Retrovirology



Poster presentation



# P04-25. Exposure of HIV-1 pseudovirus to soluble CD4 increases the breadth of neutralization with sera from macaques immunized with recombinant glycoproteins

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## Background

When HIV-1 envelope glycoproteins bind to CD4, conformational changes expose a site where the co-receptor can bind. Epitopes associated with this site are known as CD4-induced (CD4i) and give rise to antibodies which neutralize a wide range of HIV-1 isolates. Immunogens can be engineered to present these epitopes. Here, we show that exposure to soluble CD4 also sensitises pseudovirus to allow cross-neutralization of heterologous isolates by antibodies elicited by trimeric glycoproteins that have not been specifically modified to expose CD4i sites.

## Methods

Sera were taken at six weeks after the final immunization of rhesus macaques with trimeric recombinant HIV-1 envelope glycoproteins from HIV-1 461 (subtype A), HIV-1 SF162 (subtype B) and/or HIV-1 TV1 (subtype C) and have not been further engineered to enhance exposure of CD4i epitopes. SHIVSF62P4, SHIVSF62P3, SHIVKB9 (≡ SHIV89.6P, subtype B), HIV-1 TV1 or HIV-1 MJ4 (subtype C) pseudoviruses were exposed for 1 hour to sufficient soluble CD4 to reduce their infectivity by 50%. Dilutions of sera were then added to these mixtures and subsequently incubated for a further hour at 37°C before exposure to TZMbl cells. After 48 hours in culture the production of luciferase was quantified. Similar assays were performed with monoclonal antibodies.

## Results

Sera from immunized macaques neutralized homologous SHIVSF162P4 or HIV-1 TV1 pseudoviruses but not heterologous SHIV KB9 or HIV-1 MJ4. If the pseudovirus is first exposed to soluble CD4 there is no increase in the neutralization titre against homologous isolates. However, the heterologous isolates are neutralized. A similar sensitization of neutralization was seen with monoclonal antibodies to the V3 region (447-52D) or gp41 (4E10).

## Conclusion

Recombinant HIV-1 envelope glycoproteins induce antibodies which neutralize homologous pseudoviruses. However, the same immunogens also induce antibodies which can cross-neutralize heterologous isolates provided these have been pre-exposed to soluble CD4.