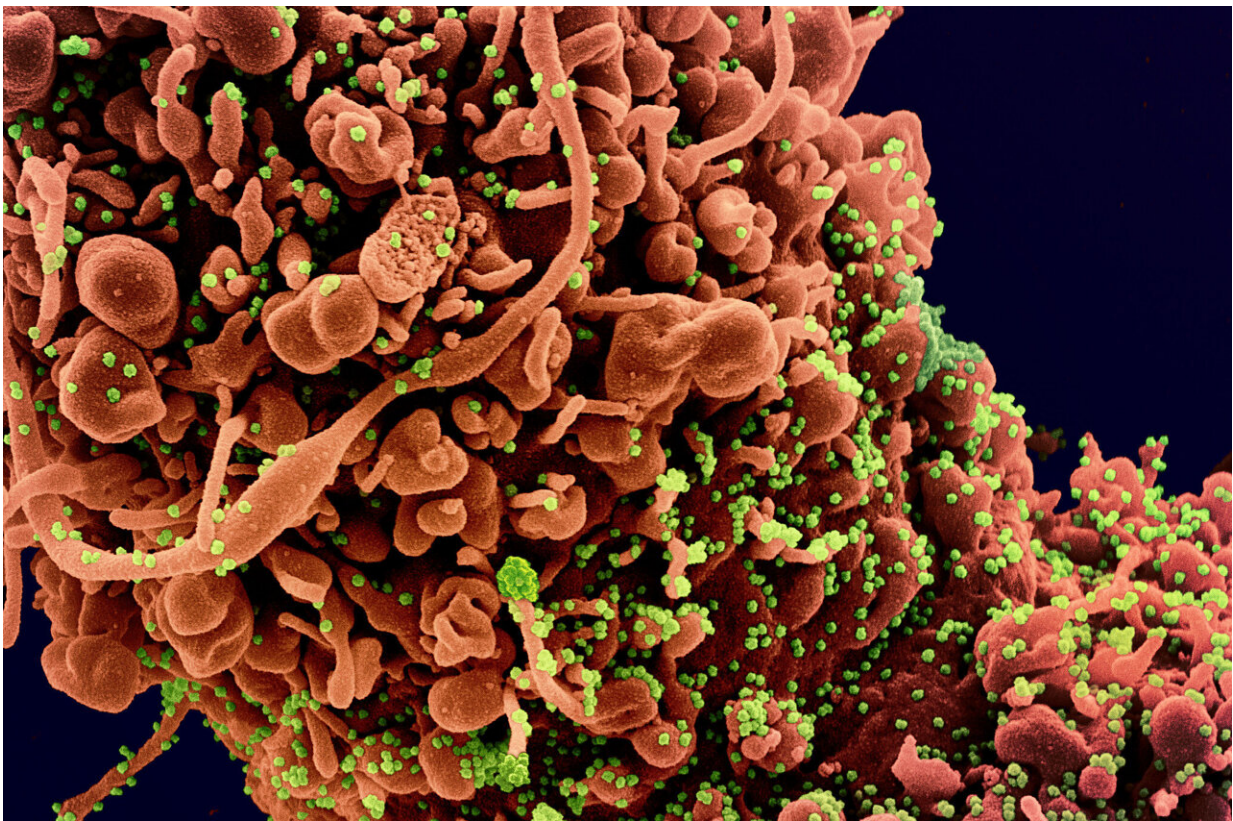


Moderna COVID-19 vaccine spurs lasting immune response: new study

September 14 2021



Transmission electron microscope image shows SARS-CoV-2, the virus that causes COVID-19, isolated from a patient in the U.S. Virus particles are shown emerging from the surface of cells cultured in the lab. The spikes on the outer edge of the virus particles give coronaviruses their name, crown-like. Credit: NIAID-RML

A new study from La Jolla Institute for Immunology (LJI) scientists helps answer the question: how long does immunity against COVID-19 last in vaccinated people?

As they report in *Science*, a low dose of the Moderna vaccine lasts for at least six months, and there is no indicator that vaccinated people will need a booster shot.

"This time point is critical because that is when true immune memory has formed," says LJI Research Assistant Professor Daniela Weiskopf, Ph.D., who co-led the study with LJI Professors Alessandro Sette, Dr.Biol.Sci., and Shane Crotty, Ph.D.

