How 'Long COVID' affects our immune systems

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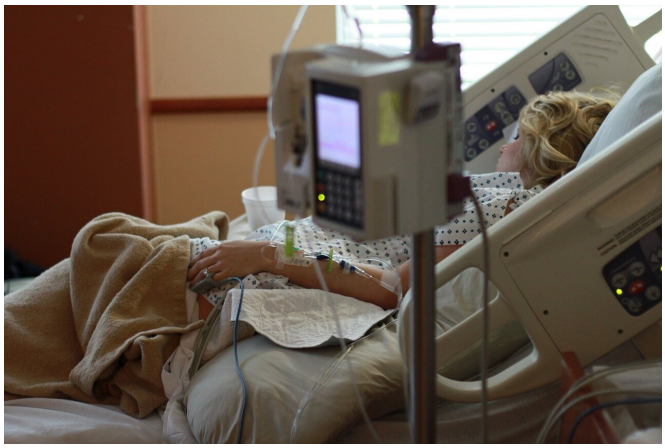

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A world-leading research collaboration in South Australia has delivered crucial insight into the lasting immune system dysregulation caused by COVID-19.

The study, conducted by experts at SAHMRI, Flinders University, the University of Adelaide, the Women's and Children's Hospital and the Royal Adelaide Hospital, showed that people's immune systems were significantly altered six months after their COVID-19 infection, with the immune cells and gene expression experienced during this post-infection period holding clues to the intriguing 'Long COVID' symptoms affecting some patients.

The immune systems of 69 participants between 20 and 80 years of age 'COVID-19 SA' were examined over a six-month period, following infection with the original strain of SARS-CoV-2, the virus that causes COVID-19. Of the total cohort, 47 were recovering from mild infection, six from moderate and 13 were recovering from severe or critical COVID-19 disease.

The unique longitudinal analysis examined antibody responses, the expression of thousands of genes in the blood, and approximately 130 different types of immune cells, via blood samples taken at 12, 16 and 24-weeks post infection. Responses were compared to healthy controls.

Flinders University Professor David Lynn—the Director of SAHMRI's Computational & Systems Biology Program—says the results show that the immune system of people previously infected with SARS-CoV-2 was significantly altered until at least six months post-infection.

"The study found substantial dysregulation of immune cell numbers that was strongest at 12-weeks post infection but was still evident in most cases for up to six months and potentially even longer," Professor Lynn says.

In addition to an increased number of immune cells and antibodies, there was also strong dysregulation of gene expression, particularly in those genes linked to inflammation. Gene expression refers to information stored in DNA that regulates how cells respond to changing environments.

This can include controlling when and how much response is made against an invading virus.

Professor Simon Barry, Head of Molecular Immunology Group at the University of Adelaide's Robinson Research Institute, says deep immunophenotyping will develop our understanding of how rare immune cells help repair the damage and set up immunity to COVID-19.

"By taking a deep dive into the immune cells in these patients, we've found some new players linked to the disease, and these may help understand why some people have more severe disease, or get Long COVID," he says.

The study didn't have the capacity to analyse the extent to which participants were experiencing the

symptoms commonly associated with Long COVID, such as fatigue, shortness of breath, chest pain and brain fog.

However, Professor Lynn says it's likely these symptoms are related to the upheaval of immune cells and gene expression.

"One could logically infer that this dysregulation is linked to the physical symptoms of Long COVID, however further research is needed to prove this," Professor Lynn says.

The reason why some individuals are so harshly affected by Long COVID, while others are barely affected, remains a mystery.

"At present there are no treatments for Long COVID sufferers and as the world slowly transitions to living with COVID, we will need to find answers and better solutions to prevent and treat Long COVID in the years to come" says Dr. Branko Grubor-Bauk, Head of Viral Immunology Group and THRF Mid-Career Fellow at the University of Adelaide and Basil Hetzel Institute for Translational Health Research.

Surprisingly, the research did not find a strong correlation between severity of infection and the severity of immune dysregulation post infection. Immune dysregulation was evident even in those patients who experienced mild infection.

"We've seen a very broad spectrum in the rate of recovery and we still don't understand why some people are recovering so much quicker than others," Professor Lynn explains.

"The level of disease severity doesn't translate directly to the level of immune dysregulation and we haven't been able to find any patterns indicating that an individual's age or sex is a differentiating factor governing differences in recovery. Clearly there are other factors at play that need to be explored," he says.

The study has also added further evidence that those who've had COVID-19 become immune to the virus.

Participants antibody titers indicated a high level of immunity for at least six months post infection, but it's unknown whether the same result would be true for those who contract other strains.

"All patients involved in this study were infected with the original virus, so whether the same level of immunity and dysregulation would occur with variants such as Delta is unknown," Prof Lynn adds.

The study was jointly led by Professor Lynn, Professor Barry and Dr. Grubor-Bauk and involved an in-depth assessment of a South Australian patient cohort, termed 'COVID-19 SA', set up by Dr. Grubor-Bauk, Professor Michael Beard and Professor Barry from the University of Adelaide in collaboration with Associate Professor David Shaw and Dr. Benjamin Reddi from the Royal Adelaide Hospital.

The researchers will continue to follow the participants for three years to document how the immune system continues to respond long term.

The 'COVID-19 SA' study results have been published on a preprint server ahead of peer review—"Long-term perturbation of the peripheral immune system months after SARS-CoV-2 infection" (2021) by CM Hope, MG Masavuli, MA Lynn, ZA Mekonnen, AEL Yeow, P Garcia-Valtanen, Z Al-Delfi, J Gummow, C Ferguson, S O'Connor, BAJ Reddi, D Shaw, C Kok-Lim, JM Gleadle, MR Beard, SC Barry, B Grubor-Bauk and DJ Lynn.

More information: Feargal J. Ryan et al, Long-term perturbation of the peripheral immune system months after SARS-CoV-2 infection, (2021). DOI: 10.1101/2021.07.30.21261234

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