

For something once considered as fixed as a TV show telephone vote, fresh evidence reveals that gene activity can be altered by your lifestyle – and slick start-ups promise to exchange a swab of your saliva for bespoke health advice. Is this a genius upgrade in the quest for health and longevity, or are we spitting in the wind?

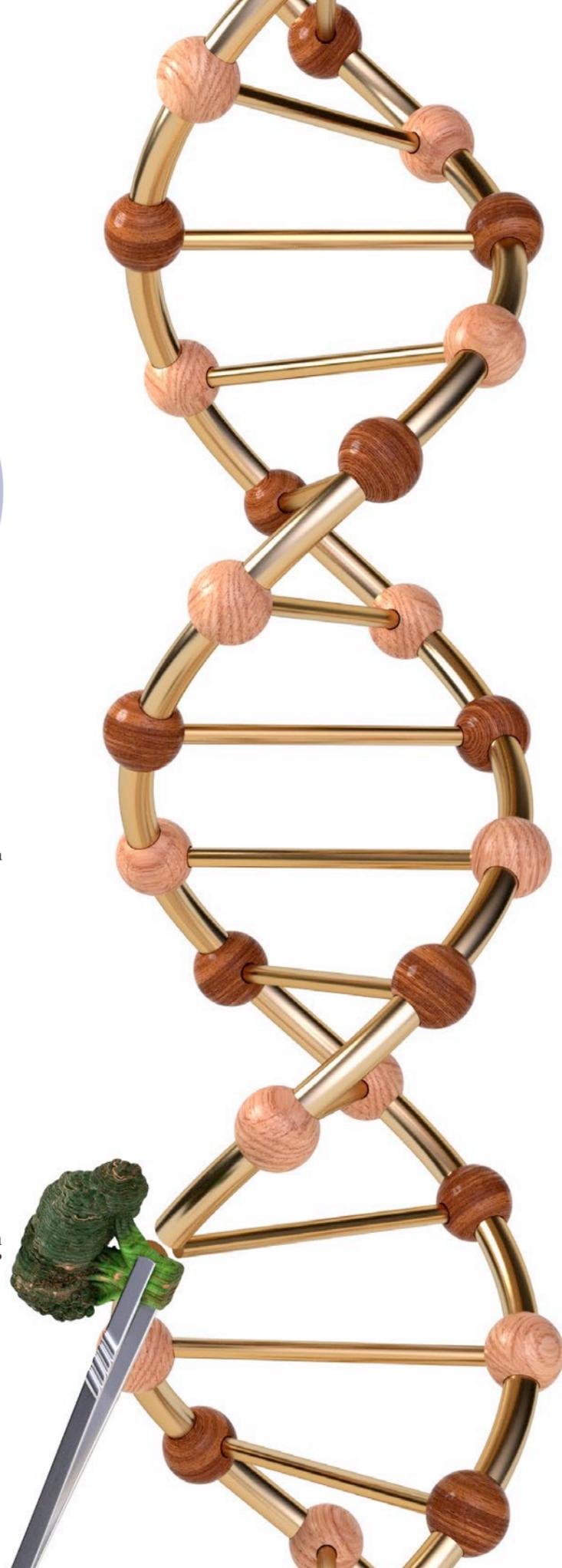
WORDS GEMMA ASKHAM





ould you happen to share a carriage with Julia and Tracey on the train from Hampshire to London – a trip they take together every four years for tests at St Thomas' Hospital – little about them would reveal that they're two of the most medically studied women in the world. It's only when you look past their different hair colours (brunette, blonde) and fashion choices (Breton stripes, florals), and double-take at the similarity in their smiles, uncanny chin dimples and shared button noses, that you spot their uniqueness – or lack of it. Julia and Tracey, both 52, are identical twins and, for health researchers like those at TwinsUK – the biggest twin register in the UK, linked with King's College London – they're a winning lottery ticket. But the twins' megabucks value isn't from their perfectly matched DNA sequence, it lies in their different lifestyles.

If only one twin were to develop a condition, such as Julia's anxiety or Tracey's type-2 diabetes, it shows that something could have changed one twin's genetic activity in a way that the other was immune to. This is epigenetics in action: 'epi' from the Greek meaning 'in addition to', plus genetics, your fixed DNA sequence. The hottest pursuit in labs right now is unravelling how influences like your postcode, workout habits and food shop can lead to chemical alterations that tinker with the way your genes work. Now, the quest is moving into the preventative healthcare market, via the launch of DNA and epigenetics testing kits. But can parting with your saliva, along with hundreds of pounds, tell you anything useful, or influence your day-to-day behaviour?



TRAIT EXPECTATIONS

If this sounds like the nature versus nurture debate from year 10 biology, it kind of is – with scientists now judging it a draw, agreeing that *both* play their part. 'Epigenetics is the study of changes in gene activity, which vary according to body tissue, stage of life and in response to your experiences and environment,' confirms Dr Jess Buxton, senior lecturer in medical genetics at Kingston University. While a complete set of genetic instructions (a genome) is written in every cell of your body, they don't all require the full set of instructions to fulfil their function. So, cells pick and choose on a need-to-use basis, like when you buy a new microwave and ignore the 11 manuals written in languages you don't understand.

