Capitalizing on cancer immunotherapy techniques to develop a potential variant-proof treatment for COVID-19

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Derya Unutmaz in his lab at The Jackson Laboratory. Credit: Tiffany Läufer

Millions have died due to COVID-19 infection, and millions more continue experiencing the chronic condition, Long COVID, which makes discovering practical, accessible, and powerful SARS-CoV-2 preventatives and COVID-19 treatments essential.

At the nonprofit biomedical research institution, The Jackson Laboratory for Genomic Medicine, Derya Unutmaz, M.D., and his team have adapted what is typically a cancer therapeutic technique, CAR T cell therapy, for the purpose of eliminating SARS-CoV-2 virus. The study, published in *Clinical & Translational Immunology*, demonstrates several immuno-based strategies to explore the treatment and prevention of COVID-19.

The first immunotherapy method focuses on the spike protein present on SARS-CoV-2 and the receptor on the host cell, angiotensin-converting enzyme 2 (ACE2). The spike protein is the molecule on the surface of the virus that is responsible for infecting healthy host cells. The protein enters the cell via the ACE2 receptor, allowing the viral RNA to begin its takeover. In the Unutmaz study, T cells were engineered with anti-spike and anti-ACE2 CAR-T cells to target either the spike protein or the ACE2 receptor, with high specificity and efficiency across various infected cell types.

The second immunotherapy method provides an antibody-based means for preventing COVID-19 infection. T cells were engineered with a bispecific antibody fused with ACE2 to activate the patient's own T cells to destroy infected cells that present the SARS-CoV-2 Spike protein on their surface. Rather than having cells, modified outside of the body, kill the infected cells, ACE2-bispecific therapy activates the healthy T cells within the individual to target Spike+ cells post-infection.

Unlike most present therapeutics, ACE2-bispecific modified cells take advantage of the ACE2 receptor to target the different presentations of the Spike protein across all SARS-CoV-2 variants, including Delta, Omicron and more. The ACE2-bispecific therapy can therefore provide more efficient elimination of variants with more powerful ACE2 binding. It can also act as a decoy to block viral entry into cells, offering a possible preventative strategy.

Both the proposed COVID-19 CAR-T cell and ACE2-bispecific-based therapies offer promising potential strategies for future COVID-19 treatment and prevention.

More information: Mikail Dogan et al, Targeting SARS?CoV ?2 infection through CAR?T ?like bispecific T cell engagers incorporating ACE2, *Clinical & Translational Immunology* (2022). DOI: 10.1002/cti2.1421

Provided by Jackson Laboratory

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