Chioma M. Okeoma, Ph.D, University of Iowa
Abstract

Cocaine alters semen exosome cargo composition and anti-HIV activity

It is over 30 years since the discovery of the Human Immunodeficiency Virus (HIV) and more than 34 million people are living with the virus globally. Despite extensive research efforts, much remains to be learned about the transmission and spread of HIV. Previously, we showed that exosomes from semen of healthy men have the potential to inactivate the infectivity of HIV virions. Given that HIV infection, transmission, and progression to AIDS are now entangled with the epidemics of drug abuse, it is pertinent to understand how illicit drugs, such as cocaine affect HIV infection and spread. Here, we compared the physical, compositional, and functional characteristics of semen exosomes isolated from donors who use or do not use cocaine. Dynamic light scattering and molecular biology assays suggest that cocaine does not alter the physical characteristics of exosomes in human semen. In addition, cocaine does not alter exosomal RNA quality and protein footprint. However, our results highlight two important aspects of the effect of cocaine on exosomal composition and function. First, cocaine markedly reduced protein and mRNA content of exosomal CD63, which is a type II cellular membrane protein that plays multiple important roles in HIV infection. Second, we found evidence that functional traits of exosomes from non-cocaine users and cocaine users differ significantly. While exosomes from non-cocaine users potently inhibit HIV infection, the exosomes isolated from cocaine users did not inhibit HIV infection. Our results suggest that cocaine may i) modulate semen exosome bio-signatures by perhaps altering the composition of exosomes during biogenesis and ii) undermine exosome-driven host protection mechanisms. The observed distinctive effects of cocaine on semen exosome composition and anti-HIV activity support the proposition that illicit drugs may fundamentally alter the compositional and functional profile of exosomes. These findings call for in-depth evaluation of the effect of illicit drugs on semen exosome compositional, epigenetic, and functional reprogramming. Such knowledge may be useful in identifying illicit drug-driven predictive bio-signatures that may influence host health and disease.