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Poster presentation

P12-05. Using combinatorial phage-display libraries as a source of mimetic peptides of three HIV-1 envelope epitopes

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Background

Mimotopes selected from combinatorial phage-peptide libraries by monoclonal and polyclonal antibodies may better reflect properties of native viral epitopes in contrast to synthetic peptide versions.

Methods

Using phage display random libraries and IgG of HIV-1 infected patients or the monoclonal antibody 2F5 (mAb 2F5), we select collections of mimotopes of the CSGKLIC loop epitope (CKC), ELDKWA from the MPER region and GPGR located on the apex of V3 loop in gp120.

Results

Related to CSGKLIC immunodominant epitope, a library of 10E9 sequences were converted into a homogeneous population in which 79% of peptides contained only the CxxKxxC-motif (x represent a non-epitope amino acid). The mimotopes displayed structural, antigenic and immunogenic features of the HIV-1 immnudominant loop epitope. In the case of GPGR epitope, two motifs were most interesting G(P/Q)GP from linear and PxxxGPG from constrained library. After four immunizations with both peptide groups, anti-sera showed a strong reactivity in ELISA with synthetic peptides containing V3 GPGR epitope sequences from different HIV-1 strains, as contrast to the narrow specificity of the patient sera. The rabbit anti-sera were able to decrease the fusion of gp120/gp41-CD4 complex in two Jurkat cell lines. Finally, when mAb 2F5 screened for structures resembling its natural epitope, it retrieved preferentially peptides with sequences longer than DKW as in previous reports. Nevertheless, in constrained 7 mer library the selection was restricted only to C-DKWAxx-C or C-xxLDKWA-C sequences, rejecting every amino acid variation. The selected mimotopes indicated that two additional residues, the Ala (DKWA) and Leu (LDKWA) residues are involved in the minimal epitope. The data imply that the 7 mer constrained peptide forming a loop represents an adequate structural context for the natural epitope core-like conformation.

Conclusion

Mimotope collections are source of information on functional viral epitopes and promise to become a new tool for designing immunogens with broad neutralizing potential.