Retrovirology

Poster presentation

P04-33. Mechanisms of HIV-1 antibody mediated inhibition in Monomac-1 and MDM

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Background

Understanding the role of the multiple and complex mechanisms of antibody mediated HIV inhibition may be key to the rational design of antibody based vaccines. Primary macrophages and the monocyte cell line Monomac-1 may offer an important tool for evaluation of classical and non-classical (particularly Fc mediated) antibody mediated neutralization of HIV.

Methods

Monocyte derived macrophages (MDMs) were isolated from PBMCs, while Monomac-1 cells were obtained from DSMZ. Expression of CD4, HIV-1 co-receptors and FcRs were analysed by FACS staining. Antibody inhibition was determined by p24 release. FcRs involvement was determined using blocking antibodies. Cytokine release was quantified by in house multiplex bead immunoassay. Antibody and immune-complex binding to HIV and FcRs were assessed using an optical SPR Imager. HIV intracellular trafficking was studied by fluorescent microscopy.

Results

In spite of differences in relative HIV-1 co-receptor expression, Monomac-1 and MDM were both susceptible to HIV-1 BaL and primary R5 isolates. However, X4 HIV-1 LAV was only able to infect Monomac-1 cells. Antibody inhibitory activity did not correlate with antibody binding affinity for HIV-1. Most inhibitory antibodies tested revealed more potent activity on Monomac-1 compared to MDM, although a few only inhibited HIV-1 infection of MDM. The activity of some antibodies showed an FcRs dependent mechanism of inhibition. These data were confirmed by the analysis of immune complexes binding affinity for FcRs, and by microscopy, which revealed a high level of co-localization of HIV viral particles with the endosomal marker CD63 in presence of 2F5 monoclonal antibody. However, a second category of antibodies appeared to work via an FcR independent mechanism linked to the secretion of HIV inhibitory chemokines.

Conclusion

Monomac-1 cells and MDM represent a useful tool for screening humoral responses to potential vaccine candidates and for probing the complex mechanisms behind antibody-mediated HIV-1 inhibition.