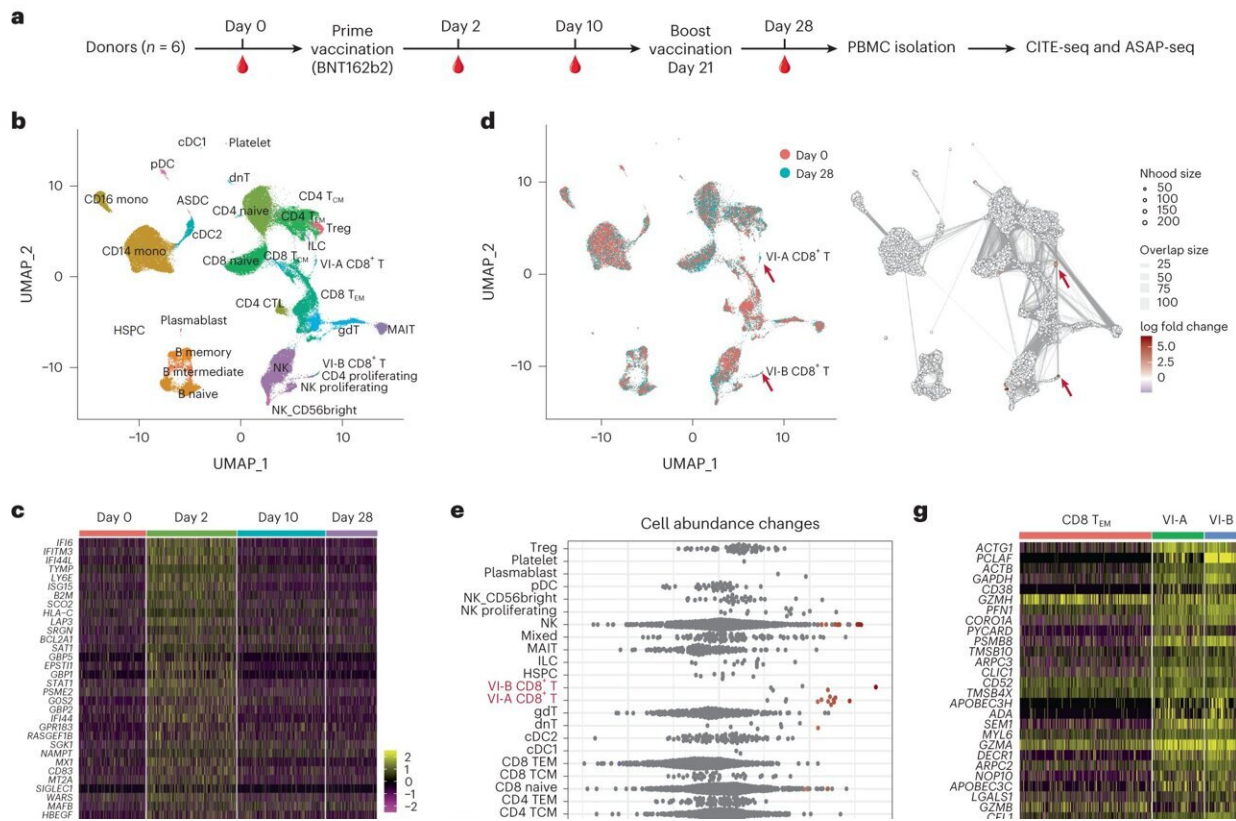


Study details immune cells vital to success of vaccines against coronavirus

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Multimodal identification of SARS-CoV-2 mRNA vaccine-induced CD8+ T cells. Credit: *Nature Immunology* (2023). DOI: 10.1038/s41590-023-01608-9

A study has revealed new details about a key population of immune system cells critical to successful vaccination against the pandemic virus,

SARS-CoV-2.

Led by researchers at NYU Grossman School of Medicine and New York Genome Center, the current study focused on T cells, which along with B cells, compose the human immune system's response to invading viruses and bacteria. A subset of T cells, labeled with the surface protein CD8, produce molecules that directly kill infected cells. B cells produce antibody proteins that neutralize and label infected cells for removal from the body.

Without risking infectious disease itself, vaccines expose patients to a piece of an invading microbe to generate responses that include B and T cell activation, such that the system is ready for the invader should it be encountered again. The mRNA vaccines deployed against COVID-19 were based on RNA, a [genetic material](#) used to encode the spike protein that the virus needs to attach to [human cells](#). Once injected, mRNA instructions are read, the spike is built, and the [immune response](#) is triggered.

