Immune-enhancing treatment may destabilize HIV reservoirs

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Although antiretroviral therapy (ART) can reduce the amount of HIV in the blood to an undetectable level in most chronically infected people, it cannot eliminate reservoirs of HIV that persist in latently infected immune cells. Findings presented at the 21st International AIDS Conference (AIDS 2016) in Durban, South Africa, suggest that combining ART with an immune-enhancing treatment may destabilize viral reservoirs in macaques infected with simian immunodeficiency virus (SIV), the monkey equivalent of HIV. The work was funded by the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, and led by Rama Amara, Ph.D., of Emory University.

HIV infects the CD4+ T cells of the immune system. Other immune cells, called CD8+ T cells, help eliminate HIV-infected CD4+ cells, but their ability to do so wanes over time. Studies have shown that loss of CD8+ T cell function is associated with high levels of a cell-surface protein called PD-1 and that HIV reservoirs concentrate in PD-1+ CD4+ T cells.

In the current study, investigators administered five infusions of either a PD-1-blocking antibody or a placebo to SIV-infected monkeys 10 days before starting the animals on ART. Monkeys that received the anti-PD-1 antibody produced more activated antiviral CD8+ cells. Following ART initiation, blood levels of SIV became undetectable in an average of 42 days in antibody-treated monkeys compared with 140 days in those that received placebo.

Eight months after starting ART, the monkeys were given three monthly infusions of anti-PD-1 antibody or a placebo. PD-1 blockade caused transient increases in blood levels of SIV, suggesting that the treatment may have destabilized latent SIV reservoirs.

According to the investigators, these findings highlight the potential of PD-1 blockade to work synergistically with ART and other therapeutic agents to improve CD8+ T cell function and destabilize HIV reservoirs in humans. Ultimately, such strategies potentially could be tested in people in an attempt to diminish HIV reservoirs and reduce the amount of HIV in a person's body to the point where the immune system could control the infection without antiretroviral drugs.

RR Amara *et al.* PD-1 blockade synergizes with ART for restoring anti-viral CD8 T cell function and possibly destabilizing the viral reservoir in SIV-infected macaques. Oral presentation at the 21st International AIDS Conference (AIDS 2016) in Durban, South Africa.

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