HIV-2 Vpx: Modeling and Probing Stucture/Function

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HIV-1 and HIV-2 have evolved somewhat altered mechanisms by which viral cDNA can be carried to the nucleus in preparation for host DNA integration. An ancient horizontal transfer event from HIV-1 has lent an additional gene to HIV-2, known as Vpx, which is homologous to Vpr in both viruses. However, the functions of Vpr as seen in HIV-1 appear to be split between Vpr and Vpx in HIV-2. A prominent function is a nuclear localization activity of Vpx. Here, we model a core structure of Vpx onto an HIV-1 Vpr NMR template. A flexible loop between helices two and three is predicted. We show that an insertion in this region is tolerated, resulting in active Vpx-containing preintegration complexes. The mutant protein is also correctly packaged into viral particles. The C-terminal region of Vpx remains unmodeled but likely adopts a polyproline II helix joined to the core via a flexible linker. We have probed this region for binding partners via phage display and present a few candidate genes. Finally, we find that the human invariant chain protein (important to MHC class II antigen presentation), when fused to Vpx, acts as a chaperone, making Vpx soluble and stable under a variety of conditions.