Innate immune system worsens the situation in severe COVID-19

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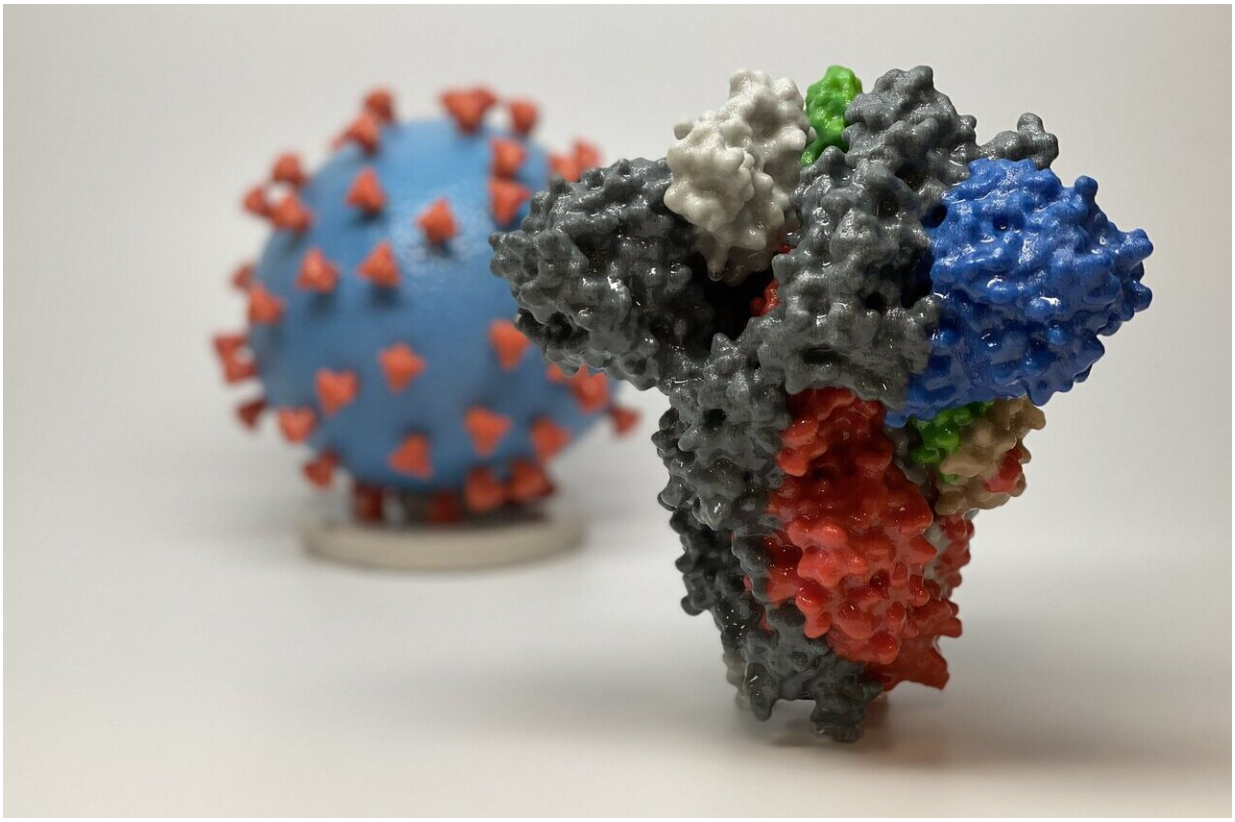

3D print of a spike protein of SARS-CoV-2, the virus that causes COVID-19—in front of a 3D print of a SARS-CoV-2 virus particle. The spike protein (foreground) enables the virus to enter and infect human cells. On the virus model, the virus surface (blue) is covered with spike proteins (red) that enable the virus to enter and infect human cells. Credit: NIH

In patients with severe COVID-19, the innate immune system overreacts. This overreaction may underlie the formation of blood clots (thrombi) and deterioration in oxygen saturation that affect the patients. This is shown in an Uppsala University study published in the journal Frontiers in Immunology.

Blood contains numerous proteins that constitute the body's primary barrier, by both recognizing and destroying microorganisms, including SARS-CoV-2 (the virus that causes COVID-19). These proteins are part of the intravascular innate immune system (IIIS), which consists of certain white blood cells, platelets and what are known as the cascade systems of the blood.

Only 5% of present-day animal species have an immune system that includes T cells and B cells, while the rest rely solely on the natural immune system, which consists largely of the IIIS. With its innate ability to recognize and eliminate foreign substances and particles, such as microorganisms and damaged cells, the IIIS serves as a kind of waste disposal system.

In the present study, in 2020, the researchers studied 66 hospital inpatients with severe COVID-19 who were receiving care in the intensive care unit, and found pronounced activation of the IIIS.

"It's probably the tissue damage, with dead cells in the lungs, that initiates this activation. It can potentially lead to clot formation and poor oxygen saturation due to increased leakage into the blood vessels," says Bo Nilsson, Professor at the Department of Immunology, Genetics and Pathology, who led the study.

The degree of activation is, in prognostic terms, connected with survival and lung function. Accordingly, the new findings support the notion that the IIIS is among the drivers of severe COVID-19. One explanation why,

in some patients with COVID-19, the IIIS acts in this way may be that the cell damage is so extensive that the IIIS overreacts and, rather than helping to clean out the tissue, makes matters worse.

If the IIIS plays the part that the scientists suspect, it might be possible to use drugs that are already approved and used for treating the disease hereditary angioedema for treating severe COVID-19 as well.

More information: Miklós Lipcsey et al. The Outcome of Critically Ill COVID-19 Patients Is Linked to Thromboinflammation Dominated by the Kallikrein/Kinin System, *Frontiers in Immunology* (2021). DOI: 10.3389/fimmu.2021.627579

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