

Conclusions: This study shows that Tregs represent an important fraction of HIV-specific T cells. Tregs impact the frequency and the capability of effector cells to control viral replication. Thus the ability to measure the inducibility of Tregs and/or to modulate those responses prior to vaccination is important for more efficient strategies in future vaccines.

P24.02

Seminal Plasma Modulates Dendritic Cell Function Favoring the Generation of CD25+/FOXP3+ T-cells

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Background: Unprotected sexual intercourse is the most common mode of HIV-1 transmission being semen the most important vector for this infection. Dendritic cells (DCs) are abundantly located on mucosal surfaces and play different roles during HIV infection: promote HIV spread by boosting CD4+ T cell infection and activate the HIV specific adaptive immune response. As semen has been shown to promote immune tolerance in different models, we hypothesize that components present in plasma seminal (SP) might modulate DC function promoting a tolerogenic immune response. To test this, we study the ability of complete SP to modulate DC function and the ability of these cells to induce CD25+/FOXP3+ regulatory T cells.

Methods: SP was obtained from healthy donors. Monocyte derived DCs were cultured during 24 hs with SP samples (diluted 1/100) in the absence or presence of LPS (10ng/ml). DC phenotype was studied by flow cytometry. Cytokine secretion was measured in culture supernatants by ELISA. After SP treatment, DCs were cultured with allogeneic CD4+ T cells and the induction of CD25+/FOXP3+ T cells was analyzed by flow cytometry.

Results: We found that SP inhibited IL-12, IL-6, TNF-alpha and IL-1, but not IL-10 production by LPS stimulated DCs (percent of inhibition respect to LPS alone: 81.2 +/- 11.07% p < 0.0001 for IL-12, 43.45 +/- 2.87% p < 0.001 for IL-6, 69.8 +/- 17.31% p < 0.001 for TNF-alpha, 37.5 +/- 13.15% p < 0.05 for IL-1, 6.1 +/- 15.6% p = 0.6 for IL-10). SP also boosted the ability of LPS stimulated DCs to induce CD25+/FOXP3+ T cells (PS + LPS = 20.4% vs LPS alone = 6%, p < 0.05). We observed no changes on the expression of HLA-DR, CD80, CD86, CD83, CD40 and CD1a on immature or LPS-maturated DCs after incubation with SP.

Conclusions: SP modulates DC function, inhibiting the secretion of pro-inflammatory cytokines and favoring the induction of CD25+/FOXP3+ T cells. In this way, we speculate that SP might modulate the adaptive immune response against sexual transmitted pathogens.

P24.03

In Vivo Viral Control in a HLA-B*35:01 Homozygous Individual after the Vaccine-induced Response to a Well-defined, HIV Gag-derived HLA-B*35 CTL Epitope

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Background: Virus-specific CD8 T cell responses to epitopes restricted by HLA-B*35:01 are generally believed to be ineffective in mediating *in vivo* control of HIV infection. We report a case of a patient homozygous for HLA-B*35:01 who showed successful viral control after vaccination with MVA-B vaccine combined with a drug to reactivate HIV-1 replication (disulfiram), and who subsequently underwent an analytical treatment interruption (ATI).

Methods: Therapeutic vaccination consisted of 3 intramuscular injections of MVA-B at 0,4,16 weeks and a 4th dose followed by 2 months of disulfiram. cART was discontinued 8 weeks after last vaccination. IFN-γ ELISPOT was used to assess immunogenicity and proviral reservoir was determined over time. Viral rebound dynamics were assessed during ATI.

Results: The patient had a past history of high viral load set point (362,000 copies/ml) and cART was initiated during chronic infection. After ATI the patient remained with low level viral load < 200 copies/ml for > 24 weeks without showing a significant decay in CD4 T-cell counts. At baseline, the patient showed a broad (19 different specificities) and strong (9,189 SFC/10⁶PBMC) T cell response, which increased to 14,470 SFC/10⁶PBMC after three vaccinations. Responses to three novel T-cell epitopes present in the vaccine insert (Nef A*03-QK10, Gag A*03-RK9 and Pol B*35-VY10) were induced upon 3 vaccination. A dominant HLA-B*35:01 restricted response to the Gag-p24 B*35-PY9 epitope (PPIPVGDIY) of 3,330 SFC/10⁶PBMC was detected before ATI. No changes in proviral reservoir or viral expression (mRNA) were observed in CD4+ T-cells after disulfiram treatment.

Conclusions: The expansion of a dominant response towards the HLA-B*35- restricted Gag RY9 epitope could potentially explain the observed viral control on this subject suggesting that certain HLA-B*35:01 restricted responses may have the potential to significantly contribute to viral control, providing important guidance for vaccine immunogen design covering non-beneficial HLA alleles.

P24.04

Evolution of Polyfunctional and Proliferative CD8+ T-cell Responses from Early to Chronic HIV-1 Infection

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Background: The limited success of HIV vaccine candidates to date highlights our need to better characterize protective cell-mediated immunity (CMI). HIV-infected subjects that experience slower progression to AIDS, provide a valuable model for the study of CMI responses that may be capable of controlling