Introduction

We humans are fascinated with ourselves. What causes the similarities between us, and what makes us different? Why is it that some people live long and healthy lives, and others don't? For centuries, the brightest minds have sought to determine what it is that makes us who we are, but also how we might live better, stronger and longer.

Genomics – that is, the study of all of our thousands of genes – is finally offering some answers to some of the biggest, longest-held questions about humanity, as well as the world we live in. DNA studies were once long and mystifying processes, but groundbreaking sequencing technologies now mean that, at the press of a button, scientists are able to create a map of all the genes we contain – and deduce a lot of the key messages those genes send.

This map is called a genome, and it contains many important clues about us, from our ancestry to the way

our bodies respond to diseases, medication and ageing. In fact, genomics can be applied to just about every part of who we are and what we do – from the different traits we inherit and our resistance to drugs to humanity's ability to solve crimes and reduce the impacts of climate change. The possibilities are vast and have the ability to transform the way we think about ourselves and the world around us.

At the same time, many of us would be willing to admit that we don't know much about genomics at all. That's understandable, considering the term itself didn't exist until the late 1980s, when an international moonshot initiative was launched to create a full blueprint of all human genes for the first time. Back then, the research was largely experimental and, as many point out, some of its practices wouldn't be considered ethical today. Researchers would take samples of their own blood to examine in the lab, for example, or draw straws among colleagues to see whose sample would be taken for that day's work. Today the practice is much better understood,

regulated and shared – and the technologies to have been born out of it are used within an incredibly wide range of research disciplines.

It's entirely likely that one day soon, your genome will be sequenced by a small machine in your GP's office to help determine the best course of treatment for anything from antibiotics to drugs for anxiety and depression. Genome sequencing can also offer clues as to how to best modify treatments, and even tailor them to the individual – bringing us one big step closer to the dream of precision medicine.

And yet, as the saying goes, with great knowledge comes great responsibility – and there are many unknown paths left to go down in terms of ethics and the way we use genetic DNA going forward. For decades, popular culture as well as the media has warned of the dangers of creating 'designer babies' and playing God to potentially disastrous effect. Some of that has already become a reality: would-be parents can use genomics to check the DNA of embryos to see if they like what's there. The

technology is only currently being used to screen against inheritable diseases, but it could be used in the future to select for intelligence and aesthetic traits. Scientists already have the tools they need to repair, modify or cut out unwanted genes entirely should they wish to – but the long-term impacts of this are unknown and experts haven't yet worked out what the rules of the game might be or how to play it.

As a society we are confused by the ethics of genomics. For example, we may express concerns over data protection, and yet at the same time send away for home-testing DNA kits, eager to share our most personal data to learn what traits we might carry in accordance with our genes. Many of us may well be appalled at the idea we might curate our children's looks or characteristics, pick one eye colour over another, even build a new biological hierarchy. And yet for some people, the ability to choose traits is a tempting prospect, something they believe would give their offspring the best chance of success. Whatever we think about the

potential of genomics to help us, we have to be aware of the fact that, at its extreme, it can so easily merge with eugenics, the advocacy of controlled selective breeding beloved by twentieth-century fascist regimes and so rightly shunned.

Clearly, genomics, and specifically gene editing, is an ethical minefield that will only raise bigger and tougher questions as the research continues to evolve. What we choose to do with these tools as a society is up to us: but the first key to decision making is understanding. Rightly or wrongly, genomics will shape the future of our health, the future of our planet – our entire existence as a species – and so it's crucial we get it right.

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How to map a life

When DNA was first identified in the late 1860s, scientists advanced one step further in their understanding of how the human body works, and even how it might be manipulated. But there was still a long way to go before theory could meet reality. In fact, experts didn't learn the full picture of how our DNA links together until around 140 years later, through a $2.7 billion (£2.2 billion) moonshot initiative called the Human Genome Project (HGP).

Arguably the most ambitious research project of modern times, the HGP was led by an international group of researchers with the aim of mapping the entire human genome – that is, a detailed reference for our complete genetic code. Launched on 1 October 1990, the project was initially funded by the US government, and later by the UK's Medical Research Council and the Wellcome Trust.

