

Researchers identify genetic factors that may influence COVID-19 susceptibility

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A new Cleveland Clinic study has identified genetic factors that may influence susceptibility to COVID-19. Published today in *BMC Medicine*, the study findings could guide personalized treatment for

COVID-19.

While the majority of confirmed COVID-19 cases result in mild symptoms, the virus does pose a serious threat to certain individuals. Morbidity and [mortality rates](#) rise dramatically with age and co-existing health conditions, such as cancer and cardiovascular disease. However, even young and otherwise healthy individuals have unpredictably experienced severe illness and death. These clinical observations suggest that [genetic factors](#) may influence COVID-19 disease susceptibility, but these factors remain largely unknown.

In this study, a team of researchers led by Feixiong Cheng, Ph.D., Genomic Medicine Institute, investigated genetic susceptibility to COVID-19 by examining DNA polymorphisms (variations in DNA sequences) in the ACE2 and TMPRSS2 genes. ACE2 and TMPRSS2 produce enzymes (ACE2 and TMPRSS2, respectively) that enable the virus to enter and infect [human cells](#).

Looking at 81,000 [human genomes](#) from three genomic databases, they found 437 non-synonymous single-nucleotide variants in the protein-coding regions of ACE2 and TMPRSS2. They identified multiple potentially deleterious polymorphisms in both genes (63 in ACE2; 68 in TMPRSS2) that offer potential explanations for different genetic susceptibility to COVID-19 as well as for risk factors. Several ACE2 variants were found to be associated with cardiovascular and pulmonary conditions by potentially altering the angiotensinogen-ACE2. In addition, germline deleterious variants in the coding region of TMPRSS2, a key gene in prostate cancer, were found to occur in different cancer types, suggesting that oncogenic roles of TMPRSS2 may be linked to poor outcomes with COVID-19.

These findings demonstrate a possible association between ACE2 and TMPRSS2 polymorphisms and COVID-19 susceptibility, and indicate

that a systematic investigation of the functional polymorphisms these variants among different populations could pave the way for precision medicine and personalized treatment strategies for COVID-19.

However, all investigations in this study were performed in general populations, not with COVID-19 patient genetic data. Therefore, Dr. Cheng calls for a human genome initiative to validate his findings and to identify new clinically actionable variants to accelerate precision medicine for COVID-19.

"Because we currently have no approved drugs for COVID-19, repurposing already approved drugs could be an efficient and cost-effective approach to developing prevention and treatment strategies," Dr. Cheng said. "The more we know about the genetic factors influencing COVID-19 susceptibility, the better we will be able to determine the clinical efficacy of potential treatments."

More information: Yuan Hou et al, New insights into genetic susceptibility of COVID-19: an ACE2 and TMPRSS2 polymorphism analysis, *BMC Medicine* (2020). [DOI: 10.1186/s12916-020-01673-z](https://doi.org/10.1186/s12916-020-01673-z)

Provided by Cleveland Clinic

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