# Researchers identify genetic factors that may influence COVID-19 susceptibility

July 15 2020

Credit: CC0 Public Domain

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

Provided by Cleveland Clinic