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OA05-05. Impact of *in vivo* CD4 binding during HIV-1 Env trimer immunizations of rhesus macaques

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Background

We recently reported that immunization with cleavage-defective soluble HIV-1 envelope glycoproteins (Env) trimers in monkeys, but not in rabbits, results in the elicitation of antibodies directed against the co-receptor binding site of gp120. This finding demonstrates that the high affinity interaction between Env and primate CD4 results in an alteration of Env immunogenicity. To further investigate the impact of Env-CD4 *in vivo* interactions during vaccination, we immunized rhesus macaques with wild type (wt) and CD4 binding defective Env trimers.

Methods

Groups of five adult rhesus macaques were immunized with wt trimers or CD4 binding defective trimers, with either retained or abrogated capacity to form the co-receptor binding-site. Plasma and PBMCs were collected 2 weeks post-immunization. Frequency of Env-specific B and T cells were assessed by ELISpot analysis and flow cytometry. Serum antibodies were measured by ELISA and neutralization assays. Four weeks following the last immunization, control and vaccinated animals were challenged with SHIVSF162P4.

Results

Antibodies against the co-receptor binding site were elicited in animals immunized with wt trimers, but not in animals immunized with the CD4-binding defective mutants. Elimination of the Env-CD4 *in vivo* interaction did not affect vaccine-induced Env-specific T cell responses or levels of total elicited binding antibodies. However, differences in the quality of the *in vitro* neutralizing antibody response were observed between the three groups. A comparable decrease in plasma viral loads compared to unvaccinated controls was also measured following challenge in all three groups.

Conclusion

These results confirm that the wt Env trimers used here interact with host CD4 *in vivo* affecting the quality of the elicited antibody response. As Env-based vaccines progress from small animals to primates, the effects of high affinity CD4 interaction may need to be considered in regards to immunogen design.