Retrovirology

Poster presentation

P19-28. The V3 region of HIV-1: from NMR to vaccine design

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Background

The V3 loop is one of the few epitopes to which broadly neutralizing antibody response can be directed. The most potent and most broadly neutralizing anti-V3 antibody to date is the human monoclonal antibody 447-52D. Using NMR spectroscopy, we studied the conformation of several V3 peptides in complex with 447-52D. The flexible V3 peptides were found to adopt a β-hairpin conformation when bound to this antibody. Using disulfide bonds we constrained V3 peptides to adopt a conformation similar to those of V3 peptides bound to 447-52D.

Methods

Two cyclic peptides, P2 and P3, based on the consensus sequence of clade-B R5 viruses were synthesized in the form of a C4-V3 construct and compared with the linear peptide (P1). The peptide P2 was constrained by a disulfide bond at positions T303C/I323C and included the entire 447-52D epitope (R304-E322); the peptide P3 was constrained closer to the GPGR turn at positions K305C/T320C. Sera of rabbits immunized with these three peptides were tested for the ability to neutralize a panel of HIV-1 isolates.

Results

The peptide constrained at position T303C/I323C (P2) elicited a more potent HIV-1 neutralizing response in comparison with the linear P1 or the constrained peptide P3. All 4 sera of rabbits immunized with P2 neutralized 5 out of the 7 strains tested. For the SF162 strain, which differed by three mutations from the immunizing V3-peptide, 50% neutralization was achieved with average titers greater than 1,580, at least 20-fold and 40-fold better than the linear peptide (P1) and the other constrained peptide (P3) immune-sera, respectively.

Conclusion

We have demonstrated that constrained V3 peptides can elicit strong HIV-1 neutralizing response that is considerably more potent in comparison with linear peptide immune-sera given that the constraint is optimally located within the V3 epitope to include the entire V3 epitope recognized by the 447-52D antibody.