Contribution of lncRNAs in Establishment of HIV Latency in Central Memory CD4 T Cells

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HIV cure research has been hampered by the existence of a latent viral reservoir that persists in infected individuals receiving antiretroviral therapy. To date, most of the cure research has focused on protein-coding genes but recently the interest in the study of long non-coding RNA (lncRNA) has risen, as these molecules could provide insight in new therapeutic strategies and further complete insight in the HIV life cycle.

Transcriptome profiling was performed (total RNA-Seq) in two primary HIV latency models of central memory CD4 T cells (T\textsubscript{CM}) to investigate changes in lncRNA expression. Subsequently, differentially expressed mRNAs and lncRNAs were identified in both models and a guilt-by-association analysis was implemented to infer biological roles for the lncRNAs in HIV latency.

In the primary HIV latency models, we respectively identified 826 & 471 mRNAs (87.8\% & 76.2\%) and 115 & 147 lncRNAs (12.2\% & 23.8\%) that were significantly differentially expressed (FDR<0.05) between uninfected and latently infected T\textsubscript{CM} cells. Between models, 10 lncRNAs were overlapping (oa. NEAT1 and PVT1) and many of these lncRNAs were associated with pathways involved in cell cycle regulation and pathways with a link to HIV latency: IL-7, PTEN, CSK and CCR5. In addition, a cluster of 17 lncRNAs was associated with the p53 pathway and corroborate earlier findings in this T\textsubscript{CM} model that illustrated p53-dependent latency establishment. One of these upregulated p53-linked lncRNAs, 7SLRNA, has a characterized inhibitory role in the p53 pathway and would suit as a possible new therapeutical target.

Altogether, this study demonstrates that several lncRNAs play a role in HIV latency and can be linked to biological pathways with importance in HIV latency establishment and maintenance. Some of these lncRNAs, i.e. NEAT1, PVT1 or 7SLRNA, represent possible targets for reversing HIV latency and contribute to a HIV cure.