Project 3: Interaction of HIV-1 VpU with host cell proteins CD4 and Tetherin

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Summary

Successful replication of human immunodeficiency virus HIV-1 in host cells requires molecular interactions between viral and host proteins. HIV-1 accessory protein VpU plays a prominent role in down regulation of human proteins CD4, the main receptor of the HI virus, and tetherin, an antiretroviral defense factor. Tetherin features two membrane anchors – one N-terminal transmembrane helix and one C-terminal GPI anchor. Tetherin retains new virions at the plasma membrane of the host cell and prevents release of enveloped viruses. There are indications for direct interactions of VpU with CD4 and tetherin, respectively. We have previously determined the structure of the cytoplasmic domain of VpU and of a CD4 fragment comprising the cytoplasmic and transmembrane domains of CD4 in membrane mimicking detergent micelles and studied their interactions using NMR spectroscopy. The aim of the project is a better understanding of the role of the transmembrane domain of VpU in the interaction with CD4 and tetherin. The affinity between full length VpU and lipid membrane anchored CD4 and tetherin fragments, respectively, will be studied with biophysical techniques. The three dimensional structure of one of these membrane protein complexes in nanodiscs or bicelles will be characterized by NMR spectroscopy.