

## Happy 10th Birthday, draft of the human genome

*It's been 10 years since the draft of the human genome was completed and a "beautiful, fragile and powerful force for great good or evil" was given to the world. What has happened since? Has this power been successfully harnessed, or was the world-wide collaboration an overhyped white elephant?*

*We've gathered together Sanger Institute researchers - those involved in creating the draft and those who are now using the map - to find out.*

### This is what you are made of

On 26 June 2000, the world's media gathered in Washington DC and London to hear President Bill Clinton and Prime Minister Tony Blair declare the completed draft of the human genome as *"the most wondrous map ever produced by human kind"*. Speaking on behalf of the Wellcome Trust, who funded much of the research, Dr Michael Dexter described it as an *"outstanding achievement, not only of our lifetime, but in terms of human history."* How do the Institute's researchers remember that momentous day?

Director of the Sanger Institute, Professor Mike Stratton, recalls the day like it was yesterday. But then he was at the press conference. Mike's eyes fire up: *"There can be few more wonderful moments as a scientist than to be able say to people, 'This is what you are made of'."*

### A day like any other

Surprisingly, for many of those who worked so hard to piece the map together, the day felt much like any other. Lucy Matthews was leading a team of "finishers" at the time, who were responsible for sticking together the fragments of DNA sequence into a coherent whole. *"It is hard to remember exactly what I was doing when the draft was announced,"* she confides. *"Our work was an ongoing process and the announcement felt like another step on the journey to producing the final human genome"*.

Another Institute researcher working closely on the project, Sarah Sims, has an equally hazy recollection of the announcement. Sarah was a production group leader, supplying the finishers with the DNA sequences to piece together: *"I can't remember where I was, but it was memorable in the fact of what we had achieved. Being able to say you were part of the team that sequenced the first human genome is amazing, a huge milestone and makes me part of history. My children will be able to say my Mum was involved with that (and their Dad, too)"*.

Darren Grafham, a fellow finisher, agrees that the day's significance is something that has become



Ten years on: Sir John Sulston, Dr Francis Collins and Professor Mike Stratton come together in front of journalists to remember the completion of the draft



more apparent over time: *“It is rare in science that something you have been part of becomes taught in classes to the next generation of people during your lifetime, let alone within 10 years.”*

However, for other researchers the announcement of the draft genome had an immediate career-changing effect. Dr Nicole Soranzo is a team leader at the Institute, uncovering novel mechanisms that underlie complex diseases such as heart disease and diabetes. *“I was in Italy, working on population genetics of trees,” she remembers. “I realised immediately the advantages of working with a sequenced genome. I decided to abandon plant genetics in favour of human genetics, despite having to start all over again.”*

### Waste of science funding?

But not everyone shared Dr Soranzo’s excitement. As Darren Grafham recalls: “People had questioned whether it could be done. They argued that it was a waste of UK science funding and would never amount to anything.”

Lia Chappell, a PhD student now working at the Institute, was 14 years old and in secondary school 10 years ago. “At the time my impression from the media was that this was an expensive proof of principle experiment, with no immediate applications. I remember discussions in the media and in school of how this money could have been better spent on ‘real’ research.”

The naysayers continue to argue today that the human genome project has failed in its promise to deliver benefits for mankind. Do our researchers agree that the project has proved to be an overhyped white elephant? Akin, perhaps to another “gift to the nation” in 2000 - the Millennium Dome?

The answer is a resounding no.

### A gift to humanity

At the time, Mike Stratton declared that: *“Today is the day that we hand over the gift of the human genome to the public. It is very fragile and beautiful and a powerful force for great good or evil.”* Is this a statement that he now feels was a little overstated? Absolutely not, he affirms: *“I didn’t plan to say that - it just came out of my mouth - but I don’t back off from it. The genome is genuinely a gift to humanity.”*



Professor Mike Stratton - ‘The genome is genuinely a gift to humanity’.

