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P05-08. Eliciting antibodies against cryptic, conserved, conformationally dependent epitopes of HIV envelope glycoprotein gp120: A strategy

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Background

Novel strategies are needed for the elicitation of broadly neutralizing antibodies to HIV gp120. Experimental evidence suggests that combinations of antibodies broadly neutralizing in vitro may protect against challenge with SHIV in nonhuman primates. A small number of these antibodies have been selected by repertoire sampling of B cells and by the fractionation of antiserum from some patients. Yet no strategy for eliciting these antibodies or additional broadly neutralizing antibodies has been successful to date. We postulate that additional cryptic epitopes of gp120 are present against which neutralizing antibodies might be elicited, even though these antibodies are not elicited by gp120, and that many of these epitopes may be accessible to antibodies should they be formed. If they are of sufficient affinity, some antibodies against additional epitopes might be broadly neutralizing.

Methods

We demonstrate a novel strategy for eliciting antibodies in mice against selected cryptic, conformationally dependent conserved epitopes of gp120 by immunizing with Multiple identical Copies of Peptides (MCPs) covalently linked in branched structures using the α and ε amino groups of lysine, representing conserved domains of gp120. This has been achieved with MCPs representing 3 different domains of gp120: (residues 105–117 α helix; 363–384 CD4 binding region; 426–441 or 419–439 β20β21 loop).

Results

Antibodies elicited by MCPs bind to native but not denatured gp120, are not elicited by immunization with gp120, and are not present in human HIV immunoglobulin. Some antibodies bind to trimeric gp120 on cells infected with multiple genotypes of HIV, bind to gp120 with relatively high affinity, and one of the monoclonal antibodies has modest neutralizing activity. Binding of antibodies to gp120 is blocked by incubation specific MCPs. Once elicited, these antibodies can be used to determine if the epitopes are accessible on native gp120.

Conclusion

MCPs can elicit antibodies to conserved cryptic conformational epitopes of gp120.