

Immunomodulatory effects of THC on the immune cells of people with HIV on ART

Background- People with human immunodeficiency virus type-1 (HIV-1) infection (PWH) on antiretroviral therapy (ART) experience chronic inflammation and persistent immune activation. To alleviate inflammation symptoms, recreational and medicinal cannabis (CB) use, known to be anti-inflammatory, is common among PWH but the molecular effects are unknown.

Methods- In this study, we investigate the effects of Δ^9 -tetrahydrocannabinol (THC), the chief psychoactive compound of CB, on the transcriptome of peripheral blood mononuclear cells (PBMCs) from $n=3$ PWH on ART and $n=1$ seronegative donor using single-cell RNA sequencing. The PBMCs were exposed to 500nM THC for 6 hours.

Results- We compared the differential gene expression between untreated, and THC treated PBMCs and observed that monocytes showed the most differential gene expression. In our dataset, a subset of CD14⁺ monocyte cluster from 2 out of 3 PWH on ART showed high expression of proinflammatory cytokines such as IL1 β and NF- κ B pathway in untreated condition. Post THC exposure, the frequency of this pro-inflammatory monocyte cluster significantly decreased along with pro-inflammatory cytokines, constituents of NF- κ B pathway and NLRP3 inflammasome. In the HIV seronegative donor, THC exposure caused increase in oxidative phosphorylation and cytoplasmic translation activity in all immune cell compartments.

Conclusions- Chronic inflammation in PWH on ART drives the expedited immune aging called “inflammaging” responsible for several co-morbidities. THC-mediated inhibition of the inflammasome/NF- κ B pathway in monocytes, may contribute to its anti-inflammatory effects. This investigative pilot study alludes to important immune-modulatory effects of CB on the immune cells of PWH. Further work investigating the mechanism of action of THC and whether its effect is beneficial or detrimental for PWH will be an important avenue of future research.

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