In the rush to develop vaccines against SARS-CoV-2, and with the rapid testing of thousands of patients required, [clinical trials](#) relied mostly on antibody levels, where efficient tests were available, to judge whether patients' immune responses to mRNA vaccine candidates were protective.

The resulting clinical protection, however, was evident as early as ten days after the first vaccine shot, well before neutralizing antibodies could possibly be generated. T cells were suspected to be at least as important to this protection, but standard methods for tracking them were too slow, and so careful analyses of CD8⁺ T cell responses were sidelined.

Published online September 21 in *Nature Immunology*, the new study

describes a fast (high-throughput) method to track T cell responses, confirms them to be vital to early protection provided by mRNA vaccines against COVID-19, and reveals the T cell subsets most responsible for it.

"Our study identified markers for the CD8⁺ T cells that arise from mRNA vaccination and that track closely with successful vaccination, which had previously been difficult to quantify on the population level," says co-first study author Rabi Upadhyay, MD, assistant professor in the Department of Medicine at NYU Langone Health, and faculty in its Perlmutter Cancer Center.

"Although our study looks at mRNA vaccination against coronavirus, the antigen-specific CD8⁺ T cell subpopulations we uncover represent key features of immune responses more broadly, and may help us to study T cells in other disease settings."

For the current study, the research team analyzed gene expression over time in single T cells collected before and after immunization with the mRNA vaccine produced by BioNtech and Pfizer against SARS-CoV-2. The researchers found distinct subsets of CD8⁺ T cells that reliably multiplied (proliferated) 21 days after the original vaccination, specifically targeting and attacking key proteins (antigens) that make up the pandemic virus.

In looking at the genetic make-up of the most effective T cells, the researchers observed that cells lacking a surface protein called KLRG1, which stands for co-inhibitory receptor killer-cell lectin like receptor G1, were the most likely to multiply quickly after mRNA vaccination and specifically attack. When study authors checked for these profiles in hospitalized COVID-19 patients, those with the most "properly programmed" T cells—lacking KLRG1 but expressing other markers such as CD38 and HLA-DR—were the most likely to successfully

recover from their infections.

Quicker answers on cancer

In the years since the pandemic began, mRNA vaccines, first used against the virus, are now in clinical trials wherein they direct the body's immune system to attack cancerous cells. By clarifying T cell markers (e.g., KLRG1, CD38, HLA-DR), and the timeline for when CD8⁺ T cells arise in the blood after vaccination, the new work may enable clinical teams to tell which patients are responding to the vaccines within days or weeks, say the authors.

That compares to the more than two months that oncologists must currently wait after mRNA vaccination to perform CT scans and assess whether their lung, breast, or prostate cancer patients responded to an mRNA vaccine. If they are validated in this setting and dramatically shorten such wait times, the new profiling methods promise to help patients pivot more quickly to other treatments if necessary, the researchers say.

Furthermore, the study authors refer to [a recent study](#) led by a different research team which found that T cells with very similar attributes—again involving KLRG1, CD38, and HLA-DR—were the most effective at attacking cancer cells after treatment with an immune system-triggering drug (immunotherapy), just as they were the most effective at attacking the SARS-CoV-2 virus in the current study.

"It is remarkable that T cell attributes found after treatment with an effective immunotherapy mirrored those that we found to track with patient recovery from COVID-19," says co-corresponding author Dan Littman, MD, Ph.D., the Helen L. and Martin S. Kimmel Professor of Molecular Immunology in the Department of Cell Biology at NYU Langone. "This pattern suggests that the close monitoring of antigen-

specific CD8⁺ T cell subpopulations will be central to future efforts to design treatments and vaccines against either viruses or tumors."

Along with Upadhyay and Littman, study authors from NYU Langone were Marie Samanovic, Ramin Herati, Jordan Axelrad, and Mark Mulligan. Study authors from the New York Genome Center were co-first author Bingjie Zhang, Yuhan Hao, John Blair, and co-corresponding author Rahul Satija. Littman is also a member of Perlmutter Cancer Center and a Howard Hughes Medical Institute (HHMI) investigator.

More information: Bingjie Zhang et al, Multimodal single-cell datasets characterize antigen-specific CD8⁺ T cells across SARS-CoV-2 vaccination and infection, *Nature Immunology* (2023). [DOI: 10.1038/s41590-023-01608-9](https://doi.org/10.1038/s41590-023-01608-9)

Provided by NYU Langone Health

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