Consumer genomics

Taking your genes in hand

Personal genetic testing is advancing rapidly.

But beware of overselling

GENETIC testing promises a lot. In particular, it promises to tell people things ranging from their risks of developing ailments as diverse as heart disease, cancer and autism to how much coffee they can safely drink. It also promises a lucrative market for those doing the testing. Single-gene tests, such as those for particular forms of genes that predispose people to breast cancer, have been available for a while. This year, however, has seen the arrival of commercial versions of techniques that can sample a person's entire genetic make-up, and do so in a way that will enable him to benefit from future discoveries as well as existing knowledge.

In many cases, knowing the risk will also allow (and might, indeed, encourage) someone to modify his behaviour to avoid a disease he is at risk of—or, failing that, to mitigate its consequences. Nevertheless, concerns are being raised about the accuracy of some tests now on the market, and also their usefulness when the results are supplied direct to consumers, rather than with professional medical advice.

Last year America's Government Accountability Office said that genetic tests it had bought from four websites misled consumers into thinking they were at

risk of ailments such as heart disease, osteoporosis and type 2 (late onset) diabetes. In some cases, firms tricked consumers into buying “personalised supplements” that were actually no better than ordinary vitamins, but cost $1,200 a year. More recently, on December 4th, the British government's Human Genetics Commission published a review calling for greater regulation of genetic tests. One member of the commission recently went so far as to brand them a “waste of money”.

Testing times

Fraudsters can, of course, be found in any industry. But another part of the problem has been the science itself. Eric Brunner, an epidemiologist at University College, London, points out that he and his fellow researchers have struggled for years to try to understand the genetic basis of common diseases. The field is plagued by small, weak studies that are hard to turn into statistically robust conclusions. As a consequence, most findings of associations between diseases and particular genes (which often get reported widely in the media when they are announced) do not stand up to later scientific scrutiny. Yet the pace of commercialisation means that companies have often started selling tests based on the earlier studies by the time their results are discredited.

Paul Pharoah, an oncologist at Cambridge University and a critic of some gene-testing firms, says that in the past tests for a gene called SOD2 have been available, with companies claiming it was associated with an increased risk of breast cancer. However, Dr Pharoah and his colleagues recently published the results of a large study which showed that SOD2 is not associated with breast cancer after all.

With luck, this sort of thing will become rarer as scientists gather more data. However, some people worry that even those tests that do what they say on the packet may not actually give the consumer useful information. A possible example of this is a gene called TCF7, which is the subject of a test marketed by deCODE, an Icelandic firm. One form of the gene, TCF7L2, is strongly linked to type 2 diabetes. Having two copies of TCF7L2 (one from each parent) doubles your risk of getting diabetes—that much is well established. But some researchers reckon that if you do not have any of the other risk factors for diabetes, your chance of getting the disease will be so low in the first place that this doubling is not worth knowing about.

The processes that lead to most diseases are not, however, the result of a

single genetic failure. Instead, they involve hundreds if not thousands of genes interacting with one another. In the past geneticists have concentrated on genes that have large individual effects when they go wrong, because such effects are easy to spot. But particular combinations of genes that are not individually significant may also be important.

This raises the question of how many genes a test needs to look at to yield a meaningful estimate of risk. Though the answer is not yet clear, Dr Pharoah reckons it is likely to be more than just two or three. Tests that look at only a handful of genes, he thinks, are simply not useful.

The answer to that, of course, is more information. And it is here that the new generation of genome-wide tests comes in. These tests (which are being offered by deCODE and also by 23andMe, a Californian company) analyse the pattern of hundreds of thousands of bits of DNA known as single-nucleotide polymorphisms (SNPs, often pronounced “snips”). A SNP is a point on a chromosome where DNA routinely varies from one person to another. Many SNPs are associated with disease-causing forms of genes, and more associations are being discovered every month. Indeed, this year has seen a bumper harvest of strong, well-replicated associations between SNPs and diseases such as cancer and diabetes.

Analysing SNPs is not the same as analysing a full genetic sequence. For that to happen routinely, the technology will have to improve a lot (see article). However, deCODE and 23andMe are offering individuals a far broader look at their genes than has been possible before—and, in the case of deCODE, are backing their opinions with original research done by the firm, rather than merely drawing on literature published by others.

Yours, for a SNP

Both firms take pains to point out that what they are offering is an “information service”, not a “test”, and certainly nothing that is intended to diagnose a medical condition. And with his firm's existing test for TCF7L2, Kari Stefansson, deCODE's boss, seems to agree that testing for this gene should be prescribed “in most instances” by a physician. However, he concedes that the wide-ranging SNP test will also tell customers how many copies of TCF7L2 they have, whether they have been through a doctor or not.

