Retrovirology

Poster presentation

P04-51 LB. The epitopes of two newly identified broad and potent neutralizing antibodies, PG9 and PG16

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Background

It is widely accepted that the elicitation of a broadly neutralizing antibody (bNAb) response will be crucial for an effective vaccine against HIV-1. Although a handful of bNAbs have been isolated, these antibodies recognize epitopes on the virus that have failed to elicit bNAb responses when incorporated into a diverse range of immunogens. Therefore, it is of high priority to identify new bNAbs that bind to epitopes that may be more amenable to immunogen design. As a first step toward this goal, we have recently employed high-throughput direct functional screening to identify two new broad and potent neutralizing antibodies, PG9 and PG16, from the memory B cells of a clade A infected donor with broadly neutralizing serum.

Methods

MAbs were characterized using flow cytometry, ELISA, pseudovirus neutralization assays, alanine scanning mutagenesis, and mixed envelope (Env) trimer analysis.

Results

PG9 and PG16 were shown to bind almost exclusively to native trimeric Env with very little binding to recombinant Env preparations. Epitopes were mapped to conserved regions of the V2 and V3 loops of gp120. Certain N-linked glycans were found to be critical in forming the epitope, and although neither antibody neutralized HIV-1_{SF162} or HIV-1_{JR-FL}, single point mutations in the V2 loop of gp120 were sufficient to restore the PG9 and PG16 epitopes in both of these isolates. The preference for trimeric HIV-1 Env was shown to be governed by gp120 subunit presentation in the context of the trimeric spike rather cross-linking of gp120 monomers.

Conclusion

Our results show that a conserved region of V2 and V3 presented on a single gp120 unit of the HIV-1 trimer is a novel vaccine target. Future immunogens, designed to focus the immune response on this region, will determine its utility in the context of a vaccine for HIV-1.