Retrovirology



Poster presentation



# P04-09. Induction of cross-clade neutralizing antibodies with a prime/boost vaccine strategy focused on a neutralizing epitope

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## Background

Experiments were designed based on the hypothesis that recombinant vaccine constructs can focus the immune response on shared HIV-1 neutralizing epitopes, and that if not diverted by other biologically irrelevant epitopes, high titers of cross-clade neutralizing antibodies (ccNAbs) will be induced. Indeed, previous experiments showed that when the immune response was focused on V3, ccNAbs were induced (Zolla-Pazner et al, Virology, 2008).

## Methods

A prime/boost regimen was used in which rabbits were primed (3×) with clade C gp120 DNA and boosted (2×) with: 1) a fusion protein in which the consensus clade C V3 sequence was fused to the C-terminus of MuLV gp70 (V3-gp70), or 2) the same V3 sequence was inserted into a structurally compatible site on cholera toxin B (V3-CTB). Sera were tested for neutralizing activity in TZM-bl cells against a panel of primary isolates and a selection of Tier 1, Tier 2 clade B, and Tier 2 clade C pseudoviruses (psVs) from the standard panel.

## Results

Sera from rabbits boosted with V3-CTB neutralized four primary isolates from clades A, AG and B with higher 50% neutralizing titers (NT50) than sera from V3-gp70-boosted rabbits. For example, sera from all five V3-CTB rabbits neutralized Bx08 (with a geometric mean titer [GMT50] = 1:153) whereas only one of five V3-gp70 rabbit responded (1:11). Similarly, serum titers in response to V3-CTB were greater than those to V3-gp70 against 4/4 Tier 1 clade B and C psVs (GMT50 = 1:188 vs. 1:60 for V3-gp70-immunized rabbits). Tier 2 clade C psVZM109F was also neutralized by sera from V3-CTB rabbits (GMT50 = ~1:20).

## Conclusion

A prime/boost vaccine regimen using gp120 DNA and V3-scaffold protein immunogens induced ccNAbs. A newly designed V3-CTB protein boost induced the strongest ccNAb response.