T-cells more important in the fight against the COVID-19 virus than initially thought

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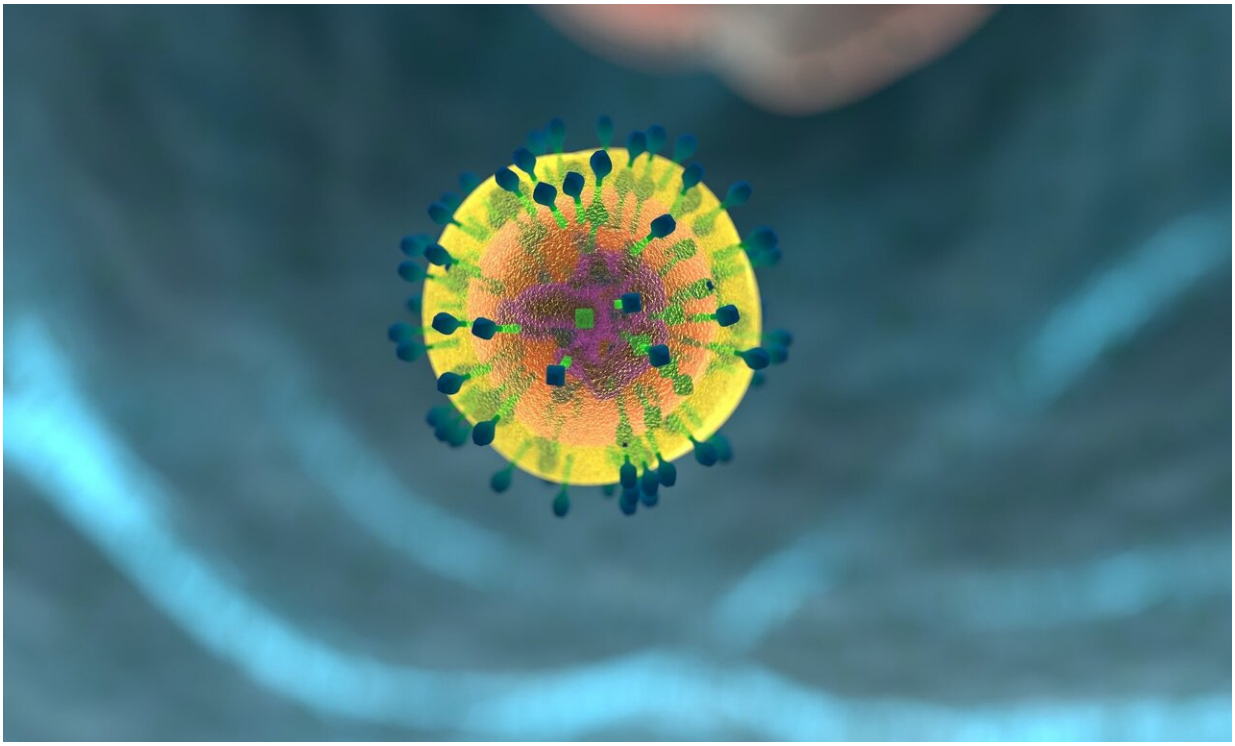

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A COVID-19 vaccine that specifically instructs the immune system to produce T-cells rather than antibodies is shown to provide good protection in a mouse model, Leiden University Medical Center (LUMC) researchers report in *Nature Communications*. According to them, the alternative vaccine may offer a solution for people with a

weakened immune system, since these individuals don't respond as well to the current ones available.

Ever since the pandemic set off in 2019, most of us have at least heard about 'antibodies.' They bind to the spike proteins of the virus which causes COVID-19, preventing it from infecting our cells. COVID-19 vaccines, therefore, mainly aim to stimulate the production of antibodies. Less known is that we can also stimulate the so-called CD8 T-cells of our immune system. "And that shouldn't be the case," says immunologist Ramon Arens, "because these cells roam our bodies like true knights in order to eliminate each cell that has been infected."

The recent study published in *Nature Communications* demonstrates the importance of T-cells and emphasizes they deserve more attention. "We showed that a vaccine that specifically stimulates CD8 T-cells protect mice very well against an otherwise deadly COVID-19 infection—provided we vaccinate them three times," Arens notes. And that is not all: T-cell-stimulating vaccines may offer more resistance to novel virus variants, as well as longer protection compared to current COVID-19 vaccines.

Common spikes

For this study, Arens and colleagues produced a peptide vaccine in cooperation with ISA Pharmaceutical and Immunetune. It contains a very small part of the virus spike protein that is specifically recognized by CD8-T cells. "Especially after the third vaccination dose, we saw an enormous increase in the number of CD8-T cells. T-cells were also located in parts of the body where we wanted to see them—such as in the lungs of the mice—indicating the virus is being attacked immediately once it enters their system." The part of the spike protein contained within the vaccine is also found in spike proteins of other SARS viruses. This indicates that it may play an important role in the

functioning of the virus and thus will not mutate quickly. Arens says that "as a result, this vaccine is probably effective against old and new variants of the virus."

Antibodies vs. immune cells

This is the first study describing that CD8 T-cells, stimulated by a vaccine (and without the help of other immune cells and antibodies), offer protection against the virus that causes COVID-19. "However, we are not suggesting that antibodies are no longer needed," says Arens. "Despite focusing on antibodies, current vaccines also increase T-cells. You really need both to fight the virus, so combining vaccines could be a potentially good option."

Promising alternative

These findings are particularly interesting for individuals with a weakened immune system, such as patients who undergo transplants or who have reduced B cells (the factories that make antibodies). Researchers are also considering broader applications for the technology. Arens says that "in general, I think booster vaccinations that elicit a strong CD8 T-cell response are a promising strategy to improve future vaccination programs." Now, Arens and colleagues are investigating the role of T-cells in current mRNA vaccines to find out whether the new vaccine would work in humans. To this end, they have initiated collaborations with a number of companies and hope to eventually bring a product to the market.

More information: Iris N. Pardieck et al, A third vaccination with a single T cell epitope confers protection in a murine model of SARS-CoV-2 infection, *Nature Communications* (2022). DOI: 10.1038/s41467-022-31721-6

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