



# A life decoded

We're on the brink of a DNA revolution – where your genetic code could be read to gain an insight into how your life will pan out. **Andy Ridgway** took a genetic test to take a glimpse at his future...

IN THE 72ND MINUTE OF A FOOTBALL international between Cameroon and Colombia, tragedy strikes. One of Cameroon's star players – former Manchester City midfielder Marc-Vivien Foé – suddenly collapses in the centre circle at the Stade de Gerland in Lyons, France. No other players are near him. After attempts to resuscitate him on the pitch, he's stretchered off and medics fight for 45 minutes to restart his heart, but to no avail. At 28, and at the peak of his career and physical fitness, Foé is pronounced dead at the stadium's medical centre.

Foé's first postmortem was inconclusive, but the second revealed he had suffered from a heart condition

called Hypertrophic cardiomyopathy – a condition he could well have inherited. Foé's death in the 2003 FIFA Confederations Cup is an extreme example, but it does illustrate a point: we're all at the mercy of our DNA – the code that makes us who we are. Even today, that code is something we have no control over – it's simply the stack of cards we're dealt.

The trouble is we've never been able to take a look at our genetic hand of cards, so there's been no way of knowing whether we've been lucky or whether we're playing on borrowed time. But now that could be changing. A growing number of companies are springing up which say they can ➔



## “In spite of the problems inherent in looking for genetic links, there’s been a tidal wave of announcements that a given condition’s genetic source has been unmasked”

➔ give you a glimpse of your genetic make-up – and insight into which particular illnesses you’re susceptible to. Their claims are, however, somewhat controversial.

As I sit in a smart Harley Street doctor’s surgery, I’m hoping my cards are about to be laid out in front of me. The person sat on the other side of the desk is Dr Paul Jenkins. Smartly dressed and well spoken, he’s a co-founder of Genetic Health, a predictive genetics company. In spite of the rather grand surroundings (and a big dose of bravado), sitting in this room waiting to hear what my genes have in store for me is not an entirely comfortable experience.

“I’ve been through this,” says Dr Jenkins. “It’s personal. It’s *really*

personal. Suddenly when you look at your genetic report, you think, that’s you: it’s your personal barcode and there’s nothing you can do about it.”

My journey of genetic enlightenment started a month before my Harley Street appointment, when I took a sample of cells from the inside of my mouth. A simple process with the rather unattractive-sounding name ‘buccal smear’, it involved rubbing a long cotton bud inside my cheek and sticking it in the post. It was then just a case of waiting: a wait that an increasing number of people are experiencing thanks to a predictive genetics industry that’s growing at an exponential rate. Some companies – such as 23andMe, which is partially financed by Google – offer the test and results over the net. In my case, I was sent a written report on over 45

pieces of my DNA as well as having the consultation with Dr Jenkins – a service which usually costs £900.

The predictive genetics industry has sprouted up out of nowhere in the last two to three years, thanks to the completion of the Human Genome Project in 2003, and then the HapMap project in 2007. The genome project identified the 25,000 genes that make up the human genetic code; HapMap took things one step further.

Dr Richard Gibbs at the Baylor College of Medicine in Texas was involved with both projects. “The Human Genome Project was the foundation,” he says. “It gave us the genetic sequence in the vast majority of people. HapMap shows us how that sequence is different in different people and enabled us to look at how those differences can lead to diseases.”

### How it works

My sample of cells was sent to a private lab run by Genetic Health at Northwick Park Hospital in northwest London where, after being processed (see ‘Test sequence’, below), it was placed in a gadget the size of a large oven. This machine looks for the all-important single nucleotide polymorphisms (SNPs) – pronounced ‘snips’ – in my DNA. Having a particular SNP may indicate whether or not I’ll be struck down by a disease.

