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Poster presentation

P05-04. Neutralizing antibodies induced by immunization with liposomal gp41 peptide simultaneously bind to both the 2F5 or 4E10 epitope and lipid epitopes

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Background

The purpose of this study was to produce peptide-and-lipid-induced murine monoclonal antibodies (mAbs) that replicate the characteristics of the 2F5 and/or 4E10 human antibodies for binding both to the membrane proximal external region (MPER) of gp41 and the adjacent lipid bilayer for neutralizing HIV-1 infection of CD4+ lymphocytes.

Methods

Liposomes containing both a synthetic MPER peptide (662-LELDKWASLWNWFDITNWLWYIK-684) as a peptide antigen, phosphatidylinositol-4-phosphate (PIP) as a lipid antigen, and monophosphoryl lipid A as a potent adjuvant were used as a formulation to immunize mice. MAbs were then produced and tested for binding to MPER, gp41, and PIP and for the ability to neutralize a replication-competent molecular clone of HIV-1 encoding a primary envelope protein and Renilla luciferase as reporter in human peripheral blood mononuclear cells (PBMC).

Results

Multispecific IgM MAbs were produced that bound PIP and that simultaneously bound to either the core MPER site of 2F5 or that overlapped with the 4E10 site. The mAbs also bound to negatively charged phospholipids, including cardiolipin, and lipid A. They had lipid binding specificities similar to those observed for 4E10 (Matyas et al., BBA, 2009; 1788: 660–5). In contrast to 4E10, these murine mAbs bound weakly to cholesterol and not to galactosyl ceramide. While these murine mAbs neutralized HIV-1 less well than 2F5 IgG, they inhibited more efficiently than the IgM isotype of 2F5.

Conclusion

This study employed widely used, clinically acceptable, safe, generic antigen-adjuvant constituents that potentially could be used for human immunization. Using liposomes containing MPER peptide and PIP as antigens and lipid A as an adjuvant for immunization, multispecific antibodies that simultaneously bind gp41 MPER and adjacent lipid and neutralize HIV-1 infection in a PBMC assay were induced. This is the first time that both the peptide and lipid binding specificities of 2F5 (or 4E10) have been induced experimentally in a neutralizing antibody.