believer4.9.qxd 6/23/03 9:42 AM Page 62

KARI STEFANSSON, M.D.

"WHAT IS IT THAT GENERATES THE SOUL? CAN YOU FIND IT IN THE DNA SEQUENCE?"

Genetics of a Viking revealed:
Swords and hallucinogenic roots
The stroke gene
Volcanoes under the midnight sun
The soul as machine
Black designer T-shirts
The oldest woman in the world

I. THE VIKING IN NEW YORK (DECEMBER, 2001)

In the Icelandic Sagas*, the Viking explorer Ingolf Arnarson departed Norway c. 874, looking for plunder and territory. With the genetic fortitude of an ox crossed with a great white shark, Arnarson and his Vikings sailed out in long boats, carrying swords, a few goats, and a hallucinogenic root they chewed that made them go berserk in battle. First, they grabbed women in Scotland and Ireland before heading northwest toward a mysterious island found a few years earlier by Viking marauders far off in the murk, where legend said monsters and mermaids lurked deep in the frigid sea beyond the edge of the Earth.*

I first met Kari Stefansson in New York City in December, 2001, at the New York Academy of Sciences headquarters at Sixty-third and Fifth Avenue. Lean and six feet four inches with a pointed, white beard, the fifty-four-year-old Stefansson is a direct descendant of Arnarson (and of Erik the Red and Leif Eriksson). Lately, he had been embarking on his own saga, this time into the murky unknown of nucleotides and entrepreneurism. Trained as a physician in Iceland, he was medium famous in genetics circles at Harvard University as a neurologist delving into the mechanics of multiple sclerosis and other neurological disorders. Before scientists could easily study DNA, he cut open the brains of people who had died from MS and other maladies of the mind. After several years of slow progress, however, Stefansson found the academic approach maddeningly slow and too small-scale.

In 1996, Stefansson returned to Iceland to found deCode Genetics. Raising $12 million—and later hundreds of millions more—he became an instant rock star in Reykjavík, the

Illustration by Gilbert Hernandez

believer4.9.qxd 6/23/03 9:42 AM Page 63

second most famous Icelander after Björk. In Reykjavík, he built a fantastic genetic palace of blond wood and glass for his company, one of the largest structures in Iceland. Stefansson's idea was to peruse the genetics of Iceland's entire population of 290,000 people, looking for patterns in genes that cause schizophrenia, asthma, Alzheimer's, anxiety, and dozens of other maladies. Thanks to meticulous genealogical records kept for 1,000 years in Iceland and written in the Islendingabok, *the "Book of Icelanders," Stefansson could tap into the records of 680,000 people who had lived on the island since Arnarson, using computers to pick out how families inherited disease. More controversially, he convinced the Althing, Iceland's parliament, to release Icelanders' individual medical records to him—with consent, and as long as the details were kept private.*

Now, in New York five years later, Stefansson was explaining to investors and journalists the details of a $300 million deal with F. Hoffmann-La Roche, in which deCode agreed to provide the pharmaceutical kingpin with genetic tests for several diseases. He also announced the discovery of genetic markers for rheumatoid arthritis. Usually, Stefansson wears tight, black, designer T-shirts to show off his remarkably fit physique and well-pumped biceps, maintained each day in a Reykjavík gym or in hotel gyms on the road. For the announcement, he wore a chic dark suit that made him look like an Armani Thor amidst the less inspired pinstripes of the drug lords. But what really struck me was Stefansson's eyes: dark green, fiery, penetrating, the eyes of a man who in another era might have killed you at the least provocation. He could barely sit still during the proceedings, even if this deal marked a great personal triumph. Afterward, I had a quick exchange with him:

DAVID EWING DUNCAN: You had this prestigious position at Harvard studying brains. Why give that up and return to Iceland?

KARI STEFANSSON: Things weren't happening fast enough. I was in academia for twenty-five years, and I was a little bit bored. Biotech was beginning to take off, to give us the tools we need to study large numbers of genes at once, instead of one at a time. I needed a population to identify genetic disease traits, and Iceland works well, because we have been isolated and have similar genes, but it's still big enough to have a diversity of diseases. So Icelanders are reasonably good lab animals for the kind of testing we do. Later, we will test this information on Americans and others to see if it is relevant to them.

