

## PE48

### Broadly specific, cytolytic T cell responses and lower inflammatory responses correlate with durable viral remission following therapeutic DNA vaccination in SIV-infected macaques

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**Background:** We previously reported (DOI: 10.1371/journal.pone.0033715) that an adjuvanted DNA vaccine that stimulated mucosal CD8+ T cell responses in the gut of SIV-infected macaques during antiretroviral drug therapy (ART) induced 3 different virological outcomes: Viral rebound within 6 months after stopping ART (5/14 vaccinated animals and 6 controls), protection from viral rebound for 12-18 months after withdrawing drugs (5/14 animals) or no detectable virus (4/14 animals) for over 30 months (duration of the study) after stopping ART.

**Methods:** At study end, macaques were necropsied to determine the impact of vaccination on residual virus in the gut and lymphoid tissues. To define what immune responses contributed to long-term viral control, lymphocytes were isolated from blood and gut tissues and T cell responses and inflammatory cytokines in the blood and gut were measured by ICS, ELISPOT and cytometric bead array. Results in macaques that had no detectable virus or exhibited a significant delay in viral rebound after stopping ART were compared to macaques that exhibited immediate viral rebound within 6 months after stopping ART.

**Results:** The 4 macaques with no detectable virus in the blood had detectable viral RNA and/or DNA in at least one lymph node or in gut tissues demonstrating the vaccines substantially reduced residual virus but did not clear the virus. Animals that exhibited delayed viral rebound or no viral rebound had a higher frequency of CD8+ T cells with cytolytic effector function, higher CD4+ T cell proliferation, and broadly specific mucosal SIV-specific CD8+ T cell response targeting more conserved viral sequences in Gag when compared to animals that rebounded within 6 months after stopping ART. In addition, lymphocytes isolated from macaques that exhibited delayed or no viral rebound post-ART expressed lower levels of the inflammatory cytokines (TNF- $\alpha$ , IL-6) prior to stopping ART when compared to macaques that exhibited immediate viral rebound within 6 months post-ART.

**Conclusions:** These results show that immunotherapeutics that can broaden virus-specific T cell responses against more conserved viral sequences and at the same time, reduce inflammation during HAART may be an effective approach to achieve durable viral remission.