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Peripheral immune cell pro- and anti-nociceptive gene expression in chronicbinge alcohol administered SIV-infected rhesus macaques

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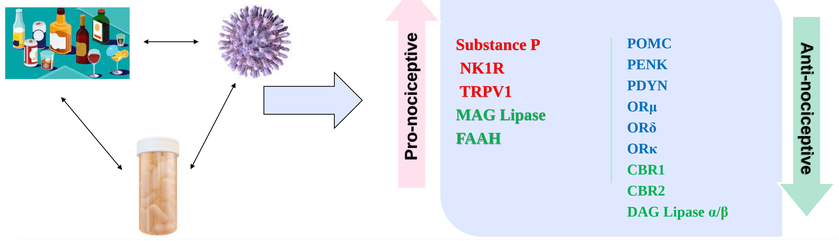
Introduction

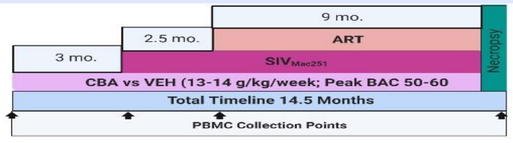
- People living with HIV (PLWH) have a 2-fold higher prevalence of chronic pain compared to the general population.
- People consume alcohol to self-medicate pain
  - Chronic alcohol use, HIV infection, and anti-retroviral therapy (ART) all independently lead to altered pain states, yet the underlying pathophysiology is poorly understood.
- PBMC gene expression are used as surrogate markers for altered states of inflammation and nociception in diseases such as IBS, Cardiac Syndrome X, and polyneuropathy
- This study investigated gene expression of the endocannabinoid, opioid, and nociceptive pain receptor systems in PBMCs as indicators and potential markers of alcohol, ART, and HIV associated alterations in pro and anti- nociceptive pathways in a relevant preclinical model of HIV-infection.

Hypothesis

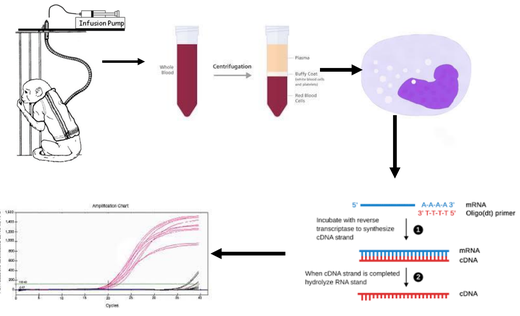


Chronic binge alcohol increases expression of pro-nociceptive and decreases anti-nociceptive genes of peripheral mononuclear cells in SIV-infection.

Materials and Methods

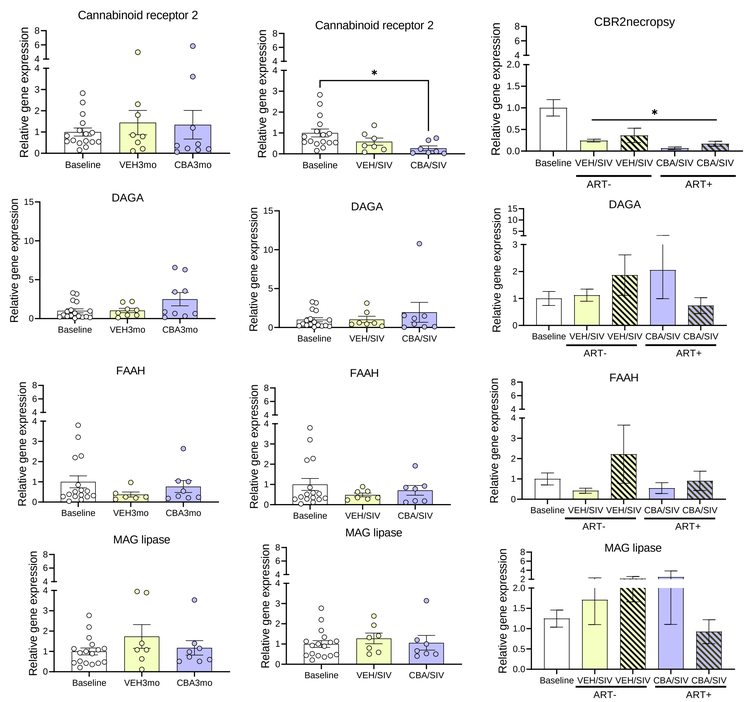


- Four experimental groups were studied; VEH/SIV/ART-; VEH/SIV/ART+; CBA/SIV/ART-; and CBA/SIV/ART+ (N=5-7/group). mRNA was isolated from PBMCs collected at 4 timepoints: baseline, 3 months of CBA/VEH administration, viral setpoint, and at study end point (11.5 months post-SIV infection).

