choose a jury?'" He said, "First, I take out all people who wear bow ties because they are not likely to be part of a team. Then I get rid of everyone of Northern European descent. They are too trusting and they all believe in authority. When the police testify, Northern Europeans and Scandinavians tend to believe they are telling the truth." At first I was outraged and considered it a complete stereotype. But I sat there and thought about it for five minutes and I realized he was completely right. I happen to be proud of that quality and I think it says something about why we are willing to put ourselves forward and make this database work. It's not just the dangers that deserve to be considered but the possibilities for good for Iceland and maybe for humanity. I know the doctors are very angry. And I wish they weren't. But many of their complaints just aren't valid. We could have passed this bill six months ago after a day of debate, but we wanted to hear how it could be improved, and we listened. Even the biggest

opponents, if you can get them to calm down, will tell you it's a better bill now than it was in April. But they are not happy, and I suspect some of them never will be. So the question for me is simple: should the doubts and fears of the minority outweigh the seventy per cent of parliament and the sixty per cent of the public who want to do this? We have discussed the plan in our press all year. I doubt any issue in the history of this republic has received as much attention. The response has been clear. Go talk to normal people on the street. Let them tell you what they think."

I took his advice, and made a highly unscientific pilgrimage to the Kringlan Shopping Mall, which, except for its self-described distinction as "the mall at the top of the world," might just as well be in Paramus; it has that familiar mix of chain stores, hamburger joints, and cinemas that tend to show American films. My survey could never be published in a peer-reviewed, scientific journal, but for anybody who has done this sort of thing in America the results were revealing: nobody was too busy to answer my questions. Every person knew what I was talking about, and most knew about it in impressive detail. I asked all of them the same questions: Did they support the database, and would they be willing to be listed in it?

Of forty people, two had no answers, two were opposed, because they just didn't trust computers, and two said they needed to think about it. The rest said they would sign up tomorrow. "It is so silly to talk about privacy here," said Thor Palmisson, an engineer. He then took out his wallet and showed me his Visa card, an air-traveller card (for Saga Business Class on Icelandair), and a video-rental card. "Every one of these has my national I.D. number on it," he said. "You can't rent a video without it, and you can't move or get a job. The numbers are easy to figure out. To me, this seems it's all just a giant attack on Kari. What is it that they are accusing him of? Is he trying to get rich? Fine, that's O.K. with me. Is he trying to get famous? I can stand that, too. I have seen him discuss this issue more than once. I don't believe he is motivated by greed. If he takes a few drops of my blood and gets rich curing cancer, that's absolutely fine with me."

The bill passed the Althing on December 17th, by a margin of thirty-seven to twenty (with six members not voting). Instead of ending the battle over the stewardship of Iceland's gene pool, however, the campaign against Decode became even more intense. The legislation was "a totalitarian act which casts a dark shadow over Iceland in the international scientific community," a leftist member of parliament, Hjorleifur Guttormsson, said that day. Overwhelmed by their defeat, critics compared the database project to the Nazi experiments with racial hygiene and the exploitation of poor blacks in the Tuskegee study.

"Anyone who can mention Nazi experiments and this database in the same sentence does not deserve to live in Iceland," Stefansson told me on the telephone as the opposition rhetoric veered out of control. Earlier, I had asked him if he ever regretted his decision to come home. "Not for a minute," he replied. "This happens to matter more than any of us do." Lowering his voice almost to a whisper, he went on, "You know, my brother is schizophrenic. I am not saying that that is what motivates me. It isn't. But, of course, it is there, hovering in the background. And I always know it. I can never know whom it will affect. Maybe my son, my cousin, a grandchild. You can't know that. It's a basic truth."

He went on to say, "I need to convince everyone I was not given a gift. I know that. But look at it logically. Should the government run this database or should private enterprise? Let's assume that the government has no idea how to create value from an enterprise like this. That is my assumption—after all, I did not spend fifteen years at Milton Friedman's university for

nothing.... So does the government have the right, after I put this together, to hand it over to somebody else? Yes, technically it has the absolute right. But this is my intellectual property."

Steffansson will spend at least the next six months negotiating with the government over the terms of the license. During that time, he will have to improve his relationship with many people he has alienated in the past year: scientists in Iceland are already threatening legal action on the ground that the bill offers Decode an unfair monopoly and that it violates human rights in its use of research subjects. Steffansson understands that he will need full cooperation from Iceland's physicians, too. The database will need accurate information—on patients, their diseases, symptoms, medications, and treatments—or it will be useless. "But don't forget the possibilities here," Steffansson said on the day the bill passed. "This fails. We go bankrupt. We lose money. Our investors lose, too. Or possibly we barely make it. Or maybe we make a fortune. There are real risks. And the people who criticize me—they have absolutely no idea what they are talking about. None."

The fact is, however, that many of them do. The field of genomics will certainly grow rapidly, and not much imagination is required to see how genetic information could be misused. To take one obvious concern, should insurance companies or employers have the unfettered right to purchase data that tell them who is most likely to die from coronary-artery disease or cancer at an early age? That isn't a problem in Iceland, where access to healthcare is guaranteed, but it would be in most countries. And what about a genetic trait that increases the viral abilities of H.I.V.? Or makes you more likely to become an alcoholic or addicted to drugs? Steffansson's research into longevity is novel and exciting, but if Decode discovers genes for longevity, most insurance companies would be eager to know who has them. What if it turns out that you don't?

"None of these questions can be answered," Sigurdur Gudmundsson, Iceland's recently-appointed Surgeon General, said. "I have done loops in the air all year long. And it has been painful. Of course there are serious dangers. Is it scary? Very. But we have to find a way to make this happen. The benefits just outweigh the problems. It doesn't mean there are no doubts. We are walking into a new world. But I don't think it is wild to say this may turn out to be a tool like none other. And I don't think this country can just sit here and say, Nope, sorry, we are going to stand on rules that existed in a different era for a different world." In the end, Gudmundsson, like many others who are just as thoughtful and just as anxious, believes that that would be the most foolish risk of all.