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Transcriptome-wide association study for frequent cocaine use identifies gene dysregulation in CD4+ T cells linked to immune response and cancer pathways

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Cocaine use is known to affect immune cell populations in ways that increase susceptibility to infectious diseases, such as HIV, and development of health disorders. However, little is known regarding modulation of immune-related gene expression by cocaine and how it relates to disease pathogenesis. To better characterize transcriptomic effects of frequent cocaine use, we tested for differential gene expression in CD4+ T cells by cocaine use status. We generated RNA-seq data for CD4+ T cells isolated from 259 peripheral blood samples. Samples were from the Women's Interagency HIV Study with self-reported frequent cocaine use (at least once per week, N=64) or no cocaine use (N=195) within 6 months prior to blood draw. All samples were from women living with HIV who had an undetectable HIV RNA viral load in blood for a minimum of 6 months.

Transcriptome-wide differential expression testing was conducted using negative binomial regression, resulting in 824 differentially expressed genes (DEGs; FDR<0.05) by cocaine use status. Of these a significantly higher proportion showed increased expression with frequent cocaine use (624 DEGs; binomial test p<2.2e-16). DEGs were enriched in Gene Ontology and biological pathway terms related to immune response such as GTPase activity, cell migration, and T cell activation and proliferation (FDR<0.05). DEGs were also overrepresented in cancer-related pathways, including EGFR signaling, PI3K signaling, and oncogenic MAPK signaling (FDR<0.05). Together, these results highlight potential genes and pathways by which cocaine use may alter immune function and health outcomes.