Gene predictions tell an ever-changing story

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by Peter Aldhous

THE DNA you are born with stays with you for life, but health predictions based on it can alter dramatically. That's the message from an analysis conducted for New Scientist showing how new discoveries in genetics change the assessments by personal genomics firms of an individual's health risks.

Shifting predictions could undermine people's faith in the value of personal genetic information, warns Cecile Janssens, an epidemiologist at Erasmus University Medical Center in Rotterdam, the Netherlands, who led the analysis. This in turn might discourage them from acting on health advice based on such data.

This warning chimes with previous suggestions from some doctors and geneticists that commercial genome scanning services were launched too soon. But the firms offering such scans insist that people have a right to learn about aspects of their genetic make-up that might affect their health, even if the information is incomplete. "Medicine does not wait to discover all risk factors before implementing the ones that it does know," says Jeff Gulcher, chief scientific officer with Decode Genetics of Reykjavik, Iceland, which offers a personal genomics service called deCODEme.

The firms scan customers' genes for up to 1 million single-letter variations in the genetic code known as single nucleotide polymorphisms, or SNPs. As studies link more of these SNPs to the likelihood of developing particular diseases, this information can be incorporated into customers' risk predictions and their personal online accounts can then be updated accordingly.

To determine the extent to which these updates change the risk predictions communicated to customers, New Scientist asked Janssens's team to examine Decode's predictions for type 2 diabetes, which around 25 per cent of Europeans succumb to over their lifetime.

People's reactions to changing predictions are an important aspect of how genome scans are used

When the deCODEme scan launched in November 2007, customers of European ancestry were given a type 2 diabetes risk prediction based on eight SNPs. Since then, there have been two updates, and predictions are now calculated from 15 SNPs.

Using data from Decode on the frequency of the SNPs among Europeans, Janssens's colleague Raluca Mihaescu generated 1000 simulated populations of people with different combinations of SNPs. For each population, she used the risks associated with each SNP to calculate how the predictions would have changed with the updates. After the first update, more than 11 per cent of people went from being told they were at above-average risk to below-average or vice versa; after the second update more than 10 per cent were similarly reclassified (see chart).
Customers of another personal genomics firm, Navigenics of Foster City, California, may have had a similar experience. The company launched its service in April 2008 with a type 2 diabetes prediction based on 11 SNPs, and added seven more in May 2009. For those who have bought scans from 23andMe of Mountain View, California, changes are still to come: the firm has not yet updated the nine SNPs it uses for type 2 diabetes.

Faced with shifting predictions of genetic risk, people may lose the motivation to change their diet and lifestyles in response, says Janssens. “They will say: if it may change over time without me doing anything, then why should I bother?”

Gulcher interprets the results differently. Those with very high risks, who have the biggest need to adopt a healthier lifestyle, are unlikely to see their results dip to below average as they are updated, he points out. His own deCODEme scan provides an extreme example of this. He has been dealt an exceptionally bad genetic hand for type 2 diabetes, having SNPs that make him 3.78 times as likely as a typical European to develop the disease. While this number has changed with the updates - the initial relative risk was put at 3.28 - the message was always that he needs to lose weight to reduce his likelihood of becoming diabetic. "Now I meet with a fitness trainer three times a week," he says.

In Mihaescu's simulations, all the people whose predicted risk shifted from above to below average started with a relative risk about 25 per cent above average, or less. While a risk elevated by this magnitude is hardly worth worrying about, it's not yet clear how a typical customer would perceive this information, or react when it changes. "People are likely to be confused," says Michael Christman, president of the Coriell Institute for Medical Research in Camden, New Jersey, which is running a study to test the clinical value of genome scans.

Researchers are starting to recognise that people's reactions to changing predictions are an important aspect of how genome scans are used. "You bring up a really important topic," says Eric Topol, director of the Scripps Translational Science Institute in La Jolla, California, who has begun a study to investigate how people use genome scans.

For more on the Dutch researchers' methods and related analyses, see their new paper in Genetics in Medicine: DOI: 10.1097/GIM.0b013e3181b13a4f, in press.