Pollution, smoking, ageing, stress and weight are all thought to influence changes in your genes

The kind of genetics that's controlled by your cells, in line with their job descriptions, is pretty stable. As for those epigenetic changes spurred by your environment, they're more dynamic. They occur due to a process called DNA methylation. Not the title of a new Radiohead album, but the addition of a methyl – what we'll think of as a cellular highlighter pen – that flags up whether a specific gene's activity should be turned up or down. Pollution, smoking, ageing, stress and weight are all thought to influence this chemical change – and variations away from normal methylation over time have been linked with the development of cancer, autoimmune problems and neurological disorders, such as dementia and Alzheimer's. During the past 10 to 20 years, identifying exactly how DNA methylation varies in health and disease has been a busy area of research, according to Dr Buxton. 'We now know that methylation levels in the gene involved in regulating cell growth are different in smokers compared with non-smokers,' he

says. 'What's more, this difference is reversible – quit smoking and this epigenetic biomarker eventually begins to resemble that seen in non-smokers. There's a lot of interest in how this kind of information could be used to monitor changes in people's health and develop new ways of preventing and predicting disease.'

TESTING TIMES

It was with preventative medicine in mind that, in 2018, a biotech start-up called Chronomics, founded by three Cambridge University PhD researchers, launched a saliva test to measure DNA methylation in genetically curious consumers. Combining a sample of your finest froth with answers to one of the most detailed questionnaires you'll ever complete (orgasm frequency, anyone?), Chronomics uses complex algorithms and epigenetic data to build a picture of how you're looking internally. Log on to the glossy website and you'll find out your biological age – which, unlike the date on your birth certificate, is more a measure of how hard you've lived than how long you've lived – your cigarette smoke exposure (firsthand or otherwise), your metabolic state (a glimpse at your metabolism speed via your diet and exercise habits), plus, your cumulative alcohol intake (your long-term health hangover from booze). You'll also see how your scores compare with those of people of a similar age in your region, and get general tips (eat less processed food, do more yoga) to help you reverse the clock. 'The majority of diseases that affect us today

are things that creep up on you over years, such as heart disease, largely because of the lifestyle choices you make,' explains Chronomics CEO Tom Stubbs, who notes that the majority of customers – currently numbering in the low thousands – are aged between 35 and 55, have experienced the first hint of their own mortality via a health scare or ageing parents. Such data would no doubt prove useful to someone in need of a health-based kick up the arse; but it's arguably less so for those for whom healthy habits are part and parcel of their routine, as *WH* Editor-In-Chief Claire Sanderson discovered. 'I was looking to fine-tune my wellness routine – to find out what kind of training I'm best suited to or whether I'm particularly sensitive to carbs – but all I really got was confirmation that I lead a healthy lifestyle,' she explains. Aged 41, the news that her biological age was 34 was 'a lovely pat on the back', as was the news that she could live until 110 free from major diseases if she continued to follow her current healthy lifestyle. 'But I would expect to get results like this as I'm very aware of my own health – I barely drink, I don't smoke, I exercise loads. I imagine this test would be better suited to someone who hasn't lived a particularly healthy lifestyle and needs a bit of a shock to change their habits – and statistics tell us that there are a lot of people who could benefit from this kind of advice – but, for someone like me, I felt it lacked actionable advice.'

Epigenetics tests only look at *modifications* to DNA, rather than your actual full sequence – the latter

being the unchangeable genetic code inherited from your parents that's analysed in ancestry and genetic tests – so you only find out data that you can do something about. Other companies are cherry-picking the best bits of both worlds. When British firm Muhdo was founded in 2016, it specialised in providing nutrition-focused genetic information and eating plans to elite athletes. In 2019, it added epigenetic profiling to its one-off DNA test, and now offers tailored testing and dietary programmes to regular punters as well as sports stars. While Muhdo won't delve into disease diagnostics, it does offer detailed insights into the genes surrounding nutrition. Muhdo's director of nutrigenomics James Brown, who devised dietary plans for Formula 1 drivers before the loss of two cousins to cystic fibrosis spurred him to go back to university to study genetics, explains that the absorption of vitamin D alone involves three or four genes. 'We all have these genes, but I might absorb vitamin D from a food source at a rate of 80% and you might absorb it at a rate of 20%,' he explains. 'Once you know someone's rate – and that's where epigenetics comes in – you can improve it.' In this case, by taking a supplement and increasing intake of dark green leafy veg, which is rich in sulforaphane, a nutrient that improves absorption of vitamin D. Muhdo applies this methodology to every nutrient its tests analyse; it then provides tools – recipes, sleep modifications, workout plans



and supplements – to help you make relevant lifestyle changes. Mudho then recommends that users take a saliva-based epigenetics test every 12 months to monitor whether their biological age is really doing a J-Lo and looking younger every time you see it.

ALL IN THE MIND?

