Retrovirology

Poster presentation

P04-06. Evolution of an anti-MPER gp41 antibody response that mediates broad HIV-1 cross-neutralization

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Background

The membrane proximal external region (MPER) of the HIV-1 envelope is recognized by three of the few broadly cross-neutralizing antibodies described so far. Recent studies have reported anti-MPER antibodies in plasmas from some HIV-infected individuals with broadly cross-neutralizing activity. Here we followed the evolution of anti-MPER antibodies in an individual that developed broad neutralization.

Methods

Multiple plasma samples from participant CAP206 from pre-seroconversion to 3 years post-infection were tested for heterologous neutralization against 42 viruses from various subtypes and HIV-2/HIV-1 MPER chimeric viruses. Envelope clones were generated at 2-weeks (transmitted virus), 2-, 6-, 12- and 21-months post-infection by single genome amplification and used in neutralization assays. Anti-MPER antibodies were depleted from plasma by adsorption onto MPER-peptide-coated beads and tested in anti-MPER ELISA and neutralization assays.

Results

Antibodies able to mediate autologous neutralization of the transmitted virus developed at 8-weeks post-infection. Neutralization escape occurred rapidly with envelope clones from 2-months post-infection showing reduced neutralization sensitivity compared to the transmitted variant. Anti-MPER antibodies were detected at 22-weeks post-infection using the HIV-1/HIV-2 chimera C1C, however this participant did not show neutralization breadth at this time-point. At 81-weeks these anti-MPER antibodies became independent of W670 for neutralization. This change in specificity corresponded with the emergence of antibodies able to neutralize 18 viruses. Depletion of anti-MPER antibodies using peptide-coated magnetic beads removed this heterologous activity. Anti-MPER antibodies eluted from the beads also neutralized the early autologous virus.

Conclusion

We described the evolution of a cross-neutralizing anti-MPER antibody response and its relationship to the autologous response. Our data suggest that affinity maturation of the anti-MPER antibodies may have resulted in neutralization breadth. Further study of the evolution of these antibodies and characterization of the virus quasispecies in this individual may provide useful information for the design of vaccine immunogens that induce anti-MPER antibodies.