DD: Why is this important?

KS: One day, you will walk into a doctor's office and they will test you, and they can tell you if you will get a disease, even if you're healthy, and they can know how to treat you in the future.

DD: You mean, if this works on the Icelandic lab rats, we Americans might make good lab rats, too?

KS: You are the best lab rats, because you are the rats we want to sell our drugs to.

DD: I'd like to come to Iceland to get tested for these genes—for stroke or whatever.

KS: Yes, yes, come, and we will be happy to subject you to our tests. We will tell you if you are crazy, or if you might die of a stroke. You will become our first American lab rat.

II. THE VIKING AT WORK (AUGUST, 2002)

In Reykjavík, the deCode building sits like a gigantic piece of Skandia furniture on a field of hardened volcanic ash. This is hardly a descriptor in this bleak landscape, where the black rock everywhere remains raw, hardened in waves and eddies, once lava-hot, covered only by a thin veneer of lime green moss. Overhead, the sky boils with immense gray-white clouds that turn nearly black above a ridge of distant mountains where active volcanoes still blow off whiffs of sulfuric steam. The land looks ripped from a primeval moment in history, when volcanoes roared and Titans and centaurs roamed the earth.

Other than deCode and an oversize church up the hill, Reykjavík is a small city of mostly squat, functional, wood-framed buildings that seem hunched over, as if holding their heads down in a storm. Rain does fall here frequently, though the nearby Gulf Stream usually keeps the temperature above

believer4.9.qxd 6/23/03 9:42 AM Page 64

freezing, even in the winter. Yet this close to the Arctic Circle you don't have to go far to find glaciers crawling across the hardened lava fields in Iceland's interior.

Inside deCode, three towers containing labs, computers, and offices are connected by a glass-enclosed atrium four stories high, a small city crisscrossed with open bridges between the towers. Hanging down from the ceiling, over the lunchroom, a gigantic model of a double helix turns slowly, picking up the dull, gray light from outside like an elongated disco ball. In one tower a supercomputer composed of twenty-three computers, one for each human chromosome, can process a person's entire genetic code in twenty minutes; a retinal scan is required to get into the area where the computers hum.

Stefansson's office is across a bridge from the spinning DNA model; his large windows overlook the old Reykjavík airport and the vast sweep of lava and mountains. He's wearing his tight black T-shirt and is about to drink two glasses of a Pepto-Bismol–colored drink he says is a protein supplement. I see Yeats's Ghosts *and the* NASDAQ Rule Book*, among other volumes, in his bookcase. He's about to tell me the results of one of the tests run on my DNA, extracted from white blood cells in a tube of my blood, which I had mailed to Iceland from San Francisco.*

KS: The DNA from you is, of course, a scary substance.

DD: I have friends who say I come from an other planet.

KS: You did not come from another planet, but I will tell you in a minute where you came from. One of the things we did was that we looked at the genes that confirm a stroke. We have established that you have a series of [genetic] markers that give you something like a two to seven times greater risk for developing a stroke than if you don't. You have this entire haplotype [gene profile], so you probably have three times the risk. If this turns out to be the case in the American population, you are genetically predisposed to stroke.

DD: Oh, hmm. Stroke? But I've had no stroke in my family, other than my grandmother when she was eighty-three years old. Doesn't my own family history weigh in here?

KS: The only thing you have done is to inherit a predisposition. What does that mean eventually? It means that if you stay in a certain environment, or if you are born in a certain environment, you will develop stroke.

DD: This is because most diseases are a combination of bum genes and the environment—that is, the environment can trigger diseases, or not?

KS: Yes.

DD: But this isn't good news for me. One day I'll be watching a movie or walking down the street, and, suddenly, I'll go limp with a stroke.