While your epigenetic age *may* decrease, your savings certainly will. An annual test with Chronomics costs £699 – for 30 quid more, you’ve got your hands on a brand new iPhone 11 – while Mudho’s DNA and epigenetics kit is £279.88 a year (£59.99, plus an 11-month subscription of £19.99). While experts

see what would happen when people were told they had a genetic trait that they actually didn’t (you wouldn’t want to play poker with this guy...). He found that telling participants they had reduced lung capacity actually knocked their athletic performance, suggesting a kind of placebo effect. This points to a whole other realm of interest for genetic and epigenetic data: not just the question of whether it can

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agree that the information around epigenetic age and smoke exposure is accurate, evidence that this will give your life a health upgrade doesn’t yet exist. Professor John Mathers, director of the Human Nutrition Research Centre at Newcastle University, recently did a peer review of nutritional intervention studies to assess the effectiveness of personalised nutrition advice. Of three studies in which people were given genetics information, only one recorded a positive change in health behaviour – a reduction in salt intake – while levels of physical activity and intakes of fat and sugar weren’t improved. Meanwhile, at Stanford University’s psychology department, researcher Brad Turnwald wanted to

impact habits, but around its ability to influence your mindset and emotions. ‘It’s important for people to understand the range of personal effects this information can have,’ warns Professor Mathers.

CALL OF NATURE

For those at the cutting edge of epigenetic research, the field is both thrilling and frustrating. Jonathan Mill, professor of epigenetics at the University of Exeter Medical School, believes some incredible investigation is currently underway, using epigenetics to track brain development, explore its link with cancer and create drugs that could rewrite epigenetic information, as opposed to your trickier-to-access genetic code. But then comes the, well, but.

‘Oh, at the same time, there’s huge, huge hype,’ Professor Mill says. ‘You can now get epigenetic yoga, epigenetic perfumes, epigenetic shampoo, epigenetic dentistry... Businesses feel that if they put a scientific-sounding name to something, then it’s instantly more marketable, but these are pseudoscience.’ Professor Mill is particularly sceptical of claims that epigenetic tests can reveal insights about the brain – say, to improve cognitive performance. ‘The epigenetic profile from a saliva sample looks very different to the epigenetic profile from a neuron because they’re different cell types,’ he adds. Consensus among the academics *WH* spoke to is that you yield the most relevant data by studying the specific cell type you’re interested in, and some go as far as to claim that epigenetic markers in saliva may actually have no relevance at all to what is going on in your brain, lower gut or muscles. ‘It might be

more believable if they asked you to mail off a bit of your brain,’ offers Professor Mill, before adding: ‘But obviously that’s not going to work.’

Nonetheless, there’s huge scope here for genetic interventions to transform healthcare. The NHS Genomic Medicine Service, which aims to be a world leader in gene-based diagnostic medicine, has extracted DNA from 70,000 patients; it’s even thought that we’re moving towards being DNA-sampled at birth in order to foster a more proactive rather than reactive approach to healthcare. Testing at birth could allow parents to find out from the get-go if their child faced heightened risks of certain diseases, and then get more tailored preventative treatment. This is also where twins-based research, like the regular studies on Julia and Tracey, come in handy. For now, epigenetics – like its name – comes ‘in addition to’ all this. ‘Epigenetics tests *are* interesting and fun,’ adds Professor Mill. ‘But the science is still not well enough understood to tell you anything useful. Sure, you can tell someone’s age and if they smoke, but you don’t need to pay lots of money to do that, do you?’ The idea of understanding your DNA and how you can control the factors that manipulate it is, undoubtedly, alluring – particularly if you’re sold the ability to turn back the years on your internal clock. But selling is what’s at stake here. Your saliva, your genetic data and £700 for a number on a screen that may or may not even be accurate. Does the maths – even at a molecular level – really add up? **WH**

TESTING TESTING

‘I WANTED AN HONEST ASSESSMENT OF HOW BAD THINGS WERE’

WH contributor Georgie Lane-Godfrey, 32, took a Chronomics test – here’s her verdict



Working in the *WH* office can be an eye-opener in terms of how unhealthy you are – my lowlight was eating a sharing-size packet of Dairy Milk Buttons for lunch during the time it took a colleague to go for a run – so I genuinely thought this test would tell me that my body was harbouring an inner biological hag. So I was astounded – and, let’s be honest, smug – when my biological age came back as 25. I’m not the fittest person and don’t always have the best diet, so I couldn’t help but wonder how much of this was based on my actual DNA and how much was based on an algorithm drawn from my answers to the lifestyle questionnaire. After all, I’d only given a small saliva sample, but I’d answered a laborious list of questions covering everything from my traffic, chemical and blue-light exposure to my income levels and experience of recent trauma. I have no doubt that the test would be a useful wake-up call for those who believe they’re healthy, but in reality lead less-than-healthy lifestyles; I have friends who have healthy BMIs but are chronically stressed and call themselves social smokers. But for someone like me, who doesn’t consciously lead a super-healthy lifestyle, it didn’t feel all that useful.

BREAK THE CODE

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