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IL-21 repairs immune function in primate model of HIV infection

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Antiretroviral drugs can suppress HIV for years, but a residual inflammatory imbalance contributes to health problems in infected individuals who are infected with the virus. A novel combination treatment aimed at repairing the immune system has shown encouraging effects in a nonhuman primate model of HIV infection, both during and after a course of antiretroviral drug treatment.

The results are scheduled for publication in *Journal of Clinical Investigation* on November 9, 2015.

Scientists at Yerkes National Primate Research Center, Emory University, were testing the effects of a fusion protein based on the immunity stimulator IL-21. They found that when combined with antiretroviral drugs, IL-21 could help restore certain types of intestinal immune cells, which are depleted by SIV (simian immunodeficiency virus) infection and thought to be important for mucosal integrity.

IL-21 has been tested in clinical trials with people fighting skin and kidney cancer, but, so far, not in people who have HIV infection.

"We found IL-21 is effective at reducing residual inflammation and improving the reconstitution of Th17 and Th22 cells, which are critical for intestinal immunity," says senior author Mirko Paiardini, PhD, assistant professor of pathology and laboratory medicine at Yerkes National Primate Research Center, Emory Vaccine Center and Emory University School of Medicine.

Co-first authors of the paper are postdoctoral fellow Luca Micci, PhD, and research specialist Emily Ryan.

In the study, the researchers treated SIV-infected rhesus macaques with the IL-21 fusion protein starting two months after they were infected. All 16 monkeys, eight IL-21-treated and eight controls, received a combination of antiretroviral drugs.

Antiretroviral drug treatment continued for seven months and then was withdrawn. IL-21 was given in three once-per-week cycles, including one cycle just after antiretroviral drugs were stopped.

After drugs were stopped, SIV still reappeared in both the IL-21-treated group and controls. However, in IL-21-treated animals, levels of SIV RNA in the blood stayed at a level that was five times less than in controls, extending out to eight months. A similar effect was seen on viral DNA levels in intestinal tissues and blood CD4 T cells. In addition, IL-21 treatment appeared to have other benefits, in terms of both reduced immune activation and signs of improved antimicrobial immunity.

"This was an important test of the concept that an intervention that reduces immune activation during antiretroviral therapy can also limit viral persistence," Paiardini says. "Our data provide a rationale for additional preclinical studies on IL-21, as part of a novel combination strategy aimed at limiting the size of the latent viral reservoir and contributing to a remission or functional cure."

Provided by Emory University