Antigen Boosting Promotes Expansion of HIV-Resistant Dual CAR T Cells and Enables Viral Control

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HIV-1-specific chimeric antigen receptor (CAR) T cells (CARTs) have shown promises for controlling viral rebound following analytical treatment interruption (ATI). However, their expansion and persistence remain challenging in the setting of suppressive antiretroviral therapy (ART), where HIV-1 antigen levels are low or absent. We hypothesized that providing exogenous HIV-1 Env antigen during ART could enhance CART expansion and increase the number of effector cells available to control viral rebound following ATI. To test this, we evaluated three Env-expressing vaccine platforms, including two replication-competent adenovirus-based vaccines (Vaccine 1 and Vaccine 2) and one replication-deficient vaccinia virus-based vaccine (Vaccine 3). Among the three, Vaccine 1 induced robust expansion of HIV-1-specific CARTs in vivo and was associated with superior control of viral replication following ATI. These findings suggest that vaccine-mediated antigen boosting can enhance HIV-1-specific CARTs expansion and improve their capacity to control viral rebound.