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Mapping of SIVmac T-cell epitopes in cynomolgus macaques immunized with auxo-GTU-MultiSIV DNA by the intradermal route followed by electroporation

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Background

Intradermal immunization with electroporation using auxo-GTU-MultiHIV DNA encoding Gag, Nef, Rev and Tat induces strong and sustained T cell responses in cynomolgus macaques. Here, we used an equivalent vaccine encoding SIVmac239 antigens (Gag, Nef, Rev, Tat, Vif, Vpx and Vpr) and we described the breath of this T cell response.

Methods

Naïve male mauritian cynomolgus macaques were immunized with auxo-GTU-MultiSIV DNA encoding Gag, Nef, Rev and Tat (n=14) or by a combination of auxo-GTU-MultiSIV DNA and auxo-GTU-SIV-vifvprvpx (n=12) by the intradermal route followed by electroporation. MHC class I and class II haplotypes were determined by microsatellite analysis. T-cell epitopes were mapped by IFN-γ ELISPOT in PBMC by using matrix of 15-mer (overlapping by 11) SIVmac239 Gag, Nef, Rev, Tat, Vif, Vpx and Vpr peptides. Sequence and length of candidate epitopes were further optimized.

Results

Immunization induced intense and sustained IFN-γ ELISPOT responses in peripheral blood. T-cell responses against MHC class I epitopes were evidenced: two in Gag p15 (KA10(28-37) presented by Mafa-B*011:01 and EL10 (58-68) presented by a MHC-Ia molecule from haplotype M3), two in Gag p27 (HL9(146-154) presented by Mafa-B*075:01 and LA9(189-197) presented by a MHC-Ib from haplotype M1), three in Nef (AS10(4-13) presented by a MHC-Ib molecule from haplotype M3; RM9(103-111) presented by Mafa-A1*063:02; LD10(146-155) presented by a MHC-Ia from haplotype M1M2M3), one in Rev (SP10(59-68) presented by Mafa-B*075:01), one in Tat (CF9(59-67) presented by Mafa-A1*063:02), four in Vif and two in Vpx. One MHC class II epitope was identified in Gag p27 (haplotype M3). Among these, to our knowledge, AF11 is a newly described epitope in cynomolgus macaques.

Conclusion

Auxo-GTU-MultiSIV DNA vaccination followed by electroporation induced multi-epitopic T cell responses, essentially CD8+ but also CD4+. Determination of SIV T-cell epitopes in cynomolgus macaques facilitates the monitoring of specific immune responses and pre-clinical vaccine development in this model.

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