Retrovirology

Poster presentation

P04-42. Molecular design of a mimotope that preserves conserved structural elements of the HIV-1 V3 crown

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Background

Identifying conserved structural elements in neutralizing epitopes of the HIV-1 Env can facilitate immunogen design for the development of an AIDS vaccine. The highly immunogenic third variable region (V3) of HIV-1 gp120 is capable of eliciting broadly reactive antibodies (Abs) in humans, and hence is a natural immunogen target. We previously demonstrated that the V3 crown has conserved structural elements recognized by broadly neutralizing monoclonal Abs (mAbs); these are the ''arch'' at the V3 tip, the hydrophobic core of the ''circlet'', and the positively-charged band. We hypothesized that a structural motif preserving conserved V3 elements would bind to broadly reactive human mAbs and could induce broadly neutralizing anti-V3 Abs.

Methods

We have designed a ''reverse'' V3 mimotope, V3rev with amino acid sequence ACQAFYASSPRKSIHIGACA, which is a cyclic peptide with swapped N- and C-terminal sequences and without the highly conserved GPGR/Q motif of the V3 crown. We determined a 2.5 Å resolution crystal structure of this peptide in complex with the broadly reactive anti-V3 human mAb 2557.

Results

Structural data showed that V3rev forms a β-structure like the regular V3 crowns and retains other structural elements of V3 such as the band and the circlet's core. It binds mAb 2557 in a manner strikingly similar to that of the native V3 loop with almost all the antigen/Ab interactions in the circlet and band preserved.

Conclusion

The atomic structural details of the 2557/V3rev complex further support the existence of conserved structural elements in the V3 region which are recognized by broadly neutralizing human anti-V3 Abs. These elements provide opportunities for structure-based immunogen design targeting the V3 epitope.