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Oral presentation

Sequence-Specific Vpr Binding to HIV-1 LTR C/EBP Binding Sites and Adjacent Regions

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Human immunodeficiency virus type 1 (HIV-1) Vpr is a virion-associated protein that transactivates the HIV-1 long terminal repeat (LTR), as well as other eukaryotic promoters. Here we used the electrophoretic mobility shift assay to demonstrate the direct binding of purified Vpr (strain pNL4-3) to HIV-1 LTR sequences that span the adjacent C/EBP site I, NF-kB site II, and ATF/CREB binding site. Binding between HIV-1 Vpr and the LTR C/EBP site II was also observed. A total of 94.7% of LTRs derived from peripheral blood displayed high relative Vpr binding affinity with respect to C/EBP site I, while only 5.3% exhibited a low relative Vpr binding affinity. Virtually all LTRs derived from peripheral blood exhibited a high relative Vpr binding phenotype relative to C/EBP site II. Additional studies have demonstrated that naturally occurring sequence variation within C/EBP site I and II can dramatically alter the relative affinity of Vpr for these cis-acting elements. Studies have also suggested a competitive interaction between C/EBP factors and Vpr for this region of the LTR. These studies suggest that Vpr may regulate the interaction of members of the C/EBP transcription factor family with the viral LTR.