KS: Maybe, but here's the beauty of the genetic profiling. It's not going to lead to a genetic determinism like that. You are not going to develop stroke, all right? You now know that you have three times the possibility of the average individual to develop stroke. So you have a strong incentive to take measures to prevent stroke. One of them is to make sure that you don't have high blood pressure; one of them is that you will not smoke. One of them is you will drink alcohol only moderately, because intake of large amounts of alcohol, binges, increases dramatically the probability that you will develop a stroke. You take young people who develop stroke, there's considerable danger to young people who drink, people less than thirty-forty years of age, when they have consumed lots of alcohol.

DD: The doctor speaking—thanks for the advice. But this genetic profile for stroke has not been tested for Americans. Right?

KS: What we have here is one of our basic discoveries. Before you can get too excited as an individual, you have to do a clinical trial in the population where you can use it, like in the American population. But this is a fairly interesting example of what genetic profiling is going to do, how it's going to impact the delivery of health care.

DD: How common is this stroke gene for Icelanders?

believer4.9.qxd 6/23/03 9:42 AM Page 65

KS: In Iceland, this is a haplotype that you find in about thirty percent of patients with stroke. You find it in about fifteen percent of controls [those without stroke]. And then you say, "Wow, fifteen percent of controls with no stroke." But this is an inheritable predisposition. We know this from our genealogical data. Of these fifteen percent, a large percentage will eventually develop stroke.

DD: So what percentage of all Icelanders carry this stroke gene?

KS: It is probably about twenty percent, if you take individuals who have been diagnosed with stroke plus individuals who have not been diagnosed with stroke. But most of these people carrying this haplotype will not develop stroke.

DD: That's one in five who carry the gene—but not all will get the disease. I hope that's me. Makes we want to go and have a drink.

KS: You cannot drink anymore.

DD: Oh, right. But why do some people—

KS: Remember, stroke is a common disease. And when people are thinking about common diseases versus the old Mendelian diseases [in which one gene equals one disease], there is a dramatic difference in the complexity…. In Mendelian disorders, if you have a mutation you will develop the disease; if you don't have a mutation you won't. And with the common diseases, you're looking at a fairly complex relationship. The Mendelian disorders are basically accidents in evolution. However, the common diseases are variations of genes that contribute to human diversity. And if you would get rid of all of the variants of all genes that contribute to human diseases, you would not only get rid of human diversity, you would get rid of man.

DD: So to be ill is to be human.

KS: You're probably best off looking at the common diseases as an expression of the limitation in designer man. We have no role after our reproductive period is over, basically. And let's say that reproductive period is over at the age of forty or something like that. Most of the common diseases do not show up until after the age of forty. And I think it was Woody Allen who once said that when the mean life expectancy of man was forty, marriage made a lot of sense. Now it is eighty and it doesn't make a lot of sense. You can basically say the same thing about the designer man when our mean life expectancy was forty. Our design made a lot of sense. Now our mean life expectancy is eighty and we're beginning to see cracks in the armor. Beginning to see these common diseases show up.

DD: What does this mean for extending life? Some of the work you're doing may influence humankind's future by curing or preventing diseases, which will result in longer life spans. Is this desirable?

KS: I'm not necessarily sure that we will prolong life very much. I hope that we will be able to make sure that man can live a healthy and productive life, and then he dies. Once, as a neurologist at the University of Chicago, I admitted the longest-living person in the United States, and all the TV networks were there, saying she is 116 years of age and she is going to die.

DD: What did you admit her for?

KS: She came with a stroke and had pneumonia. The old brain reacts to pneumonia in a funny manner. And she woke up, and she asked me, "Dr. Stefansson, do you know why I'm this old?" And I thought, Is it appropriate to try to be funny when I'm talking to the oldest living person in the United States? "Is it because you were born a long time ago?" I asked. "No, that's not the reason," she said. "The reason is that I stopped drinking." "And when did you stop drinking?" "When I was 109." And when the son came the following day—I think he was ninety-two or ninety-four years of age—he brought a family photograph from when his mother was forty years of age, and she looked like a fifteen-year-old girl at that time. She was already then genetically much

believer4.9.qxd 6/23/03 9:42 AM Page 66

younger than people her age.

