Now the **100,000 Genomes Project** has hit its target, what comes next? We look at whether we are on the cusp of a **genomic revolution**.

THE FUTURE IS GENOMIC

Predicting the future is notoriously hard. Even the brightest minds fall foul – in 1932 Albert Einstein said there is "not the slightest indication that nuclear energy will ever be obtainable". While 16 years ago Bill Gates proclaimed: "These Google guys, they want to be billionaires and rock stars and go to conferences and all that. Let us see if they still want to run the business in two to three years."

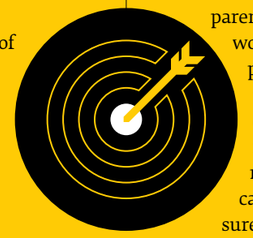
This is perhaps why Professor Mark Caulfield, the Chief Scientist at Genomics England, does not want to be pinned down when it comes to the future of the rapidly evolving branch of molecular biology – genomics.

"The longer that you are involved in life sciences, the more that you know you can never know enough," he says. "Sometimes you may be on rocky road, but you will always be learning. I don't see this as something where we can answer all the questions – when you answer a question, that opens doors to other questions that you've then got to try and answer."

Transformation

Genomics is a relatively new discipline. It was only in 2003 – the same year Bill Gates made the above statement – that the human genome was first fully sequenced. Now, just over a decade on, it is the cutting-edge field that many are investing in, from big pharma (AstraZeneca plans to sequence two million genomes over the next 10 years) to governments (the new target for England is to sequence half a million genomes from the NHS in the next five years).

"We will sequence these genomes across 22 categories of rare diseases and, at present, four cancers," says Mark. "We want to make sure that in 50 years people will look back and see genomics as an everyday routine thing... it's got a big role to play. I hope people will look back and see that we've done a transformative thing."



Uncertainty

But because the field is so new, it is not yet known exactly what kind of a transformative effect it will have (See box, overleaf, for an alternative vision, from Gerry Thomas, Professor of Molecular Pathology at Imperial College London). In the future, will everyone have their genomes sequenced as standard? Will it be so integrated and intrinsic to the NHS that when a baby is born, it will have its genome sequenced? It's something Mark has clearly considered.

"We would need to do significant research into whether society and parents would want that. It would have to be based on parental choice, but there would be a case for considering that in the future," he says. "We would need to have evidence and careful planning to make sure that our programme was

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designed with the highest quality outcomes and that it would be of utility and would not lead to anxiety."

Geneticist David Goldstein is heading up AstroZeneca's genomics initiative and is very open about the fact that he sees an uncertain future, too. "Everyone now recognises that genomics really is moving. It's not all hype anymore," he says. "A lot of the problem has been in acting like we can predict when genomic efforts will win clinically relevant insights. It's just not very predictable. He adds that much of the work will "not win insights that are commercially valuable to AstraZeneca" and that they are "not banking on a single project delivering".

While future outcomes may be uncertain, integration into the NHS is well underway. A total of 103,311 genomes have been sequenced from over 85,000 participants and 1,500 NHS staff have been involved in the work, along with 3,000 researchers and trainees worldwide. The National Genomic Medicine Service went live for certain tests in October and Mark expects it will go live for full genomes in July.

He says: "I think that what people will beginning to notice is the increase in the range of testing and uniform national coverage, so there will be no risk of a postcode lottery. The founding principle of the NHS being free at the point-of-care will be enshrined."

Volunteering

That said, could the new "genomic volunteering" scheme announced by Matthew Hancock at the end of January undercut this? The Health Secretary said: "Seriously ill children and adults with genetic conditions, including cancer, will be offered DNA analysis as part of their routine care."

He continued: "And, while healthy people should not have this service free on the NHS, there are huge benefits to sequencing as many genomes as we can – every genome sequenced moves us a step closer to unlocking life-saving treatments."

The scheme (costs and details if which have not yet been revealed) involves healthy people paying to have their genomes sequenced on the condition that they allow their data to be to used by Genomic England.

Mark says: "The intention would be that we would recover the cost of the sequencing. There's an opportunity for people to understand more about their genomes, as long as they cover their costs. We are also looking at how we could use that money to pay for people who can't afford to have their genome sequenced. We think that the natural altruism of the British people means they will be happy to do that."

