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Effects of cannabinoids on phenotype of patient monocyte-derived macrophages varies by cannabis use patterns

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Antiretroviral therapy (ART) has improved the quality of life and survival of people with HIV (PWH). However, immune activation and inflammation persist after viral suppression and these appear to be central mechanisms underlying central nervous system (CNS) dysfunction. PWH using cannabis demonstrate reduced inflammation and CNS dysfunction. We hypothesized that cannabis use may reduce inflammatory gene expression in monocyte-derived macrophages (MDM). MDMs were generated from blood specimens donated by PWH stratified into three groups: 1) naive (n=14); 2) moderate (1-6 times/week; n=5); and 3) daily cannabis users (n=3). MDMs were stimulated with THC, CBD, inflammatory cytokines and ART drugs alone or in combination for 24 hours and then analyzed for mRNA and protein expression of inflammatory genes including: NLRP3 and TREM2. CBD induced more robust responses than THC and patterns in MDM responses to CBD varied between the three groups. CBD reduced basal NLRP3 mRNA levels in ~85% of naive, all moderate, and ~66% of daily cannabis users. However, in the presence of IL1b stimulation, CBD reduced NLRP3 mRNA in ~43% of naive, 20% of moderate and ~33% of daily cannabis users. CBD rescued IL1b-induced reductions in TREM2 mRNA in 66% of MDMs regardless of cannabis use pattern. These findings suggest CBD effects on inflammatory gene expression vary in PWH by cannabis use patterns. It is likely that other factors (genetic and environmental) play a role in the effects of cannabinoids on MDMs. More detailed transcriptomic and phenotypic data on MDMs are in the pipeline and recruitment is ongoing.