

# Kári Stefánsson

Outspoken doctor Kári Stefánsson founded Iceland's deCODE Genetics to use its citizens' genealogy in the hunt for human disease genes. Here he speaks of his passion for medicine and for his homeland—and about courting controversy in both.

In the bowels of the world's most notorious biotech company, a robot, balanced on an earthquake-proof concrete slab, is shuffling the chilled blood of 100,000 Icelanders. It is a stark reminder of the propensity of this desolate island, with its jagged lava fields and steaming fissures, to shudder or explode.

The keeper of the samples is Kári Stefánsson, equally famous for his ability to blow up. One of the most controversial characters in human genetics, the Icelander cofounded deCODE Genetics in 1996 to use the island nation's meticulous genealogy records in his hunt for disease genes. Seven years on, the company has a handful of published results and its stock price is hovering around the bottom of the market.

Stefánsson's background mirrors the history of his volcano-strewn country. He can trace his family back to warrior and poet Egill Skallagrímsson, a first-generation Icelander born in AD 910. Perhaps this heritage imbued Stefánsson with a passion for literature: be it novels, poetry or biography, he always has a book on the go. "You cannot be a good scientist without reading 50–60 novels a year," he says.

Books aside, Stefánsson says his driving force is the desire to help diagnose and cure diseases. After studying medicine in Iceland's capital, Reykjavik, he joined the University of Chicago's neurology and neuropathology faculty, subsequently taking a position at Harvard University in Cambridge, Massachusetts.

It was in a coffee shop in nearby Boston that he and longtime colleague Jeffery Gulcher realized their destiny lay back in Iceland. The pair was already using Icelanders' genealogy to link distantly related people and find the genes they shared for multiple sclerosis risk. If they were to extend their hunt to other common conditions, Stefánsson realized, they needed to live in Iceland. Gulcher was less keen but eventually followed him. "The first thing you tell yourself is that it's an interesting idea but completely impractical," Gulcher now says. "But by and large [Stefánsson] ends up being right."

Stefánsson returned to Iceland to face fierce condemnation of his plans. Much of it centered on the Icelandic parliament's decision to allow deCODE to exclusively build and market a centralized health-care database containing patients' medical records, for which participants are presumed to have given consent. A second criticism has surrounded the commercial use of Icelanders' health information and genetics.

Stefánsson recalls this period as his most difficult. "I felt somewhat persecuted," he says. Outside of the health-care database, he says, blood samples—and hence genetic information—have always been donated with informed consent. In response to the second criticism, he says he could not otherwise have raised the capital, and that Iceland has benefited from the new jobs.

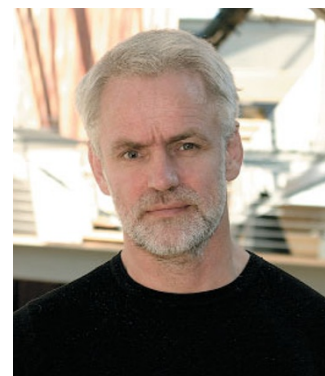
Despite his wounded feelings, Stefánsson shoulders some of the blame for eliciting criticism. One reason is his tendency to lash out or speak provocatively where others would hold their tongue. "He's used his personality to his advantage in creating attention," says friend, collaborator and fellow neurologist Allan Levey of Emory School of Medicine in Atlanta, Georgia. "We know he's earned himself a few enemies."

Some of Stefánsson's fiercest opponents have been those in the Icelandic lobby group Mannvernd. Although the health-care database is still passing security checks and has not yet been built, Mannvernd chairman and psychiatrist Peter Hauksson remains opposed to its construction. He also believes that doctors nowadays are not disclosing their financial interests, such as shares, in deCODE. "They have sold their soul," Hauksson says.

But at least on the surface, many Icelanders seem largely supportive of Stefánsson's plans. Around 100,000 of the nation's 285,000 citizens have given blood and consented to its use in deCODE's genetic studies, and polls show that the majority are in favor of the health-care database. "[Stefánsson] is a very good salesman," concedes Tomas Zoega of National University Hospital in Reykjavik and ex-chair of the Icelandic Medical Association's ethics committee. "He's a colorful personality in Iceland."

While the controversy rumbles on, Stefánsson and his team have been getting on with some science. In the absence of the notorious health-care database, the company has built up the country's genealogy,

"Somehow we became the main focus of people who believed that the study of human genetics is dangerous. I [should] probably carry some of the blame."



ogy, other medical records and genetic profiles into three linked databases. When studying a particular disease, collaborating doctors hand their patients' medical information to deCODE, where it is then encrypted and fed into the databases. From this, the researchers can identify those individuals who are even remotely related and ask doctors to approach them for blood samples for genetic analysis. Participants get a deCODE T-shirt.

A personal highlight of his work, Stefánsson says, was the discovery of a gene, dubbed neuregulin-1, implicated in schizophrenia—a condition that afflicts his own brother. "It was a bit of a poetic moment," he says. But though the deCODE team claims to have identified genes linked to conditions from hypertension to aging, the scientific community is yet to be convinced. One key test will be whether the associations between gene and disease hold up in other populations, explains geneticist Pui-Yan Kwok of the University of California, San Francisco. "We're waiting to see whether it actually works," he says.

Stefánsson clearly has no such doubts: he says he hopes to convert the disease genes discoveries into "at least ten" real drugs. By founding deCODE, Stefánsson may have chosen a rocky road on a rocky island in the North Atlantic but, he says, "I wouldn't want to be anywhere else in the world."

*Helen Pearson, Reykjavik*