Scientists Find No Signs That Well-Treated HIV Replicates in Lymph Nodes

This finding stands in sharp contrast to a controversial 2016 paper that reached the opposite conclusion.

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A research team has found no evidence of ongoing HIV replication in the lymph nodes among individuals receiving fully suppressive antiretroviral (ARV) treatment for the virus. This finding stands in sharp contrast to the conclusions of a 2016 study out of Northwestern University, published in Nature, that indicated that even in the face of ARV treatment, HIV replicates in the lymph nodes, thus helping to replenish the viral reservoir.

Today, as scientists seek means to cure the virus or provoke extended periods of viral remission without the need for regular ARVs, it is incumbent upon the overall cure research field to characterize the viral reservoir, the stubborn presence of which prevents standard ARV treatment from ridding the body of HIV. Hence, determining what role the lymph nodes may play in maintaining the reservoir is an important piece of the puzzle.

According to one scientific school of thought, despite effective ARV treatment, the virus maintains a low level of replication in the body, whether in the presence of the medications or in sanctuary sites—places in the body out of reach of HIV treatment. In an opposing school of thought, effective ARV treatment is in fact fully potent and suppresses all viral replication. The new study's findings add credence to the latter theory.

Findings from this study were presented by Mary Kearney, PhD, of the HIV Dynamics and Replication Program at the National Cancer Institute, at the 2018 Conference on Retroviruses and Opportunistic Infections (CROI) in Boston.

Kearney and her team studied five individuals living with HIV, four of whom had a viral load below 40 and had been taking ARVs for four to 13 years and one of whom had not taken treatment for the virus. The investigators took samples of peripheral blood mononuclear cells (PBMCs), which have been established as cells that harbor the latent, or unreplicating HIV, that is a chief component of the viral reservoir. They also took samples of lymph node mononuclear cells (LNMCs), drawing cells from opposing pairs of lymph nodes among the participants.

Additionally, the investigators secured samples from three of the ARV-treated participants that

predated their time on HIV treatment as well as a pair of samples from the lymph nodes located at the crease of the thigh and the torso taken a year apart in each of two HIV-treated participants.

The scientists conducted genetic analyses of the provirus—the viral genetic code integrated into the cells—of clones of infected cells and of the provirus's expression in the PBMCs and LNMCs. These analyses indicated a broad genetic diversity among the viral copies.

The researchers found no evidence of compartmentalized viral replication in the lymph tissue. Nor did they see evidence that the population of virus in the two types of cells had diverged genetically from that seen in such cells before the study subjects began taking ARVs.

These findings, the researchers concluded, were not consistent with the theory that during fully suppressive ARV treatment, the HIV reservoir is maintained by ongoing cycles of viral replication in either the PBMCs or LNMCs.

"In the blood of these individuals we did not find evidence for ongoing cycles of viral replication, which is consistent with what we found in other patients," Kearney said. "And when we looked in the lymph nodes, we also did not find evidence of viral replication. We concluded that [ARV treatment] is fully potent in the lymph nodes, just as it is in the blood."

Contacted for comment about Kearney's study, Steven Wolinsky, MD, a professor of infectious diseases at Northwestern University who is the lead author of the contrasting Nature paper, said, "We welcome the replication efforts and would be particularly keen to access their data to confirm the analytical findings."
