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Genomics is mired in misunderstanding

The cost of genome sequencing has fallen drastically, says **George Church**, *so why are so few people opting to have their genetic secrets revealed?*

Readers of *Nature*, we can assume, are bright and insatiably curious. So why have so few obtained and interpreted their own genome sequence? The answer, I suspect, is that we are failing to communicate genomic progress to the public.

For 7 years I led one of the teams registered to compete for the US$10-million Archon Genomics X Prize, and I was naturally disappointed by the abrupt cancellation of the competition in August. However, the confusion surrounding the X Prize debacle does at least highlight several problems and misunderstandings in genomics.

The first is that genomics is seen as expensive. In fact, sequencing costs have plummeted — from $3 billion for the first human genome in 2006 down to $1,000 wholesale cost today. That's not much more than the cost of a decent laptop, and much less than a car. However, people are reluctant to pay to have their genome sequenced — many feel that it should be provided for free by insurance schemes or the government. But the cost of sequencing can easily be recovered over a lifetime through the avoidance of unnecessary diagnostics, therapeutics and time spent in waiting rooms and hospitals.

Perhaps too many think that genomics is inaccurate. When it announced the cancellation, the X Prize Foundation claimed that "no company is sequencing whole genomes to the accuracy the contest required". Aside from the pre-judgemental weirdness, is this statement true? Haplotype phasing quality — a measure of accuracy — has improved from 350 kilobases in 2007 to 2,463 kilobases in 2013, and point errors have improved from 1 in 100,000 to 1 in 10 million — both well beyond the X Prize goals. Genetic searches for tandem repeats are now used in DNA fingerprinting.

Are the results uninterpretable? Even if we place the As, Cs, Gs and Ts in the right order, how does this help? Genome-wide information studies (GWAS) and studies of twins can give the impression that predicting traits from genomic sequence is a haphazard science. But since 1991 the number of highly predictive gene tests has risen from two to 3,000. Even 'complex' traits include components that can be identified and applied clinically to individuals who are not classed to be directly at risk. For example, height and diabetes GWAS have shown that a vast number of genes have small effects, but a few rare variants have large effects by altering levels of growth hormone for height and insulin for diabetes. These hormones are effective therapies even for individuals who are not mutant in them. Too often the messy results of GWAS and twin studies are down to poor selection of subjects and neglect of confounding environmental factors.

Even if they are interpretable, are the results useful? Yes! Even if there is no cure for the genetic conditions identified, there are effective preconception and prenatal options that can have a huge positive impact on the family. For example, Ashkenazi communities already use genetic screening to make lists of suitable marital partners early in life to avoid their offspring developing painful Tay–Sachs disease and dozens of similarly devastating diseases (which are not restricted to their community, by the way). Although we are tempted to restrict genomics to those with ethnic or family risks, the fact is that we are all at risk. Even the possibility of finding markers for one treatable disease (such as a cancer or cardiomyopathy) should be a sufficient reason to check one's genome.

Perhaps most provocatively, some critics assert that genomics could be harmful. The US Genetic Information Nondiscrimination Act (GINA) prevents genetics-based discrimination in health insurance and employment; however, there is not a GINA in every country, and it doesn't cover the military, life insurance or person-to-person discrimination. But the question is: do the overall benefits of genomics exceed the risks? Do the benefits of driving trump the one-and-a-quarter million traffic-related deaths per year?

A growing number of bioethicists and researchers are worried that typical consenting practices do not inform patients of the likelihood of data escape and re-identification. Certainly, conventional consents served to protect the researchers, not the volunteers. However, the huge numbers of volunteers who are willing to share their genetic data make this a moot point. Why insist on recruiting those — and setting policy around those — who would be upset if their data escapes?

DO THE OVERALL BENEFITS OF GENOMICS EXCEED THE RISKS?

In spite of, or because of, great progress in genomics, some people practise genetic modesty and do not wish to know what they can glean from their genetic details. Others will reject the opportunity, say, to reveal the genetic problems in store for loved ones such as children because they fear the social stigma that this could bring.

It is important for those of us at the sharp end of work on genomics to respect such views and not to judge those who hold them, but what about everybody else? We are not providing adequate and equal education about the risks and benefits of the genomic choices that are already available.

We already share our (very revealing) faces, voices and opinions. As we share more of our genetics, and as we develop genomic progress into precision medicine, researchers and the public alike need frank assessments of all these tests and treatments. We need the X Prize more than ever. ■

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