

Poster presentation

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PI9-54 LB. Interrogating the membrane-proximal external region (MPER) of HIV-1 gp140

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Background

The MPER of HIV-1 gp140 contains the epitopes for the cross-clade neutralising antibodies, 4E10 and 2F5. However, there is evidence that the 4E10 epitope is located in other regions apart from the MPER and that expression levels of recombinant gp140s from stable CHO lines are lower if the 4E10 epitope is included.

Methods

To investigate the contribution of the MPER to the antigenicity and immunogenicity of HIV-1 envelope glycoproteins, three lines of investigation were followed: 1 - immunisation of rabbits with C-clade gp140s with/without MPER; 2 - Biacore studies of antibody and sCD4 binding of gp140s with/without MPER; 3 - Neutralisation of pseudoviruses with/without MPER by MAb 4E10.

Results

The results indicate that the possession of the MPER 4E10 epitope by pseudoviruses is sufficient for neutralisation by the 4E10 MAb. However, the addition of the 4E10 epitope reduced expression of gp140 from stable CHO lines by over 50% and has a marked effect on the binding of the b12 MAb, which recognises the CD4 binding site, and sCD4. Finally, mean end-point antibody titres from immunised rabbits were lower in animals immunised with C-clade gp140 which contains the 4E10 epitope. An analysis of breadth and potency of neutralising responses raised in these animals is underway.

Conclusion

The data suggests that the addition of the 4E10 epitope to HIV-1 gp140 has profound effects on the structure of gp140, which affects the expression levels, antigenicity and immunogenicity of these glycoproteins.