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Impact of Opioids on HIV-induced Innate Immune Response and Pathogenesis

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Although combination antiretroviral therapy (cART) has successfully suppressed HIV replication, a persistent reservoir of latently infected immune cells remains, preventing a complete cure. Substance use disorders, particularly opioid abuse, present additional challenges by altering immune cell function, which may increase HIV susceptibility and influence viral latency. Opioids have been shown to exacerbate HIV pathogenesis in neuronal cells by increasing viral replication and promoting neuroinflammation. However, the impact of opioids on HIV infection and immune cell function remains poorly understood, with limited research on how opioids modulate innate immune responses during HIV infection. Opioid receptors are expressed on immune cells, and opioid exposure can induce molecular changes that influence HIV's ability to persist in these cells. We hypothesize that opioid-induced changes in the epigenomic and transcriptomic profiles of immune cells affect the HIV-induced immune response and influence HIV's ability to remain latent or active. Using in vitro studies, we demonstrate that morphine significantly suppresses the HIV-induced innate immune response in immune cells. Through experiments using inhibitors or viruses lacking the envelope, we show that virus entry is essential for inducing the innate immune response. Our overarching goal is to examine how opioid exposure alters immune cell gene expression and chromatin structure, and how these changes influence HIV infection and latency using single-cell RNA-seq, ATAC-seq, and Cut&Tag to create a comprehensive map of immune cell responses to opioid exposure. This work will inform future strategies for curing HIV, particularly in individuals with substance use disorders.