

Engineering CAR T Cells to Target the HIV Reservoir.

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Authors:	Wenli Mu, Mayra A Carrillo, Scott G Kitchen
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Public Summary:

The HIV reservoir remains to be a difficult barrier to overcome in order to achieve a therapeutic cure for HIV. Several strategies have been developed to purge the reservoir, including the "kick and kill" approach, which is based on the notion that reactivating the latent reservoir will allow subsequent elimination by the host anti-HIV immune cells. However, clinical trials testing certain classes of latency reactivating agents (LRAs) have so far revealed the minimal impact on reducing the viral reservoir. A robust immune response to reactivated HIV expressing cells is critical for this strategy to work. A current focus to enhance anti-HIV immunity is through the use of chimeric antigen receptors (CARs). Currently, HIV-specific CARs are being applied to peripheral T cells, NK cells, and stem cells to boost recognition and killing of HIV infected cells. In this review, we summarize current developments in engineering HIV directed CAR-expressing cells to facilitate HIV elimination. We also summarize current LRAs that enhance the "kick" strategy and how new generation and combinations of LRAs with HIV specific CAR T cell therapies could provide an optimal strategy to target the viral reservoir and achieve HIV clearance from the body.

Scientific Abstract:

The HIV reservoir remains to be a difficult barrier to overcome in order to achieve a therapeutic cure for HIV. Several strategies have been developed to purge the reservoir, including the "kick and kill" approach, which is based on the notion that reactivating the latent reservoir will allow subsequent elimination by the host anti-HIV immune cells. However, clinical trials testing certain classes of latency reactivating agents (LRAs) have so far revealed the minimal impact on reducing the viral reservoir. A robust immune response to reactivated HIV expressing cells is critical for this strategy to work. A current focus to enhance anti-HIV immunity is through the use of chimeric antigen receptors (CARs). Currently, HIV-specific CARs are being applied to peripheral T cells, NK cells, and stem cells to boost recognition and killing of HIV infected cells. In this review, we summarize current developments in engineering HIV directed CAR-expressing cells to facilitate HIV elimination. We also summarize current LRAs that enhance the "kick" strategy and how new generation and combinations of LRAs with HIV specific CAR T cell therapies could provide an optimal strategy to target the viral reservoir and achieve HIV clearance from the body.

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