Human CD4$^+$ T cells specific for dominant epitopes of SARS-CoV-2 Spike and Nucleocapsid proteins with therapeutic potential

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Abstract

Since December 2019, Coronavirus disease-19 (COVID-19) has spread rapidly across the world, leading to a global effort to develop vaccines and treatments. Despite extensive progress, there remains a need for treatments to bolster the immune responses in infected immunocompromised individuals, such as cancer patients who recently underwent a haematopoietic stem cell transplantation. Immunological protection against COVID-19 is mediated by both short-lived neutralising antibodies and long-lasting virus-reactive T cells. Therefore, we propose that T cell therapy may augment efficacy of current treatments. For the greatest efficacy with minimal adverse effects, it is important that any cellular therapy is designed to be as specific and directed as possible. Here, we identify T cells from COVID-19 patients with a potentially protective response to two major antigens of the SARS-CoV-2 virus, Spike and Nucleocapsid protein. By generating clones of highly virus-reactive CD4+ T cells, we were able to confirm a set of 9 immunodominant epitopes and characterise T cell responses against these. Accordingly, the sensitivity of T cell clones for their specific epitope, as well as the extent and focus of their cytokine response was examined. Moreover, by using an advanced T cell receptor (TCR) sequencing approach, we determined the paired TCR?? sequences of clones of interest. While these data on a limited population require further expansion for universal application, the results presented here form a crucial first step towards TCR-transgenic CD4+ T cell therapy of COVID-19.

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