Genomics 101 transcript: What is whole genome sequencing?

**Naimah:** Today we are going to be finding out a bit more about what is whole genome sequencing. I will be speaking to Greg Elgar, who is the Director of Sequencing in Research and Development here at Genomics England. So, Greg, we have spoken about a genome before, but what is a whole genome and what can it tell us?

**Greg:** So, a whole genome is all of the DNA in one of our cells. It is the end-to-end sequence of the DNA in chromosomes, and it is different to what we have often done as scientists before in that we often sequence little bits of the genome. So, we often sequence just a single gene, for example, but at Genomics England we like to sequence our entire genome, so we have all the information in one of our cells.

**Naimah:** Whenever you say sequence, what do you mean by that?

**Greg:** So, sequence is literally reading along the different bases in the genome. There are four different bases, G, A, T, and C, and it is the order of those bases that define what that DNA will code for, and we can literally read from one end of a chromosome to the other and get the whole string of bases. If we put all the chromosomes together, we end up with about 3,000 million bases of information.

**Naimah:** And whenever we read these bases, what do they tell us?

**Greg:** It is very complicated to read the sequence of a genome, and the reason for that is because it is a very simple code and because there is an awful lot of it. And so, we read it by comparing it with a reference. So many years ago, in the very, very early two thousands, a reference genome was generated from a small group of individuals and that reference genome is held in a database. When we sequence anybody's genome, we then compare the sequence of that genome with the sequence of the reference. That allows us to identify differences between the genomes, and it also allows us to identify those bits that are exactly the same.

**Naimah:** You said that whole genome sequencing is what we are doing now at Genomics England, but what did we do previously?

**Greg:** So, sequencing was only invented in any way at all in the late 1970s, and for many years it was a very slow, laborious task, and there was absolutely no way we could even think about sequencing the whole human genome. It was only in the 1990s when sequencing started to become quite automated so we could consider doing that, and even then, it was an absolutely gargantuan worldwide effort to get the whole human genome sequence that is just the sequence of one individual, essentially. Since then, methods have gotten even quicker, and now we can sequence whole genomes of individuals in a day, and we can do many of those at the same time. The difficulty really nowadays is not doing that sequencing, it is storing all the information and working out what we do with all that information afterwards.

**Naimah:** Okay, just to go back a bit, to sequence a whole genome, what is exactly entailed in that? Is this just a blood sample from a participant?

**Greg:** Yeah, so if we are simply sequencing, if you like, the normal genome of an individual, we can do that from blood, although red blood cells don't have DNA and then white blood cells do, and there's enough DNA from a tiny drop of blood to provide us with enough DNA to sequence it. If we want to sequence someone who has cancer, then we need to sequence the DNA that comes from the tumour itself, because cancer involves many changes in the genome, and so for cancer, we need to compare the genome from the tumour with the DNA from the normal blood of that individual.

**Naimah:** You've mentioned that there are some benefits to whole genome sequencing, such as it being quicker, are there any limitations or challenges to whole genome sequencing?

**Greg:** So, the interesting thing is that up until very recently, we sequenced genomes in one way because there has only really been one platform or one machine that we have been able to use to sequence human genomes really quickly. More recently, there are new machines and new ways of sequencing. The new ways of sequencing allow us to look at the genome in a slightly different way. It allows us to understand that as well as those Gs, As, Ts and Cs, there are other modifications, or add-ons, if you like, to DNA, which also may have an influence in disease. So, as the technology changes, we are starting to learn more and more about the genome, and that is why at Genomics England, we are always looking to make sure that we are using the most up-to-date methods and that we sequence in the best way possible. As the sequencing technologies change, it does give us the opportunity to look at new insights.

**Naimah:** Do you have any idea of what these future technologies might look like?

**Greg:** Yes, I think one of the great opportunities that we have is to start personalising the way that we test different individuals for different diseases. So, I think in future, medicine will become more personalised, and with the help of having genome sequence, DNA sequence of individuals, it will allow drug and treatments to be tailored so that you get the best response for a particular individual. I think, in future, the genome and the benefits that the genome can provide will end up being closer to the patient and the patient will have more control over it. I think that is really important because we need to empower individuals and give them the opportunity to make choices about what happens with their genome.

**Naimah:** So, has whole genome sequencing helped us move away from this model of one medicine fits all?

**Greg:** Yes, absolutely it is helping us move away from the one medicine fits all model, which is deeply flawed, and many people respond not only really badly to medicines, but some people just do not respond optimally to a particular dose of a medicine. So, there is a huge amount that we can do to help with that. Again, in order to do that, we need to find a way of getting the sequence and the genome closer to the patient so that the GP, for example, can make the right choices because that is often the level of where the choices are made in terms treatment.

**Naimah:** Can you give me an example of where whole genome sequencing has allowed the development of personalised medicine?

**Greg:** So, it's still very much in its early stages, and so probably the most pertinent examples at the moment are more in clinical trials where pharmaceutical companies are designing trials now so that when they test their drug, they also have the genome sequence of the individuals that they're looking at, and that will allow them to clearly see whether there is a different reaction based on different genome sequence, and that will allow future tailoring of medicine. So, it is very much in its early stage. We do not really do much personalised medicine yet, certainly not associated with the genome. The closest we get to personalised medicines is understanding when people are allergic to medicines and then we do not prescribe them. In future that will become much more subtle and much more nuanced.

**Naimah:** That was Greg Elgar explaining whole genome sequencing. If you have any more questions on this, please email us on [info@genomicsengland.co.uk](mailto:info@genomicsengland.co.uk).Thank you for listening.