Low Immune Activation and Low Numbers of HIV-target cells in the Ectocervix of HIV-Exposed Seronegative Commercial Sex Workers

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Background:
The majority of all HIV transmissions, worldwide, occur through heterosexual transmission, across mucosal surfaces. Heterogeneity in susceptibility to HIV infection has been demonstrated in HIV-exposed seronegative (HESN) individuals and the resistance against infection has been partly attributed to a low systemic and mucosal immune activation.

Aims:
To investigate:
• The number, localization and phenotype, ex vivo, of immune cells in the FGT from HESN individuals in relation to the control groups.
• If the low immune activation as well as lower number of HIV-target cells at the portal of entry (e.g. ectocervix) correlate with the partial resistance against HIV acquisition.

Study cohort:
Ectocervical biopsies were obtained from HIV infected and uninfected women from the Puwmani district in Nairobi, Kenya.

Conclusions:
• HESN FSW display a low immune activation in their ectocervix, including a low number of immune cells and low expression of proinflammatory cytokines.
• HESN FSW have low numbers of HIV-target cells in their ectocervix.
• CD4+T cells in the ectocervix are mainly located in the epithelial compartment.
• This mucosal phenotype, at the portal of entry, may be beneficial in the partial resistance against HIV infection.

Low numbers of HIV-target cells in the ectocervix of HESN FSW

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>HIV FSW</th>
<th>HIV+ FSW</th>
<th>HIV LR</th>
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<tbody>
<tr>
<td>Median or number</td>
<td>Median or number</td>
<td>Median or number</td>
<td>P-value</td>
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<tr>
<td>(range or %)</td>
<td>(range or %)</td>
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<tr>
<td>42 (27-51)</td>
<td>42 (24-58)</td>
<td>38 (24-47)</td>
<td>n.s</td>
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</tbody>
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Douching ever performed by inserting water or water and soap in the vagina.

n.s. - not significant

* P-value for HIV+ FSW vs. HIV LR
**P<0.01, Fishers exact test
***P<0.001, Fishers exact test

No differences between the groups in respect to:
- Other STI
- Hormonal contraception
- Menstrual cycle stages
- Pregnancies

Low numbers of CD4 positive cells within the ectocervix of HESN FSW

Figure 1. In situ staining and quantification of CD3, CD8 and HLA-DR expressing cells in the ectocervical tissue sections obtained from HESN FSW, HIV+ FSW and HIV LR individuals. Tissue section were stained with DAB (in brown) and with hematoxylin (in blue). Scale bar 200µm.

Figure 2. In situ staining of CD4 expressing cells in the ectocervical tissue sections obtained from HESN FSW, HIV+ FSW and HIV LR individuals. a) Tissue section were stained with DAB (in brown) and with hematoxylin (in blue). Scale bar 500 µm b) immunofluorescent double staining; CD3 in red, CD4 in green, dapi in blue. Scale bar 100µm

Figure 3. Quantification of HIV receptor expressing cells in the ectocervical tissue sections obtained from HESN FSW, HIV+ FSW and HIV LR individuals.

Figure 4. Enumeration of proinflammatory cytokine mRNA expression in the ectocervical tissue obtained from HESN FSW, HIV+ FSW and HIV LR individuals.