

Poster presentation

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Solution structure of the equine infectious anemia virus p9 protein: a rationalization of its different ALIX binding requirements compared to the analogous HIV-p6 protein

Alok Sharma^{1,2}, Karsten Bruns^{1,2}, René Röder^{2,3}, Peter Henklein³, Jörg Votteler*², Victor Wray¹ and Ulrich Schubert²

Address: ¹Department of Structural Biology, Helmholtz Centre for Infection Research, D-38124 Braunschweig, Germany, ²Institute of Virology, Friedrich Alexander University of Erlangen-Nürnberg, D-91054 Erlangen, Germany and ³Institute of Biochemistry, Charité-Universitätsmedizin-Berlin, D-10117 Berlin, Germany

* Corresponding author

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Background

The equine infection anemia virus (EIAV) p9 Gag protein contains the late (L-) domain required for efficient virus release of nascent virions from the cell membrane of infected cells. The genomic position of p9 is analogous to that of the HIV-1 p6 protein and other similar proteins from different lentiviruses. Compared to HIV-1 p6, EIAV p9 has only minimal amino acid sequence homology and a considerable variation in the predicted secondary structure. Besides the function of p9 in viral DNA production and processing of the provirus [1], p9 plays, like p6 of HIV-1, an essential role in virus release, which is governed by late assembly domains (L-domains) [2-4].

Results

In the present study the p9 protein and N- and C-terminal fragments (residues 1-21 and 22-51, respectively) were chemically synthesized and used for structural analyses. CD and ¹H NMR spectroscopy provide the first molecular insight into the secondary structure and folding of this 51-amino acid protein under different solution conditions. Qualitative ¹H chemical shift and NOE data indicate that in a pure aqueous environment p9 favors an unstructured state. In its most structured state under hydrophobic conditions, p9 adopts a stable helical structure within the C-terminus. Quantitative NOE data further revealed that this α -helix extends from Ser-27 to Ser-48, while the N-termi-

nal residues remain unstructured. The structural elements identified for p9 differ substantially from that of the functional homologous HIV-1 p6 protein.

Conclusion

These structural differences are discussed in the context of the different types of L-domains regulating distinct cellular pathways in virus budding. EIAV p9 mediates virus release by recruiting the ALG2-interacting protein X (ALIX) via the YPDL-motif to the site of virus budding, the counterpart of the YPX_nL-motif found in p6 [4,5]. However, p6 contains an additional PTAP L-domain that promotes HIV-1 release by binding to the tumor susceptibility gene 101 (Tsg101) [2]. The notion that structures found in p9 differ from that of p6 further support the idea that different mechanisms regulate binding of ALIX to primary versus secondary L-domains types.

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