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Single cell multiomic analysis of cannabis use in people with HIV on ART

Background- Despite effective control of human immunodeficiency virus-1 (HIV-1) replication with anti-retroviral therapies (ART), HIV associated chronic inflammation is a major cause of co-morbidities in people with HIV (PWH). To relieve pain, recreational and medicinal cannabis (CB) use has increased significantly among PWH. However, specific molecular mechanisms that uniquely address their effects on HIV reservoir and the complex immune milieu in PWH have not been formally assessed.
Methods- Cellular Indexing of Transcriptomes and Epitopes by Sequencing (CITE-seq) was performed on PBMCs from a cohort of ART-suppressed PWH (n=40) with confirmed plasma toxicology for CB use (heavy and moderate) or non-use. Data analysis was performed using the Scverse ecosystem. For modeling the effects of CB use on latent HIV reservoir, we measured HIV viral DNA using Intact Proviral DNA Assay (IPDA) and quantified cell associated HIV expression using HIV gag-specific qPCR.
Results- We observed that CB use significantly reduced HIV viral expression in heavy CB users as compared to moderate use while with no significant differences in the viral reservoir measurements. We also saw significant increase in regulatory T cells (Tregs) in moderate CB users as compared to non-users and lower frequencies of CD4+ terminal effector cells and CD161+ natural killer cells in CB users. We observed reduced expression of the inflammatory NF-κB pathway in some CB users. While moderate CB users show downregulation of this pathway, heavy use of CB was associated with upregulation of NF-κB pathway. Interferon responses were also upregulated in CB users while cytoplasmic translation and macromolecular processes were downregulated in all immune compartments for CB users.
Conclusion- These findings reveal that CB use can have major immunomodulatory effects based on frequency of use which could dictate its effects on the inflammation and reservoir dynamics in PWH on ART.

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