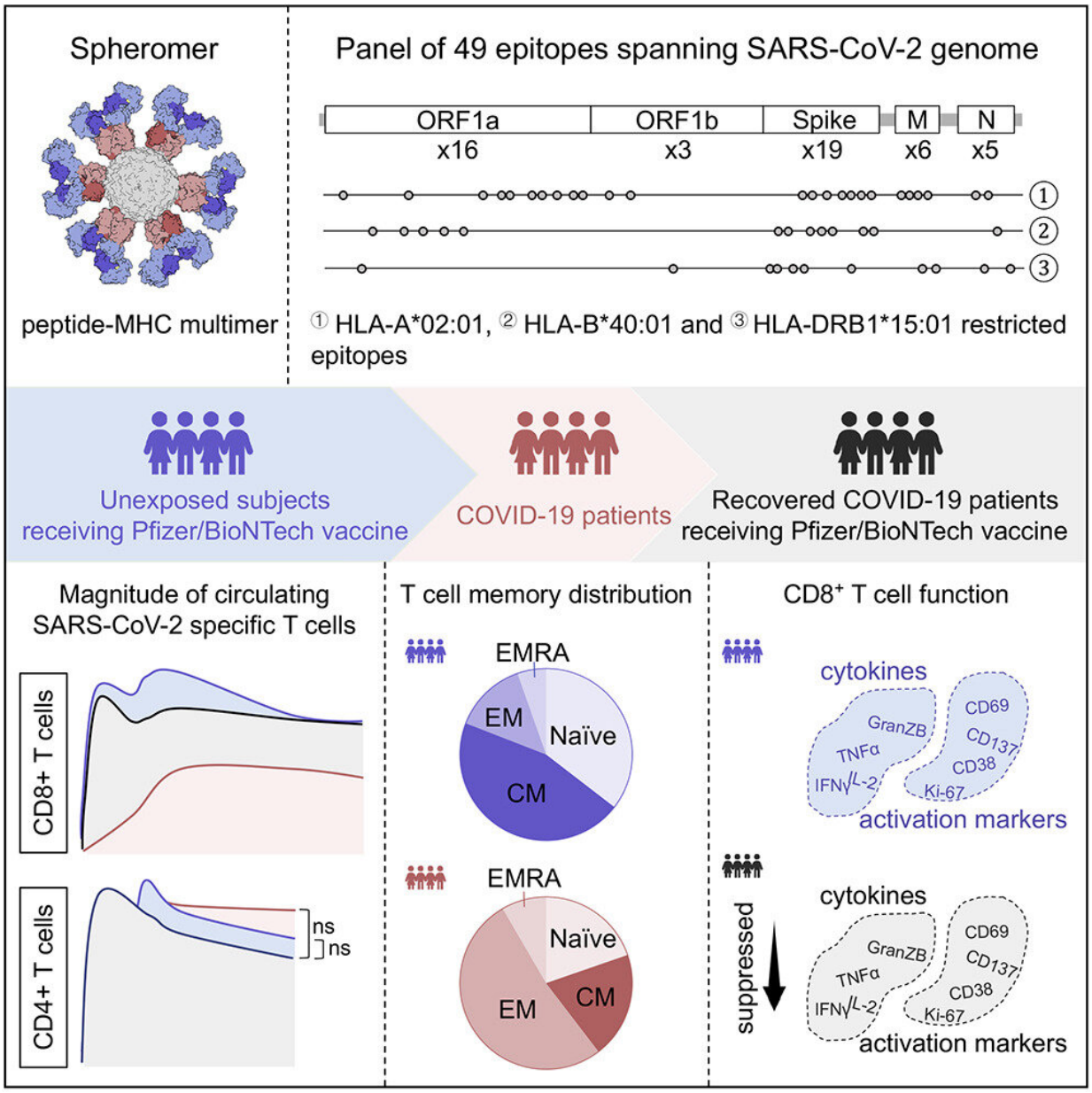
SARS-CoV-2 infection weakens immune-cell response to vaccination, suggests study

March 20 2023



Graphical Abstract. Credit: *Immunity* (2023). DOI: 10.1016/j.immuni.2023.03.005

The magnitude and quality of a key immune cell's response to vaccination with two doses of the Pfizer-BioNTech COVID-19 vaccine were considerably lower in people with prior SARS-CoV-2 infection compared to people without prior infection, a study has found.

In addition, the level of this key immune cell that targets the SARS-CoV-2 spike protein was substantially lower in unvaccinated people with COVID-19 than in vaccinated people who had never been infected. Importantly, people who recover from SARS-CoV-2 infection and then get vaccinated are more protected than people who are unvaccinated. These findings, which suggest that the virus damages an important immune-cell response, were published today in the journal *Immunity*.

The study was led by Mark M. Davis, Ph.D. Dr. Davis is the director of the Stanford Institute for Immunity, Transplantation and Infection and a professor of microbiology and immunology at Stanford University School of Medicine in Palo Alto, California. He is also a Howard Hughes Medical Institute Investigator.

Dr. Davis and colleagues designed a very sensitive tool to analyze how immune cells called CD4+ T cells and CD8+ T cells respond to SARS-CoV-2 infection and vaccination. These cells coordinate the immune system's response to the virus and kill other cells that have been infected, helping prevent COVID-19.

The tool was designed to identify T cells that target any of dozens of specific regions on the virus's spike protein as well as some other viral regions. The Pfizer-BioNTech vaccine uses parts of the SARS-CoV-2

spike protein to elicit an immune response without causing infection.

The investigators studied CD4+ and CD8+ T-cell responses in blood samples from three groups of volunteers. One group had never been infected with SARS-CoV-2 and received two doses of the Pfizer-BioNTech COVID-19 vaccine. The second group had previously been infected with SARS-CoV-2 and received two doses of the vaccine. The third group had COVID-19 and was unvaccinated.

The researchers found that vaccination of people who had never been infected with SARS-CoV-2 induced robust CD4+ and CD8+ T-cell responses to the virus' spike protein. In addition, these T cells produced multiple types of cell-signaling molecules called cytokines, which recruit other immune cells—including antibody-producing B cells—to fight pathogens.

However, people who had been infected with SARS-CoV-2 prior to vaccination produced spike-specific CD8+ T cells at considerably lower levels—and with less functionality—than vaccinated people who had never been infected. Moreover, the researchers observed substantially lower levels of spike-specific CD8+ T cells in unvaccinated people with COVID-19 than in vaccinated people who had never been infected.

Taken together, the investigators write, these findings suggest that SARS-CoV-2 infection damages the CD8+ T cell response, an effect akin to that observed in earlier studies showing long-term damage to the immune system after infection with viruses such as hepatitis C or HIV. The new findings highlight the need to develop vaccination strategies to specifically boost antiviral CD8+ T cell responses in people previously infected with SARS-CoV-2, the researchers conclude.

More information: Fei Gao et al, Robust T cell responses to Pfizer/BioNTech vaccine compared to infection and evidence of

attenuated peripheral CD8+ T cell responses due to COVID-19, *Immunity* (2023). DOI: 10.1016/j.immuni.2023.03.005