Retrovirology

Poster presentation

P12-08. Membrane-specific antibodies that simultaneously bind to gp41 of HIV-1 and membrane lipid epitopes are induced by immunization with liposomes

Z Beck*[1], N Karasavvas[2], GR Matyas[2] and CR Alving[2]

Address: [1]Division of Retrovirology, Department. of Adjuvant and Antigen Research, Henry M Jackson Foundation/US Military HIV Research Program, Rockville, MD, USA and [2]Walter Reed Army Intitute of Research/US Military HIV Research Program, Rockville, MD, USA

* Corresponding author

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Background

Two broadly neutralizing human monoclonal antibodies (mAbs), 4E10 and 2F5, have antigen binding paratopes that simultaneously bind to peptide sequences on gp41 and also to various lipids, such as phospholipids, galactosyl ceramide (GalCer) or cholesterol (Chol) (BBA 2009;1788:660-665). We aimed to create a method to induce murine polyclonal and mAbs by immunization in which the induced antibodies bind simultaneously both to gp41 sequences and to individual lipids in the adjacent lipid bilayer.

Methods

Liposomes containing lipid A as an adjuvant and either (A) both Chol and gp140 HIV envelope protein [L(71% Chol + gp140)], or (B) both GalCer and a synthetic mper48 peptide of gp41 [L(mper48 + GalCer)] as antigens were used for immunizing mice. Hybridomas producing mAbs recognizing either the lipid antigen or the protein antigen separately by ELISA, or that simultaneously bound to both the lipid and protein antigens, were obtained.

Results

The mouse pre-immunization sera had low but detectable titers of natural antibodies to lipids, but not to proteins (or peptides). After immunization with both types of liposomes the induced antisera contained Abs both to the appropriate lipid and to gp140 protein and mper48 peptide. By immunization with L(71% Chol + gp140) or L(mper48 + GalCer), IgM multispecific antibodies were induced that recognized both protein and a variety of lipid antigens.

Conclusion

Our data suggest that immunization of mice with liposomes containing lipid A and also containing both a lipid and protein (or peptide) antigen consistently induce multispecific- and membrane-specific antibodies that recognize broad topographical antigenic liposomal membrane surface patterns. The binding characteristics of the antibodies for both protein and lipid are similar to the same general property of broadly neutralizing 2F5 and 4E10 human mAbs. These membrane-specific antibodies recognize both lipid and proteins in a lipid membrane environment and such antibodies might be useful in a vaccine setting.