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Comparative Structural Studies of Vpu Peptides in Phospholipid Monolayers by X-ray Scattering

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Beamline(s): X22B

Introduction: Vpu is an 81-residue HIV-1 accessory protein, its transmembrane and cytoplasmic domains each responsible for one of its two functions[1]. Langmuir monolayers of phospholipid incorporating a membrane protein with a unidirectional vectorial orientation, on a semi-infinite aqueous subphase, provide one "membrane-like" environment for the protein. The cytoplasmic domain's interaction with the surface of the phospholipid monolayer in determining the tertiary structure of the peptide within the monolayer was investigated, employing a comparative structural study of Vpu with its sub-molecular fragments Tm and TmCy, truncated to different extents in the cytoplasmic domain, via synchrotron x-ray scattering utilizing a new method of analysis[2,3].

Methods and Materials: X-ray specular reflectivity and grazing incidence diffraction(GID) were measured from the mixed monolayers of phospholipids and proteins at various different protein/lipid mole ratios on Liquid Surface Spectromemter of X22B[4].

Results: Our interpretation on electron density profiles derived from the experimental data were that localizations of the transmembrane and cytoplasmic domains within the monolayer profile structure were similar for all three proteins, the hydrophobic transmembrane helix within the hydrocarbon chain region tilted with respect to the monolayer plane and the helices of the cytoplasmic domains lying on the surface of the headgroups parallel to the monolayer plane. The thickness of the hydrocarbon chain region, determined by the tilt of the hydrocarbon chains and transmembrane domain with respect to the monolayer plane, was slightly different for Tm, TmCy and Vpu systematically with protein/lipid mole ratio. Localization of the helices in the cytoplasmic domains of the three proteins relative to the headgroups depends on their extents. Thus, the interaction of the cytoplasmic domain of Vpu on the surface may affect the tilt of the transmembrane helix within the hydrocarbon chain region in determining its tertiary structure in the membrane.

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