CAR-T Cells Against HIV: Taking Aim at a Genetic Moving Target

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Chimeric antigen receptor (CAR) technology offers the potential for robust and durable suppression of HIV in the absence of anti-retroviral drugs, i.e. a “functional cure”. CARs can be designed to recognize the HIV envelope glycoprotein and selectively kill infected cells based on their surface Env expression. To circumvent the high susceptibility of HIV to mutational escape, we have designed CARs with targeting motifs based not on antibodies, but instead on CD4, the primary receptor for all HIV variants. Particular success has been achieved with bispecific CARs containing CD4 linked to a second moiety derived from a human protein that binds to a distinct highly conserved site on HIV-1 Env. The second moiety significantly enhances CAR potency, and prevents the CD4 from acting as an entry receptor into CAR-expressing CD8+ T cells. Flow cytometry provides critical insights in advancing pre-clinical studies on these anti-HIV CARs.
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