Everyone knows that DNA contains their genetic ‘code’. But that code is actually marked out by molecules called ‘bases’ which appear along the DNA strands. There are just four kinds

## TEST SEQUENCE



As instructed, I took a sample of cells from the inside of my mouth using a long cotton wool bud, rubbing the swab on the inside of my cheek 15-20 times. I repeated the process another five times to make sure Genetic Health had enough cells to sample, then stuck them in the post.



At the lab, chemicals broke down the cells to release the DNA. This was placed in a testing tray along with an enzyme that helped to replicate the genetic material – making it easier to identify the SNPs. Different markers were added to the wells in the tray – each testing for a different SNP.



## ASK THE EXPERT: RICHARD GIBBS

Director of the Human Genome Sequencing Center at Baylor College of Medicine, Texas

of base, and a group of them which codes for a specific instruction is what we know as a gene. On average, one in every 500 to 1000 bases differs from those found in the majority of people. When they occur in at least one per cent of the population, these variations are known as an SNP. Some of these variations don't have any influence on your health, but others can hike your chances of getting a condition, such as cancer.

Research teams around the world are now looking for links between SNPs and diseases, hoping to find the all important 'gene for...'. It's not a simple task. For a start, many *different* genes may influence your susceptibility to any one given condition.

### Is this an exciting phase in genetic testing's history?

Absolutely. More and more links to different diseases are being established. But it's important to remember that the quality of those links varies. Some genes can significantly increase your chances of getting a disease, while others only have a small influence. It's a lot to get your head around if you're not familiar with genetics, so genetic tests should not just be done in the corner drug store.

### How accurately can today's tests predict diseases?

Firstly it depends on the accuracy of the data and we've

pushed that to high levels.

You've then got to understand what that data means.

### What do you think will be the next big breakthroughs?

Genetic analysis will have a big impact on our knowledge of behaviour disorders in the next few years. I'm sure there will be bipolar genes, schizophrenia genes and autism genes.

### Was genetic testing always the dream when you were involved in the Human Genome Project and HapMap?

We're at a crossroads. We had a dream of a high road where genetic tests would

be given through the medical care system and provide you with good quality, accurate information where predictions, diagnosis and treatment are guided by your genetic make-up. The low end is you spit in a cup and get data that doesn't mean much, with a growing number of companies offering genetic testing purely to sell dietary supplements. Who knows where it's going to go.

### What's your organisation looking at currently?

Genetic links with schizophrenia, epilepsy and cancer. We're not out of the woods yet, but we've found a lot of trees.



Yet in spite of the problems inherent in looking for genetic links, there's been a tidal wave of announcements proclaiming that a given condition's genetic source has been unmasked. The difficulty for any company that wants to offer predictive tests is sorting the scientific wheat from the chaff, the true genetic links with disease from the red herrings, so it can decide which SNPs to test for. It's here that much of the controversy lies.

"Just because there seems to be a link in one group in one study, it doesn't mean there's necessarily a true association," says Dr Ron Zimmern, Executive Director of the PHG Foundation, a charity which has carried out research into genetic tests. "An association needs to be replicated in different studies involving different

populations before it can be deemed to be a true association."

Dr Jenkins at Genetic Health says a great deal of thought goes into the process of selecting which SNPs to test for. "We wouldn't use a single study, but it wouldn't necessarily have to be a full-scale meta-analysis [a study that pools lots of research]. Not all of the studies we have looked at in the past



Genetic Health are based in London's famous Harley Street

STEP 3



The tray was then placed in the genetic sequencer. This device contains a light source which encourages markers to glow. Crucially, a marker will only glow if it has been able to attach to the SNP it tests for. If the SNP isn't present, the marker doesn't glow.

STEP 4



The genetic sequencer fed information to a computer, plotting a series of graphs revealing which markers glowed and which did not. Then came the hard part. An expert had to interpret this information and predict how my SNPs could influence my health in the future.

