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Non-coding RNAs drive increased fatty acid synthesis and reduce inflammation in cART treated HIV infected cocaine users

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Survival rates of HIV+ substance users are significantly lower compared to non-users despite cART treatment and continue to be a major challenge in this population. The contribution of cocaine to the disruption of balance between pro- and anti-inflammatory pathways and its effects on metabolism are thought to contribute to the comorbidities associated with cocaine use in ART treated subjects. We utilized a systems biology approach to delineate the molecular and cellular mechanisms associated with this poor clinical outcomes in a well-characterized cohort of cART treated HIV+ cocaine users and non-users. We identified a transcriptomic module up-regulated in cocaine users and significantly enriched in non-coding RNA (ncRNA) that regulate RNA metabolism pathways. We also observed a down-regulation, in the cocaine users, of a module enriched with pro-inflammatory and interferons genes and with monocytes and neutrophils associated genes. Interestingly, up-regulation of miRNA193's targets in cocaine users, added more support to the emerging evidences of miRNAs as regulators of drug abuse and immunity and in particular to the role of miRNA193 in the modulation of lipids and fatty acids metabolism. By integrating gene expression data and metabolomic data, we show a positive association between plasma fatty acid metabolites and the ncRNA module whereas a negative association is observed between plasma fatty acid metabolites and the inflammatory/interferon module. Our results provide a framework to investigate the influence of long chain fatty acid in cocaine users in the context of HIV highlighting the role of ncRNA in controlling inflammation by impacting on cell metabolism.