Generating HIV Proviruses to Model Variation of Transcription and Latency Across Different HIV Subtypes

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Abstract

Since the development of antiretroviral therapies (ART), people living with human immunodeficiency virus (HIV) have been able to live longer and healthier lives. However, a cure for HIV still does not exist. ART treatments can prevent further viral replication within the host, but it remains unable to eradicate the virus from all infected cells. Among infected cells in the host, a subset becomes latently infected. If ART treatment is paused or discontinued, the latent reservoir immediately reactivates and supports the rebound of the virus and HIV progression. This latent reservoir of cells is what primarily contributes to the chronicity of HIV and needs to be resolved in order to develop an HIV cure. Most of what is understood about HIV latency comes from laboratory strains of HIV subtypes from the U.S. or Western Europe, which represent only a small percentage of HIV types. How regulatory sequences from other HIV clades regulate transcription and latency has not been carefully studied. The primary transcriptional element that regulates HIV transcription is the long terminal repeat (LTR), therefore understanding how different LTRs affect expression of the virus – especially generation of latent virus – is essential to discovering a cure. In this project, we generated proviral expression plasmids with LTRs from different clades. We were interested in the impact of the different LTRs on HIV's transcriptional efficiency, latency establishment, and ability to be reactivated. Preliminary results demonstrated that the LTRs respond differently to latency reversing agents (LRAs), which once further investigated could inform targeted, subtype-specific latency reversal treatments of HIV.