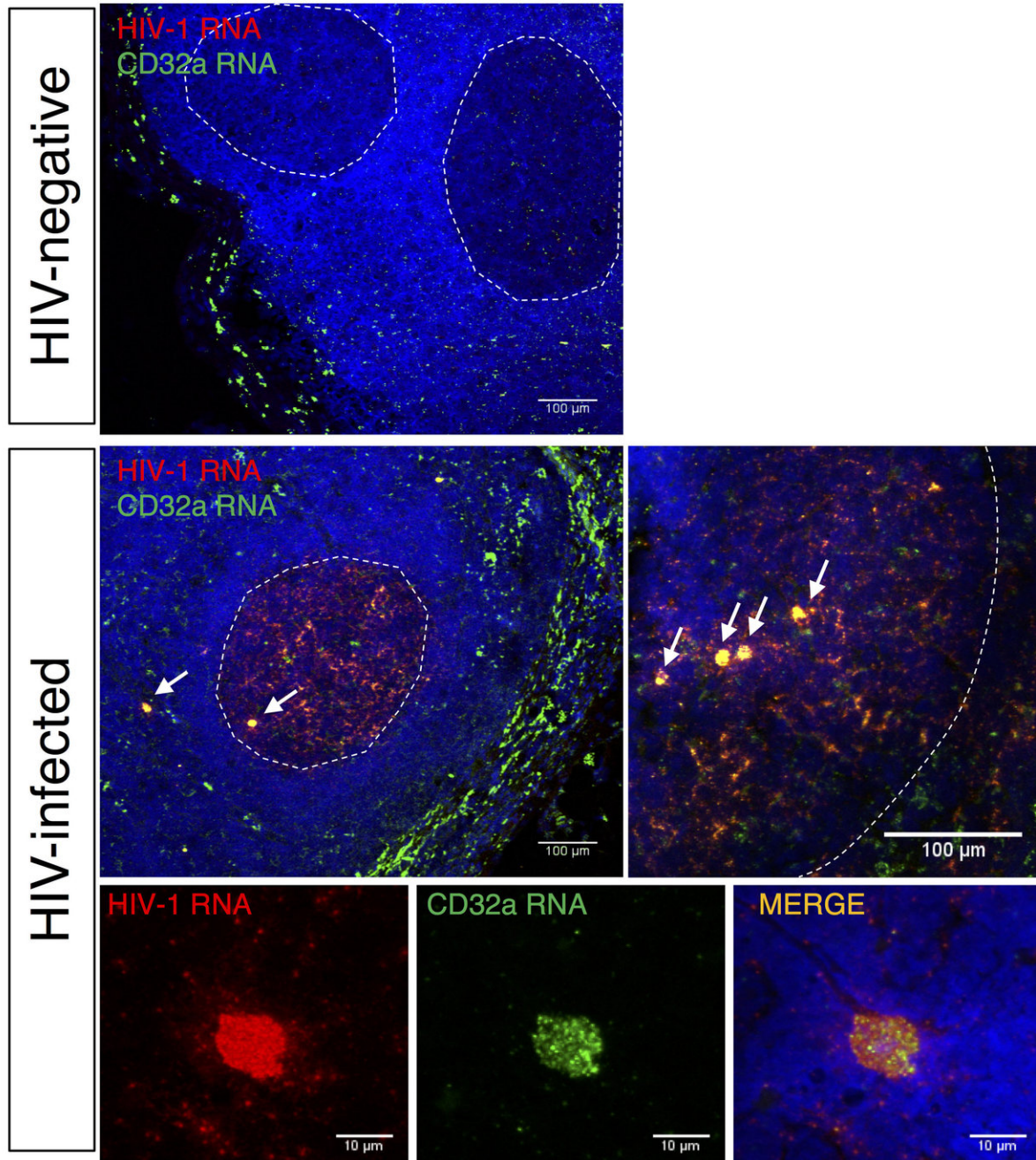


Top HIV cure research team refutes major recent results on how to identify HIV persistence

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Microscopic images showing levels of CD32 (green) and HIV-RNA (red) in lymph node tissue from an HIV-infected patient and a healthy control. The HIV-infected patient had cells expressing both HIV and CD32 (white arrows). Credit: M. Abdel-Mohsen et al., *Science Translational Medicine* (2018)

An international team focused on HIV cure research spearheaded by The Wistar Institute in collaboration with the University of Pennsylvania and Vall d'Hebron Research Institute (VHIR) in Barcelona, Spain, established that the CD32 molecule is not a preferential biomarker to identify HIV silent reservoirs within the immune system of patients undergoing antiretroviral therapy (ART), as proposed by a recent landmark study. Instead, they report that CD32 identifies cells that are actively infected in spite of ART. These results, which have impactful implications for research on HIV eradication, were published in *Science Translational Medicine*.

ART suppresses the replication of HIV in the host immune cell population and stops the progression of HIV-related disease. However, patients continue to have low but persistent amounts of virus in their blood - either in resting or activated [cells](#). The major obstacle to achieving an HIV cure is the ability of the virus to remain latent by hiding in resting CD4 T cells in a silent status, in which the virus does not actively replicate or express its proteins.

In order to understand the mechanisms of viral latency and target the HIV reservoir, researchers need to isolate latently infected CD4 T cells in vivo.

"Identifying specific biomarkers of latently infected cells is considered as the 'holy grail' in the HIV eradication field," said lead corresponding author Luis J. Montaner, D.V.M., D.Phil., director of the HIV-1 Immunopathogenesis Unit at The Wistar Institute Vaccine & Immunotherapy Center. "A recent report published in *Nature* by Descours et al. prompted great interest, as it claimed to have identified CD32 as one such marker that is selectively expressed on the majority of persistently infected CD4 T cells. In an effort to reproduce and broaden these results, we found CD32 was telling us something quite different from what was reported. By the end, our collective data challenge the

notion that CD32 identifies HIV latently infected T cells."

The team thoroughly analyzed blood and immune tissues from HIV-negative donors, HIV-positive individuals treated with ART, and HIV-positive viremic individuals, collected at several institutions around the world. They also observed similar findings in an animal model of HIV infection.

Results showed that CD32 expression is rather a marker for activated, HIV infected CD4 T cells, since it was co-expressed with other molecules that characterize immune activation. Furthermore, CD32 did not enrich for HIV DNA, which is one of the main traits of latently infected CD4 T cells, whereas the majority of HIV DNA resided in CD32-negative cells. Instead, results pointed to a direct link between CD32 expression and active HIV infection, as suggested by the concomitant presence of HIV RNA that indicates active transcription of the viral genome.

"Our work sheds light on the nature of CD32 as a molecule associated with transcriptionally active HIV and proves that targeting CD32-positive cells is unlikely to hit the HIV latent reservoir," said Mohamed Abdel-Mohsen, Ph.D., assistant professor in The Wistar Institute Vaccine & Immunotherapy Center and first author of the study. "Although CD32 may provide a helpful tool to study HIV transcription, we need to go back to the drawing board and keep searching for reliable and specific HIV latency biomarkers for the development of effective strategies towards HIV eradication and cure."

More information: M. Abdel-Mohsen et al., "CD32 is expressed on cells with transcriptionally active HIV but does not enrich for HIV DNA in resting T cells," *Science Translational Medicine* (2018).
stm.sciencemag.org/lookup/doi/.../scitranslmed.aar6759

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