

Submitter Name: Maria Cowen  
Submitter email: mcowen4@gmu.edu  
PI Name: Dr. Fatah Kashanchi  
PI email: fkashanc@gmu.edu

## **Effects of Marijuana on Viral Transcription in HIV-1 Infected Cells and Resulting Extracellular Vesicle Release**

Catherine DeMarino<sup>1</sup>, Maria Cowen<sup>1</sup>, Bianca Cotto<sup>2</sup>, Sara Jane Ward<sup>3</sup>, Ronald Tuma<sup>3</sup>, Prasun Datta<sup>2</sup>, Leah H. Rubin<sup>4</sup>, Dianne Langford<sup>2</sup>, Fatah Kashanchi<sup>1</sup>

<sup>1</sup>Laboratory of Molecular Virology, George Mason University; <sup>2</sup>Department of Neuroscience, Temple University; <sup>3</sup>Department of Pharmacology, Temple University; <sup>4</sup>Department of Neurology, Johns Hopkins University School of Medicine

As of 2016, roughly 18.2 million of the approximately 36.9 million people living with HIV globally were receiving combination antiretroviral therapy (cART). Despite decades of research and development of this complex drug regimen, which is effective in the prevention of new infections, cells with an integrated HIV-1 genome have leaky transcription which can produce viral RNAs and proteins. These viral products can then be packaged into extracellular vesicles (EVs) and released from the infected cell. EVs, specifically exosomes, produced from HIV-1 infected cells contain viral mRNAs and incubation of these exosomes with cells caused a significant increase in the production of the proinflammatory cytokines, implicating EVs as a possible mechanism for the chronic inflammation observed in the CNS of people living with HIV-1 on antiretroviral therapy<sup>1-4</sup>. Previous studies have shown that marijuana use in people living with HIV is associated with a lower viral load and high CD4+ T-cell count, suggesting a potential therapeutic application. Here, we investigated the effects of cannabinoids, CBD and THC, on viral transcription in HIV-1 infected cells and resulting changes in EV release. Our data suggests CBD and THC can act as viral transcription inhibitors, potentially through two independent mechanisms. Additionally, the results show a significant reduction in EVs released from infected cells. These studies are significant in that marijuana may provide a protective effect by alleviating the pathogenic effects of EVs in HIV-1 and CNS-related infections.