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# Long noncoding RNA landscape in the intestinal epithelium of delta-9-tetrahydrocannabinol treated chronically SIV-infected rhesus macaques

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**Background.** Medicinal and recreational cannabis use is widespread in HIV patients. We previously defined a novel anti-inflammatory gene/microRNA signature in the gastrointestinal tract of Delta-9-Tetrahydrocannabinol ($\Delta^9$-THC) treated chronically SIV-infected rhesus macaques (RMs). Long non-coding RNAs (lncRNAs) play important epigenetic regulatory roles including chromatin remodeling, transcriptional control, post transcriptional processing and show tissue specific expression. We hypothesized that modulation of lncRNA expression represents an epigenetic mechanism underlying the anti-inflammatory effects of THC. **Methods.** Using microarray, we profiled lncRNAs and protein-coding gene expression in colonic epithelium (CE) of uninfected (n=6) and SIV-infected RMs administered either vehicle (VEH/SIV; n=5) or $\Delta^9$-THC (THC/SIV; n=6). **Results.** Relative to controls, 2660 and 2664 lncRNAs ($p<0.05$) were up and downregulated, respectively in CE of VEH-SIV RMs. Interestingly, fewer lncRNAs were differentially expressed in THC-SIV RMs (1951-up and 1855-down). Well characterized HOTAIR, MALAT1, GATA6-AS1, GATA3-AS1, SPRY-IT1 were exclusively upregulated in CE of VEH-SIV RMs. Similarly, NEAT1 and IFNG-AS1 were upregulated only in THC-SIV RMs. Importantly, BISPR, an exon sense-overlapping lncRNA that negatively regulates interferon signaling showed 2.4-fold higher expression in THC-SIV relative to VEH-SIV RMs suggesting a lncRNA mechanism underlying cannabinoid inhibition of inflammatory response. LncRNA-miRNA-mRNA regulatory networks are being constructed. In vitro studies to characterize the effects of THC on BISPR and other lncRNAs are in progress. Further, THC prevented lymph node fibrosis in THC-SIV RMs by significantly upregulating the anti-fibrotic transcription factor PPAR$\gamma$. **Conclusions.** Our findings for the first time show that THC-mediated suppression of HIV/SIV induced intestinal epithelial dysfunction/inflammation involves differential modulation of lncRNA expression.