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Induction of HIV-1 Gag-specific memory T cells in Chacma baboons by MVA prime and VLP boost vaccine regimen

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Background

We previously reported induction of HIV-specific responses in Chacma baboons following immunization with SAAVI MVA-C (MVA) and HIV-1 Pr55 Gag virus-like particles (VLPs) in a prime-boost vaccination strategy. In the current study, we characterised the vaccine specific memory T cells by flow cytometry.

Methods

Peripheral blood mononuclear cells (PBMC) from baboons primed with MVA and boosted with VLPs ($n=3$) or vaccinated with VLPs only controls ($n=2$) were stimulated with HIV-1 Gag peptide pools. T cell cytokine production (multiplex TNF- α , IFN- γ and IL-2) and memory phenotype was determined by flow cytometry. Human anti-CD28 and CD95 antibodies were used to delineate effector memory (Tem) and central memory (Tcm) T cells.

Results

Vaccine specific memory responses were detectable one week after MVA prime. At peak T cell response (four weeks after VLP boost), the frequency of cytokine producing cells in prime-boost animals (mean response: $0.21\% \pm 0.012$ and $0.242\% \pm 0.049$ of CD4+ and CD8+ cells respectively) was higher than in control animals (mean response: $0.066\% \pm 0.005$ and $0.034\% \pm 0.016$ of CD4+ and CD8+ cells respectively). Gag-specific CD4+ cells from the prime-boost animals were significantly skewed towards a Tcm phenotype ($>95\%$) of total cytokine responses compared to the Tem phenotype ($<2\%$). A similar memory distribution profile of Gag-specific CD4+ cells was maintained 20 weeks after the VLP

boost. At this time, Gag-specific CD8+ cells were evenly distributed between Tcm ($\sim 40\%$) and Tem ($\sim 60\%$) phenotypes. Vaccine specific memory responses were preserved 20 weeks after the VLPs boost (mean: $0.128\% \pm 0.025$ and $0.147\% \pm 0.039$ of CD4+ and CD8+ cells respectively) in the prime-boost animals.

Conclusion

In conclusion, the MVA prime and VLP boost induced Gag-specific cytokine producing Tcm and Tem defined by expression of CD28 and CD95. These cells were detected up to 20 weeks post vaccination suggesting these vaccines could be potential HIV-1 vaccine candidates.

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