HUMAN NATURE

Justine Picardie voyages into the genetic fabric of her existence

'Escape Artist (In Levis)' (2008) by Sam Taylor-Johnson

If the global pandemic has taught us anything, it is to value the expertise of the brilliant scientists who have developed vaccines and treatments to counter the threat of the coronavirus. On a personal level, my own respect for the medical profession has also been strengthened for another reason. For in the past year, I have been privileged to participate in a pioneering genetic research project that has the potential to change all of our lives for the better. Certainly, the experience has made me realise how modern medicine is constantly pushing boundaries and moving onwards to new horizons.

I was offered the opportunity to join a pilot study of Whole Genome Sequencing by my GP, Dr Michael Sandberg, who is running a joint programme with Professor Ros Eeles, a leading geneticist at the Royal Marsden Hospital and the Institute of Cancer Research. Working alongside a specialist team, they are using a new process of genome sequencing that is infinitely more accurate than the DNA-testing kits sold online as indicators of ethnic background and ancestry. The aim of the project is to further the understanding of genetic testing, and the ways in which it can be used constructively to improve our health.

Dr Sandberg knew about my family history of cancer – my sister Ruth died of breast cancer at the age of 33; he was also aware of my father's Ashkenazi Jewish heritage (in his case, from Russia and Eastern Europe), which is linked to an increased risk of gene mutations associated with breast and ovarian cancers. Ruth died in 1997, and genetic testing was not widely available at the time, nor particularly precise. In 1994, researchers in the United States had identified a particular gene variation known as BRCA1, which caused an 85 per cent chance of developing breast cancer and a 44 per cent risk of ovarian cancer. The following year, another variation, BRCA2, was discovered, which was also found to be a risk factor for these cancers. But when Ruth was first diagnosed in London in 1996, genetic testing was not a possibility. Indeed, a project was only just beginning in New York that same year, to identify these two gene mutations that appeared to be more prevalent in Ashkenazi Jewish women suffering from cancer.

I already had two young sons when my sister died, and substantial financial responsibilities, including a large mortgage. Even if genetic testing had been made available to me, I would have been wary of having it. If I did turn out to have a BRCA1 or 2 variation, it seemed likely that such a result would affect my life insurance and mortgage options. So I tried not to dwell on the frightening thought of hereditary cancer, and mostly I succeeded.

In 2013, the topic became more widely discussed, when Angelina Jolie spoke openly about her decision to have genetic testing, after her mother died of ovarian cancer aged 56. Jolie discovered that she carried the BRCA1 gene, and took the decision to have a preventative double mastectomy. 'Cancer is still a word that strikes fear into people's hearts, producing a deep sense of powerlessness,' she wrote in an essay for *The New York Times*. 'But today it is possible to find out through a blood test whether you are highly susceptible to breast and ovarian cancer, and then take action.'

I remember reading Jolie's words, and briefly considering whether I, too, should request genetic testing. But I pushed the question out of my mind again. It was not that I was being irresponsible about my health: I had regular mammograms and ultrasounds. Yet there was always so much else to think about: the painful end of my first marriage and the upheaval of divorce; falling in love again and remarrying; motherhood, moving house, and the ceaseless demands of a challenging career as a writer and editor. The swirling currents of daily life, with all its unexpected perils and pleasures, took precedence over any pre-planned course of action that brought with it a stark reminder of heritable disease and death.

In the end, my decision to go ahead with genetic testing came down to timing and happenstance. I did not actively seek it out, but once the opportunity came up, it seemed like a good idea, and I felt psychologically ready for the process, in a way that I was not in my thirties. Age does not necessarily bring wisdom, but for me, at least, getting older has been accompanied by a growing sense of stability and resilience. I am lucky to have a supportive husband, who gives me the confidence to face challenges in the knowledge that he stands steady by my side. The involvement of Dr Sandberg was also crucial. He explained with great care and compassion what was involved, and we talked about the conceivable outcomes (such as discovering genetic variations that correlated with cancer), so that I fully understood each step that lay ahead.

It was also reassuring to learn that the research project would be concentrating on 'actionable genes', in which inherited alterations are associated with a significant, but preventable, risk of disease, rather than those related to incurable conditions such as Alzheimer's or vascular dementia. Along with the blood tests, I was given a comprehensive medical check-up, including an echocardiogram and ultrasound, which showed that I was currently in good health.

Below: Justine Picardie (front) with her sister Ruth in childhood

Then came a wait of several months for the results, during which time the first wave of the coronavirus pandemic swept across Europe and we entered a national lockdown. There was so much else to worry about that I didn't brood over the genetic testing; both of my sons and their partners were infected with Covid at the beginning of the outbreak in London, and I was more concerned about them than anything else. During the ensuing weeks, I tried to remain

calm, and as safe and healthy as possible in the circumstances.