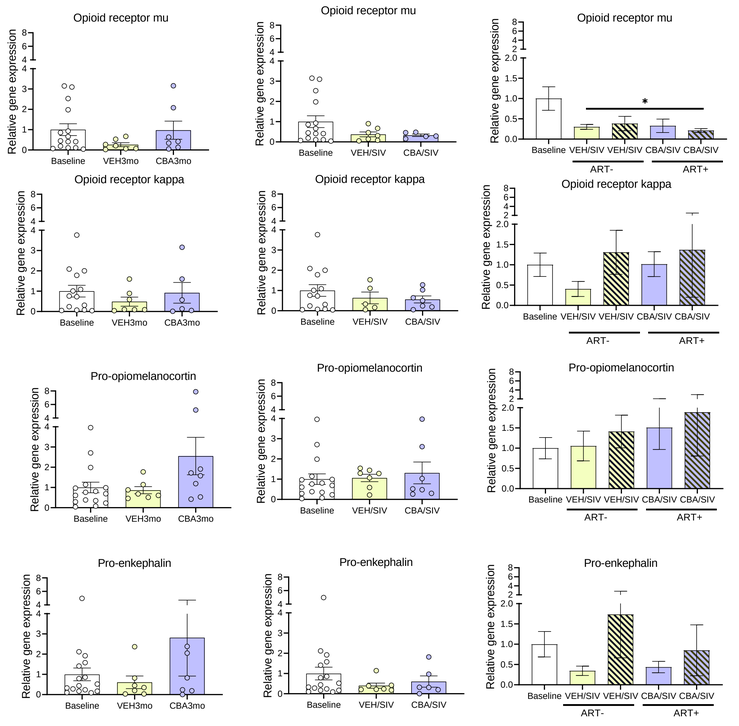


- mRNA from each sample was extracted using Qiagen RNeasy ckit
- RNA was transcribed to cDNA using Qiagen Reverse Transcriptase
- Using qPCR each sample was normalized to the housekeeping gene RPS13 and the relative gene expression calculated using Pfaffl (Delta-Delta Ct) method

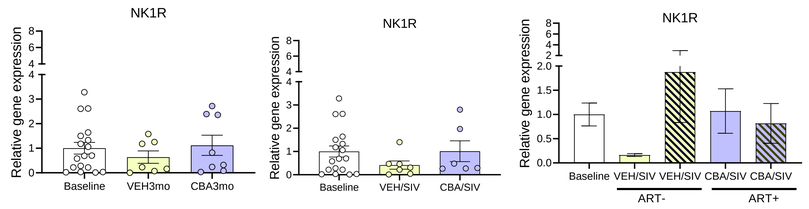
Endocannabinoid Gene Expression



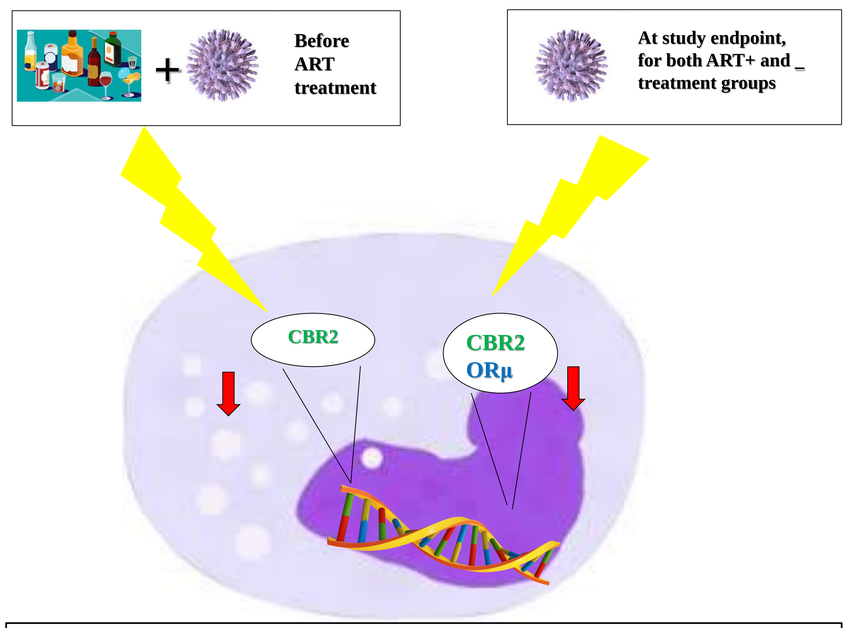
Opioid Gene Expression



Pain Receptor Gene Expression



Conclusions



- Decreased CBR2 and ORM expression at study end point in all treatment groups compared to baseline suggests that SIV significantly contributes to the pro inflammatory/ nociceptive state seen in PLWH
- Lack of significant changes in POMC/PENK/PDYN, as well as SP and NK1R suggest that the PBMCs may not be driving the pro-nociceptive state but rather responding to it and facilitating increased inflammation instead

Future Studies

- Compare target gene expression in PBMCs expression with that of frontal cortex to identify if the peripheral expression reflects that of the CNS.
- Analyze gene expression in human PBMCs of PLWH and correlate it with pain sensitivity test measures.

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