Whatever the disclaimers say (and one purpose they have is to help firms to avoid regulation) people are clearly going to be getting medical information

from such tests. For example, overweight customers who find they have two copies of TCF7L2 really do have something to think about.

In time, of course, the regulators will catch up. Indeed, Dr Stefansson hopes that deCODE's products will eventually become approved diagnostic techniques, rather than mere information services. But for the moment, this is still an area where buyer should definitely beware.

And that is probably right. The technology of testing is improving fast and regulation risks slowing progress. Moreover, physicians' calls for scrutiny should themselves be scrutinised, because genetic testing inevitably transfers power from doctors to laymen.

That transfer of power brings responsibility, of course—the responsibility of consumers, aided by the gene-testing companies themselves, to interpret their new knowledge sensibly. If they do not, doctors' surgeries may be flooded with what have come to be known as the worried well, and regulation is sure to follow. If people do take responsibility, however, a healthier life awaits them.

Genetic sequencing

DNA, direct

The race for the $1,000 genome is on

JUST as computers used to occupy entire rooms, and were able to make only a few thousand computations a second, so the first DNA-sequencing machines were able to read only about 5,000 genetic “letters” a day. Technology changes. Now it is possible for a single machine to sequence a human genome of about 3 billion letters in two months. At this rate, those 5,000 letters would take less than ten seconds.

So where next? If the X Prize Foundation has its way, it will soon be possible to sequence a genome in hours. To make that happen, the foundation, perhaps better known for its spaceflight prize, is offering the Archon genomics prize. This will be worth $10m to the first team able to sequence 100 human genomes accurately in ten days or less. (The prize is sponsored by Stewart Blusson, a philanthropist who is president of Archon Minerals, a mining company based in Vancouver.)

The Archon prize has already tempted six teams to sign up. The latest, led by George Church, a chemist at Harvard Medical School in Boston, joined in this week. One of the other competitors is 454 Life Sciences Corporation, based in Branford, Connecticut. Earlier this year 454 sequenced the entire genome of James Watson (one of the scientists who worked out the structure of DNA molecules) in two months. It is improving this technology to try to win the prize.

454's technique involves attaching single-stranded fragments of DNA to small plastic balls placed in wells—over 1.5m of them—in a set of plates. Each well is then washed with a series of solutions that contain one of the four different genetic letters (known as nucleotides and denoted by the initials A, C, G and T).

The reason DNA is able to replicate, and thus pass genetic information down the generations, is that the nucleotides like to pair up in a consistent way—A with T and C with G. This is aided by an enzyme called polymerase that runs along a single DNA strand adding the correct nucleotides in order, to build up another strand. And that process, in turn, can be made visible using a second enzyme, called luciferase. This enzyme produces a flash of light in response to

a chemical change that happens as a nucleotide is added. Recording which wells flash in response to which nucleotides means the sequence of the fragment in each well can be built up one base at a time. Add all the fragments together and you have the whole.

Other people developing sequencing technology are trying more direct ways to read the nucleotides. A team at the University of California, San Diego, which is not, at present, one of the X prize runners, does it by forcing DNA through tiny pores and logging each nucleotide as it passes. Meanwhile Reveo, a firm based in Hawthorne, New York that is going for the prize, runs microscopic knives along the surfaces of DNA molecules. The blades of the knives in question are only a few atoms across, and are thus sensitive to the ins and outs of any molecule they are touching. Since each nucleotide has a different shape, the result can be used to decode their order.

Whoever wins the race, Marc Hodosh, science director for the Archon X Prize, says their level of technology is likely to equate to a cost of $10,000 a genome. Although that is still some way short of the $1,000 genome that is reckoned to be the point at which a retail business becomes possible, Dr Hodosh thinks the process of commercialising the winner will, itself, bring about the necessary 90% fall in cost. That means the curious will be able to treat themselves to a complete scan without breaking the bank. Whether they will like the result is a different question.

A mummified dinosaur

Dinosaur bones are fairly rare fossils, but compared with what is shown in this picture, they are as common as muck. It is a piece of dinosaur skin (or, rather, its petrified transmutation). It belongs to a fossil hadrosaur (a type of herbivorous dinosaur) that lived 67m years ago in what is now Hell Creek, North Dakota. The first bones of the animal were discovered in 1999 by Tyler Lyson, now a graduate student at Yale, but then a schoolboy. A full-scale expedition to recover it has, however, only recently been mounted. The fossil's state of preservation is remarkable. Besides skin, various ligaments and tendons have been found, and the specimen is now undergoing examination in the industrial equivalent of a hospital body scanner, at a Boeing workshop in California, to see if any internal organs have been petrified, too.