Coincidentally, I was also absorbed in writing a new book, which is set during World War II. As part of the research, I had travelled to Germany, to study the archives of the Ravensbrück concentration camp. Knowing that a number of my father's ancestors had been killed in the Holocaust, I inevitably found myself thinking about the implications of my heritage. Because of my father's Jewish descent, notwithstanding my mother's Anglo-Saxon family history, as far as the Nazis were concerned, I would have been deemed a Jew and suffered the consequences.

My research also led me to read more about the wider racial ideology of Nazi Germany, and how the doctrine asserting the superiority of 'the Aryan master race' was promoted as having a scientific basis. According to Hitler's deputy, Rudolf Hess, Nazism was 'applied biology'; hence the introduction in 1933 of the 'Law for the Prevention of Progeny with Hereditary Diseases', which demanded the sterilisation of all those who suffered from mental illness, learning difficulties, congenital conditions, epilepsy, blindness and deafness. The persecution of people with disabilities escalated in 1939, as Hitler authorized 'Operation T4', a widespread programme of euthanasia. This ran in parallel with the 'Final Solution' to kill millions of Jews, as well as the extermination of others deemed to be 'subhuman', such as Slavs, Roma, Sinti and homosexuals. In the context of these relatively recent wartime events, and the disturbing legacy of Nazi eugenics, I can well understand why genetic testing could be a sensitive issue for some people. Added to our knowledge of the past is disquiet about the future, and the destructive possibilities of genetic engineering as envisaged by Margaret Atwood in her dystopian novel *Oryx and Crake*. This apocalyptic vision of a man-made pandemic, arising from a virus created in a laboratory by a biotechnologist, speaks to so many of our current anxieties.

Quite aside from the profound questions about how our identity and destiny might be defined by our genetic make-up, the subject of cancer was still taboo when I was a child. My maternal grandmother had cancer, which was never discussed openly, and my father's mother died relatively young, of a cause that remained nameless. Even when my sister was diagnosed in 1996, I remember the unease and dread with which some older friends and family members responded to the news; almost as if the disease should be shrouded in secrecy and silence, such was its terrible stigma.

Today, while cancer remains feared, it is no longer unmentionable. And thanks to the groundbreaking work of Professor Eeles and her colleagues, genome sequencing has a truly beneficial role in its prevention and treatment, as well as that of other serious illnesses. The screening that I received examined 650 genes in total, including 15 different mutations associated with breast cancer alone, and dozens of others for ovarian and colon cancers, as well as cardiac genes that can cause heart disorders. The project also extends into the fascinating new field of pharmacogenomics, by investigating how genes can affect one's response to a range of prescribed drugs.

Such is the detail contained in the testing that it not only takes time to get the final results – which are double-checked by two systems in different laboratories on either side of the world, and then scrutinised and discussed by a number of geneticists – but it also requires careful explanation. I was given the initial results by Dr Sandberg in a phone call, followed by an hour-long video consultation with Professor Eeles; and subsequently joined 26 other participants in a Zoom meeting, to listen to an overview of the research project and to give our feedback. Remarkably, we all felt it had been an entirely positive experience, even though eight major gene variants had been discovered in our group, while 85 per cent of us were found to be carriers of at least one recessive gene linked to hereditary disease.

In my case, though the tests revealed that I do not have the BRCA1 or 2 mutations, several other variants did show up, some of which are associated with my Ashkenazi heritage. Fortunately these are results that I can act upon in practical ways. One of the most useful outcomes of the genome screening is the discovery that I have a gene variant that increases the risk factor (five-fold) for blood clots causing pulmonary embolism and deep vein thrombosis. As a consequence, I now know that I must take preventative measures before surgery or long-haul flights.

Another equally helpful result concerns the relationship between genes and pharmacology; in particular, those variants that may affect a specific drug's metabolism or cause severe adverse reactions. In the future, this form of genetic testing will lead to personalised dosages and precise adjustments to drug treatments. But for now, I'm equipped with the vital knowledge that I should avoid certain medicines; for example, a particular form of chemotherapy would be likely to have a dangerously toxic effect, rather than being curative. Inevitably, I can't help wondering if it was the same agents that hastened my sister's death, because chemotherapy seemed to make her so terribly ill. And I wish with all my heart that Ruth was still alive today, and that we could talk about the intensely personal issues raised by our shared Ashkenazi heritage. Yet even as I write these painful words, I remain hopeful about what lies ahead for our children, as medical science become more sophisticated.

Of course, we cannot predict the future, nor avoid unforeseeable threats; but genome screening provides us with the means to make informed choices about our health and wellbeing. 'It's like knowing your hand of cards in a game of bridge,' explains Dr Sandberg. His is a good analogy, although I tend to think of my genetic test results as a compass and map. The survey is not yet complete – and like those ancient, illustrated atlases drawn by past voyagers, there are mysterious regions where dragons might lurk. But the exploration and discoveries will continue, shining beams of light where darkness once reigned.

For more information on genetic screening, visit www.90sloanestreet.com.

The topic became more widely discussed when Angelina Jolie spoke about having genetic testing

Justine and Ruth (front)

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