

Gene protection for COVID-19 identified

4 June 2021

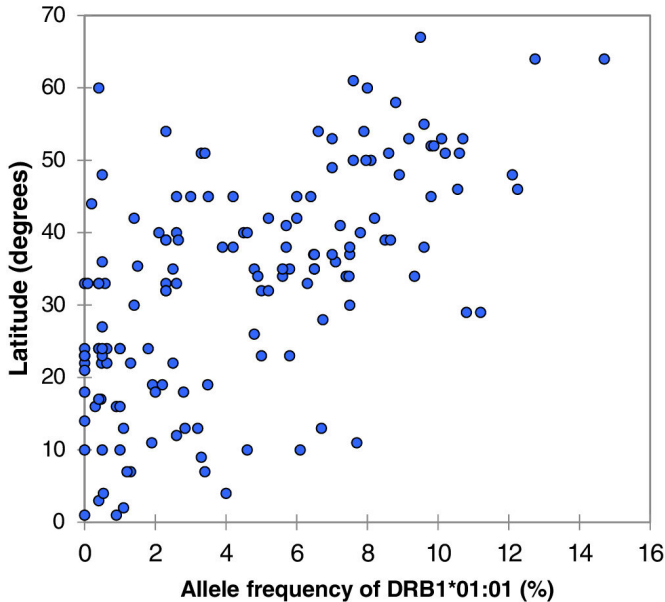


FIGURE 1 The relationship between latitude and allele frequency of HLA-DRB1*01:01 in 151 populations from around the world. Spearman rank correlation $r = .609$, $P = .001$

The first evidence of a genetic link explaining why some people who catch COVID-19 don't become sick has been discovered.

A scientific and medical team led by Newcastle University, UK, have demonstrated that the gene, HLA-DRB1*04:01, is found three times as often in people who are asymptomatic. This suggests that people with this gene have some level of protection from severe COVID.

The study, funded by Innovate UK, the UK's innovation agency, compared asymptomatic people to patients from the same community who developed severe COVID but had no underlying illnesses, and is published today in the HLA journal.

The study team believe this is the first clear evidence of genetic resistance because this study

compared severely affected people with an asymptomatic COVID group and used next generation sequencing to focus in detail and at scale on the HLA [genes](#) which are packed together on chromosome 6. Other studies have scanned the whole genome but that approach is less effective in the tissue typing complex.

Genome wide studies can be likened to a satellite image. The [high density](#) and complexity of the histocompatibility complex and variation in different populations means significant variation can be overlooked. For example, different alleles or versions of the same gene could have opposite effects on the immune response. This study was much more focused and compared symptomatic to asymptomatic in the same population revealing the "protective" qualities of the allele.

It is known that the human leukocyte antigen gene identified, HLA-DRB1*04:01, is directly correlated to latitude and longitude. This means more people in the North and West of Europe are likely to have this gene.

This suggests that populations of European descent will be more likely to remain asymptomatic but still transmit the disease to susceptible populations.

Dr. Carlos Echevarria from the Translational and Clinical Research Institute, Newcastle University who also works as a Respiratory Consultant in the Newcastle Hospitals NHS Foundation Trust and is a co-author of the paper says: "This is an important finding as it may explain why some people catch COVID but don't get sick.

"It could lead us to a genetic test which may indicate who we need to prioritize for future vaccinations."

"At a population level, this is important for us to know because when we have lots of people who are resistant, so they catch COVID but don't show symptoms, then they risk spreading the virus while

asymptomatic."

Geolocation

The effect of genes being linked to geolocation is an accepted scientific concept and it is well known that HLA genes develop over generations in reaction to disease-causing pathogens.

Study author, David Langton, whose company [ExplantLab](#) helped fund the study through an Innovate UK research award, added: "Some of the most interesting findings were the relationships between longitude and latitude and HLA gene frequency. It has long been known that the incidence of multiple sclerosis increases with increasing latitude. This has been put down in part to reduced UV exposure and therefore lower vitamin D levels. We weren't aware, however, that one of the main risk genes for MS, that is DRB1*15:01, directly correlates to latitude.

"This highlights the complex interaction between environment, genetics and disease. We know some HLA genes are vitamin D responsive, and that low vitamin D levels are a risk factor for severe COVID and we are doing further work in this area."

The study used samples from 49 patients with severe COVID who had been hospitalized with respiratory failure, samples from an asymptomatic group of 69 hospital workers who had tested positive through routine blood antibody testing and a control group from a study into the relationship between HLA genotypes and the outcomes of joint replacement surgery.

The study used next generation sequencing machines to study the different versions, or alleles, of the HLA genes in depth which was combined with a variety of expertise and modeling. The research was limited to samples from North East England during the first lockdown. This reduced variation in the study groups but more studies will be needed in the UK and other populations as there may be different copies of the HLA genes providing resistance in other populations.

The work was a collaboration between Newcastle University, Newcastle Hospitals NHS Foundation

Trust, Northumbria Healthcare NHS Foundation Trust as well as the South Tees Hospitals NHS Foundation Trust and North Tees and Hartlepool Hospitals NHS Foundation Trust.

Co-author, Professor Sir John Burn, Professor of Clinical Genetics at Newcastle University said: "SARS Cov-2 is one of the greatest threats Mankind has faced. The more we understand why some people become sick, the better we can defend ourselves against this virus and others like it in future."

More information: David J. Langton et al, The influence of HLA genotype on the severity of COVID-19 infection, *HLA* (2021). [DOI: 10.1111/tan.14284](https://doi.org/10.1111/tan.14284)

Provided by Newcastle University

APA citation: Gene protection for COVID-19 identified (2021, June 4) retrieved 10 June 2021 from <https://medicalxpress.com/news/2021-06-gene-covid-.html>

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