Retrovirology

Poster presentation

P04-37. Kinetic and thermodynamic factors determine HIV-1 neutralizing potency of MPER-specific antibodies

C Ruprecht*, L Berlinger and A Trkola

Address: Institute of Medical Virology, University of Zurich, Zurich, Switzerland
* Corresponding author

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

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):P65 doi:10.1186/1742-4690-6-S3-P65

This abstract is available from: http://www.retrovirology.com/content/6/S3/P65

Background

A considerable effort in the development of HIV vaccines has been directed towards eliciting neutralizing antibody responses that match the activities of the membrane-proximal external region (MPER) specific monoclonal antibodies 2F5 and 4E10. Recent years have broadened our knowledge in the structural composition of the MPER region, its accessibility for antibody attack, and highlighted the possibility that neutralization by MPER-specific antibodies required the recognition of their epitopes in the context of membrane lipids. The precise window of action of these antibodies and their modes of epitope recognition however still await further definition.

Methods

Here we performed detailed time-course studies of the interaction between virus and the MPER specific antibodies in comparison with neutralizing antibodies IgG1b12 and 2G12 prior to and during the infection of target cells. Virus binding was assessed directly in an ELISA-based virion capture assay and infectivity of antibody treated virus was probed on susceptible target cells (TZM-bl).

Results

We found that, while MPER-specific neutralizing antibodies bind to HIV virions before target cell and receptor interaction, this interaction is slow in the onset and requires several hours to reach its maximum. Time-dependent increase in 2F5 and 4E10 binding to virions is paralleled by an increase in the antibodies neutralization activity. Notable, this process is temperature dependent with lower temperatures obliterating the effect.

Conclusion

In sum our results strongly support the notion that the MPER of gp41 is accessible for neutralizing antibodies before receptor engagement but that the accessibility of the MPER on the virions depends on thermodynamic rearrangements in the epitope or viral membrane domain. Based on our observations, we hypothesize that the MPER on intact virions has a considerable degree of structural flexibility and is able to sample multiple conformations including structures occurring during viral entry into target cells and which expose the region sufficiently to allow antibody to dock.