Study details critical role of viral gene ORF8 in COVID-19 infection and outcomes

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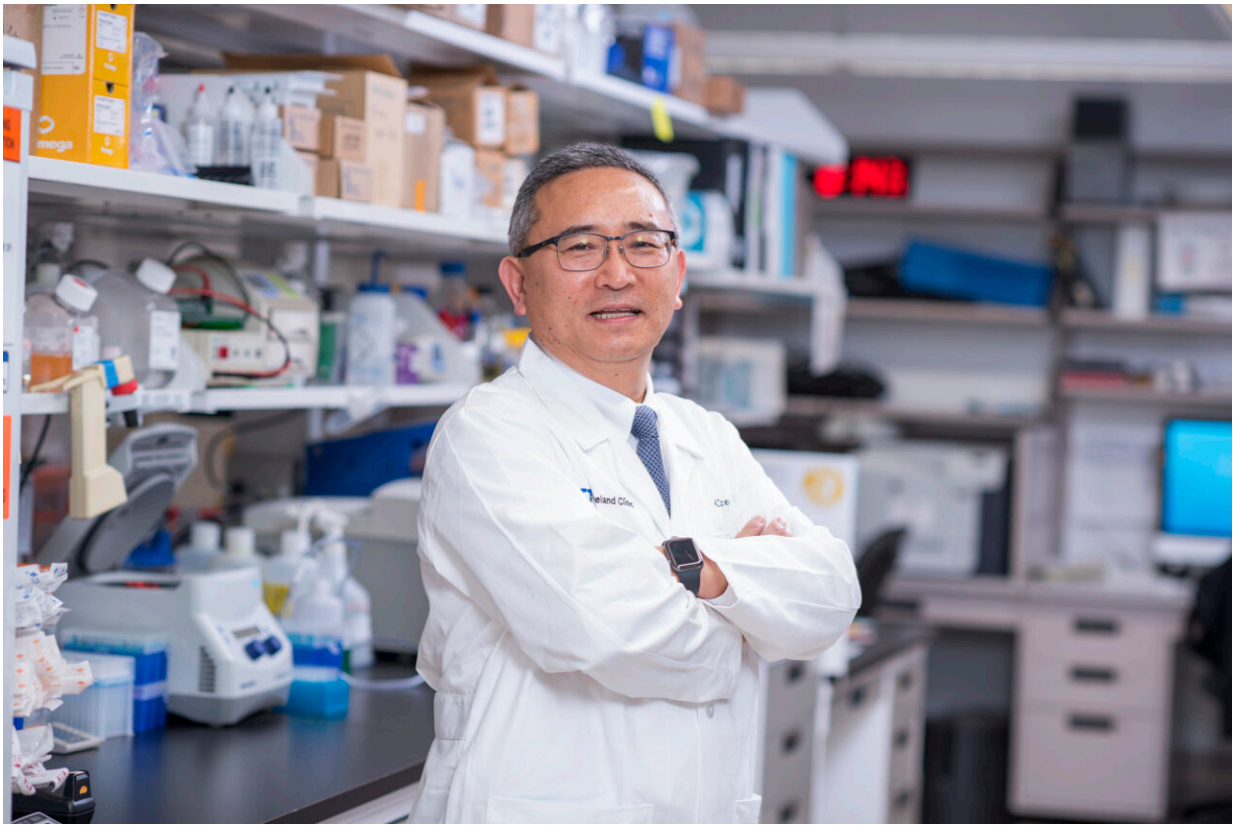

A research team led by Jae Jung, PhD, Director of Cleveland Clinic's Global Center for Pathogen & Human Health Research, has uncovered the critical role a viral gene, ORF8, plays in infection and disease outcomes of SARS-CoV-2. Credit: Cleveland Clinic

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Global Center for Pathogen & Human Health Research, has uncovered the critical role a viral gene, ORF8, plays in infection and disease outcomes of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19.

The study, published in *mBio*, provides a greater understanding of molecular mechanisms that can accelerate immune cell activation and could suggest treatments for patients with COVID-19. This is the first published study using samples from the COVID-19 registry of the Cleveland Clinic BioRepository.

"Understanding human health and disease requires studying human biological samples and knowledge of the clinical situation surrounding the disease," said Lara Jehi, MD, Chief Research Information Officer, Cleveland Clinic. "By aligning research with clinical care, the BioRepository provides an innovative and efficient way to bridge data and samples at a scale that can only be accomplished by a large research-based academic medical center like Cleveland Clinic."

While previous studies have shown that those with severe cases of COVID-19 often develop signs of acute respiratory distress syndrome (ARDS), many basic aspects of the SARS-CoV-2 virus remain unknown.

According to the new findings by Dr. Jung and his team, SARS-CoV-2 Open reading frame 8 (ORF8), a viral inflammatory protein, contributes to the severity and spread of COVID-19.

"Our team studied the triggers for cytokine meditated inflammation and identified the ORF8 as a stand out viral gene showing its mutations that were related to the virus's ability to inflame and spread," said Dr. Jung.

"We knew patients infected with SARS-CoV-2 variants that lacked ORF8 were associated with milder infection outcomes," said Dr. Xin

Wu, a postdoctoral fellow in Dr. Jung's lab who led this study. The study revealed that SARS-CoV-2 ORF8 is a viral mimic of another inflammatory protein that contributes to severe inflammation."

"The resources and COVID-19 samples provided by the BioRepository were essential in understanding the relationship between plasma ORF8 levels of SARS-COV-2 and COVID-19 disease outcomes," said Dr. Wu. "In this case, understanding the role of ORF8 can lead to new treatments that could provide benefits for patients with severe COVID-19."

Cleveland Clinic and Azenta Sciences partnered to build the state-of-the-art biorepository in the newly formed Cleveland Innovation District. The innovative cryostorage facility houses biological samples that researchers can access and analyze on-site, leading to accelerated research for the development of new disease treatments.

"The Cleveland Clinic BioRepository will transform the speed and impact of our research," said Dr. Jehi. "The work by Dr. Jung and his team is an excellent first of many more to come."

More information: Xin Wu et al, Viral Mimicry of Interleukin-17A by SARS-CoV-2 ORF8, *mBio* (2022). DOI: 10.1128/mbio.00402-22

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