Identifying a new protein that enables SARS-CoV-2 access into cells

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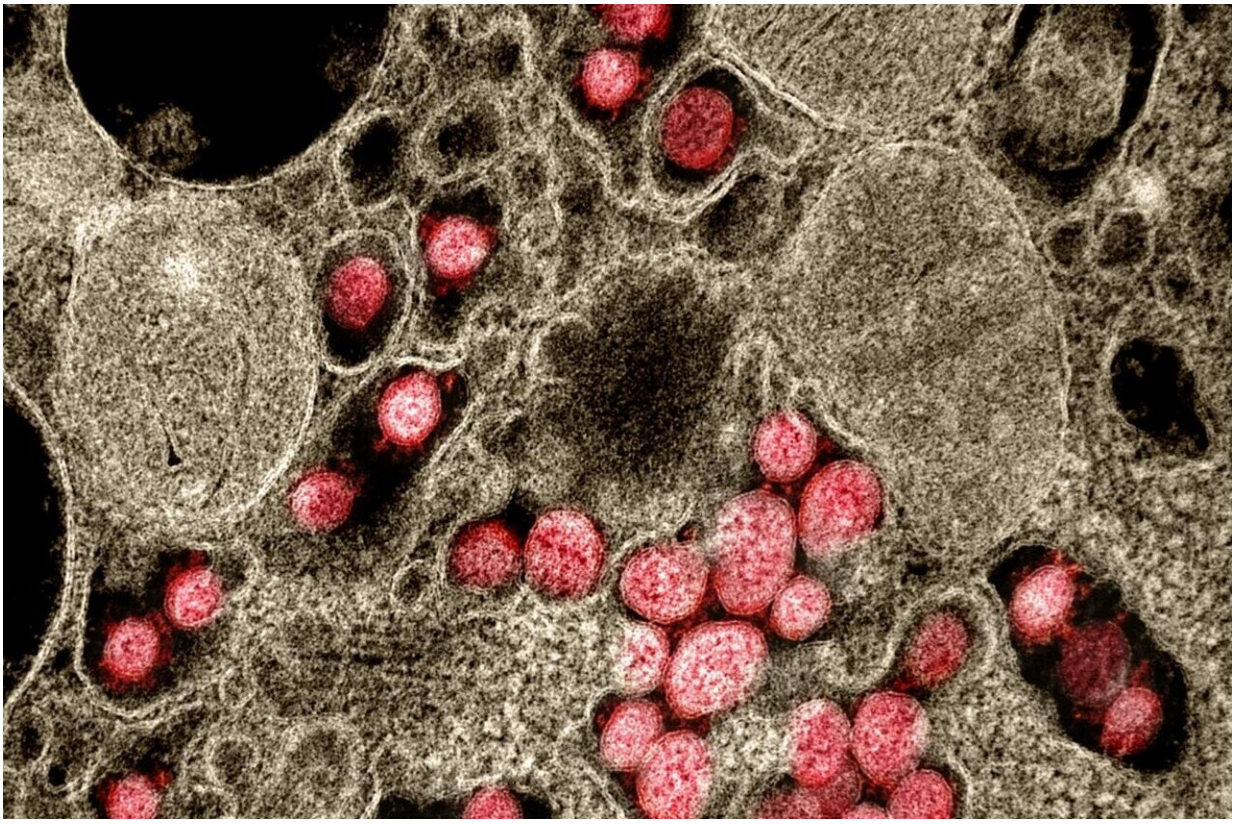

Transmission electron micrograph of SARS-CoV-2 virus particles isolated from a patient. Credit: NIAID

The entry of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into human cells is an essential step for virus transmission and

development of COVID 19. Although the lung epithelial cells are its initial target, SARS-CoV-2 also can infect endothelial cells. Endothelial cells are the major constituents of the vascular system and cardiovascular complication is a hallmark of severe COVID-19. Angiotensin-converting enzyme 2 (ACE2) is the entry receptor for SARS-CoV-2. However, the possible involvement of other cellular components in the viral entry is not fully understood.

A team of researchers from the Boston University School of Medicine (BUSM) has identified extracellular vimentin as an attachment factor that facilitates SARS-CoV-2 entry into human cells. Vimentin is a structural protein that is widely expressed in the cells of mesenchymal origin such as endothelial cells and a potential novel target against SARS-CoV-2, which could block the infection of the SARS-CoV-2.

"Severe endothelial injury, vascular thrombosis, and obstruction of alveolar capillaries (tiny air sacs scattered throughout the lungs) are common features of severe COVID-19. Identification of vimentin as a host attachment factor for SARS-CoV-2 can provide new insight into the mechanism of SARS-CoV-2 infection of the vascular system and can lead to the development of novel treatment strategies," said corresponding author Nader Rahimi, Ph.D., associate professor of pathology & laboratory medicine at BUSM.

The researchers used liquid chromatography–tandem mass spectrometry (LC-MS/MS) and identified vimentin as a protein that binds to the SARS-CoV-2 spike (S) protein and facilitates SARS-CoV-2 infection. They also found that depletion of vimentin significantly reduces SARS-CoV-2 infection of human endothelial cells. In contrast, over-expression of vimentin with ACE2 significantly increased the infection rate. "More importantly, we saw that the CR3022 antibody inhibited the binding of vimentin with CoV-2-S-protein, and neutralized SARS-CoV-2 entry into human cells," explained Rahimi.

These findings appear online in the *Proceedings of the National Academy of Sciences*.

More information: Razie Amraei et al, Extracellular vimentin is an attachment factor that facilitates SARS-CoV-2 entry into human endothelial cells, *Proceedings of the National Academy of Sciences* (2022). DOI: 10.1073/pnas.2113874119