



SARS-CoV-2 Infection Weakens Immune-Cell Response to Vaccination

NIH-funded study suggests need to boost CD8+ T cell response after infection.

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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 [March 15] [in the journal Immunity](#).

The study was co-funded by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, and led by Mark M. Davis, PhD. 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.

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