Retrovirology

Poster presentation

P05-13. Fragments of HIV-1 gp41 derivatives presented on virus-like particles with preserved binding affinity for broadly neutralizing antibodies

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Background

The induction of broadly neutralizing antibodies (bNAbs) against the envelope protein is thought to be an essential part of an effective HIV vaccine. A part of gp41 which is conserved through all HIV-1 clades, the membrane-proximal external region (MPER), bears epitopes for two of the most potent known neutralizing monoclonal antibodies. As HIV-1 virus-like particles (VLPs) provide a natural membrane setting for gp41-derived proteins, we take advantage of VLPs as carriers for membrane-anchored, truncated gp41 as immunogen.

Methods

Several versions of gp41 including the C-terminal heptad repeat (CHR), MPER, transmembrane domain and a shortened cytoplasmic tail have been designed and characterised. To stabilize the trimeric state of gp41, heterologous zipper domains have been introduced at appropriate positions. Additionally, constructs with a further truncated CHR have been designed in order to focus the immune response to the highly conserved MPER. The most truncated version only consists of the transmembrane domain and the MPER.

Results

All designed gp41 derivatives were expressed in a human cell line and incorporated into VLPs. Most of them show enhanced binding to bNAbs 2F5 and 4E10 compared to full-length gp160 and similar binding compared to full-length gp41, as measured in FACS analysis and VLP capture assay. Also the most truncated version of gp41 still seems to be properly transported to the cellular membrane and recognized by 2F5 and 4E10. All described immunogens are currently tested in the rabbit model for immunogenicity and elicitation of neutralizing antibodies. The animals are primed with DNA and boosted two times with VLPs presenting gp41 fragments.

Conclusion

Thus, we created several fragments of gp41 with preserved binding affinity for broadly neutralizing antibodies, to serve as immungens on the surface of VLPs for the elicitation of antibodies directed against the membrane proximal region of gp41.