Monitoring the Cellular Immune Profiles of COVID-Vaccinated Donors Using in silico-Designed Immunogenic Epitopes From SARS-CoV-2 Proteins

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Although the SARS-CoV-2 spike protein is researchers' primary target, more conserved non-structural proteins (NSPs) of SARS-CoV-2 can be better targets if sufficiently immunogenic. The hypothesis was to assess T-cell responses to the spike protein and non-structural proteins of SARS-CoV-2 in donors with different immunization and infection histories. Immune Epitope Database-designed 12-mer immunodominant peptide epitopes from the virus' NSPs and spike protein were cultured individually with human peripheral blood mononuclear cells (PBMCs) of donors vaccinated with either the Moderna or Pfizer mRNA vaccines, alongside control donors who had never been exposed to coronavirus. The T-cell cytokines secreted following culture were assessed by a multiplexed proteomics platform to measure the strength of the donors' functional response. Data from three specific cytokines demonstrated how donors' response differed in individuals with different immunization and SARS-CoV-2 infection history. This demonstrates that immunodominant peptides from both SARS-CoV-2 NSPs and spike protein can induce robust antigen-specific T-cell cytokine responses. Furthermore, fully-vaccinated donors showed a robust T-cell response, especially to the spike protein, while previously infected donors with no vaccination history responded greater to NSP epitopes. Longitudinal studies in fully vaccinated donors over a period of 6 months showed a reduced response to both the spike protein and NSPs. After donors received the second dose of the vaccine, the assay responses revealed that their immunity was boosted since the first dose. With further data generated by unique donors, this assay could be utilized to measure the immune memory and strength of donors to SARS-CoV-2.

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