Retrovirology

Poster presentation

P04-40. Dissecting pre- and post-attachment activity of HIV-1 entry inhibitors and neutralizing antibodies

L Berlinger*, P Rusert 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):P68 doi:10.1186/1742-4690-6-S3-P68

This abstract is available from: http://www.retrovirology.com/content/6/S3/P68

Background

HIV-1 adsorption and entry into target cells is initiated by the binding of the viral envelope glycoprotein gp120 to cell surface molecules. While the central role of CD4 as entry receptor is undoubted, it has been debated for long whether the initial contact of the virus with the target cell occurs through interaction with CD4 itself or alternate attachment molecules, such as heparan sulfate or adhesions factors, as suggested by several studies. Here we revisit this topic and dissect the actions of neutralizing antibodies and inhibitors on initial attachment to the target cell, receptor engagement and fusion.

Methods

Attachment of GFP-labelled HIV particles to target cell was assessed by flow cytometry. Virus entry was also quantified by flow cytometry using a FRET-based virion fusion assay. Infectivity was assessed using standard infection assays using primary cells (PBMC) and cell lines (TZM-bl).

Results

We found that the attachment process can only be successfully blocked by inhibitors that interfere with the engagement of CD4 such as CD4bs specific Abs, soluble CD4 and CD4-specific inhibitors. Noteworthy, the MPER-specific neutralizing antibodies 2F5, 4E10 had no impact on attachment but displayed potent inhibitory activity post CD4 engagement. A survey of patient plasma confirmed a high prevalence of antibody activity blocking virus attachment suggesting CD4bs-directed activity but also revealed the presence of a noteworthy post-CD4 engagement activity in several cases.

Conclusion

Our data indicate that attachment to target cells is almost exclusively driven by the interaction with CD4. While binding to other cell surface entities most certainly occur, these interactions are not the driving factors that influence the consecutive steps of the entry process. In addition the careful dissection of antibody activity at specific steps of virus attachment and entry allows insight into the functional activity of the antibody response elicited during natural infection.