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

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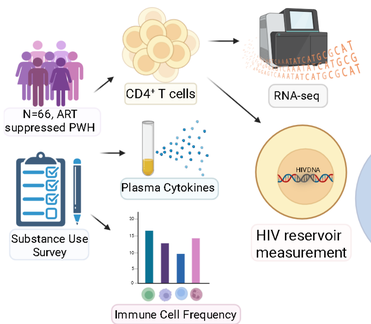
BACKGROUND

Recreational and/or medicinal substance use is prevalent among people living with HIV (PWH) on anti-retroviral therapy (ART). However, their effects on the immune system and HIV-1 latent reservoir are not fully elucidated. Our studies reveal important findings regarding effects of substance use HIV reservoir and functions of immune cells.

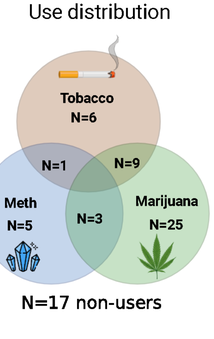
METHODS

We obtained self-reported substance use, blood differential, cytokine and reservoir measurements, and RNA sequencing data from CD4+ T cells of a cohort of 66 PWH on ART(UCSF-SCOPE, Options cohort) to assess the impact of substance use. Pydeseq2 was used for data analysis.

Experimental Setup

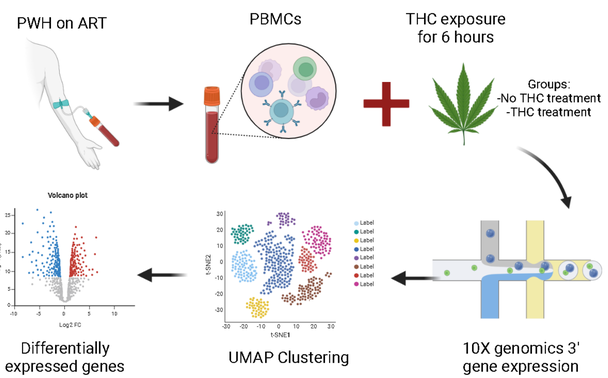


Cohort- Substance Use distribution



Ex-vivo THC exposure

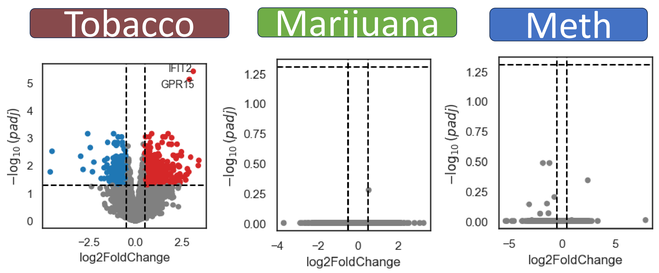
PBMCs from 3 PWH on ART were treated with 500nM Δ9-tetrahydrocannabinol (THC) for 6 hours ex-vivo. 10X genomics 3' single-cell pipeline was implemented to understand changes in gene expression using Scanpy.



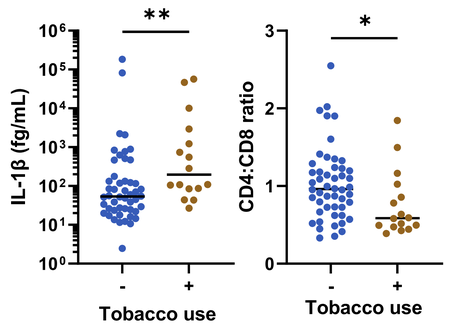
Substance Use may significantly impact HIV reservoir and inflammation.

