

Abstract

HIV-1 Envelope Glycoprotein Trafficking and Viral Transmission †

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Abstract: HIV-1 encodes an envelope glycoprotein complex (Env) containing a long cytoplasmic tail (CT) harboring trafficking motifs implicated in Env incorporation into virions. Although the requirement for the Env CT in viral transmission is known, the precise mechanism by which Env is incorporated into nascent virions and localizes to the virological synapse remains poorly defined. To further elucidate the mechanism of Env trafficking, we examined three HIV-1 strains: the lab-adapted clade B strain, NL4-3, and a transmitted/founder (T/F) clade C virus, K3016, and a T/F clade B virus, CH077. The HIV-1 Env CT contains two invariant trafficking motifs: tyrosine endocytosis motif, Y⁷¹²SPL, and C-terminal dileucine motif, LL⁸⁵⁵. Virion Env incorporation analysis revealed that Y⁷¹²SPL is necessary for efficient Env incorporation, while LL⁸⁵⁵ is dispensable. Spreading infection kinetics were analyzed in various T-cell lines and primary human PBMCs; the results indicated that both endocytic motifs contribute to efficient viral spread in culture. Analysis of Env localization to the T-cell uropod, the portion of the plasma membrane that forms a virological synapse with uninfected cells, was found to be dependent on the Env CT and the Y⁷¹²SPL motif. Cell-to-cell and cell-free transmission assays using T cells infected with HIV-1 bearing Y₇₁₂A or LL₈₅₅AA Env CT mutations are ongoing to establish a role for these motifs in both modes of viral transmission. These studies will significantly enhance our understanding of Env trafficking and viral transmission, providing insights into viral Env–host interactions in physiologically relevant cells.

Keywords: HIV-1; Env; gp41; cytoplasmic tail; transmission; endocytosis; virological synapse



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