Mapping the human genetic architecture of COVID-19

COVID-19 Host Genetics Initiative

Nature volume 600, pages472–477 (2021)

Author : Dr. Hajar Fauzan Bin Ahmad

Abstract

The genetic make-up of an individual contributes to the susceptibility and response to viral infection. Although environmental, clinical and social factors have a role in the chance of exposure to SARS-CoV-2 and the severity of COVID-191,2, host genetics may also be important. Identifying host-specific genetic factors may reveal biological mechanisms of therapeutic relevance and clarify causal relationships of modifiable environmental risk factors for SARS-CoV-2 infection and outcomes. We formed a global network of researchers to investigate the role of human genetics in SARS-CoV-2 infection and COVID-19 severity. Here we describe the results of three genome-wide association meta-analyses that consist of up to 49,562 patients with COVID-19 from 46 studies across 19 countries. We report 13 genome-wide significant loci that are associated with SARS-CoV-2 infection or severe manifestations of COVID-19. Several of these loci correspond to previously documented associations to lung or autoimmune and inflammatory diseases3,4,5,6,7. They also represent potentially actionable mechanisms in response to infection. Mendelian randomization analyses support a causal role for smoking and body-mass index for severe COVID-19 although not for type II diabetes. The identification of novel host genetic factors associated with COVID-19 was made possible by the community of human genetics researchers coming together to prioritize the sharing of data, results, resources and analytical frameworks. This working model of international collaboration underscores what is possible for future genetic discoveries in emerging pandemics, or indeed for any complex human disease

https://doi.org/10.1038/s41586-021-03767-x

**References**

1. Docherty, A. B. et al. Features of 20 133 UK patients in hospital with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *Br. Med. J*. **369**, m1985 (2020).

[Google Scholar](http://scholar.google.com/scholar_lookup?&title=Features%20of%2020%E2%80%89133%20UK%20patients%20in%20hospital%20with%20COVID-19%20using%20the%20ISARIC%20WHO%20Clinical%20Characterisation%20Protocol%3A%20prospective%20observational%20cohort%20study&journal=Br.%20Med.%20J.&volume=369&publication_year=2020&author=Docherty%2CAB)

1. Zhou, F. et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* **395**, 1054–1062 (2020).

[CAS](http://umpir.ump.edu.my/articles/cas-redirect/1:CAS:528:DC%2BB3cXkvVGktL8%3D)  [PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Abstract&list_uids=32171076)  [PubMed Central](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC32171076)  [Google Scholar](http://scholar.google.com/scholar_lookup?&title=Clinical%20course%20and%20risk%20factors%20for%20mortality%20of%20adult%20inpatients%20with%20COVID-19%20in%20Wuhan%2C%20China%3A%20a%20retrospective%20cohort%20study&journal=Lancet&volume=395&pages=1054-1062&publication_year=2020&author=Zhou%2CF)

1. Dendrou, C. A. et al. Resolving *TYK2* locus genotype-to-phenotype differences in autoimmunity. *Sci. Transl. Med*. **8**, 363ra149 (2016).

[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Abstract&list_uids=27807284)  [PubMed Central](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC27807284)  [Google Scholar](http://scholar.google.com/scholar_lookup?&title=Resolving%20TYK2%20locus%20genotype-to-phenotype%20differences%20in%20autoimmunity&journal=Sci.%20Transl.%20Med.&volume=8&publication_year=2016&author=Dendrou%2CCA)