Targeting HIV Transcriptional Machinery for a Functional Cure of HIV

Antiretroviral therapy (ART) has been used to suppress HIV, but the virus persists in latent CD4+ memory T cells through stable HIV proviral DNA. If ART is interrupted, these latent HIV reservoirs will rebound, typically within a few weeks. A developing strategy for a functional HIV cure, "Block and Lock," aims to prevent this viral reactivation by suppressing the provirus into a latent state. We examine the efficacy of two compounds to interfere with the transcriptional machinery of HIV provirus to eliminate replication. Compound A inhibits epigenetic modifications of nucleosomes, inducing a silenced structure of local chromatin at the HIV promoter. Compound B inhibits positive transcription elongation factor (P-TEFB), which is essential for HIV transcriptional elongation. 2D10 cells were treated with both compounds separately and in combination. Relative proviral expression indicates that both compounds were effective in blocking the transcriptional machinery of HIV. Interruption of treatment resulted in an initial increase in expression, but long-term silencing is still under investigation.