A novel role for the viral Rev protein in promoting resistance to superinfection by human immunodeficiency virus type 1.

Abstract:
At the cellular level, cells infected with human immunodeficiency virus type 1 (HIV-1) exhibit immunity to a second infection by the virus that initiated the first infection or by related viruses [superinfection resistance (SIR)]. In the case of HIV infection, SIR was basically attributed to downregulation of the CD4 receptors. We have recently reported on an interaction between HIV-1 Rev and integrase (IN) proteins, which results in inhibition of IN activity in vitro and integration of cDNA in HIV-1-infected cells. A novel function for the viral Rev protein in controlling integration of HIV cDNAs was thus proposed. The results of the present work suggest involvement of the inhibitory Rev in sustaining SIR. A single exposure to wild-type HIV-1 resulted in one to two integrations per cell. The number of integrated proviral cDNA copies remained at this low level even after double infection or superinfection. SIR was dependent on Rev expression by the strain used for the first infection and was eliminated by peptides that disrupt intracellular complex formation between IN and Rev. The same lack of resistance was observed in the absence of Rev, namely following first infection with a DeltaRev HIV strain. The involvement of Rev, expressed from either unintegrated or integrated viral cDNA, in promoting SIR was clearly demonstrated. We conclude that SIR involves Rev-dependent control of HIV cDNA integration.