Viewpoint: Genetics of COVID — Research into why some people never got the virus should explore genetic predisposition to long COVID

It's been over three years since the first known COVID infection. Since then, we've seen hundreds of millions of cases around the globe.

You've probably had it – at least once, if not multiple times – as has nearly everyone you know. As continued waves of infections arrive, fewer and fewer people have never caught COVID. But, even taking into account those who have had it and not realised, there are probably still some people out there who have managed to avoid the virus altogether (so far).

Last year, I wrote about people who had yet to be infected. Were they somehow immune? Did they possess some advantageous genetic mutation? Were they simply avoiding people and continuing to take precautions? Or had they just been lucky, and their time was inevitably going to come?

Unfortunately, we still don't know why some people have managed to avoid COVID for so long. Science takes time. We saw research occur at unprecedented speed in 2020 to understand SARS-CoV-2 (the virus that causes COVID) and to develop treatments and vaccines. But that level of funding and collaboration is hard to sustain in a world with so many worthwhile areas of research.

That said, some research is looking in particular at whether a genetic element helps explain why certain people have never caught COVID. But while this research is important, we shouldn't lose focus on those who are suffering from the disease and its longer-term effects.

Is immunity in the genes?

The COVID Human Genetic Effort, led by researchers in the US, has recruited people with known exposure to the virus, but who haven't had it themselves. This includes, for example, healthcare workers or people who lived in a household with a confirmed case of COVID.

Scientists will be examining their DNA and looking for unusual mutations that may explain an apparent resistance to SARS-CoV-2 infection. This may be a mutation in the cellular receptors or enzymes needed for the virus to gain entry to our cells, or perhaps a mutation in a gene involved in the immune response to infection.

Studies that look to uncover anomalies in our DNA, termed genome-wide association studies, have already been able to identify genetic mutations that make some people resistant to other infections like HIV and norovirus (the winter vomiting bug). If we can identify the reasons people may be immune to a particular virus then, theoretically, that knowledge could be used to prevent the infection.

But is it really that simple? Despite our understanding of the genetic mutations that protect a lucky minority of people against norovirus, there's no vaccine or treatment for this virus. And the infamous "CRISPR babies" (several children born in 2018 whose genomes had been edited in an attempt to make them immune to HIV), received criticism for dubious ethics, not to mention being illegal.

Genetic mutations might explain why some people have never caught COVID. Billion Photos/Shutterstock

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Genetic mutations might explain why some people have never caught COVID. Billion Photos/Shutterstock

It’s possible that it’s not a mutation in one gene, but a combination of mutations in multiple genes, that render a small number of people immune to COVID. Targeting multiple genes without causing any unwanted side-effects can be tricky and would make it much harder to harness this knowledge for anti-COVID drugs.

But understanding the genetic mutations that make someone resistant to COVID could provide valuable insight into how SARS-CoV-2 infects people and causes disease. In other words, it may be interesting scientifically, but perhaps not clinically.

While it will be some time before we have answers from these studies, scientists do believe there is a small group of people who are naturally immune to SARS-CoV-2 owing to their genes.

Time to shift focus?

As scientists, we can become fixated on certain details of our research. It’s always important to remind ourselves that there are people on the other end of these infectious diseases.

Although SARS-CoV-2 continues to infect people across the world, and is constantly mutating and evolving into new variants, its severity has in general been greatly reduced thanks to effective vaccines.

At the same time, an estimated two million people in the UK report long COVID, of which nearly one-fifth have symptoms so severe the condition significantly limits their day-to-day activities.

While there are a few theories as to what contributes to long COVID, including microclots in the blood and chronic inflammation, we don’t really know why some people are affected and others are not. So perhaps our focus should shift from the genetic determinants of immunity to SARS-CoV-2 to exploring whether some people may have a genetic predisposition to a potentially life-altering chronic disease.

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