Mainstreaming

The project has already created 21 petabytes of data (50 petabytes would be enough to store the entire written works of mankind from the beginning of history, in all languages). This is being interrogated by researchers all over the world, who are provided with access to the data on the condition that they share their findings.

But, while many researchers may have an advanced understanding of what all this data means, what about those on the frontline of the NHS? What about the biomedical scientists, doctors and nurses, all of whom will be increasingly involved as genomics becomes more widely used?

It was a subject that was under the microscope at the Festival of Genomics conference, which took place in London at the end of January. Among the dozens of sessions was a panel debate entitled "Mainstreaming Genomics and the Education of Interpretation".

Catherine Houghton, Lead Consultant Genetic Counsellor at Association of Genetic Nurses and Counsellors, said: "The pace of change is making it extremely difficult for us to have time on top of our clinical roles, in terms of the mainstreaming agenda." She added: "You can't expect someone in the mainstream to suddenly become an expert in genomics, it's about gradually increasing knowledge and taking it step by step."

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Jonathan Roberts, a Genetic Counsellor from the Wellcome Genome Campus, added: "Uncertainty is a big challenge. There is a lot of uncertainty in terms of the results and the predictive value of what those results can be. I think uncertainty is something that we are all trying to get to grips with at the moment."

Education

It is hoped that the Genomics Education Programme will resolve this uncertainty. The £20m three-year programme is supported by Health Education England as part of its responsibility to ensure the NHS has the staff it needs to deliver care now and in the future. Its role involves directly supporting those professionals involved in the 100,000 Genomes Project and microbial genomes work; supporting the wider transformation of services to integrate genomic technologies into healthcare; and upskilling existing staff so they can make the most of genomic technologies in their work.

This is being done through a range of means, including online resources and self-directed education, formal academic-based training programmes, workforce planning for the specialist staff, NHS-funded places for staff on training programmes and multi-professional clinical research fellowships and doctoral posts in genomics and bioinformatics.

But it is not just the workforce that needs to be taken into consideration. For the public, the nature of the tests is fundamentally different from the conventional tests they are used to.

Marks says: "One individual test for a single patient can have ramifications family-wide – it may not just tell them something about themselves, but their whole family."

It's an issue that Catherine Houghton addressed at the Genomics Festival. "It is important that the education of the patient happens before the tests are carried out, so that the patient knows the implication for themselves and their family. Genetic test results don't necessarily give you a definitive answer and that needs to be put across to the clinicians and the public."

Healthier for longer

This complex new world does not come cheap. Hundreds of millions have been spent and many hundreds more will be spent. "It is obviously costing a considerable sum of money," says Mark. "But you can see where the economics of this can release cash. I'm not saying we can save [the NHS] money, but we can release cash in some areas. We've got to put money in the front end to get something out of the back end."

He added: "Genomics could be the gift that keeps on giving by helping people avoid harm – we need to examine how we keep people healthy for much longer. More work is of course required, but we need to deliver a 22nd Century health service."

We don't yet know what this future will look like, and we don't know what role genomics will come to play, or the impact that it may have on managing our health. Predictions about the future are notoriously tricky, but while there are too many variables and unknown factors for any certainty, it is looking increasingly likely that the future is genomic. BMS

LOST IN TRANSLATION?

Gerry Thomas, Professor of Molecular Pathology at Imperial College London: "Introducing change into any healthcare system is not easy. Bringing in a whole new way to diagnose patients using DNA sequence rather than the tried and tested methods of biochemistry, morphology and localisation of proteins will be challenging for the NHS.

"Change is facilitated when those who are being asked to change can see the benefit of that change. The ability to be able to give a patient with a rare disease a name for their disease provides psychological benefit to the patient and has the (much) longer term potential to provide better treatments. However, the benefit to cancer patients is less clear, particularly when their care involves a complex multidisciplinary team. To make a difference clinically means turning round a test in a clinically relevant timescale and providing the information back to the doctor and the patient in a way that permits an informed choice to be made on treatment. The biggest challenge of all is the way in which genomics is rolled out in a manner that preserves the principles of ethics. Genomic medicine must be applicable to all relevant patients with the disease, and be proven to be beneficial both clinically and economically.

"It will not be the only way that diagnoses are reached and treatments are given – we are so much more than just our DNA. And only time will tell whether, as with so many other scientific 'breakthroughs', this project was the harbinger of a genomics revolution for the NHS or if it simply gets lost in translation."