DD: So even with drinking until 109, her genetics dictated she was going to live a long time.

KS: Yes.

DD: I'm feeling older after a night out in Iceland last night. People here drink all night in the midnight sun. It's a party all night.

KS: It isn't worth it, getting drunk. It takes too much out of you, as I know too well. But it can help, too. I have this younger brother, and our relationship has been really difficult for about fifteen years, and he came this spring to visit me, and we got drunk together, and since then our relationship is just like it used to be in the old days.

DD: Did you find out anything else about my DNA? Or do I want to know?

KS: We tested your ancestry to see if the population data from Iceland is relevant to you. You told us your ancestors came from Scotland. In the Icelandic *Sagas*, they said that Iceland was settled by Norwegian Vikings who stopped in the British Isles and picked up slaves and women, in Ireland and maybe Scotland. And we decided to test you by looking at your mitochondrial polymorphisms [mitochondrial DNA that exists in each cell, separate from the double helix of human DNA]. Remember, mitochondria is passed from mother to offspring. Then we looked at your Y chromosome—these both are fairly good measures of paternal and maternal lineage. When we looked at this, it turns out that when we compare it to all of Europe, about seventy percent of Icelandic mitochondria are Celtic.

DD: The Celts being Irish and British.

KS: Yeah, and about seventy percent of Icelandic Y chromosomes are Norwegian. So it looks like Iceland was settled by Norwegian boys who grabbed British girls. This is important when it comes to your mitochondrial DNA, because if we look at the mitochondrial sequence number, one that people look at mostly for ancestry, we find out that you have a haplotype that is characteristic for Europeans. However, when we look at region two, there is this very rare haplotype found only in Iceland and the north coast of the British Isles. We found this haplotype in you.

DD: Uh-oh, then this stroke gene is relevant to me.

[*Stefansson calls someone on the phone*]

KS: [*Into the phone*] I'm out of coffee and I'm in a desperate need because I'm talking to very boring fellows. [*To me*] My eighteen year-old daughter would have said, "boring dudes."

DD: So I could easily blend in with the population here in Iceland.

KS: Very easily.

DD: Let's talk about the nature of what you are doing here at deCode. You are essentially collecting information about how humans function, exploring this new continent called the human genome, all of our DNA, the 30,000 or 40,000 genes that make me me, and you you.

KS: You know, one of the things that was lost on people when they started to look at the genetics of human disease, common disease, is the amount of data you need to be able to make sense of this stuff. They didn't realize that the fundamental nature of what you're studying in human genetics is information: the fundamental units of life, little bits of information. Of all life, not only human life. And we've begun by approaching human genetics as the study of information. We invested enormously in computers and informatics and mathematics and statistics; that is the fundamental reason we can do what we do. So we run a huge monstrosity of a machine here and we have so much data.

DD: You talk as if we humans were just machines. But we're not talking about normal technology here—soft-

believer4.9.qxd 6/23/03 9:42 AM Page 67

ware for building a better carburator or tracking a FedEx package. This is life, this is our future, our children's future—this is our soul, in a sense.

KS: I'm not sure about the machine aspect. I don't feel like a machine. But what I find amazing—what I didn't grasp, although I knew it, and what I didn't understand although I was aware of it—is the fact that what we're dealing with is propagation of information. Nothing else.

DD: And we may be able to reshape that information.

KS: We can reshape that information, but the amazing thing is that what makes life unique is that it consists of self-replicating information. That's what draws the line of distinction between what is dead and alive. And therefore the species, the individual, can be replicated.

DD: But what about the soul?

KS: What is it that generates soul? Can you find it in the DNA sequence? Does the soul lie in the sequence?

DD: Well, according to some geneticists I've talked to, eventually you will. It may be generations from now, but Eric Lander [of MIT, a leader in the Human Genome Project], for one, told me that he hates to say it, he said, but we are machines when it comes down to it. We're a database. And we know such a tiny percentage of it now, but someday we probably will, if we continue on this path, know those complex interactions and know how to build a conscious being just like ourselves.

