

Name: Urja Achal Bhatt, MS

Email: urja22@email.unc.edu

Impact of Substance Use on Viral Reservoir and Immune Cell Gene Expression in People With HIV on ART

Background- People with HIV (PWH) on antiretroviral therapy (ART) maintain a viral reservoir that is resistant to ART as well as elevated levels of chronic inflammation and comorbidity. Substance use is frequent amongst PWH, but the impact of substances such as marijuana (MJ), methamphetamine and tobacco (TB) on inflammation and viral persistence during therapy is unknown.

Methods- We analyzed the viral reservoir, plasma cytokine levels, immune cell frequencies and RNA-sequencing data from CD4+T cells isolated from a cohort of 66 PWH to assess the impact of substance use on these parameters. The frequency of recent substance use was collected using a survey form. Pydeseq2 software was used for differential gene expression analysis of bulk-RNA sequencing data.

Results- Remarkably, MJ use in-vivo was associated with a significantly lower HIV-1 DNA copies per million CD4+T cells and reduced viral reservoir expression. We also found that MJ use is associated with lower counts of neutrophils and lymphocytes. We did not observe any significant differential gene expression in the CD4+T cells of MJ users. Notably, TB smoking was associated with a significantly lower CD4:CD8 ratio and higher levels of the pro-inflammatory cytokine IL-1 β in plasma. Comparison of the CD4+T cell transcriptome of TB users and non-users revealed upregulation of pro-inflammatory pathways including TNF α signaling via NF- κ B pathway, Toll-like receptor signaling pathway and Interferon-gamma response in TB users.

Conclusion- These findings reveal that MJ use is associated with distinct alterations to the viral reservoir while TB use is associated with upregulation of inflammatory pathways and lower CD4:CD8 ratio. Thus, different substance use can have complex pleiotropic effects on the immune cells in PWH on ART.

Authors:

Submitter: Urja Achal Bhatt, PhD Student, 3rd year, University of North Carolina, Chapel Hill,
Edward Browne, PhD, University of North Carolina, Chapel Hill
Steve Deeks, MD, University of California San Francisco
Frederick Hecht, MD, University of California San Francisco
Rebecca Hoh, MS, University of California San Francisco
Sulggi Lee, MD, PhD, University of California San Francisco
David Margolis, MD, University of North Carolina, Chapel Hill