In fact, while the Moderna COVID-19 vaccine (mRNA-1273) led to strong CD4+ (helper) T cell, CD8+ (killer) T cell and antibody responses for at least six months after clinical trial participants were fully vaccinated, it is likely that the immune response could last much longer. The researchers also show that this strong immune memory lasted in all age groups tested, including in people over age 70, a demographic especially vulnerable to severe COVID-19.

"The immune memory was stable, and that was impressive," adds Crotty. "That's a good indicator of the durability of mRNA vaccines."

Comparing Moderna vaccine to natural immunity

The researchers compared recovered COVID-19 patients to vaccine trial participants who received a 25-microgram dose of the Moderna vaccine during the phase 1 clinical trials (supported by the National Institute of Allergy and Infectious Diseases, National Institutes of Health).

"We wanted to see if a quarter of the dose is able to induce any immune response," says study first author Jose Mateus Triviño, Ph.D., a

postdoctoral fellow at LJI. "We had the opportunity to receive the samples from the original Moderna/ NIH phase 1 trial participants who had received two 25-microgram injections of the vaccine, 28 days apart."

This vaccine dose is a quarter of the 100-microgram Moderna dose given emergency authorization by the Food and Drug Administration (FDA). While researchers don't know whether this smaller dose is as effective as the standard dose, this new study shows that the T cell and antibody response in the smaller dose group is still strong.

In fact, the researchers found that the Moderna vaccine spurs an adaptive [immune response](#) to the SARS-CoV-2 spike protein (a key target) nearly identical to the immune system's response to a natural SARS-CoV-2 infection. "The response is comparable," says Weiskopf. "It's not higher and it's not lower."

The new study does not show that a lower dose of the Moderna vaccine provides the same protection as the standard dose. "It would take a clinical trial to tell you how protective the lower dose is," says Crotty.

Common cold viruses do prep the immune system

The new research also shows the power of "cross-reactive" T [cells](#). In a 2020 *Science* study, the LJI team showed that T cells in people who had recovered from common cold coronaviruses could respond to the novel coronavirus, SARS-CoV-2. At the time, they didn't know whether this cross-reactivity could actually protect against COVID-19.

"Understanding the role of cross-reactive T cells is important because T cells play an important role in the control and resolution of COVID-19 infections," says Sette.

For the new study, the researchers found that people with cross-reactive T cells had significantly stronger CD4+ T cell and [antibody responses](#) to both doses of the vaccine.

"If you have this immune reactivity, your immune system may kick in faster against the virus," says Sette. "And multiple studies have shown that how quickly the immune system reacts is key."

Moderna vaccine activates "killer" T cells

The team also filled in an important gap in COVID-19 vaccine research. Until now, many studies had shown an effective CD4+ T cell response to the Moderna vaccine, but CD8+ T cell data was lacking.

"We know naturally infected and recovered people develop excellent CD8+ T cell responses against SARS-CoV-2; however, there was concern about the generation of CD8+ T cells by mRNA vaccines," says Mateus Triviño.

The new study shows a strong CD8+ T cell response to the low dose Moderna vaccine, similar to the response after a patient fights a natural SARS-CoV-2 infection, says Sette, a renowned T cell expert.

"We see a robust CD8+ T cell response—and we showed that using multiple assays," adds Weiskopf.

Coming up:

Will this same vaccine durability hold true for the other types of COVID-19 vaccines? Weiskopf and her colleagues are investigating. In the meantime, Weiskopf says real-world data suggest immune memory does last.

"The people in the hospitals are the ones not vaccinated," she says.

The researchers are also interested in how the durability of the Moderna [vaccine](#) compares with other COVID-19 vaccines in use.

More information: Jose Mateus et al, Low-dose mRNA-1273 COVID-19 vaccine generates durable memory enhanced by cross-reactive T cells, *Science* (2021). [DOI: 10.1126/science.abj9853](https://doi.org/10.1126/science.abj9853)

Provided by La Jolla Institute for Immunology

Citation: Moderna COVID-19 vaccine spurs lasting immune response: new study (2021, September 14) retrieved 15 February 2024 from <https://medicalxpress.com/news/2021-09-moderna-covid-vaccine-spurs-immune.html>

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