Introduction

Increasing evidence suggests that innate responses may be key determinants of the outcome of infection, particularly the role of Toll-like receptors (TLRs) which have recently been shown to be important in early host defense and instruction of adaptive response (Biasin et al., 2010).

The aim of this study was to understand the earliest event in mucosally transmitted HIV-1 infection in a group of women whose exposure to HIV is almost exclusively through the genital mucosa.

To better understand the correlates of mucosal protection against mucosally transmitted HIV which is largely unknown, a viral challenge was used, this consisted a live attenuated influenza vaccine (FluMist®) administered intranasally to stimulate the mucosal system.

Blood was collected prior to (day 0) and following vaccination day 7 and 30. We hypothesized that the HESN will have heightened innate immune responses compared with HIV-negative/susceptible individuals both before and after mucosal challenge.

Methods

The study population was drawn from the Majengo sex worker cohort, Nairobi, Kenya comprising 2 groups: HESN or HIV resistant; short term HIV exposed uninfected (New Negative/susceptible, HIV-S).

Peripheral blood mononuclear cells (PBMCs) from the subjects were isolated by Ficoll Hypaque (Histopaque-1077) density gradient centrifugation procedure from heparin-treated blood.

PBMCs isolated from the study participants were incubated with agonists specific for TLR9 (CpG ODN) and TLR7/8 (ssRNA40), unstimulated cells served as negative controls (Media) while SEB served as positive control.

Supernatants from these cultures were quantified for presence of pro and anti-inflammatory cytokines and chemokines using multiplex assay on Luminex.

Results

Stimulation of PBMCs with TLR 7, 8 and 9 ligands led to a significant increase in IL-2 production at baseline in HIV-R compared with HIV-S (p=0.0159). Also significant increase in IP-10 at day 7 (p=0.00952) and 30 (p=0.0317) in HIV-R compared to HIV-S was observed.

Figure 1 : Chemokine and Cytokine responses (y-axis pg/ml) following stimulation of PBMCs from HIV-R and HIV-S individuals (x-axis ) with TLR 7/8 and 9 ligands before (a) and after FluMist vaccination (b, c)

Conclusion

HIV-resistant women had stronger IL-2, IFN-γ and IP-10 responses to TLR ligands compared to HIV-susceptible. This may point to an important protective role of innate mechanisms in influencing susceptibility to HIV-1 infection, and has a potential for augmenting prevention or therapeutic interventions.

Literature cited


For more information contact: Irene Adhiambo Onyango
adhiambo.onyango@gmail.com
4971-00200, Nairobi, Kenya