SARS-CoV-2 induces inflammation, cytokine storm and stress in infected lung cells

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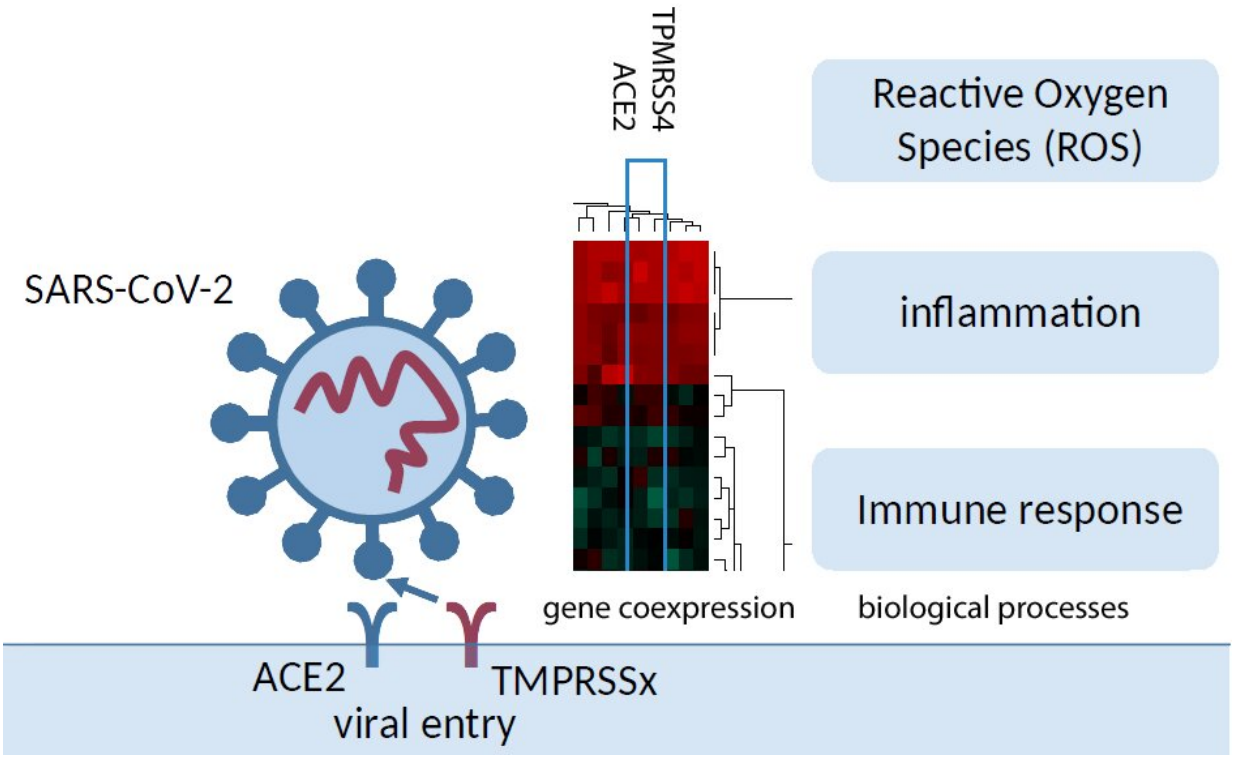

The coronavirus SARS-CoV-2 docks with its spike protein onto the receptor-ACE2 found on the surface of lung cells. The levels of co-expressed genes with the human receptor-ACE2 were calculated from several publicly available datasets pertaining to lung epithelial cells infected with SARS-CoV-2. The resulting gene-signature consisted of members from the Trans-Membrane-Serine-Protease (TMPRSS) gene family which prime the virus spike protein for cell entry. Other genes from the gene-signature are associated with reduced immune responses and activated inflammation, Reactive Oxygen Species (ROS) and

cellular stress. Credit: WruckW /AdjayeJ, HHU Duesseldorf, Germany

The researchers Wasco Wruck and Prof. James Adjaye from the Institute of Stem Cell Research and Regenerative Medicine, Medical Faculty of Heinrich-Heine-University Duesseldorf, Germany, employed a bioinformatic approach on transcriptome data pertaining to human lung epithelial cells infected with SARS-CoV-2. The meta-analysis unveiled several adversely affected biological processes in the lung which no doubt also applies to other infected organs such as the heart and kidney. Their study is published in *Scientific Reports*.

With a current estimation of more than 60 million infected people and more than 1.4 million recorded deaths worldwide, COVID-19—the disease caused by the coronavirus SARS-CoV-2, and classified as a pandemic by the WHO—poses a threat to public health, national economies and society as a whole. Although effective vaccines are becoming available, we still need a better understanding of the molecular mechanisms underlying the etiology of COVID-19 to enable more effective therapies in the future.

Wasco Wruck, first author of the study, says: "We initially viewed the results of the analysis in an unbiased manner. To our surprise, we noticed that several Transmembrane Serine Proteases besides the already known TMPRSS2 were highly correlated with ACE2 expression. Furthermore, in a more in-depth analysis, the gene-signature could be annotated with numerous biological processes. Among these were regulation of viral life cycle, immune responses, pro-inflammatory responses, several interleukins such as IL6, IL1, IL20 and IL33, IFI16 regulating the interferon response to a virus, chemo-attraction of macrophages, and cellular stress resulting from activated Reactive Oxygen Species.

Prof. James Adjaye, senior author of the study, summarizes: "We have shown that not having access or the necessary infrastructure to carry out research with the deadly coronavirus SARS-CoV-2 should not preclude progress in dissecting the etiology underlying COVID-19. There are currently numerous transcriptome-based datasets related to experiments carried out on numerous cell types infected with SARS-CoV-2 which can be retrieved and analyzed to identify adversely affected biological processes with the hope of identifying putative druggable targets which can be used to better manage COVID-19 in the future."

More information: Wasco Wruck et al. SARS-CoV-2 receptor ACE2 is co-expressed with genes related to transmembrane serine proteases, viral entry, immunity and cellular stress, *Scientific Reports* (2020). DOI: 10.1038/s41598-020-78402-2

Provided by Heinrich-Heine University Duesseldorf