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Background

Identifying the immune correlates of reduced susceptibility to HIV remains a key goal for the HIV vaccine field, and individuals who are HIV-exposed, seronegative (HESN) may offer important clues. Reduced systemic immune activation has been described in HESN individuals. Conversely, pro-inflammatory T cell subsets, particularly CD4⁺ T cells producing the cytokine IL17 (Th17 cells), may represent a highly susceptible target for HIV infection after sexual exposure. Therefore, we characterized the cellular pro-inflammatory and IL17/IL22 cytokine immune milieu in the genital mucosa and blood of HESN female sex workers (FSWs).

Methods and Results

Blinded lab personnel characterized basal and mitogen-induced gene and cytokine immune responses in the cervix and blood of HESN FSWs (n = 116) and non-FSW controls (n = 17) using qPCR and ELISA. IL17 and IL22 production was significantly reduced in both the cervix and blood of HESNs, both in resting cells and after mitogen stimulation. In addition, HESN participants demonstrated blunted production of both pro-inflammatory cytokines and - chemokines.

Discussion and Conclusions

We conclude that HIV exposure without infection was associated with blunted IL17/IL22 and pro-inflammatory responses, both systemically and at the site of mucosal HIV exposure. It will be important for further studies to examine the causal nature of the association and to define the cell subsets responsible for these differences.