HIV and substance abuse may influence the evolution of exosomes (exosome speciation): Implication for biosignature

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HIV infection co-occurs more frequently with psychiatric disorders, such as drug abuse. Although combination antiretroviral therapy (cART) can inhibit viral replication and slow the progression to AIDS, cognitive impairment seen in drug abusers may result to discontinuation of or intermittent adherence to cART. Poor adherence to cART may result in poor outcomes including increased risk for opportunistic infections, and potentially emergence of resistant HIV strains. Cocaine is one of the most abused drugs in people living with HIV. Given its tendency to enhance HIV replication, cocaine may have an immune and/or epigenetic modulatory function that may be imprinted in extracellular vesicles, such as exosomes. We therefore hypothesized that illicit drug-mediated effects on host cells may be detected in exosomes. To test our hypothesis, we obtained blood from rats repeatedly exposed to cocaine or saline. Further, we obtained blood from HIV negative and HIV positive donors who do or do not abuse drugs. Using a novel technique—Tandem-Preparative-Analytical protocol (TPA), developed in our laboratory, we analyzed the physicochemical properties of exosomes from these groups. Our results reveal interesting interactions between HIV, exposure to drugs, and exosome speciation. First, exosomes secreted into the blood of poly-drug users are different in size and concentration compared to that of drug-naïve controls. This finding was confirmed with data from rat, where repeated exposure to cocaine results in secretion of different exosome species compared to rats exposed only to saline. Second, HIV infection alone or in the setting of drug abuse altered the biophysical properties (size, concentration, and charge) of blood exosomes. These findings indicate that the profile of exosomes in body fluids, such as blood may serve as biosignature for identifying possible co-occurring HIV/drug addiction. Such biosignature may help in early intervention to reduce the risk of comorbidity.