Study: Infection with common cold coronaviruses can trigger broad cross-immunity against SARS-CoV-2 proteins

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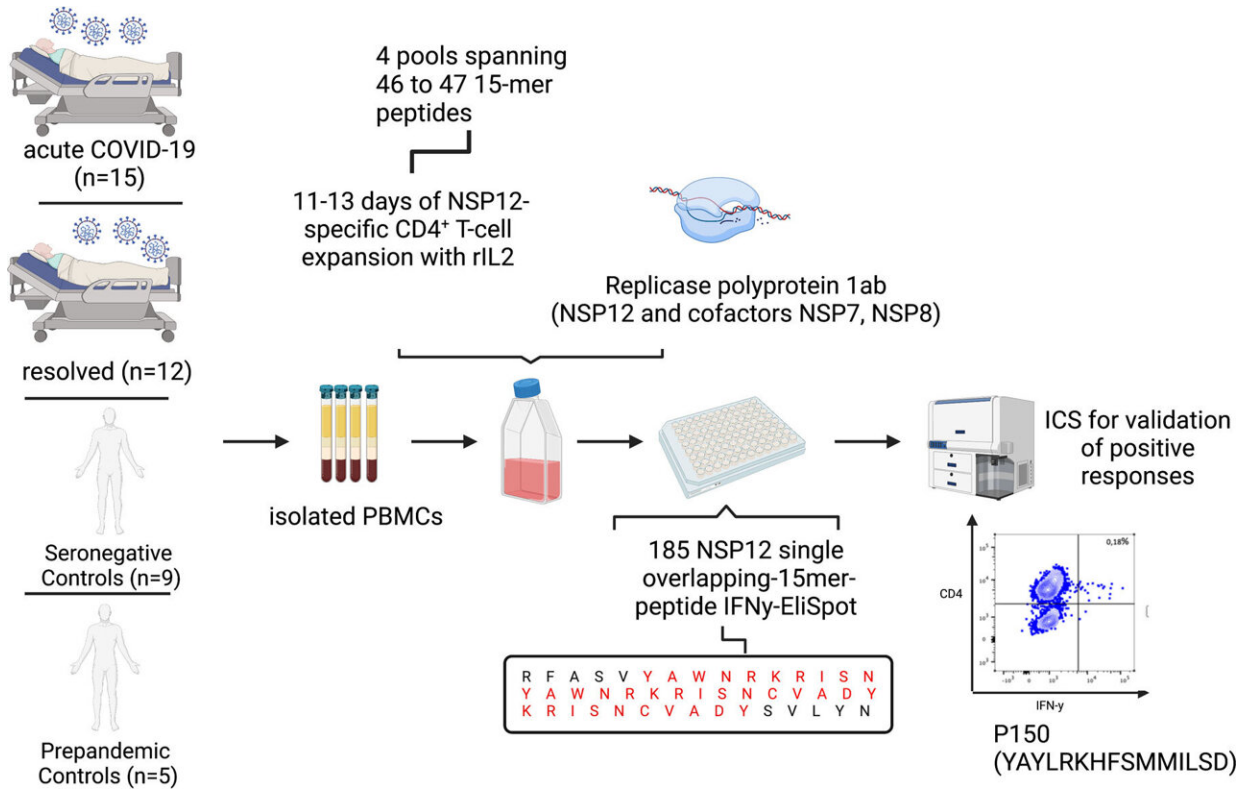

Experimental setup of the 15-mer single-peptide IFN-γ-ELISpot after 11–13 days of in vitro peptide-specific culture with different peptide pools, each spanning 46 to 47 peptides, and ICS after single-peptide re-stimulation for validation of positive peptide-specific T-cell responses. Credit: *Frontiers in Immunology* (2023). DOI: 10.3389/fimmu.2023.1182504

Researchers at the University Medical Center Hamburg-Eppendorf have demonstrated cross-reactive immune responses to another SARS-CoV-2 protein besides the spike protein. The research team found a broad immune system T cell response to the RNA-dependent RNA polymerase of SARS-CoV-2 in blood samples from COVID patients as well as from subjects who were never infected with SARS-CoV-2.

The T cells of the never-infected probands presumably arose from previous infection with other common cold coronaviruses and cross-reacted with the SARS-CoV-2 RNA polymerase in the tests.

The response of the T cells of the immune system plays an important role in combating COVID-19 as well as with regard to disease progression during infection. The immune response has so far been studied mainly for the spike protein of SARS-CoV-2, as it forms the basis for vaccination with an mRNA agent.

SARS-CoV-2 is an RNA virus with a large genome encoding at least 29 proteins, including structural (such as the spike protein), accessory and non-structural proteins. Previous studies had shown that exposure of the immune system to structural proteins can trigger a virus-specific response of CD4+ T cells—among these was a study led by the DZIF scientist Prof. Julian Schulze zur Wiesch of the University Medical Center Hamburg-Eppendorf that investigated the response of CD4+ T cells to the structural SARS-CoV-2 spike protein.

In a new study, the team now compared the specific T cell response to SARS-CoV-2 RNA-dependent RNA polymerase—a non-structural protein—in blood samples of COVID-19 patients and of subjects who had never had COVID, including pre-pandemic samples. In all samples the researchers detected a broad immune system T cell response.

The T cells found in the samples from people who had never been

infected with SARS-CoV-2 therefore presumably arose in response to an earlier infection with other common cold coronaviruses and cross-reacted in the tests with the SARS-CoV-2-poymerase protein.

In addition, the scientists compared the potential specific cross-reactivity of SARS-CoV-2 RNA-dependent RNA polymerase with that of other proteins of related cold coronaviruses to gain further insight into SARS-CoV-2-specific T cell responses.

"These data provide further evidence of the complexity of the body's immune response to SARS-CoV-2 and what a long way we still have to go to fully understand it. Further research can now build on this publication and more intensively investigate the interaction between different respiratory viruses," says the study's first author Tim Westphal.

The research, published in the journal *Frontiers in Immunology*, may help advance the development of vaccines and therapies against corona- and other respiratory viruses.

More information: Tim Westphal et al, Evidence for broad cross-reactivity of the SARS-CoV-2 NSP12-directed CD4+ T-cell response with pre-primed responses directed against common cold coronaviruses, *Frontiers in Immunology* (2023). DOI: 10.3389/fimmu.2023.1182504

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