The effects of cannabidiol and HU308 on viral transcription in HIV-1 infected cells and resulting extracellular vesicle release

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As of 2021, roughly 28.7 million of the approximately 38.4 million people living with human immunodeficiency virus (HIV) globally were receiving combination antiretroviral therapy (cART). cART has extended the lives of many people living with HIV (PLWH) but, there are still lifelong ailments associated with HIV-1 such as HIV-associated neurocognitive disorder (HAND), which encompasses a wide range of neurocognitive disorders. The CNS is thought to be a main HIV-1 reservoir, and these infected cells have “leaky” transcription of the viral genome that leads to the eventual packaging of viral RNA and proteins into extracellular vesicles (EVs). These EVs are released from the cell and have been shown to cause an increase the production of proinflammatory cytokines on recipient cells. Previous studies have shown that marijuana use in PLWH is associated with decreased pro-inflammatory cytokines. Here, we investigated the effects the major non-psychoactive molecule of marijuana, cannabidiol and its synthetic molecular cousin, HU308, on viral transcription in HIV-1 infected cells and resulting changes in EV release. Our data suggests that CBD or HU308 can act as an EV release suppressor, which contain cytokines and viral products, both in mono- and 3D culture. Additionally, the results show a significant reduction in classical exosomes released from infected cells. These studies are significant in that CBD or HU308 may provide a protective effect by alleviating the pathogenic effects of EVs in HIV-1 and CNS-related infections.