

Researchers uncover diabetes as a potential risk factor for COVID-19, and possible mechanisms

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Researchers from the School of Biomedical Sciences of the Faculty of Medicine at The Chinese University of Hong Kong (CU Medicine) have recently applied an advanced statistical approach to analyze risk factors that may be causally related to COVID-19 infection. Results suggested that diabetes may be a risk factor leading to increased susceptibility to or severity of COVID-19 infection through changes in ACE2 expression, which is a key receptor for the virus. A substantial proportion of COVID-19 death cases in Hong Kong suffered from diabetes. There is an urgent need to confirm risk factors and the mechanisms in order to protect the susceptible groups and identify effective treatments. The current study results were recently published in the international scientific journal Diabetes Care.

High ACE2 receptor expression in diabetes patients may lead to increased susceptibility to or severity of COVID-19 infection

The COVID-19 pandemic has affected more than a hundred countries or regions worldwide, and more than 11 million confirmed cases have been reported. It is urgent to seek solutions to control

the spread of the disease to susceptible groups, and to identify effective treatments. A better understanding of its pathophysiology is also desperately needed.

A research team at the School of Biomedical Sciences at CU Medicine applied an advanced statistical approach known as Mendelian randomisation to analyze <u>risk factors</u> that may be causally related to the disease. The team made use of "big data" from <u>genome-wide association studies</u> to explore diseases and blood proteins causally linked to altered ACE2 expression in the lung. There is sound evidence that ACE2 is a key receptor for COVID-19, and high expression of ACE2 may increase susceptibility to infection.

Through a screen of over 500 diseases or traits, the most consistent finding was tentative evidence of an association between diabetes-related traits and increased ACE2 expression. Significant and positive associations with ACE2 expression were observed across multiple diabetes datasets and analytic methods for type 1 and 2 diabetes as well as related traits including early start of insulin. The results suggest that diabetes may be a risk factor leading to increased susceptibility to or severity of COVID-19 infection through changes in ACE2 expression.

Study results may guide drug repositioning in the future

As an exploratory analysis, blood proteins linked to altered ACE2 expression were also found and examined by the team, which may help elucidate potential molecular mechanisms, and serve as potential biomarkers and guide drug development or repurposing in the future.

Dr. Hon Cheong SO, Assistant Professor of the

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School of Biomedical Sciences at CU Medicine, who led the study, said, "There is great potential for using genomic big data to uncover risk factors and treatments for COVID-19. One important aspect of this study is that we employ Mendelian randomisation, which is better at delineating causal relationships than observational studies. We emphasize that our study is largely exploratory and the present findings are still preliminary; however, we hope the current work will shed light on new research strategies and lead to more confirmatory studies in this area in the future."

More information: Shitao Rao et al. Exploring Diseases/Traits and Blood Proteins Causally Related to Expression of ACE2, the Putative Receptor of SARS-CoV-2: A Mendelian Randomization Analysis Highlights Tentative Relevance of Diabetes-Related Traits, *Diabetes Care* (2020). DOI: 10.2337/dc20-0643

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