Effective chimeric antigen receptor T-cells (CAR-Ts) against SARS-CoV-2

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Current therapies to treat coronavirus disease 2019 (COVID-19) primarily involve vaccines against the spike (S) protein S1 of SARS-CoV-2. Here, we outline an alternative approach involving chimeric antigen receptors (CARs) in T-cells (CAR-Ts). CAR-T recognition of the SARs CoV2 (RBD) peptide induced ribosomal protein S6 phosphorylation together the expression of CD69 and effector molecules, interferon- γ (IFN-γ), granzyme B (GZMB), perforin and Fas-ligand (FasL) on overlapping and distinct populations of CAR-Ts. CAR-Ts also showed killing of RBD, S1 peptide loaded target cells or target transduced to express the entire S1 protein. The efficacy of killing varied with different sized hinge regions, while time-lapse microscopy showed cluster formation with targets and cytolysis as mediated by GZMB/perforin. Lastly, we showed successful *in vivo* killing of S1-expressing cells by our SARS-CoV-2 CAR-T cells in mice. The successful generation of SARS-CoV-2 CAR-Ts represents a potential therapeutic approach for the treatment of COVID-19.