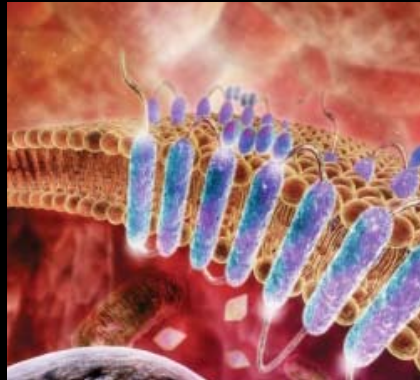
# Predictive genetics

## YOUR GENES AND YOUR LIFE

It's not just about knowing how likely you are to get cancer

### YOUR HEALTH

As well as indicating whether you'll suffer from certain conditions, your genetic make-up might also influence how effective medicines will be. Your genetic code could mean not having a certain receptor on your cells, so a medicine can't bind to it and have an effect, or you could have an enzyme that breaks the drug down so slowly that it produces side-effects. In Europe, new patients prescribed HIV drug abacavir are tested for a gene called HLA-B\*5701, which has been linked with adverse reactions. In the US, the Federal Drug Administration also suggests genetic tests are carried out before patients are prescribed anti-cancer drug Purinethol or the blood clot-preventing warfarin. More tests are around the corner.



### YOUR WORK

If left unregulated, the potential impact of genetic testing on your chances of getting or keeping a job could be huge. An employer could find out exactly who they were getting, particularly if genetic links with personality traits are discovered, which is highly likely. The signs are already there – basketball player Eddy Curry, who has an irregular heartbeat, was asked by his club the Chicago Bulls to take a predictive genetic test for a heart condition. He refused and was traded to the New York Knicks, who made no such demand. In the US, legislation is currently on the table which would mean only patients and doctors would have access to the results of a genetic test. There is presently no such legislation in the UK.

### YOUR MONEY

Knowing what your genes hold in store would be gold dust to any company offering life insurance. If you've been landed with a 'risky' set of genes, life insurance could cost you an arm and a leg – or you might be branded uninsurable. In the UK, insurance companies have introduced a voluntary moratorium on using genetic data when assessing any form of medically-related insurance, whether it's life cover or medical protection. But, says Jonathan French of the Association of British Insurers: "If you have a genetic test and you don't carry the gene that means you're at greater risk of having say breast cancer, it will have an advantageous effect on your premiums." Again, some feel legislation will be needed.



### GENETIC SECURITY

Your genetic information is a valuable asset, and is likely to get even more valuable in the future. "As more genetic links are established, we may even start to predict people's behaviour," says Dr Paul Jenkins of Genetic Health. If you don't want any Tom, Dick or Big Pharma to be able to get their hands on your DNA profile – and use that information to their own ends – it will be vital to have control over who gets their hands on your DNA. Genetic Health label all samples with just a code number, so only a limited number of people know your identity, and once tested, the samples are destroyed and your records kept securely. Such security measures will become increasingly vital.



Brian Whitley, MD of Genetic Health

→ were based on thousands of people, but the ones coming out now are. There are small studies we would look at and say that's not enough evidence."

But even if a link is statistically established, says Dr Zimmern, the size of the effect an SNP has is also important. If the influence on the likelihood of getting a condition is minuscule, he says it should not be included in a predictive genetic analysis because it is much more likely to be drowned out by other factors, such as a person's lifestyle and the rest of their genetic make-up. "The additional risk varies enormously between genes," says Dr Jenkins. "That's why it's important to get a medical consultation with your results. Below a 25 per cent increase in risk, I don't think it would be relevant."

