Genome Study Predicts DNA of the Whole of Iceland

Large genome databases are starting to reveal critical health information—even about people who have not contributed their DNA.

By Antonio Regalado on March 25, 2015

Maps show how common certain risk-causing DNA mutations are around Iceland.

The CEO of an Icelandic gene-hunting company says he is able to identify everyone from that country who has a deadly cancer risk, but has been unable to warn people of the danger because of ethics rules governing DNA research.
The company, DeCode Genetics, based in Reykjavík, says it has collected full DNA sequences on 10,000 individuals. And because people on the island are closely related, DeCode says it can now also extrapolate to accurately guess the DNA makeup of nearly all other 320,000 citizens of that country, including those who never participated in its studies.

That’s raising complex medical and ethical issues about whether DeCode, which is owned by the U.S. biotechnology company Amgen, will be able to inform members of the public if they are at risk for fatal diseases.

Kári Stefánsson, the doctor who is founder and CEO of DeCode, says he is worried about mutations in a gene called BRCA2 that convey a sharply increased risk of breast and ovarian cancers. DeCode’s data can now identify about 2,000 people with the gene mutation across Iceland’s population, and Stefánsson said that the company has been in negotiations with health authorities about whether to alert them.

“We could save these people from dying prematurely, but we are not, because we as a society haven’t agreed on that,” says Stefánsson. “I personally think that not saving people with these mutations is a crime. This is an enormous risk to a large number of people.”

The Icelandic Ministry of Welfare said a special committee had been formed to regulate such “incidental” findings and would propose regulations by the end of the year.

The technique used by DeCode to predict people’s genes offers clues to the future of so-called precision medicine in other countries, including the U.S., where this year President Barack Obama called for researchers to assemble a giant database of one million people (see “U.S to Develop DNA Study of One Million People”). A large enough U.S. database could also be used to infer genes of people whether or not they had joined it, says Stefánsson, and could raise similar questions about whether and how to report health hazards to the public.

“This technique can be applied to any population,” says Myles Axton, chief editor of Nature Genetics, the journal in which DeCode today presented some of its findings. He said the tiny island’s detailed genealogical records are why “it was achieved first in Iceland.”

Various legal and ethical obstacles currently prevent DeCode from warning people who are at risk. Volunteers who signed up for DeCode’s studies were promised anonymity, and also that they wouldn’t learn of research findings. Bioethicists recognize that people have a right “not to know” of genetic hazards, which means they can’t simply be told.
“The rule is that you can only use and expose genetic data if you have the permission from the individual in question,” says Gísli Pálsson, an anthropologist at the University of Iceland. “But this is beyond informed consent. People are not even in the studies, they haven’t submitted any consent or even a sample, yet the company claims to have knowledge about these people and that there is a health risk.”

Pálsson says traditional notions of medical ethics are now in open conflict with the aims and capabilities of precision medicine. He believes such standards will need to be adjusted in fundamental ways in the future, so that more weight is given to public health benefits over individual privacy rights.

The life expectancy of women with the BRAC2 mutation is 12 years less than for women without it because 86 percent of those who have it will develop cancer. Men are also affected because the mutation raises the chance of prostate cancer. Stefánsson says many of those deaths could be avoided by preventive surgery, like a mastectomy.

“We could in Iceland, at the push of a button, find all women with a mutation in the BRCA2 gene,” says Stefánsson. “It is one tiny little example of what you can do. You can use this in preventive medicine like never before.”

DeCode’s data might also be able to predict who in the population is at elevated relative risk for Alzheimer’s disease or who has an undiagnosed learning disability.

DeCode was started in 1996 with the idea of linking DNA research to Iceland’s national health system (see “Population Inc.”). The country’s situation is unique because of its carefully kept genealogical records, which go back to the Ninth Century, when the island was settled. That also means most Icelanders are at least distant cousins.

DeCode has generated rough gene maps, called genotypes, on about 150,000 Icelanders. More recently, advances in DNA sequencing technology have allowed it to obtain complete genome sequences of about 10,000 people, Stefánsson says, or about one in 30 Icelanders. Results from the first 2,636 full genomes were reported by the company today in *Nature Genetics*.

Combined with genealogical tables, these data are what allow DeCode to “impute” the genomes of nearly everyone born of Icelandic parents. That is because once the full genome of some people in a family tree is known, the genes of the others can be inferred.

Sean Harper, head of R&D at Amgen, calls DeCode’s ability to guess people’s DNA a “conundrum.” He says it is not an unfamiliar problem to geneticists, however, since routine DNA tests of one person often reveal information about close relatives. But it has never before occurred at the level of an entire nation.
“It’s a gray area from a bioethics perspective, but we would be inclined to provide the data or at least a notice,” says Harper. He says Amgen, which uses gene information from DeCode to guide its drug research, had no plans to charge anyone for the risk information it has developed. “It would not be appropriate [to] try to make it a commercial process,” he says.

The U.S. lacks a similar national database, although some private companies, like 23andMe and Ancestry.com, have generated rough gene maps of several million people altogether. The National Institutes of Health is planning to spend millions in the coming years on accumulating full genome data on tens of thousands of people.

That means the entire world will soon confront the same types of ethical dilemmas that Iceland now faces, says Pálsson. “Do you have the right to fiddle with people’s lives on a massive scale? You can tell your neighbor, ‘You are smoking too much.’ But it’s another thing to approach 1,000 people and say, ‘You have the BRCA2 mutation,’ ” he says.

Credit: Infographic courtesy of deCODE Genetics; Headshot courtesy of deCODE Genetics | Chris Lund

Tagged: Biomedicine, genetics, human genome, genomics, Amgen

Reprints and Permissions | Send feedback to the editor