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OA05-02. Analysis of DNA compared to Ad5 vaccination, as single and mixed modalities, demonstrates robust induction of cellular immune responses in macaques

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Background

We have previously reported dramatic increases in immune responses induced by DNA vaccines delivered by electroporation (EP), resulting in improved control of viral replication following a SIVmac251 challenge. We compared the immunogenicity of DNA+EP to the Ad5 vaccine, the most potent recombinant viral vector for the generation of CTL responses in macaques and humans. Futhermore, we were interested in examining the effect of prime/boost strategies using these two platforms on the magnitude and phenotype of the immune response.

Methods

Three groups of rhesus macaques (n = 5) were immunized with consensus SIVmac gag, env, pol constructs with plasmid IL-12 by EP (DNA+EP), Ad5SIVgag, pol, nef (Ad5) or saline alone (Naive). The DNA+EP group received 4 immunizations and the Ad5 group received 3 immunizations. Five months following the last immunization the DNA+EP group was boosted twice with the Ad5 vaccine and vice versa. Cellular responses were assessed by IFNγ ELISpot, CFSE proliferation, and ICS for polyfunctional populations.

Results

The Ad5 group had an early three-fold enhancement of IFNγ responses compared to the DNA+EP group (1925 ± 610 and 666 ± 297 SFU/106 PBMCs, respectively). Subsequent Ad5 immunizations failed to boost responses while the DNA+EP group reached a robust 9776 ± 1589 SFU/106 PBMCs. Proliferation was five-fold better and the magnitude of the polyfunctional CD8+ T cell response was a log higher in the DNA+EP group compared to the Ad5 group (1.31% and 0.11%, respectively). When boosted with DNA, the Ad5 polyfunctional response increased six-fold (0.67%) and the DNA+EP group had a 7-fold increase (8.28%) following an Ad5 booster immunization.

Conclusion

Following the initial series of immunizations the DNA+EP group surpassed the Ad5 group in terms of magnitude, proliferation, and polyfunctionality. However both groups demonstrated a boost in all responses following crossover immunizations. These results have significant implications for HIV vaccine development and warrant further study.