ROLE OF THE CYTOPLASMIC DOMAIN OF THE LENTIVIRAL ENVELOPE GLYCOPROTEINS IN MEMBRANE FUSION AND ENVELOPE INCORPORATION INTO VIRIONS

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The mature form of the envelope (Env) glycoproteins of lentiviruses is a heterodimer composed of the surface (SU) and transmembrane (TM) subunits. The TM consists of an ectodomain containing a fusion peptide, a membrane anchor and a carboxy-terminal cytoplasmic tail (CT). Mutagenesis studies of the 164-amino acid-long CT of the simian immunodeficiency virus (SIV) TM allowed us to demonstrate that domains within this region modulate incorporation of the Env glycoprotein into virions, SU-TM complex stability and virus infectivity. Feline immunodeficiency virus (FIV) possesses a TM with an unusually short CT of 53 amino acids. To investigate the relevance of the FIV TM cytoplasmic domain to Env-mediated viral functions, we characterized the biological properties of a series of Env glycoproteins progressively shortened from the carboxyl terminus. All the mutant Env proteins were efficiently expressed and processed in feline cells. Deletion of 5 or 11 amino acids from the TM C-terminus did not affect Env functions whereas removal of 17 or 23 residues reduced Env-mediated cell-to-cell fusion. Further truncation of the FIV TM by 29 residues impaired Env cell surface expression, fusogenicity and packaging into virions. Remarkably, deletion of the TM C-terminal 35 or 41 amino acids restored or even enhanced Env biological properties. Interestingly, truncation of the TM CT to only 6 amino acids did not affect Env incorporation into virions but abrogated Env fusogenicity. Finally, removal of the entire TM CT or deletion of 6 amino acids into the membrane-spanning domain abrogated Env functions. Our results demonstrate that the SIV and FIV TM cytoplasmic domains play an important role in modulating Env structure and function.

Keywords: Simian immunodeficiency virus, Feline immunodeficiency virus, Envelope glycoprotein, Fusogenic activity.