

Altered CD4 and NK Cell Profile with Inverse IFN γ and IL-10 Antiviral Response in HIV-1+ Pregnancies

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Introduction: HIV-1⁺ mothers experience increased incidence of pre-term delivery and lower neonate birth weight in both resource rich and poor settings. Pre-term labour is linked to maternal inflammation and the activation of fetal lymphocytes; antiretroviral therapy (ART) treated HIV-1 infection is associated with chronic immune activation, potentially caused by persisting HIV-1 reservoir, and other viral co-infections. Parallels between HIV-1 infection and pre-term labour are apparent, therefore this study aims to use HIV-1 infection as a model, and determine differences in maternal lymphocyte composition and antiviral function in HIV-1⁺ and HIV-1⁻ pregnancies.

Methods: Participants were recruited from the Chelsea and Westminster Hospital, consented, and blood sampled. Peripheral blood mononuclear cells (PBMC) were isolated and flow cytometric analysis performed to determine the expression of activation, differentiation and exhaustion markers. IFN γ and IL-10 ELISpot assays on PBMC were undertaken to measure responses against Flu and CMV antigens. Responses to Gag and Nef peptides were tested by ELISpot in HIV-1⁺ individuals only. Statistical analysis was carried out using Prism version 6.0. Intergroup variation was assessed by unpaired two-tailed t tests, intragroup variation by Wilcoxon matched pairs test, and statistical significance defined as $p < 0.05$.

Results: Phenotypic analysis showed increased frequency of exhausted CD4⁺PD-1⁺ effector memory T cells in HIV-1⁺ women ($p = 0.0117$). CD11b and NKp30/NKG2A markers revealed a decrease of anergic NK cell subsets in HIV-1⁺ mothers ($p = 0.0174$). There was a statistically significant increase in IFN γ response to Flu and CMV ($p = 0.0123$ and $p = 0.0005$ respectively), and a decrease in IL-10 response in the HIV-1⁺ group. All HIV-1⁺ women were IFN γ responders to Gag, and 7/8 (87.5%) were Nef responders.

Conclusions: Pregnancy may modify T-cell differentiation towards effector memory subset while maintaining fetal tolerance. Despite ART HIV-1 persists, as shown by Gag and Nef responses, and skews T cells to an exhausted profile. Differences in cell populations reflect prolonged activation and disrupted tolerance, confirmed by altered NK cell phenotype. Together these findings show the impact of viral persistence on innate and acquired immunity, and identify cell populations that may be integral in the cause of pre-term labour.