### Red alert

The first indication of the stack of cards I have been handed arrived in the form of a 50-page report from Genetic Health. In it were bars indicating the chances of my contracting a host of conditions, based on my genetic make-up. The bars range from green, indicating a low risk, to red, a high risk. There are bars for cardiovascular disease, thrombosis, osteoporosis, prostate cancer and others, but a quick heart-stopping scan of the results revealed no conditions in the red zone. However, the presence of certain SNPs had put me in the 'moderate risk' zone for a few things, Alzheimer's disease being among them. My report told

me that my increased risk of getting Alzheimer's later in life was down to a gene called apolipoprotein E (ApoE) which comes in three forms. Unfortunately I have one copy of the ApoE4 SNP, the one associated with an increased risk of Alzheimer's. But what does it mean? "It means you've got a one in four chance of getting Alzheimer's by your late 80s," says Dr Jenkins in my consultation. "The average probability is one in eight."

Other conditions, such as the risk of high blood pressure, were also in the moderate (orange) zone of the spectrum – so nothing to cause huge concern. But as there's nothing I can do about my DNA, what's the point in knowing? The answer is, what you *can* alter is how you live – what you eat, whether or not you smoke and how much exercise you do. The idea is that the predictive test may reveal aspects of your life you need to change, and whether you could do with another test such as a heart scan. Some companies

(though not Genetic Health) will even sell you nutritional supplements based on your results.

I'd approached the test feeling quite confident, as most of my close family is fairly long-lived. The only chink in my confidence – and my main source of concern in my consultation – was that finding any duff genes in my DNA could have had consequences for my two-year-old son, who will have inherited some of my SNPs. But thankfully, it seems I've been handed quite a good deck of cards. Had I not, the psychological consequences could have been huge.

#### Testing times to come

The sheer volume of research being carried out in this field will mean that genetic links will be found to more and more conditions – even mental illnesses such as schizophrenia and epilepsy. And it seems likely that predictive genetic tests will become more prevalent – perhaps even the



Swabs are stored at -80°C, and marked only with a code number

norm. If it helps to prevent early deaths, like that of Marc-Vivien Foé, that has to be a good thing. But there needs to be careful thought about the wider implications. Could a bad genetic hand bar you from certain jobs, or from getting life insurance? And what if commercial companies get hold of your genetic information?

Even Dr Jenkins, who is a vociferous proponent of genetic testing, is aware of the potential impact on society. "I think genetic testing is fascinating," he says, "and the science behind it is extremely strong. But there are enormous questions we need to discuss, as a society, about what to do with this knowledge."

**Andy Ridgway is news editor of Focus**

#### » FIND OUT MORE

[thepersonalgenome.com](http://thepersonalgenome.com)  
Blog on personal genomics by Jason Bobe at Harvard Medical School

<http://tinyurl.com/46pktc>  
House of Lords inquiry into genomic medicine

[www.hapmap.org](http://www.hapmap.org)  
HapMap website with details on SNPs

[www.hgsc.bcm.tmc.edu/](http://www.hgsc.bcm.tmc.edu/)  
Human Genome Sequencing Center at the Baylor College of Medicine, Texas

## GENETIC DISCRIMINATION

### How DNA profiling could affect your children's future prospects

In the 1997 film *Gattaca*, society is divided into a super-race of genetically-selected individuals known as 'valids', who land all the best jobs, and naturally-conceived 'invalids' who only have access to menial jobs, as they're assumed to be more susceptible to disease. But even if society doesn't start selecting genetically-elite embryos – which seems highly unlikely – there is real concern that children could be discriminated against because of their genetic make-up.

Earlier this year, the House of Lords started an inquiry into 'genomic medicine'. Research group GeneWatch UK wrote in, saying legislation is needed to prevent genetic discrimination. Yet Richard Gibbs at Baylor College of Medicine in Texas



says predictive genome testing will become widespread. "A handful of genetic tests are currently done at birth, but I think there will be a full spectrum in the future. It's not a matter of if, but when."

The range of known genetic links with diseases – and even our physical ability and psychological characteristics

– is likely to balloon over the next few years: an Australian company is already offering the first genetic test which could indicate whether you would make a good sprinter or not. As we learn more about the code that defines us, we'll have to work hard to ensure that our DNA doesn't spell out the course our life will take.