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Defining the impact of cannabis use on immune cell phenotypes and the latent viral reservoir in people with HIV.

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HIV infection remains incurable due to the persistence of a viral reservoir during antiretroviral therapy. This reservoir is formed by a set of infected cells in which the virus is maintained in a reversibly silenced latent state by epigenetic and chromatin-based modifications that restrict viral gene expression. Cannabis (CB) use is prevalent amongst people with HIV (PWH), but the impact of CB on the latent HIV reservoir has not been investigated. Peripheral CD4 and CD8 T cells from a cohort of CB-using PWH and a matched cohort of non-users on antiretroviral therapy were evaluated for expression of maturation/activation markers, HIV-specific T cell responses, and the frequency of intact proviral DNA. CB use was associated with increased abundance of naïve T cells, reduced effector T cells, and reduced expression of activation markers. While the abundance of intact proviruses was not significantly affected by CB use across the whole cohort, we observed that, for participants with high frequency of NKG2A or CD16 expression in NK cells, CB use was associated with a smaller intact HIV reservoir. In vitro stimulation of latently infected T cells with THC followed by analysis using single cell RNAseq/ATACseq demonstrated a transient reduction in HIV transcription and accessibility, as well as suppression of ribosomal gene expression. This analysis is consistent with the hypothesis that cannabinoids induce a hypometabolic state in HIV infected cells that limits activation, exhaustion and senescence in the T cells of PWH and may influence the size of the latent HIV reservoir.