Killikelly et al. Retrovirology 2012, 9(Suppl 2):P67
http://www.retrovirology.com/content/9/S2/P67

RETROVIROLOGY

POSTER PRESENTATION Open Access

# Biophysical dissection of the antigen-antibody interaction of the broadly reactive anti-V3 human mAb 447-52D

A Killikelly[1*], H Zhang[1], B Spurrier[1], C Williams[2], MK Gorny[2], S Zolla-Pazner[2], X Kong[1]

*From* AIDS Vaccine 2012
Boston, MA, USA. 9-12 September 2012

## Background

The immunogenic third variable region (V3) of HIV-1 gp120 is a target for AIDS vaccines. V3 is recognized by mAb 447-52D, known for its ability to neutralize viruses with a GPGR beta turn motif at the apex of V3, which is characteristic of clade B viruses. Interestingly, 447-52D can also bind non-clade B V3 peptides containing a GPGQ motif. A detailed biochemical and biophysical dissection of the antigen-antibody interaction of 447-52D was undertaken to understand this disparity.

## Methods

We cloned and produced large amounts of the Fv fragment of 447-52D and a panel of mutations. We then measured their epitope binding characteristics by Isothermal Titration Calorimetry (ITC).

## Results

We assessed the Fv-V3 binding by ITC for the following mutations in residues of the mAb that are thought to mediate three key interactions: (i) $Y^{H100j}$ of the heavy chain (H) to T ($Y^{H100j}T$) or $Y^{H33}A$. These two aromatic residues form a pi-cation interaction, sandwiching the side chain of $R^{315}$ of the GPGR motif in the V3-peptide. These mutations reduce binding affinity by 56 and 171-fold, respectively. (ii) $W^{L91}$ of the light chain (L) to A ($W^{L91}A$). This residue packs against $P^{313}$ of the V3 GPGR turn. This mutation reduces binding 230-fold. (iii) $D^{H95}R$ of the heavy chain or $R^{315}Q$ of the epitope. These two residues form a salt bridge between the antigen and the antibody. These mutations reduce binding by 224 and 171-fold, respectively. These data suggest a hierarchy of interactions and the salt bridge plays an important role in the affinity.

## Conclusion

mAb 447-52D binds non-clade B peptides with the R315Q variation with much less affinity, explaining why it cannot neutralize non-clade B viruses. Through probing specific contributions of individual residues by mutagenesis and ITC, we were able to fully characterize the interactions between V3 and 447-52D.

**Author details**
[1]New York University Medical Center, New York, NY, USA. [2]Veterans Affairs New York Harbor Healthcare System, New York, NY, USA.

Published: 13 September 2012

doi:10.1186/1742-4690-9-S2-P67
**Cite this article as:** Killikelly *et al.*: Biophysical dissection of the antigen-antibody interaction of the broadly reactive anti-V3 human mAb 447-52D. *Retrovirology* 2012 **9**(Suppl 2):P67.



[1]New York University Medical Center, New York, NY, USA
Full list of author information is available at the end of the article