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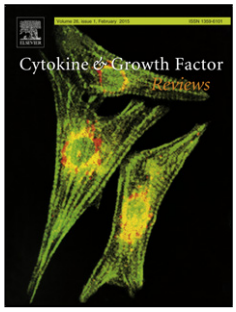

Title: Multilayered and versatile inhibition of cellular antiviral factors by HIV and SIV accessory proteins

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Multilayered and versatile inhibition of cellular antiviral factors by HIV and SIV accessory proteins

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Highlights

- Vpr, Vpu and Nef target antiviral factors directly and suppress their expression
- Accessory HIV and SIV proteins act as versatile adaptors
- Synergisms between accessory HIV-1 proteins are critical for immune evasion

Abstract

HIV-1, the main causative agent of AIDS, and related primate lentiviruses show a striking ability to efficiently replicate throughout the lifetime of an infected host. In addition to their high variability, the acquisition of several accessory genes has enabled these viruses to efficiently evade or counteract seemingly strong antiviral immune responses. The respective viral proteins, i.e. Vif, Vpr, Vpu, Vpx and Nef, show a stunning functional diversity, acting by various mechanisms and targeting a large variety of cellular factors involved in innate and adaptive immunity. A focus of the present review is the accumulating evidence that Vpr, Vpu and Nef not only directly target cellular antiviral factors at the protein level, but also suppress their expression by modulating the activity of immune-regulatory transcription factors such as NF-κB. Furthermore, we will discuss the ability of accessory proteins to act as versatile adaptors, removing antiviral proteins from their sites of action and/or targeting them for proteasomal or endolysosomal degradation. Here, the main emphasis will be on emerging examples for functional interactions, synergisms and switches between accessory primate lentiviral proteins. A better understanding of this complex interplay between cellular immune defense