In order to help facilitate the research, in 1992 Wellcome set up the Sanger Institute, a dedicated laboratory on a factory-sized scale near Cambridge. Similar dedicated spaces were built in California and Texas, but sequencing took place at numerous universities and research centres across the UK, US, France, Germany, Japan and China.[1] By the time of the HGP's completion in 2003, at least eighteen countries had contributed in some form or another.

The reason such large labs and so many contributors were necessary was in part because of the huge scale of the project: there are 3.2 billion letters of DNA in the human body, and each one had to be identified and recorded. At a time when technology was much more limited, the project required all the expert eyes and ears possible and so researchers split up tasks evenly across labs, countries and continents. A crude map was created to allow contributors to each add in their respective pieces of the puzzle. But more than this, the HGP was designed to be collaborative, involving as many different laboratories and nationalities as possible to ensure the

work was inclusive and reflective of the genetic expertise found all over the world. Moreover, it was important to both funders and scientific leaders that this was a global project, both to share the huge costs involved and to prevent any one party claiming ownership of the human genome – the secrets of our existence.

For the many, many researchers involved in mapping the first human genome, the project itself presented an opportunity to be part of history. 'It was the complete opposite of the lingering old-fashioned belief that science was for the alpha male, the brilliant lone genius, all that rubbish,' says Julian Parkhill, who joined the Sanger Institute in 1997 and eventually became its head of pathogen genomics. 'This was a very large community of scientists all working together towards a common goal.'

Stephan Beck, a leading medical genomicist, was head of human sequencing at the Sanger Institute for some of that time, where he played a leading role in the sequencing and analysis of human and mouse genomes. He remembers the excitement of the time well: 'We knew it

was going to be a unique project – no species has ever been capable of sequencing its own genetic content before and this was something that was only going to happen once,' he says. Multiple donors were required throughout the project in order for researchers to collect enough human DNA to work with (using blood and sperm samples), but their identities were kept anonymous. 'In my experience, there was never any shortage of volunteers,' says Beck.

But with so much at stake, tension was growing between the public and private research sectors, each vying to win the prize of being the first named group to solve the puzzle of human existence. By the late 1990s an American biotechnologist and entrepreneur named Craig Venter was making his frustrations over the slow pace of public projects known. Formerly an employee at the US National Institutes of Health (NIH), Venter had pioneered new techniques in genetics research which were quicker than those being used by the HGP partners, and he saw a business opportunity in the mapping of the human genome. Confident that he could do better, Venter sought

funding from the private sector and went about hiring his own research team to map the human genome himself.[2] 'Government-funded efforts were painstakingly slow,' says Parkhill. Meanwhile, 'here was this private industry individual saying, "I've got some money, I'm going to do it all myself." And he tried to persuade the US government to let him do it instead.'

Venter's intervention became a sore point in the research community for several reasons. For one thing, the HGP's public networks had been established on the condition of openness and transparency. This was formalised in a meeting in Bermuda in February 1996, when the HGP partners agreed to share their progress on public research databases every twenty-four hours. The move towards open data made researchers accountable for their work and helped to ensure that work was not accidentally repeated across borders. It allowed for a more collaborative approach – research teams could cross-check data and point out any potential errors – but it also adhered to the principles of making publicly

funded science openly available for the public good, rather than hidden away behind paywalls or lost in private storage drives.

Venter declined to be part of the arrangement, initially keeping his data locked away from other contributors. He also accused the US government of wasting public funding by making the operation so far-reaching, involving 'armies of scientists' without any plan in place to make the money back through innovation. Venter's plan, by contrast, was to patent the genes he mapped out and sell access to the data through a subscription service.[3] Publicly funded researchers taking part in the open approach to data questioned Venter's motives and lack of transparency.[4]

Ultimately, Venter's mission didn't result in the public efforts being shut down as some might have feared. If anything his private company, Celera, helped to speed up the public effort by adding a huge amount of pressure on governments to get the job done first. With the HGP facing the prospect of losing its claim to the discovery