Female genital epithelial cells from HIV-exposed seronegative commercial sex workers express a discrete cytokine/chemokines profile upon toll-like receptor activation

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Background: Majority of human HIV-1 infections are acquired through heterosexual transmission across female genital mucosa. Epithelial cells that line the genital mucosa express toll-like receptors (TLR) and act as first line of defense against mucosal infections. Immune locale orchestrated by TLR mediated activation of female genital epithelial cells can be a critical determinant of HIV-1 resistance or susceptibility. HIV-1-exposed seronegative (HESN) women have been shown to have a distinct pattern of cytokines and chemokines as measured in CVL samples. In this study we investigated the role of TLR signaling in female genital epithelial cells in determining the local mucosal cytokine /chemokines milieu.
Methods: Endoervical cytobrsuh samples were obtained from Pumwani CSWs cohort in Nairobi, Kenya. HESN (n=22), HIV- (n=24) and HIV+ (n=23).Cervical epithelial cells (CECs) were purified through a series of nylon membrane filtrations. Purity and viability of CECs was assessed by Ber-EP4 expression and MTS assay, respectively. CECs were cultured with or without TLR3 ligand (poly:IC) or TLR1-9 ligand combined for 24 h. Cytokine/chemokines levels in the supernatants were determined using the Milliplex MAP multiplex kit (Human Cytokine/Chemokine I) and analyzed on the BioPlex-200 according to manufacturer's protocol.
Results: We tested 22 cytokines and chemokines (EGF, GM-CSF, IFNalpha2, IFN gamma, IL-1b, IL-2, IL-6, IL-7, IL-8, IL-10, IL-12 (p40), IL-12(p70), IL-15, IL-17, IP-10, MCP-1, MCP-3, MDC, MIP-1alpha, MIP-1beta, RANTES, and TNFalpha). CECs from HESN individuals expressed significantly lower levels of interferon-γ-induced protein 10 (IP-10) and IL-8 upon TLR3 or combined TLR1-9 stimulation compared with controls. Both of these cytokines and chemokines have important functions in inflammatory and immune cell recruitment.
Conclusion: These results highlights the role of TLR signaling in CECs and support the immune quiescence model of HIV-1 protection, whereby lower target and inflammatory cell recruitment at the genital mucosal compartment reduces HIV-1 target cell numbers.