KS: Although I have a certain tendency to want to disagree with Eric, I cannot disagree with him that we will gradually learn more and more about the nature of this machine. But I think that he underestimates a little bit of the complexity of the function of the brain. You see, if the ultimate function of the brain is consciousness, and you divide consciousness into two components, the alertness and the concept of consciousness, we understand perfect about alertness today. But how we generate the concept of consciousness is much less clear. We know only little bits and pieces. And even if you take a step back and you say, "Let's define one of the elementary components of the function of brain as the instrument of concept of consciousness," and you say, "Let's see how we can define a thought," a singular thought is a very, very elementary component of what constitutes a human being. But we don't have a clue; we don't even have a definition.

DD: And you're a neurologist, so—

KS: Not to mention the complexity of the mechanism that leads to it. I think that if Eric is waiting with bated breath for the day that, through reading the sequence of the human being in the form of a relatively simple linear stretch of information, we can figure out how people will be when it comes to the personality of the soul, he has a long wait. He's going to be blue.

DD: I think he'll be dust, probably. But others have said this, too. Brain geneticists…

KS: Give me a break. Don't listen to people who say that, because they haven't the faintest idea. You are talking to people who are good geneticists, who have very little idea about the phenotype that they are looking at. You see, what you are basically doing with genomics is that you are looking at the level of least complexity. You're looking at a simple code, in a linear form.

DD: Right.

KS: You sitting there, scribbling on a piece of paper, you are basically the human being in its most complex form. And it is more difficult to systematically analyze you in this form than in any other form. However, after having spoken to you for a few minutes, I probably know more about you now than I would spending ten years analyzing the pieces of your genome. But it's going to be much easier for me to learn about the nature of people who share some components of your phenotype by going to this level, because I can look at it over a population of people who behave as you do.

believer4.9.qxd 6/23/03 9:42 AM Page 68

DD: I hear you like to play basketball.

KS: It is, at least when you're my age, very important to get a little more exercise so you feel better. The basketball thing is just an option to do the battle one-on-one in a friendly manner.

DD: Like the Vikings? So you're a very competitive person?

KS: I don't know whether I'm more competitive than the next man.

DD: Because that's part of being an entrepreneur?

KS: I don't know that. As I said, I'm not sure that I'm more competitive than the next man. I'm not all that competitive, my guess is.

III. THE VIKING AT PLAY (AUGUST, 2002)

That night, Stefansson met me for drinks after dinner at an Italian restaurant that served, among the usual pasta and veal, horse meat, apparently an Icelandic staple. He quickly became flush as he drank, and he admitted that this happens when he's nervous. I asked him why he was nervous, and he said that the business side of deCode was getting intense. The stock had dropped from over $30 a share two years earlier to just under two dollars. Hardly unusual for the battered tech and biotech segments of the market, but it was worrying because deCode's market cap was nearing the value of its cash in the bank, making it a possible takeover target.

DD: So what's a doctor like you doing running a company, anyway?

KS: There is a business side to this. The investors gave us a large amount of money to build our computers and have fun with genetics. But we have to run a business.

DD: Had you any previous business experience?

KS: No. But I had a good story, so I got money easily. But now it's not so easy in this economy. The company is doing well, but the market is shit. And that's all I have to say about it, because I'm trying to enjoy my wine.

After drinking enough wine to give me a stroke for sure, we walked up the main drag of Reykjavík—there is only one, though the bars, clubs and restaurants are as sophisticated as any in the world. Icelanders travel incessantly and bring back music, art, dancing—and genetics—from elsewhere, integrating with their own sensibility. In one bar near a CD store where Björk used to sing early in her career, heads turn when Stefansson walks in. He towers over most people and is known by everyone. I step over to the bar to order beers, and two Icelandic women say hello. One of them says she is in love with Stefansson, the other is annoyed with him, because, she says, like most of Iceland she bought deCode stock and watched it drop. Stefansson comes over and is sullen—he's had a long day, but we drink until three a.m. As he says goodnight—and it's still light out—Stefansson tells me that drinking tonight will kill me, that I'll have a stroke by morning.

