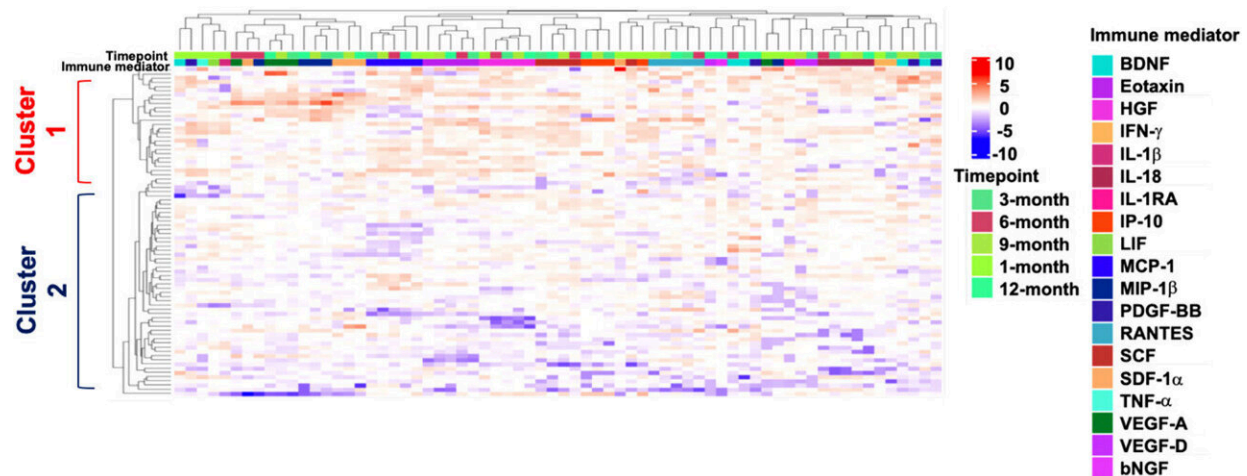


Prolonged inflammation associated with long COVID restored to healthy levels within two years post-infection: Study

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A 12-month longitudinal systemic cytokine analysis of COVID-19 patients reveals a cluster of patients with persisting elevations of proinflammatory cytokines. Longitudinal plasma samples were collected across 5 time points up to 12 months post-illness onset from 78 COVID-19 patients. Concentrations of 45 immune mediators were quantified using a 45-plex microbead-based immunoassay. Clustering of individuals based on their systemic cytokine responses at 1, 3, 6, 9, and 12 months was carried out using hierarchical clustering with complete-linkage and Euclidean distance measure. Credit: *Journal of Medical Virology* (2023). DOI: 10.1002/jmv.28774

The long-term symptoms observed in some individuals post-COVID-19

are associated with a sustained systemic inflammation, according to researchers from the A*STAR Infectious Diseases Labs (A*STAR ID Labs) in Singapore and the National Centre for Infectious Diseases (NCID). Their study, published in the *Journal of Medical Virology*, demonstrates that the prolonged inflammation observed in patients hospitalized with COVID-19 is restored to healthy levels within two years after the initial infection.

COVID-19 typically causes illness in individuals for a few days or weeks following the onset of the first symptoms. However, some individuals continue to experience symptoms that can last for several weeks or longer. This syndrome is commonly referred to as long COVID, or after-effects of SARS-CoV-2 infection. Those suffering from long COVID typically report one or more symptoms such as [chronic fatigue](#), shortness of breath, joint or muscle aches, cough, difficulty concentrating, problems with memory, heart palpitations and insomnia, among others. The exact causes behind the development of long COVID remain unknown, but it occurs more often in individuals who have experienced severe COVID-19 or those who have not been vaccinated against SARS-CoV-2.

To shed light on why some people develop long COVID, A*STAR researchers conducted a [longitudinal study](#) over a period of 24 months. Doctors at NCID and Changi General Hospital (CGH) recruited 78 individuals who were admitted to hospital with COVID-19, some of whom had a severe infection. After being discharged, patients were followed up for up to 24 months post-illness onset to assess for COVID-19 aftereffects.

After the first-year post-infection, approximately 37% of the patients reported symptoms. A*STAR scientists observed that patients with persistent symptoms had sustained inflammation with increased blood [inflammatory cytokines](#) and abnormal activation of immune responses

for up to 24 months after the [initial infection](#). Additionally, they found that older individuals with more severe disease outcomes after the initial infection were more likely to have prolonged systemic inflammation after recovery. However, symptoms that last after two years may or may not be related to COVID-19.

Dr. Fong Siew-Wai, Research Scientist at A*STAR ID Labs and lead author of the study, said, "Our study provides valuable insights into the relationship between COVID-19, inflammation and post-recovery symptoms. It revealed that the immune cells of individuals who experience persistent inflammation show signs of aging. This breakthrough in research helps us better understand the long-lasting effects of COVID-19 experienced by patients. It also opens up new possibilities for developing treatments that specifically target the root cause of these prolonged symptoms."

In this study, all patients were given one dose of mRNA vaccine after the same infection at 12 to 16 months and their immune profiles at 12 and 24 months were compared. The findings showed that persistent inflammation and immune activation presented by patients suffering from long COVID were alleviated after 24 months since most of the inflammatory markers and dysregulated immune cells recovered to levels comparable to healthy vaccinated individuals. Importantly, the research revealed that there was no worsening of symptoms or increased [inflammation](#) among COVID patients after receiving the vaccine. Therefore, it is advisable for long-haulers to be vaccinated in order to gain protection against reinfection.

Associate Professor Barnaby Young, Head of the Singapore Infectious Disease Clinical Research Network at NCID, who led clinical recruitment for this study, said, "Long COVID is a puzzling and frustrating condition for patients. While research into the condition is gathering pace around the world, it remains poorly understood. We hope

our study offers reassurance to sufferers that their symptoms will resolve with time and that it will accelerate the search for a treatment that can speed up recovery."

More information: Siew-Wai Fong et al, Prolonged inflammation in patients hospitalized for coronavirus disease 2019 (COVID-19) resolves 2 years after infection, *Journal of Medical Virology* (2023). [DOI: 10.1002/jmv.28774](https://doi.org/10.1002/jmv.28774)

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