Identification of new genomic regions that influence the severity of COVID-19 disease

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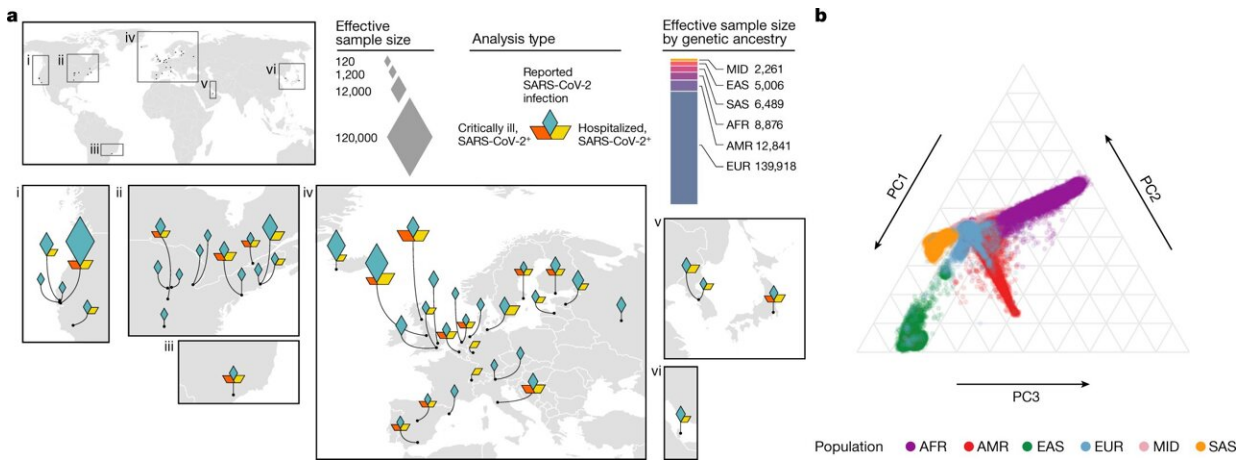

Overview of contributing studies in Host Genetics Initiative data freeze 6. A, Geographical overview of the contributing studies to the COVID-19 Host Genetics Initiative and composition by major continental ancestry groups. Ancestry groups are defined as Middle Eastern (MID), south Asian (SAS), east Asian (EAS), African (AFR), admixed American (AMR) and European (EUR). B, Principal components analysis highlighting the population structure and the sample ancestry of the individuals participating in the COVID-19 Host Genetics Initiative. This figure is reproduced from the original publication by the COVID-19 Host Genetics Initiative with modifications reflecting the updated analysis from data freeze 6. Credit: *Nature* (2022). DOI: 10.1038/s41586-022-04826-7

An international collaboration of human geneticists involving researchers

at Queen Mary University of London and the Genes & Health study has identified 11 new genomic regions that influence the severity of COVID-19 disease.

The results will help the team better understand why people get infected with SARS-CoV-2, and why some people get very severe disease, for example becoming hospitalized with COVID-19.

The paper "A first update on mapping the human genetic architecture of COVID-19" published in *Nature* on Wednesday, August 4, 2022, presents a genome-wide association study meta-analysis of more than 125,000 cases and over 2.5 million control individuals across 60 studies from 25 countries for three COVID-19-related phenotypes.

These phenotypes include individuals critically ill with COVID-19 who required respiratory support in hospital or died from the disease; individuals with moderate or severe COVID-19 hospitalized due to symptoms associated with the infection; and all cases with reported SARS-CoV-2 infection regardless of symptoms.

The study found that genetic variation in the gene that codes for lung surfactant proteins can affect the severity of COVID-19 disease. Lung surfactant helps "grease" lung movement when breathing and protects against some infections.

One variation in the Surfactant Protein D (SFTPD) gene confers risk for hospitalization and has been previously associated with increased risk of other lung diseases such as chronic obstructive pulmonary disease and decreased lung function. SFTPD encodes surfactant protein D (SP-D), which participates in innate immune response, protecting the lungs against inhaled microorganisms.

Another genetic variation in an area named SLC22A31 also confers risk

of hospitalization. SLC22A31 belongs to the family of solute carrier proteins that facilitate transport across membranes and is co-regulated with other surfactant proteins.

Professor David van Heel, Professor of Genetics at the Blizard Institute and Chief Investigator and Joint Lead for East London Genes & Health, said, "Some risk factors for COVID-19 disease severity have already been identified, such as obesity and older age. We also have protective treatments such as vaccines and drugs, but we wanted to know what role your genetic make-up plays.

"The COVID-19 pandemic continues to pose a major public health threat, especially in countries with low vaccination rates. The more we can understand about viral infection, the more we will know should there be any future pandemics."

The Genes & Health study hosted at the Blizard Institute at Queen Mary was one of many international cohorts who contributed to the multiple phenotype analyses of the initiative by providing data on British south Asians, who have had some of the worst health outcomes in the U.K. from COVID-19. Many other genetic studies have focused on people of white European ethnicity.

Thanks to this type of data, the initiative was able to test whether the effect of COVID-19-related genetic variants was markedly different across ancestry groups. The study did not detect obvious differences between ancestry groups, attributing observed differences in the effect of COVID-19-related genetic variants to the differing inclusion criteria across studies in terms of classifying COVID-19 severity. However, it was also noted that these differences across the studies might mask the true underlying differences in effect sizes between ancestry groups.

More information: A first update on mapping the human genetic

architecture of COVID-19, *Nature* (2022). DOI: 10.1038/s41586-022-04826-7