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Abstract

Elucidating the Role of HIV-2 Viral Protein X †

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Abstract: Human immunodeficiency viruses type 1 and 2 (HIV-1 and HIV-2) are the causative agents of the acquired immunodeficiency syndrome (AIDS). While both viruses share a similar structural and genomic organization, a difference in replication dynamics and the clinical course of infection is evident between the two. Patients dually infected were shown to have lower viral loads and generally a slower rate of progression to AIDS than those who are mono-infected. While the roles of the unique accessory proteins have been studied in detail for HIV-1, those of HIV-2, including viral protein X (Vpx), remain largely uncharacterized. In our previous experiments, Vpx of HIV-2 was found to be involved in decreasing the infectivity of HIV-1 in dual infection cell culture assays. We set out to elucidate the function of this accessory protein, identifying protein–protein interactions of HIV-2 Vpx with cellular and possibly HIV-1 proteins in dual infection, using in-vitro proteomics techniques and proximity ligation assays. Results showed that wild-type Vpx interacted with many cellular proteins involved in splicing, packaging of pre-mRNA, nuclear export, and translation. Of particular interest was the interaction between HIV-2 Vpx and the pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15, which is required for HIV-1 viral DNA synthesis, and the eukaryotic translation initiation factor 2 subunit 3 (EIF2S3), involved in the early steps of protein synthesis. Additionally, Vpx was found to interact directly with the cellular transcriptional repressor C-Terminal Binding Protein 2 (CTBP-2). Moreover, Vpx was shown to hinder the function of HIV-1 reverse transcriptase in in-vitro assays. These findings shed light on the functions of this accessory protein and add to our understanding of the replication dynamics of HIV-2 and its role in dual infection.

Keywords: HIV-2; Vpx; viral replication; protein-protein interaction; dual infection; CTBP-2

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