The epigenetic effects of alcohol and cannabinoids, AM630, and JWH-015 on monocyte-derived dendritic cells

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Previous studies have demonstrated that substances of abuse such as alcohol (Aroor et al., 2014) and marijuana (Yang et al., 2014) play a role in epigenetically modifying gene expression in immune system cells through site-specific histone modifications. Interestingly, THC, the main psychotropic constituent in marijuana, is also known to interact with differentially associated genes responsible for cellular functions such as cell cycle regulation and metabolism (Yang et al., 2014). THC and related synthetic cannabinoids such as JWH-015 and AM630 are functionally similar in that they all bind to the two main cannabinoid receptors, CB1 and CB2 (Fattore & Fratta, 2011). Our own preliminary data analyzing histone modifications clearly revealed the ability of alcohol and the synthetic cannabinoid, JWH-015, to alter the presence of histones H3 and H4 in a previous model where treatments were administered chronically. In this model, alcohol and cannabinoids will be administered to monocyte-derived dendritic cells (MDDCs) at specific time points (24, 48, and 72 hours). Cells will be treated *in-vitro* with varying concentrations of alcohol (0.05, 0.1, 0.2, 0.3, and 0.4 %), the CB2 receptor agonist: JWH-015 (1,5, and 10 μM), and the CB2 receptor antagonist: AM630 (1,5,10 μM), in order to assess the ability of these substances to epigenetically modify the function of these key immune system cells. H3 and H4 histone quantification will be performed after treatments. The role of histone deacetylases will be confirmed by the use of histone deacetylase inhibitors, TSA and MGCD0103. Results emanating from this study will elucidate the epigenetic mechanisms of alcohol and cannabinoids on dendritic cell regulation.