A Viral Tool to Reactivate Latent HIV

Britt Glaunsinger
University of California, Berkeley
Basic Biomedical Sciences
2014

A key problem precluding an HIV cure is the fact that patients possess reservoirs of infected T cells that contain non-replicating (latent) HIV. Despite the effectiveness of highly active antiretroviral therapy (HAART) at reducing the actively replicating HIV, the virus can persist as a silent, integrated genome in a variety of cell types; during this latent phase the infection is essentially invisible to both the immune system and to antiretroviral drugs. Latently infected cells pose a risk to patients as they can spontaneously reactivate, igniting new rounds of viral replication—thus forcing patients to remain on antiretroviral therapy for life. It is for this reason that there is immense interest in discovering ways to reactivate latent virus so they become susceptible to therapy.

Our goal is to explore methods to stimulate reactivation of this latent reservoir of HIV so that the infected cells can be purged by antiretroviral therapy. Our preliminary data suggest a novel strategy to drive HIV reactivation using a protein from another virus often associated with AIDS patients, termed Kaposi's sarcoma-associated herpes virus (KSHV). KSHV is a prominent AIDS-associated pathogen. Previous studies have shown that infection of cells containing HIV-1 with KSHV leads to potent stimulation of HIV-1 gene expression by activating the HIV-1 promoter, termed the LTR. We compared the ability of various KSHV proteins to activate gene expression from the HIV-1 LTR and found a single potent activator, termed ORF45. We aim to discover how ORF45 stimulates HIV gene expression, as this information may help in the design of new strategies to force HIV-1 out of the latent state so that infected cells can be eliminated.