**Genomics 101 transcript: What is a rare condition?**

**Ana Lisa Tavares**

**Naimah:** What is a rare condition? Today I’m joined by Ana Lisa Tavares, clinical lead for rare disease research at Genomics England, and she’s going to explain more.

**Ana Lisa:** There are thousands of rare conditions. I hesitate to say a number as we’re learning all the time, so this keeps changing. There are estimated to be perhaps around 10,000 different rare conditions, as an order of magnitude. Many rare conditions start in childhood, 75% or three quarters affect children. A little over 10% affect adults, only adults, and some, around 20% can start in children or adults.

**Naimah:** So, what makes a condition rare?

**Ana Lisa:** A rare condition can be defined as affecting less than one in 2,000 people in the general population. This is a definition that’s used in Europe. Different parts of the world use slightly different numbers and definitions, so for example, the number of people with a rare condition living in that country, there isn’t one single universal definition.

The important part I think is that this is a practical way to help shine a spotlight on rare conditions, which collectively affect a lot of people, and the particular challenges in making diagnoses and finding treatments for rare conditions. So together, it’s estimated 7% of people are affected by a rare disease in their lifetime, or one in 17, so that means that there are 3 and a half million people in the UK affected by a rare disease, and in the world, probably somewhere between 250 to 450 million people, so perhaps 350 million people, a really huge number.

When you look into these numbers, there are rare conditions that are much more common than others. So, 80% of people with a rare condition have one of the 150 most commonly occurring rare conditions. Cystic fibrosis would be an example that many people will have heard of, and if you look at those numbers from a different angle, 85% of rare conditions affect less than one in a million people, so are very rare, and it’s important to bring together these different voices to solve some of the common challenges.

**Naimah:** Can you explain to me how these differ from more common conditions?

**Ana Lisa:** The simplest answer is that they are defined by the frequency, so how often they happen in the general population, and one reason for grouping together thousands of rare conditions is to highlight some of the particular challenges. This includes delays in getting a correct diagnosis that can often take years, an increased chance of a misdiagnosis before getting to an accurate diagnosis, and treatment challenges, as 95% of rare conditions don’t have a specific treatment. This is a very good question, and I would like to note that it’s also an artificial distinction to some extent. So, human conditions have a range of underlying causes that can be broadly grouped together, including genetic and environmental, such as a viral infection.

However, it gets complicated, for example, a proportion of common conditions that may have many different causes will have a genetic component, so for example causing an early onset familial form of a condition, such as diabetes. And in fact, genetic causes may give or can give the clue or the key that’s necessary to develop a new drug therapy that can then help many people with the condition, so those that may have a rare genetic cause and those that have a more common cause, such as for high cholesterol.

So, one other way that rare and common conditions can differ, not just based on frequency, is the causes of those rare conditions and common conditions. I’ll start by saying that there are lots of rare conditions that aren’t genetic, and there are common conditions that do have a genetic basis, so none of these observations are absolute, but there’s a spectrum of different causes for rare and common conditions. So, I would say there are more rare conditions that are caused by a single genetic cause, and there are more common conditions that might be caused by many very small genetic effects acting together, and also many different environmental causes.

**Naimah:** So, are rare conditions always genetic?

**Ana Lisa:** The short answer is no [laughter]. Many rare conditions do have a genetic cause, perhaps 70 to 80% of rare conditions, so if you had 10 people with different rare conditions together in a room, the chances are that 8 of them will have a genetic component to their rare condition. And when we talk about genetic causes, these can of course be very varied, from a single letter change in the DNA code to an extra chromosome with several hundred genes. Rare conditions include ones without any known genetic cause, so for example some rare infectious diseases and some rare cancers. And I think it’s important to say that there’s a lot that we collectively don’t know yet about rare conditions, so our understanding is incomplete and imperfect, and there’s still a huge amount to understand.

**Naimah:** And it would be good to understand what challenges patients with rare conditions might face.

**Ana Lisa:** There are many challenges in achieving an accurate diagnosis, getting well organised, coordinated care, and the fact that 95% of rare conditions don’t have a specific treatment. There’s a big impact on emotional wellbeing for those with rare conditions and their parents and carers. Genomic Alliance did a survey showing that 88% of those with a rare condition felt emotionally exhausted from having their rare condition, and there are big impacts on other aspects, such as education, employment, etc.

**Naimah:** And what do you think the future looks like for the treatment of patients with rare conditions?

**Ana Lisa:** So, this is a huge question with many answers. I think key is coordinated care, and I’m personally really excited about the potential for new rare therapies to be made for particular types of genetic causes that perhaps one day could be modified to treat many different types of rare conditions. To me, this would be incredibly powerful and would be a dream to transform therapies for rare conditions.

**Naimah:** That was Ana Lisa Tavares explaining what a rare condition is. I’ve been your host, Naimah Callachand, and if you want to hear more Explainer episodes like this, you can find them on our website at [www.genomicsengland.co.uk](http://www.genomicsengland.co.uk). Thank you for listening.