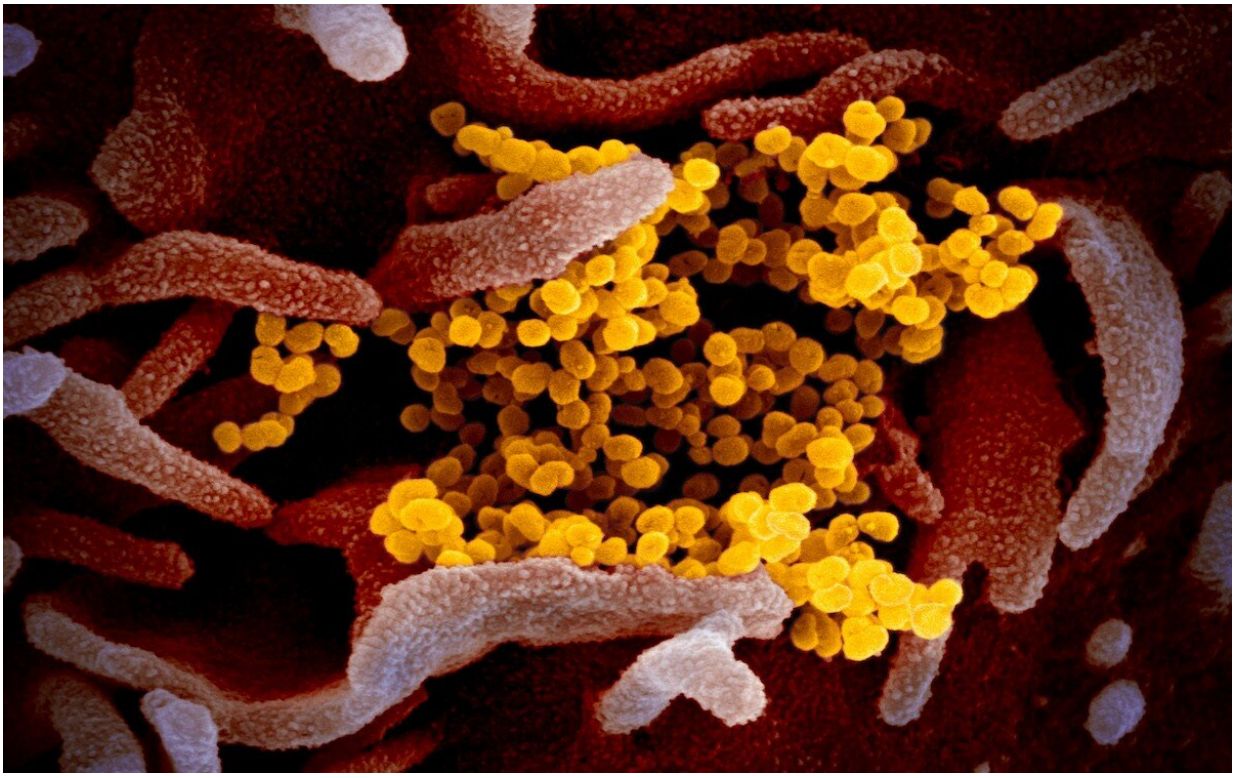
COVID-19: Enzyme targeted by virus also influences gut inflammation

November 5 2020



The novel coronavirus as seen under a microscope. Credit: Courtesy of the National Institutes of Health.

An enzyme that helps COVID-19 (coronavirus) infect the body also plays a role in inflammation and patient outcomes in inflammatory bowel disease (IBD), according to a new study led by Cedars-Sinai. The

findings raise the possibility that anti-inflammatory drug therapies for IBD may aid recovery from coronavirus.

The multisite study, led by Cedars-Sinai and published today in the journal *Gastroenterology*, focused on angiotensin-converting enzyme 2 (ACE2), which normally plays a crucial health role by activating a hormone that helps regulate blood pressure. But in COVID-19 infections, the SARS-CoV-2 virus binds to ACE2 and uses it to invade and infect cells, "hijacking" them to spread the virus.

To learn more about how ACE2 affects the body, investigators examined its role in Crohn's disease and ulcerative colitis—two types of IBD that can cause inflammation and scarring (fibrosis) in the digestive tract along with diarrhea, cramping and loss of appetite.

"We chose these disorders because COVID-19, while known for attacking the lungs, frequently causes gastrointestinal symptoms," said Dermot P. McGovern, MD, Ph.D., the Joshua L. and Lisa Z. Greer Chair in Inflammatory Bowel Disease Genetics and senior author of the new study. "It was important for us to understand how COVID-19 might affect IBD patients who are treated with anti-inflammatory medications. Also, there is increasing evidence that the GI tract may serve as an alternate route for uptake of SARS-COV-2 in general."

By examining records of nearly 1,000 patients at Cedars-Sinai, Washington University in St. Louis, Missouri, and multiple other centers across North America, the team found that levels of ACE2 in the small bowel were lower in Crohn's patients and higher in the colons of ulcerative colitis patients than they were in patients without IBD. The differing ACE2 levels were associated with poorer outcomes and more severe disease in the IBD patients.

"We saw that the effect of ACE2 depended on both its specific location

in the gastrointestinal tract and the specific disease involved," said McGovern, professor of Medicine and Biomedical Sciences. "So, this enzyme was a double-edged sword."

In both types of IBD, treatment with infliximab, an anti-inflammatory drug, normalized the levels of ACE2 and was associated with improved disease outcomes in patients. This finding suggests these drugs, commonly used in autoimmune diseases, also might improve outcomes in COVID-19, the investigators said.

"Overall, our study supports the potential paradoxical function of ACE2 in inflammation and COVID-19," McGovern explained. "Individuals with higher ACE2 expression may be at increased risk of infection with SARS-CoV-2. But judging from our discoveries of how ACE2 works in IBD, this enzyme likely has anti-inflammatory and anti-fibrotic functions that also could help certain COVID-19 patients recover from the virus."

Further research is needed to delineate the processes involving ACE2 and what they might mean for treating COVID-19 patients, he said. In support of that effort, the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health recently awarded a two-year grant of $677,036 to McGovern to examine overlaps in the mechanisms that drive inflammation in IBD and COVID-19.

More information: Alka A. Potdar et al, Altered intestinal ACE2 levels are associated with inflammation, severe disease and response to anti-cytokine therapy in IBD, *Gastroenterology* (2020). DOI: 10.1053/j.gastro.2020.10.041

Provided by Cedars-Sinai Medical Center