Many COVID-19 patients produce immune responses against their body's tissues or organs

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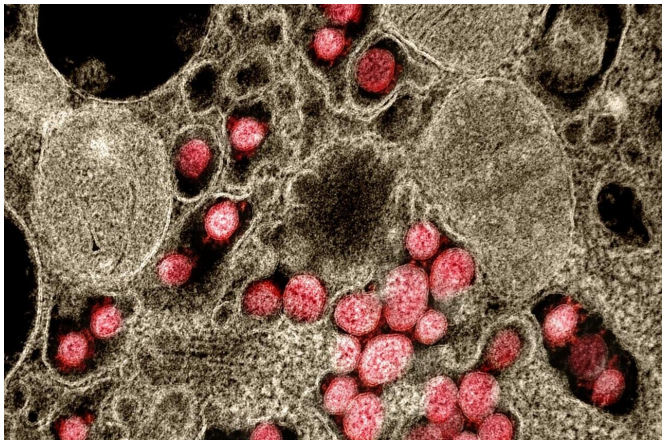

Transmission electron micrograph of SARS-CoV-2 virus particles isolated from a patient. Credit: NIAID

A University of Birmingham-led study funded by the UK Coronavirus Immunology Consortium has found that many patients with COVID-19 produce immune responses against their body's own tissues or organs.

COVID-19 has been associated with a variety of unexpected symptoms, both at the time of infection and for many months afterwards. It is not fully understand what causes these symptoms, but one of the possibilities is that COVID-19 is triggering an autoimmune process where the immune system is misdirected to attack itself.

The study, published today (June 4) in the journal *Clinical & Experimental Immunology,* investigated the frequency and types of common autoantibodies produced in 84 individuals who either had severe COVID-19 at the time of testing or in the recovery period following both severe COVID-19 and those with milder disease that did not need to attend hospital. These results were compared to a control group of 32 patients who were in intensive care for another reason other than COVID-19.

An autoantibody is an antibody (a type of protein) produced by the immune system that is directed against one or more of the individual's own proteins and can cause autoimmune diseases. Infection can, in some circumstances, lead to autoimmune disease. Early data suggest that SARS-CoV-2 infection can trigger long-term autoimmune complications and there are reports of SARS-CoV-2 infection being associated with a number of autoimmune disorders including Guillain-Barre Syndrome.

Supported by UK Research and Innovation (UKRI) and the National Institute for Health Research (NIHR), the study found higher numbers of autoantibodies in the COVID-19 patients than the control group and that these antibodies lasted up to six months.

Non-COVID patients displayed a diverse pattern of autoantibodies; in contrast, the COVID-19 groups had a more restricted panel of autoantibodies including skin, skeletal muscle and cardiac antibodies.

The authors also find that those with more severe COVID-19 were more likely to have an autoantibody in their blood.

First author Professor Alex Richter, of the University of Birmingham, explained: "The antibodies we identified are similar to those that cause a number of skin, muscle and heart autoimmune diseases.

"We don't yet know whether these autoantibodies are definitely causing symptoms in patients and

whether this is a common phenomenon after lots of infections or just following COVID-19. These questions will be addressed in the next part of our study."

Senior Author Professor David Wraith, of the University of Birmingham, adds: "In this detailed study of a range of different tissues, we showed for the first time that COVID-19 infection is linked to production of selective autoantibodies. More work is needed to define whether these antibodies contribute to the long-term consequences of SARS-CoV-2 infection and hence could be targeted for treatment."

Professor Paul Moss, Principal Investigator of the UK Coronavirus Immunology Consortium and Professor of Haematology at the University of Birmingham added: "This is an interesting study that reveals new insights into a potential autoimmune component to the effects of COVID-19. Research like this has been made possible by the huge collaborative efforts made by those that are a part of the UK Coronavirus Immunology Consortium. This study is another important step towards delivering real improvements in prevention, diagnosis, and treatment of COVID-19 to patients."

The study participants were separated into four cohorts:

Group one: 32 individuals sampled during their stay in intensive care for reasons other than COVID-19. 41% of individuals had autoantibodies. In this group, there were many different causes of their illness (over half was pneumonia) and autoantibodies were found against nearly all of the different autoantigens examined, indicating a more random distribution.

Group two: 25 individuals who were sampled during their stay in intensive care following a diagnosis of severe COVID-19. 60% had autoantibodies. Of those who tested positive for autoantibodies, 41% had epidermal (skin) antibodies, while 17% had skeletal antibodies.

Group three: 35 individuals who had been admitted to intensive care with COVID-19, survived and were sampled three to six months later during routine outpatient follow up. 77% of individuals had autoantibodies. Of those who tested positive for autoantibodies, 19% had epidermal (skin) antibodies, 19% had skeletal antibodies, 28% had cardiac muscle antibodies; and 31% had smooth muscle antibodies.

Group four: 24 healthcare workers sampled one to three months after mild to moderate COVID-19 that did not require hospitalisation. 54% of individuals had autoantibodies. In those who tested positive for autoantibodies, it was against only four autoantigens: 25% had epidermal (skin) antibodies; 17% had smooth muscle antibodies; 8% had anti-neutrophil cytoplasm (ANCA) antibodies that target a type of human white blood cells; and 4% had gastric parietal antibodies which are associated with autoimmune gastritis and anaemia.

More information: Alex G. Richter et al, Establishing the prevalence of common tissue?specific autoantibodies following SARS CoV?2 infection, *Clinical & Experimental Immunology* (2021). DOI: 10.1111/cei.13623

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