Poster Presentation

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Structural study of the transmembrane and membrane proximal domains of HIV-1 gp41

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The transmembrane subunit (gp41) of the envelope glycoprotein (Env) of HIV-1 associates non-covalently with the surface subunit (gp120) and together they play essential roles in viral mucosal transmission and infection of target cells. The membrane proximal region (MPR) of gp41 is highly conserved and contains epitopes of broadly neutralizing antibodies. The transmembrane (TM) domain of gp41 is involved in many essential biological functions and its primary role is to anchor the Env in both viral and cellular membranes. Despite having many important biological functions, the atomic structure of gp41 TM domain remains unknown. While high-resolution X-ray structures of some segments of the MPR were solved in the past, they represent the prefusion or post-fusion conformations, which could not be recognized by the broadly neutralizing antibodies 2F5 and 4E10. Here we describe the expression, purification, biophysical characterization and crystallization of a chimera construct including maltose binding protein (MBP) and MPR-TM of gp41. The purified MBP-MPR-TM protein reacts with the broadly neutralizing antibodies 2F5 and 4E10 with nanomolar affinities and thereby may represent an immunologically relevant conformation mimicking a pre-hairpin intermediate of gp41. Crystals could not be obtained initially when MPR-TM was fused to the C terminus of MBP with linker 1 (MBP-linker1-MPR-TM) but could be obtained after changing the linker (MBP-linker2-MPR-TM). The crystal belongs to space group P32 with unit cell constants of a=172 Å, b=172 Å, c= 70 Å and alpha=beta=90 and gamma=120. The 2.5 Å crystal structure reveals the conformation of MBP and part of the linker region of this chimera, but the MPR-TM segment is unstructured.

Keywords: transmembrane and membrane proximal domains of HIV-1 gp41, Biophysical determination, X-ray crystallization