RESULTS

Substance use (right) Vs non-use (left)

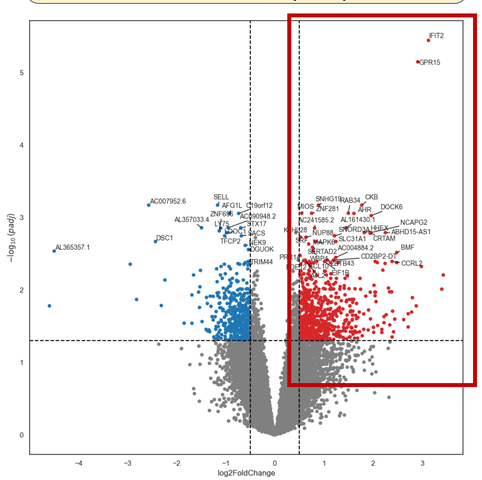


Differential gene expression analysis was performed for substance use vs non-use. Tobacco use resulted in up- and down-regulation of several genes in CD4+ T cells

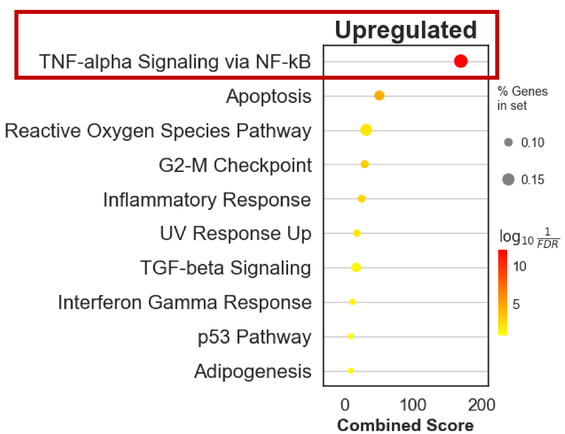


Tobacco use is associated with higher level of IL-1β, an inflammatory cytokine and decreased CD4:CD8 ratio, associated with non-AIDS comorbidities in PWH

Volcano plot- Tobacco use (right) vs non-use (left)

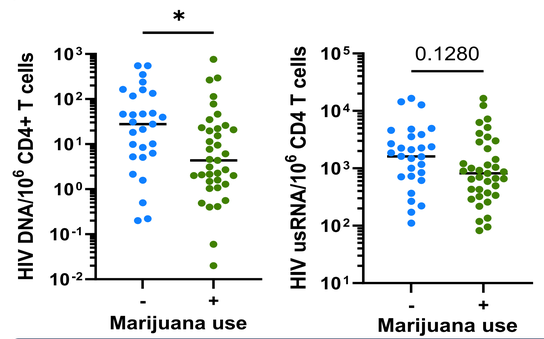


Gene Set Enrichment analysis on Tobacco use upregulated genes



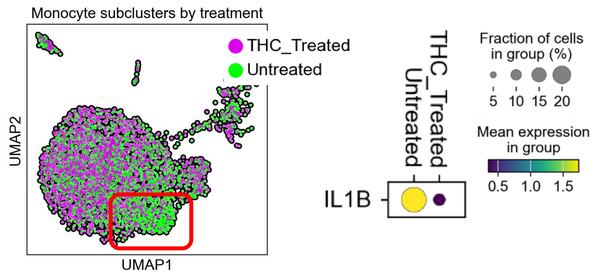
Tobacco use was found to upregulate several genes; a substantial number of upregulated genes belong to the Nf-κB pathway, responsible for driving an inflammatory response.

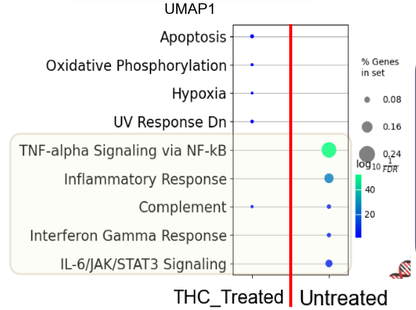
Marijuana use and HIV reservoir



Marijuana use is associated with a smaller HIV reservoir with no significant changes in viral RNA.

Ex-vivo THC exposure





We found transcriptomic downregulation of monocyte-derived pro-inflammatory cytokines and pathways for THC treated PBMCs from PWH on ART

PLAIN LANGUAGE SUMMARY

- Tobacco use upregulates inflammatory pathways.
- Marijuana use is associated with smaller HIV reservoir.
- THC treatment downregulates the inflammatory signals in monocytes.
- Mechanisms driving the effects of marijuana are unknown.

References: PMID-38243412, PMID: 31779701, PMID: 38019897

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