Alan Tracey, an Institute finisher who is responsible for ‘completing’ more than 1 per cent of the entire human genome, explains that the true value of “this gift to humanity” may take many years to develop. *“It isn’t something where the benefits are immediately obvious,” he says. “But the important thing is the research that continues off the back of it and will be going on for years.”*



Yet, the potential of the map to benefit mankind was almost lost to commercial interests and locked away in intellectual property rights. As Sancha Martin - a research administrator at the Institute - reveals, publishing the draft as a freely available resource for all researchers, was a momentous event in itself. *“To have data publicly available to anyone who wanted to work with it was unheard of at the time. It was a landmark change in the approach to data release from scientific studies, I think. It was the beginning of something very special.”*

Dr Nicole Soranzo agrees that much of today’s research could never have taken place without the unparalleled cooperation and collaboration fostered by the human genome project. *“Completing such a visionary project has helped the human genetics community gain confidence in its ability to succeed in large international collaborative projects involving private and public partners, as well as providing key infrastructure and technological advancements.*

*It has prompted further large-scale projects such as the HapMap, which has been instrumental in designing the tools for genome-wide association studies. These in turn have led to the discovery of hundreds of common genetic risk factors for complex diseases, and provided much insight into novel biological and physiologic mechanisms underlying human disease.”*

### It’s hard to imagine how biology worked without it

Lia Chappell has only known a research world where the human genome map has been available to guide investigators’ studies. *“From my point of view the human genome has always been there, and it’s hard to imagine how biology worked without it,”* she says. *“When I think about a gene, one of the first things I ask is where it is in a genome. Before the draft genome was released, I can only imagine that it must be like trying to find your way around a new city with only a couple of souvenir postcards instead of a street map!”*

However, the work of the human genome project was only the first step on the journey to understanding the role of genetics in disease. Sir John Sulston explains: *“The draft human genome was a step in an ongoing process, rather than the discovery of a new principle like the structure of DNA, or Mendel’s findings in his garden or Darwin’s observations on the Beagle. Science goes on. So long as it is open we can find out everything, in due course.”*

### Asking impossible questions

Darren Grafham echoes Alan’s thoughts: *“The draft genome enabled scientific questions to be asked that were impossible before the draft existed and led the way for genomics to proceed in the subsequent 10 years. Without the draft, the mouse and other genomics projects would not have been funded or initiated.”*

One benefit of the human genome project has been the exponential increase in the speed of DNA sequencing. Sarah Sims explains: *“The next big thing will be being able to sequence anybody’s genome cheaply. The structure of DNA was discovered only 50 years ago, it*



Sir John Sulston - ‘The initial announcement of the first reference human genome was really symbolic: it was like firing a starting gun’.

*took 10 years to sequence the first human draft, and now a draft can be done in days. It's only a matter of time before a genome can be done in hours/minutes. Genetics has come a long way!"*

Yet this increase in sequencing speed comes with new challenges. *"It opened up the vast world of sequencing individual human beings so that you can compare one with another and more and more finely see what the results of variations are,"* John Sulston notes. *"It's an enormous data set that is hugely complex and we are only just beginning to explore. We don't know where all that is going, but it is changing so fast that the initial announcement of the first reference human genome was really symbolic: it was like firing a starting gun."*

## Cancer in our sights

Cancer research is one area where the Sanger Institute is now exploiting this explosion of knowledge in identifying disease-causing genetic variations. Sancha Martin is excited by the possibilities: *"The thing that thrills and challenges me every day is my work for the International Cancer Genome Consortium. I now oversee the administration of a project which aims to sequence the whole genomes of 1,500 breast cancers. From these cancer genomes we hope that researchers in the cancer community will be able to identify possible therapeutic targets or biomarkers for prognosis. These data will be a springboard to a huge range of possible downstream analysis that could lead us anywhere we are willing to go."*

Sir John Sulston shares her enthusiasm: *"A particular bridgehead where I would hope to see continued quite rapid progress is in cancer because I think the efforts now to identify the changes in cancer cells are going to be increasingly successful with all this sequencing going on."*

However, he cautions, such discoveries may take time to be translated into clinical therapies that will benefit patients. *"Whether we will be anywhere near understanding everything is another matter. There is a vast amount of 'dark matter' in the human genome still to be uncovered and understood. And we may find added complexity that may still stop us. And then there is the matter of engineering - of whether one can deliver drugs based on the discoveries we make."*

So, today's genomic researchers continue to face a daunting challenge: to read the "fragile and beautiful" instruction manual for mankind in ever finer detail and unlock its undoubted power "for good or evil". But, perhaps, the bigger question is: are we ready for what we will find?