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The feline immunodeficiency virus envelope protein precursor: functional analysis of a leader deletion mutant

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One of the distinguishing features of lentiviruses is their induction of a number of gene products in addition to the characteristic viral proteins gag, pol, env in infected cells. These accessory proteins are generated in various ways, most often by translation of spliced mRNAs. The feline immunodeficiency virus (FIV), as well as other non-primate lentiviruses, generate one of their proteins by cleavage from an extended envelope protein precursor (Olmsted et al., 1989; Talbott et al., 1989). In contrast to other lentiviruses of which the precursor contains just the hydrophobic signal sequence at its amino terminus, the FIV presequence is the longest of all lentiviruses known and constitutes a 2O kD polypeptide, which is cleaved off at least in part post-translationally (Verschoor et al., 1993; Pancino et al., 1994). Thus, processing of the FIV glycoproteins resembles that described for the ungulate caprine arthritis and encephalitis virus (CAEV; Knowles et al., 1991). Adding to the complexity of these viruses, the amino-terminal 80 residues of this polypeptide also constitute the first exon of the rev gene and are thus shared with the rev protein (Phillips et al., 1992). Apart from this, nothing is as yet known about the structure of the polypeptide, its intracellular destination, its possible membrane-association through the signal peptide present at its carboxy terminus, or about its possible incorporation into viral particles. As a first attempt to probe for its function we deleted part of the presequence of the envelope precursor protein gene. In order not to interfere with other processes directed by the genomic sequence involved, such as rev production

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and envelope protein membrane assembly, we made a deletion that removed some one-third of the polypeptide. The FIV deletion mutant was viable and produced infectious virus, implying that at least the membrane integration function was unperturbed. The mutant virus was tested for replication on a large number of different cell types. Similar replication kinetics were observed as for the parental FIV-Petaluma in cultured Crandell feline kidney (CRFK) cells, feline thymocytes, feline peripheral blood mononuclear cells (PBMC) and bone marrow derived macrophages. However, in cells of astroglial origin (G355-5 cells, feline astrocyte-derived cell line FBDC) replication was strongly reduced to almost absent in primary astrocytes. Clearly, the large deletion in the presequence had affected the leader protein's functioning. However, why this function is only required in particular cell types and not essential in others remains to be established. It will be important to characterize the leader polypeptide by making an antiserum and to test the replication kinetics of the deletion mutant in vivo.

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