

## **Broad HIV-1 inhibition *in vitro* by vaccine-elicited CD8<sup>+</sup> T cells in African adults**

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**Background.** Addressing HIV-1 variability is a major scientific challenge, because vaccine-induced immune responses must recognize multiple HIV-1 variants. One approach focuses on conserved HIV-1 sequences that are common to majority of variants and cannot easily mutate. We tested HIV-1 prime-boost vaccine regimens combining conserved regions of HIV-1 (HIVconsv) and full-length clade A Gag-RT-Int-Nef (GRIN).

**Methods.** Seventy two HIV-uninfected adults at KAVI-ICR, Nairobi participated in a phase II trial, with 3 groups, 20:4 vaccine:placebo; human adenovirus 35-GRIN (Ad35-GRIN) followed by modified vaccinia virus Ankara (MVA.HIVconsv) at week 8 (**AM**); pSG2.HIVconsv DNA at baseline, weeks 4 and 8, Ad35-GRIN at week 12 and MVA.HIVconsv at week 20 (**DDDAM**) or DNA delivered by electroporation (**DEPDEPDEPAM**). ELISPOT and intracellular cytokine staining (ICS) assays were performed on fresh, and epitope mapping and multi-clade 8-virus panel viral inhibition assays (VIA) were performed on cryopreserved PBMC.

**Results.** In the ELISPOT assay, all (100%) volunteers responded to vaccination. The mean total peak IFN- $\gamma$  ELISPOT frequencies were 3016, 3836 and 3453 SFC/10<sup>6</sup> PBMC in AM, DDDAM and DEPDEPDEPAM, respectively. An average of 6 peptide pools were recognized in ELISPOT, with a predominance of Gag and Pol. CD4 and CD8 T-cells were oligofunctional, secreting IFN- $\gamma$ , TNF- $\alpha$  and IL-2. Every vaccinee (100%) inhibited at least 1 virus in VIA. The average inhibition breadth after the last vaccination was 4.1, 4.6 and 3.1 out of 8 viruses for the AM, DDDAM and DEPDEPDEPAM regimens, respectively

**Conclusion.** Robust broadly-specific T-cell responses to conserved regions were detected by ELISPOT, oligofunctional CD4 and CD8 T cells by ICS and functional T cells by VIA. After the last administration of MVA.HIVconsv, the response rate and magnitude of T cells was similar across all groups. The DNA prime did not significantly enhance the response rate, magnitude or functionality of T-cells at the time point measured. Furthermore, electroporation enhanced DNA, but not the final T-cell frequencies.