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Oral presentation

Detection of Novel Neutralizing Antibody Reactivities Against The Membrane Proximal External Region (MPER) of gp41 in HIV-1 Infected Humans

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Background

Previously, we employed site-directed mutagenesis to introduce HIV-1 4E10 and 2F5 epitopes into the corresponding region of a functional HIV-2 envelope glycoproteins (AIDS Vaccine 2005, abstract #A210). The resulting "chimeric" viruses were used to screen HIV-1 infected human plasma for 4E10 or 2F5-like neutralizing antibodies (Nabs). Among 177 subjects infected with HIV-1 representing ten different subtypes or circulating recombinant forms, none had significant Nab titers directed toward these epitopes.

Materials and methods

Here, we tested the same HIV-1 positive plasma specimens for neutralizing activity against chimeric HIV-2 viruses in which we substituted the complete 25 amino acid HIV-1 MPER (designated clone C1) or non-overlapping amino-terminal or carboxy-terminal portions of it (designated C3 and C4, respectively) using a single-cycle infectivity assay (Nature 422:307, 2003).

Results

HIV-2 viruses containing the C1, C3 or C4 MPER, and the parental virus HIV-2/7312A, were infectious and equally susceptible to neutralization by T1249, sCD4, the anti-HIV-2 Env mAb 1.7A, and polyclonal anti-HIV-2 antibodies. This result demonstrates that none of the chimeric HIV-2 viruses was "globally sensitive" to neutralization. Surprisingly, 60 out of 165 (36%) of HIV-1 plasmas tested contained MPER specific Nabs. IC50 titers ranged from 0.0005–0.02 (mean 0.006; median 0.004; standard deviation 0.004). Anti-MPER Nab reactivities were mapped to C3 (6 subjects) or C4 (14 subjects) regions of the HIV-1 MPER or to epitopes spanning them (13 subjects). None of the 60 subjects with Nabs to C1, C3, or C4 had antibodies that neutralized HIV-2 viruses containing 2F5 or 4E10 epitopes only.

Conclusion

These results indicate that the MPER of HIV-1 elicits Nab responses in a substantial proportion of infected patients and that the epitopes recognized by these Nabs are distinct from those recognized by 4E10 or 2F5.