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Modulation of HERV family expression after treatment with HDAC inhibitors

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Background: Human Endogenous Retroviruses (HERVs) comprise about 8% of the human genome. Some autoimmune diseases and cancers have been associated with the expression of HERV-K, which is the most recently integrated family of endogenous retroviruses. The production of HERV-K derived proteins in HIV infected cells provides a potential target for HIV eradication. Latently HIV infected remain as the major obstacle for HIV eradication. Use of histone deacetylase inhibitors (HDACis) to induce HIV expression in resting cells is a promising strategy for HIV latency reversal.

Methods: In this study we quantified the reactivation of five different families of HERVs by three non-selective HDACis (Vorinostat, Panobinostat and Romidepsin) in a latently HIV-1 T-cell model.

Results: After a 5-hour pulse with each HDACis, Vorinostat (1000nM), Panobinostat (50nM) and Romidepsin (50nM), we detected a 23.8%, 32.1% and 58.9% reactivation of HIV-1, respectively by measuring intracellular KC57 expression by flow cytometry. We also detected an increase in the gene expression of tested HERV families (R, K, H and P), with Panobinostat having the strongest ability to induce expression HERV-K. Further analysis within the HERV-K family, revealed that the pol gene was the most expressed gene compared to gag and env.

Conclusions: These data demonstrate the dynamic regulation of HERV expression after treatment with HDACis and future HIV-1 therapeutic strategies should consider the influence of the reactivation of endogenous retroviruses in infected cells.