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A Novel Post-transcriptional Block in Gene Expression Contributes to HIV-1 Latency In Vivo

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HIV-1 latency represents a major barrier to eradication. We describe a novel post-transcriptional block in HIV-1 gene expression in latently infected cells. Multiply spliced HIV-1 RNAs encoding the critical positive regulators Tat and Rev exhibited strict nuclear localization in latently infected primary resting CD4+ T cells. Proteomic analysis identified polypyrimidine tract binding protein (PTB) as a HIV-1 RNA binding protein which allows cytoplasmic accumulation of HIV-1 RNAs and subsequent release of replication-competent virus by latently infected cells. Thus a post-transcriptional block in resting cells interrupts a positive feedback loop and contributes to latency. This work suggests novel approaches for reversing latency.