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Oral presentation

OA04-03. Characterization of cell-mediated immune responses generated by recombinant modified vaccinia Ankara (rMVA)-HIV-1 in a phase I vaccine trial

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Background

Potency of the cell-mediated immune response is now the critical metric for down-selection of candidate HIV-1 vaccines. Here we characterize the potency (magnitude and quality) of cell-mediated immunity generated in response to a multigenic rMVA-based HIV-1 (CRF01_AE-derived) vaccine.

Methods

49 healthy, vaccinia-naive volunteers were enrolled in a phase I randomized, double-blind, dose-escalation, route-comparison, placebo-controlled trial to assess the safety and immunogenicity of MVA-CMDR HIV-1 vaccine. The study was divided into Part A: low-dose 10^6/pfu ID versus 10^7 pfu/IM and Part B: high-dose 10^7 pfu/ID vs 10^8 pfu/IM. Vaccinations were given at months 0, 1 and 3 with an active:placebo ratio of 10:2. Chromium-release CTL, IFNγ Elispot, and polyfunctional flow cytometry (IL-2/IFNγ/TNFα/MIP-1β/CD107a), were performed on all volunteers. Synthetic peptide pools and GLP-grade MVA were used to assess insert (Gag/Pol/Env) and vector immunogenicity respectively.

Results

Vector-specific responses were robust (> 80% response rate at high-dose), durable (maintained at least 6 months), and exhibited a dose-dependent increase in both magnitude and response rate among the 4 arms of the trial. HIV-insert-specific responses were detected using all assay platforms, but were lower than the vector-specific responses in both magnitude and response rate in all arms of the trial (~60% at high-dose by CTL, Elispot and ICS assays). Specifically, polyfunctional analysis revealed a TNFα/IL-2/IFNγ bias in CD4+ T cells and a MIP-1β/CD107a/IFNγ bias in CD8+ T cells, with CD4+ T cell responses more frequent than CD8+ T cell responses to the HIV inserts. Vector-specific immune responses showed a boosting effect from the 2nd to the 3rd immunization.

Conclusion

rMVA vaccination induces a dose-dependent, robust and durable polyfunctional cellular immune response as measured by IFNγ Elispot, CTL and intracellular cytokine stimulation assays. Although vector-specific responses tend to dominate over insert-specific responses, the data supports further exploration of MVA as a vector modality in prime-boost vaccination strategies.