

A BASIC RESEARCH GOAL: “SHOCK” HIV OUT OF LATENCY

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From Research to the Real World: Sharing Science Symposium

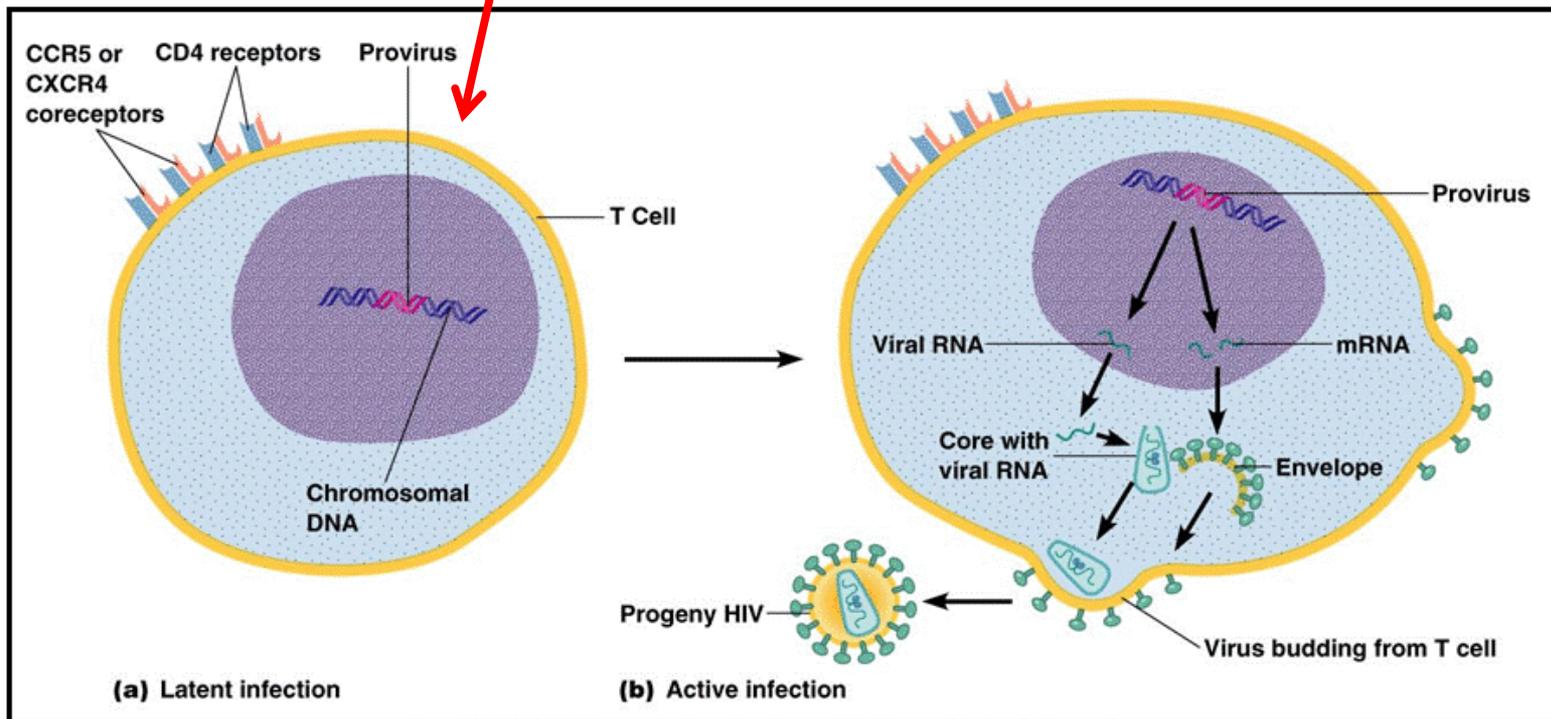
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Why We Did this Study

- Current anti-HIV medications inhibit viral replication – they target cells that are active
- Current drugs do not cure infection – a silent viral reservoir remains in “resting” CD4 T cells – **“Latent Infection”**
- If medications are stopped, HIV starts replicating again
- A “shock and kill” strategy has been proposed to cure infection:
 - “shock”: develop new medications to activate latent virus
 - “kill”: develop methods to enhance immune system’s ability to clear cells with reactivated virus

Why We Did This Study: To Understand Latent HIV Infection

Latent and Active HIV Infection in CD4 T-cells



What We Did

- Previously, we identified key cellular factors that regulate HIV replication and are shut-off when cells are resting
[*key factors: CDK9 and Cyclin T1 – an enzyme (kinase)*]
- We isolated CD4 T cells from healthy blood donors
- We infected cells with HIV under conditions where latent infection is established
- We treated cells harboring latent HIV with small molecules (*Histone deacetylase inhibitors*) that we thought would activate our key cellular factors

What We Found

- Treatment of cells with these agents turned on our cellular cofactors (*CDK9 and Cyclin T1*)
- We observed that latent HIV started replicating to some extent
- Reactivation of these key factors is probably not potent enough by itself to “shock” all latent virus in patients

What Our Results Mean and Why this Matters

- Activation of these key cellular cofactors is essential to reactivate latent HIV
- These key cellular cofactors are an important target for a “shock” strategy
- In combination with other activation agents to potently “shock” latent HIV and an effective “kill” strategy, our work may contribute to a functional cure of HIV infection

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