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Modulation of microRNA profiles in extracellular vesicles by HIV infection and opiates

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Opiate abuse increases the risk of Human Immunodeficiency virus(HIV) transmission and exacerbates HIV neuropathology by increasing inflammation and modulating immune cell function. Theoretically this occurs in part to biomolecules within exosomal extracellular vesicles(xEVs) that have crossed the blood-brain-barrier introducing their biomolecules (lipids, nucleic acids, and proteins) to cells in the brain. Here, we examined in the context of HIV infection and opiate exposure changes in microRNAs (miRNAs), non-coding RNA molecules detected in xEVs. Given that miRNAs regulate protein expression through targeted binding to specific mRNAs, xEV miRNA content may serve as both a mediator and biomarker of HIV disease pathology and opiate use disorder(OUD). Preliminary findings showed that the xEVs derived from morphine-exposed or HIV-infected PBMCs modulated neuronal cell line SH-SY5Y function and viability. Nanostring microRNA array results showed that both HIV infection and opiate(morphine) exposure altered miRNA xEV profile. HIV modulated 164 miRNAs, while opiate(morphine) treatment altered expression of 151 miRNAs, and 97 were common to all treatment groups. Webgestalt and GO slim analysis revealed five specific miRNAs differentially altered by HIV and morphine exposure, which target critical genes involved in viral replication, apoptosis, and neuronal cell function: miR-1290, miR-627-5p, miR-378-e, miR-150-5p, and miR-1246. These miRs may represent a biosignature relevant to OUD in context of HIV infection. Of note, miR-1246, which targets the OPRM1 (mu opioid receptor) gene, was up-regulated in xEVs of morphine-treated cells 12-fold. Taken together, targets of this potential miR-xEV-based signature may identify mechanisms of action or novel therapeutic targets for OUD and HIV neuropathology.