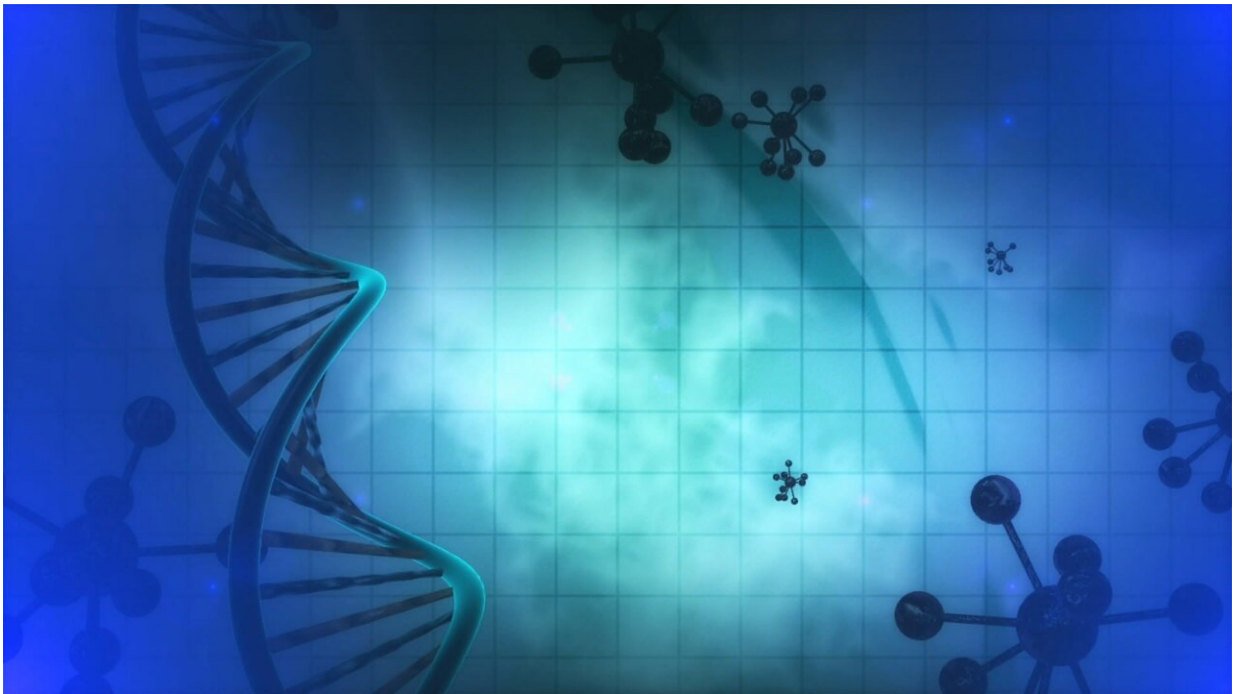


Gene variant that protects against COVID-19 identified

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An international metastudy led by researchers at Karolinska Institutet has identified a specific gene variant that protects against severe COVID-19 infection. The researchers managed to pinpoint the variant by studying people of different ancestries, a feat they say highlights the importance of conducting clinical trials that include people of diverse descents. The results are published in the journal *Nature Genetics*.

In addition to old age and certain underlying diseases, genetics can influence whether we become severely affected or only suffer mild illness from COVID-19. Previous studies on mainly people of European ancestry have found that individuals carrying a particular segment of DNA have a 20 percent lower risk of developing a critical COVID-19 infection. This DNA segment encodes [genes](#) in the [immune system](#) and is inherited from Neanderthals in about half of all people outside Africa.

This region of DNA is, however, packed with numerous genetic variants, which makes it challenging to disentangle the exact protective variant that could potentially serve as a target for medical treatment against severe COVID-19 infection.

Studied people of different ancestries

To identify this specific gene variant, researchers in the current study looked for individuals carrying only parts of this DNA segment. Since the Neandertal inheritance occurred after the ancient migration out of Africa, the researchers saw a potential in focusing on individuals with African ancestry who lack heritage from the Neanderthals and therefore also the majority of this DNA segment. A small piece of this DNA region is, however, the same in both people of African and European ancestries.

The researchers found that individuals of predominantly African ancestry had the same protection as those of European ancestry, which allowed them to pinpoint a specific gene variant of particular interest.

"The fact that individuals of African descent had the same protection allowed us to identify the unique variant in the DNA that actually protects from COVID-19 infection," says Jennifer Huffman, the first author of study and a researcher at the VA Boston Healthcare System in the U.S.

The analysis included a total of 2,787 hospitalized COVID-19 patients of African ancestry and 130,997 people in a [control group](#) from six cohort studies. Eighty percent of individuals of African ancestry carried the protective variant. The outcome was compared with a previous, larger metastudy of individuals of European heritage.

Key for COVID drug development

According to the researchers, the protective gene variant (rs10774671-G) determines the length of the protein encoded by the gene OAS1. Prior studies have shown that the longer variant of the protein is more effective at breaking down SARS-CoV-2, the virus causing the disease COVID-19.

"That we are beginning to understand the genetic risk factors in detail is key to developing new drugs against COVID-19," says co-author Brent Richards, senior investigator at the Lady Davis Institute of the Jewish General Hospital and professor at McGill University in Canada.

Underscores need for diversity

The COVID-19 pandemic has spurred considerable collaboration among researchers in different parts of the world, which has made it possible to study genetic risk factors in a wider diversity of individuals than in many previous studies. Even so, the majority of all clinical research is still being done on individuals of predominantly European descent.

"This study shows how important it is to include individuals of different ancestries. If we had only studied one group, we would not have been successful in identifying the gene variant in this case," says the study's corresponding author Hugo Zeberg, assistant professor at the Department of Neuroscience at Karolinska Institutet.

More information: Hugo Zeberg, Multi-ancestry fine mapping implicates OAS1 splicing in risk of severe COVID-19, *Nature Genetics* (2022). [DOI: 10.1038/s41588-021-00996-8](https://doi.org/10.1038/s41588-021-00996-8).
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