Single cell imaging flow cytometry as a novel epigenetic tool to detect post-translational modifications and extracellular histone release induced by substance abuse

Marisela Agudelo, Ph.D., Tiyash Parira, M.S., and Gloria Figueroa, B.S.

Department of Immunology, Herbert Wertheim College of Medicine, Florida International University, Miami, 33199.

Histones are the key proteins in nuclear chromatin and epigenetic modifications of histones play a major role in the regulation of gene transcription; however, extracellular release of histones elicit toxic and neuro-inflammatory effects. Nevertheless, whether these histone proteins are release into the periphery during substance abuse and whether they play a major role during substance abuse-induced inflammation has not been elucidated yet. Our lab has developed a novel method using single cell imaging flow cytometry to detect post-translational modifications in human monocyte-derived dendritic cells (MDDCs) and to elucidate the role of histone modifications during abuse of substances such as alcohol and synthetic cannabinoids. In the current study, we have evidence of the effect of alcohol drinking on the release of extracellular histones in human plasma and our results confirm the presence of circulating histones in plasma from alcohol users, and surprisingly, a significant increase of circulating histones in female drinkers when compared to male drinkers. In addition, when MDDCs were treated *in vitro* with JWH-015 (5 uM) and EtOH (0.2%) there was a differential effect on the release of histones and on the regulation of histone modifications. Our findings, for the first time, demonstrate the presence of extracellular histone proteins in human plasma from alcohol drinkers, a gender-specific effect on the extracellular release of histones, and a differential histone modulatory effect induced by the synthetic cannabinoid, JWH-015. In summary, the detection of post-translational modifications and extracellular histones may serve as a promising tool to measure the inflammatory consequences of substance abuse and even serve as a biomarker for substance abuse disorders.

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