

Researchers support new strategies for HIV control

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HIV-1 Virus. Credit: J Roberto Trujillo/Wikipedia

The search for an AIDS cure has partly focused on ways to eradicate infected cells. Now, new research from Karolinska Institutet in Sweden and the University of Pennsylvania in the U.S. shows that this approach may not be necessary for a functional cure. In a study focusing on a subset of HIV-positive individuals who can live with the virus without treatment, the researchers found that these people's lymphocytes suppress the virus but do not kill off infected cells.

AIDS is a persistent global health issue with no existing vaccine or cure. HIV infection typically leads to a loss of CD4+ T cells, a type of white blood cell that, together with the CD8+ T cells, attacks and destroys infections. The fewer CD4+ T cells a person has, the worse are the symptoms. But fewer than 1 percent of HIV-positive people have stable CD4+ T cell counts and undetectable HIV viremia, and are thus able to live with the virus without therapy. This group, known as elite controllers, has more effective CD8+ T cells—the cells that kill off viruses—than most HIV-positive people.

In this study, published in *Science Translational Medicine*, the researchers wanted to find out exactly how the CD8+ T cells of elite controllers keep the HIV virus from replicating and progressing to AIDS. They collected [blood samples](#) and lymph node tissue biopsies of a total of 51 HIV-positive individuals, including 12 elite controllers, from three sites in the U.S. and Mexico.

Using single-cell RNA sequencing analyses, a method used to study individual cells, the researchers found that elite controllers had more HIV-specific CD8+ T cells in their lymphoid tissue than the others, but that these were so-called non-cytolytic cells, meaning they didn't kill off infected cells. Instead these CD8+ T cells of [elite controllers](#) had a distinct transcriptional profile and were able to suppress HIV replication through an enhanced ribosomal function, meaning they were better at translating proteins from amino acids. This led to the production of more

and a greater variety of cytokines, small protein molecules that are important in cell communication, and boosted the cells' polyfunctionality.

"These findings go against the paradigm of HIV control that focuses on killing off infected [cells](#) to find a cure," says Marcus Buggert, assistant professor at the Department of Medicine, Huddinge, at Karolinska Institutet. "While these strategies may still work, our research supports a model in which viral suppression rather than viral eradication can in fact serve as a functional cure."

More information: S. Nguyen et al., "Elite control of HIV is associated with distinct functional and transcriptional signatures in lymphoid tissue CD8+ T cells," *Science Translational Medicine* (2019). stm.sciencemag.org/lookup/doi/10.1126/scitranslmed.aax4077

Provided by Karolinska Institutet

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