Retrovirology

BioMed Central

Oral presentation



# OA021-04. HIV-1 gp41 envelope MPER mutation altered epitope conformation in lipid and increased sensitivity to 2F5 and 4E10 neutralizing antibodies

X Shen*, M Dennison, F Gao, DC Montefiori, L Verkoczy, B Haynes, M Alam and G Tomaras

Address: Duke University, Durham, NC, USA
* Corresponding author

*from* AIDS Vaccine 2009
Paris, France. 19–22 October 2009

Published: 22 October 2009

*Retrovirology* 2009, **6**(Suppl 3):O16 doi:10.1186/1742-4690-6-S3-O16

This abstract is available from: http://www.retrovirology.com/content/6/S3/O16



## Background

The conserved membrane-proximal external region (MPER) of HIV-1 envelope is a target for the rare broadly neutralizing 2F5, Z13 and 4E10 monoclonal antibodies (mAbs). However, MPER antibodies are rarely found in HIV-1 infected subjects nor arise following envelope immunization. A potential strategy to elicit such antibodies more frequently is to design an envelope protein with increased exposure of the 2F5 and 4E10 mAb epitopes.

## Methods

Using pseudotyped virus neutralization assays and surface plasmon resonance (SPR) assays (with both peptides and peptide-liposome conjugates), we characterize an HIV-1 envelope mutant pseudovirus that is ~300 fold more sensitive to 2F5 and 4E10 neutralization than wildtype.

## Results

The mutation responsible is a single leucine to serine substitution at position 669 in the gp41 Env MPER. A non-neutralizing MPER mAb, 13H11, which binds peptides with gp41 669 leucine but not 669 serine, did not interact with L669 peptide-lipid conjugates, consistent with previously observed masking of L669 when peptide is lipid-associated. In contrast, the 2F5 mAb, which recognizes an epitope C-terminal to the 13H11 mAb, bound more stably, with a slower off-rate, to MPER L669S mutant peptide-lipid conjugates than to wild-type peptide-lipid conjugates.

## Conclusion

These data suggest that the L669S mutation in the gp41 MPER creates a virus that is more susceptible to neutralizing MPER antibodies because of enhanced exposure of the neutralizing epitope. Inactivated pseudotyped virus or subunit immunogens with the L669S gp41 MPER mutation may be candidates for induction of MPER neutralizing antibodies.