

Public Abstract

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Title:VIRAL ENVELOPE PROTEINS AND THE HIV-1 ACCESSORY GENE VPU MEDIATE SELECTIVITY OF VIRAL AND HOST PROTEINS IN RETROVIRAL ASSEMBLY

Retroviruses are enveloped RNA viruses that assembly primarily at the plasma membrane of the host cell. During budding from the membrane, they acquire their own glycoproteins as well as a lipid bilayer derived from the cell. The assembly process is complex and involves specific interactions between viral components and the cell. Compatibility during retrovirus assembly appears to be mediated by multiple factors: physical compatibility between glycoproteins and viral structural proteins, trafficking of proteins to appropriate locations, lipid interactions between Gag, Env and the plasma membrane, and microdomain association. In addition to mediating coalescence of appropriate factors, retroviruses appear equally equipped at excluding select host cell proteins and have evolved a number of genes to do so.

Here we present work outlining contributions of the envelope protein from murine leukemia virus to assembly with the lentiviral vector human immunodeficiency virus-1 (HIV-1). We subsequently observed an interesting phenotype, where an HIV-1 accessory gene Vpu restricts the envelope protein from gibbon ape leukemia virus (GaLV Env) from assembling with HIV-1. Further studies from our lab demonstrated that Vpu recognizes GaLV Env in a manner almost identical to CD4, the natural cellular target of Vpu, and that GaLV Env is essentially a CD4 analogue. We have found that Vpu restricts both target proteins in a manner that does not fit with the previously described Vpu-restriction model for CD4. Collectively, the GaLV Env model offers a new tool for more carefully investigating how the HIV-1 accessory gene Vpu downmodulates the host cell receptor CD4.