Study shows vaccines may protect against new COVID-19 strains—and maybe the common cold

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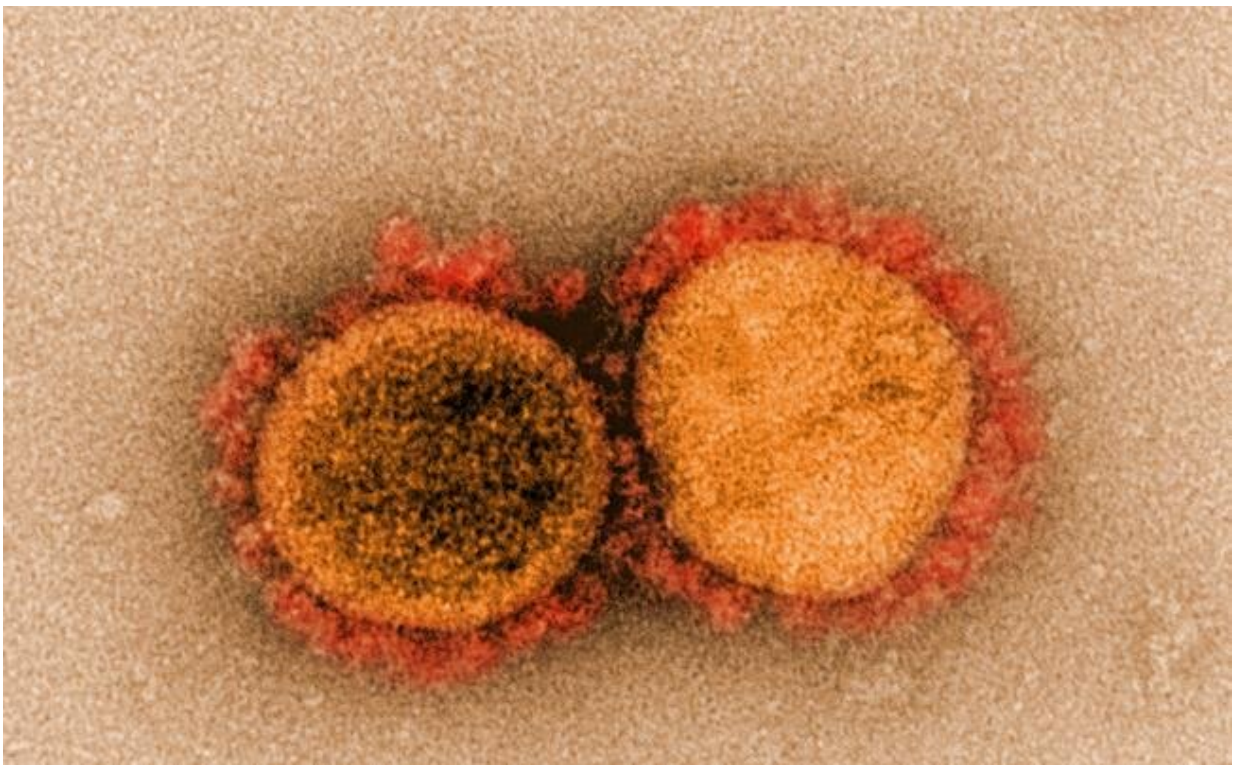

Transmission electron micrograph of SARS-CoV-2 virus particles, isolated from a patient. Image captured and color-enhanced at the NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland. Credit: NIAID

A new study by Johns Hopkins Medicine researchers provides evidence

that CD4+ T lymphocytes—immune system cells also known as helper T cells—produced by people who have received either of the two messenger RNA (mRNA) vaccines for COVID-19 caused by the original SARS-CoV-2 strain also will recognize the mutant variants of the coronavirus that are rapidly becoming the dominant types worldwide.

The researchers say this suggests that T cell responses elicited or enhanced by the vaccines should be able to control the current SARS-CoV-2 variants without needing to be updated or modified. They also found that the same T cells may provide some protection from another member of the coronavirus family that is responsible for one type of the common cold.

The findings were reported April 6, 2021, in the *Journal of Clinical Investigation*.

CD4+ T cells get their "helper" nickname because they assist another type of immune cell, the B lymphocyte (B cell), in responding to surface proteins—antigens—on cells infected by invaders that include viruses such as SARS-CoV-2. Activated by the CD4+ T cells, immature B cells become either plasma cells that produce antibodies to mark infected cells for disposal from the body or memory cells that "remember" the antigen's biochemistry for a faster response to future infections.

In the case of SARS-CoV-2, the antigen is the protein making up the spikes that protrude from the surface of the virus. The mRNA vaccines—known by their manufacturer's names, Pfizer-BioNTech and Moderna—provide genetic instructions to a vaccinated person's immune system to recognize the spike protein and start production of antibodies against SARS-CoV-2.

CD4+ T cells also send out chemical messengers that attract another type of T cell—known as the CD8+ T cell (or "killer T cell")—so that the

virus-infected cells can be removed.

To conduct their helper T cell study, the researchers evaluated blood samples from 30 healthy health care workers and laboratory donors who had not previously tested positive for SARS-CoV-2—both before and after two doses of a COVID-19 mRNA vaccine. The participants, 12 women and 18 men, ranged in age from 20 to 59.

CD4+ T cells extracted from the blood samples were analyzed for their responses to various components (protein fragments known as peptides) from the original strain SARS-CoV-2 spike protein and three common cold coronaviruses.

The researchers discovered that vaccine recipients—as expected—had broad T cell responses to the original strain SARS-CoV-2 spike peptides.

"We identified 23 distinct T cell-targeted peptides, of which only four appear affected by the mutations that created the variant coronaviruses first seen in the United Kingdom and South Africa," says study senior author Joel Blankson, M.D., Ph.D., professor of medicine at the Johns Hopkins University School of Medicine. "That means the other 19 peptides are the same in the original SARS-CoV-2 and the newer strains, so the mRNA vaccines should induce T cells that respond well to the variants."

Blankson says this is important because previous studies showed that antibodies don't recognize the SARS-CoV-2 variants as well as the CD4+ T cells.

"So the T cells may help prevent the variant viruses from causing severe COVID-19 disease even if antibodies don't stop them from infecting a person," he explains.

When the researchers looked at the vaccine-induced T cell response to the spike proteins of three common cold coronaviruses, they saw a three-fold increase for one, HCoV-NL63, but not the other two.

"Further studies are needed to determine why this occurred," says Blankson. "We suspect that HCoV-NL63 may have more epitopes [peptides that elicit an immune response] in common with SARS-CoV-2 than the other common cold coronaviruses."

In a recent and related study, Blankson and Johns Hopkins Medicine colleagues looked at blood from convalescent patients who had recovered from a SARS-CoV-2 infection and identified the unique receptors on memory CD4+ T cell that recognize the spike proteins of both the original strain of SARS-CoV-2 and four common cold coronaviruses.

Blankson says that characterizing these T cell receptors may be helpful in guiding development of future vaccines for a variety of coronaviruses.

More information: Bezawit A. Woldemeskel et al. SARS-CoV-2 mRNA vaccines induce broad CD4+ T cell responses that recognize SARS-CoV-2 variants and HCoV-NL63, *Journal of Clinical Investigation* (2021). DOI: 10.1172/JCI149335

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