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Role of long non-coding RNAs (lncRNAs) in HIV latency

Abstract: Therapeutic reversal of HIV latency and elimination of the latent reservoir is the final frontier towards a complete cure of HIV infection. However, current therapeutic strategies fail in settings, and the inability to design effective therapeutic options that control HIV gene expression reflects gaps in our understanding of how HIV transcription and viral latency are regulated. While the mechanisms by which host proteins govern HIV gene expression and viral latency have been extensively investigated and are relatively well- understood, there remains a significant gap of knowledge regarding the emerging role of the non-coding transcriptome, specifically long non- coding RNAs (lncRNA) in understanding the steps that establish viral latency.

We present preliminary results that suggest that the lncRNA CYTOR is a novel activator of HIV gene expression that is recruited to the HIV promoter and activates HIV gene expression. CYTOR also suppresses viral latency establishment, and facilitates latency reversal. These functions stem from the direct association of CYTOR with the cellular transcription elongation machinery that mediates RNA-polymerase pause-release and transcription elongation and modification of the chromatin landscape around the viral promoter. Indirectly, CYTOR regulates down-stream gene targets to promote T cell activation and actine remodeling. Overall, our study provides new insights on the regulation of HIV transcription and the role of lncRNAs in the control of viral latency, as we obtain a comprehensive understanding of the role of CYTOR in HIV gene expression and latency establishment.

Keywords: HIV; non-coding RNA; latency; RNA Polymerase II; transcription control

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