IV. THE VIKING IN SAN FRANCISCO (JANUARY, 2003)

Stefansson has just finished giving his standard twenty-minute spiel about his company to a room full of investors. He's testy; deCode's stock is still scrapping along below two dollars a share, despite the company's success, and these investor meetings are no fun anymore. I pick him up at the Mandarin Oriental Hotel and take him to my gym. He works out in a huff and won't talk much, except about the amazing similarity of the women in the gym. Most are blond and thin. The gym is in a part of San Francisco people sometimes call Ken and Barbie Land, with some justification. He says we should test the genes of this population to find out why they all look the same. Then he decides he really doesn't want to know.

At dinner, we again drink what seems like an endless bottle of wine. Having now followed Stefansson for over a year, I watch him eat, this volcanic, playful Viking dressed like a Boss model, and I wonder—Can we nonscientists trust him? Can we trust these geneticists and entrepreneurs to do the right thing with this potent new information about life itself?

I remember a conversation I had with Stefansson about the

believer4.9.qxd 6/23/03 9:42 AM Page 69

Human Genome Project, the mapping of the 30,000 or so genes that constitute human beings. We talked about the geneticist Craig Venter, the mercurial visionary and entrepreneur whose company, Celera, engaged in a very public race with a government-funded effort to solve the genome. Venter rankled nearly everyone with his brash style, but his methods won out in the end. A few months earlier, Venter had announced that the genome solved by Celera was his own, despite assurances that the genome used was a mix of several people of different ethnicities, chosen randomly. He had always hinted that his genome was one of those used, but not the sole genome to be used in his company's contribution to the multi-billion dollar solving of the human genome. A public relations coup that helped land him a lucrative book contract, the news of his duplicity disturbed me, and I brought it up with Stefansson.

KS: There is no process to protect anonymity that takes away from me, or Craig Venter, the right to reveal to the world whatever you want to reveal about the self. The process is not set up to take away from you the right to self-determination. It's to protect your right to self-determination. So when Venter stands up and says, "This is my genome," it displays his narcissism and his love for the spotlight, but he's simply exercising what is his right.

DD: Of course he has a right to do it, but he himself set up a system through his scientific board which promised to keep this anonymous and to use people other than himself.

KS: He said that he would use someone other than himself?

DD: Yeah, there were forty people they were drawing DNA from, and they were supposed to randomly choose, I think—I forget the exact number—six or seven people whose genomes would become components of the human genome.

KS: These are trivial things!

DD: The point is that we have to trust scientists. We the public have to trust you to keep your word, even about something that you say is trivial. But when we hear that you're circumventing processes like that, especially for personal gain or glory, it makes us worry that other processes might be subverted…

KS: Can I tell you something? At the time when Venter was starting off with this [the Human Genome Project], there was enormous public debate on the use of genetic information, and there were tremendous pressures to make the system so safe and reliable that it was almost impossible to work in it. He should probably not have made a commitment to do it this way if he was not going to do it, but it doesn't constitute a major breach of confidence or commitment between him and the rest of the world.

DD: It's not a major breach. But it feeds into a paranoia that's already out there that scientists sometimes don't keep their word.

KS: Scientists do keep their word, but let me share with you that I think the scientists are probably just in the dead center when it comes to the commitment to keep their word. They're no different from other people and they shouldn't be.

I wonder if this is true as we sup on a cold, wet San Francisco evening. Are geneticists really no different from other people? They're probably not, though maybe they should be more accountable than most. After all, we nonscientists are essentially placing in their hands the future of our species, and possibly of the entire planet.

I ask Stefansson what's going on at deCode, and he's still in a bit of a funk after the investor meeting. He's tired and scowls at me, but the Arnarson fire of the Sagas *is less deadly for the moment as this Viking rests.*

KS: I don't want to talk now. You can keep asking me questions, but I will not answer them. Let me eat in peace.

After dinner, Stefansson says goodnight. There will be no more drinking this evening. Tomorrow, he flies off again to fight more battles, the Viking as geneticist sallying forth into the mysterious land of DNA. ✶