Exogenous CCL27 causes an elevation in CD3+CD4+ T cells in the epithelium of inner foreskin but not outer foreskin. This potentially increases the susceptibility of the inner foreskin to HIV relative to the outer foreskin.

**Background and aims**

Previous studies have shown that the inner foreskin is more susceptible to HIV infection. This has been postulated to be due to the higher density of HIV target cells (CD4+ T cells) in the inner foreskin and increased inflammatory markers in the tissue compared to the outer foreskin and the glans penis. The chemokine responsible for homing T cells to skin, CCL27 [1], was found to be 7-fold higher in the inner foreskin relative to the outer tissue. We hypothesized that CCL27 can recruit CD3+CD4+ T cells to the foreskin epithelium. The aim of this study is to provide a better understanding of the differences in the susceptibility of the inner compared to the outer foreskin.

**Study design and methods**

1 cm² Inner and outer foreskin tissue explants were exposed to three conditions for 48 hours at 37°C:
- complete R10 media (unstimulated).
- TNFa (100ng/ml) in R10 media (+ve control).
- CCL27 (400ng/ml) in R10 media.

Explants stained for CD3-FITC, CD4-CYS and DAPI. A Deconvolution microscope with Delta Vision imaging system was used to acquire fluorescent images. CD3+ and CD4+ cells were highlighted and the area of epithelium measured using SoftWorX. Analysis done using IDL.

**Results**

We observed an increase in the density of CD3+CD4+ T cells in the epithelium of the inner foreskin that was exposed to CCL27 but not the outer foreskin. The data showed a 2- to 3-fold (p<0.001) increase in CD3+CD4+ T cell numbers in the epithelium after stimulation with TNFa (from 60 cells/mm² to 138 cells/mm²) and CCL27 (from 60 cells/mm² to 147 cells/mm²) compared to the unstimulated samples while the outer foreskin tissue samples showed no significance between TNFa, CCL27 and unstimulated samples.

**Conclusion**

Exogenous exposure of foreskin tissue to CCL27 significantly increased the population of CD3+CD4+ T cells in the inner foreskin compared to the outer foreskin. This increase is suggested to be due to the migration of CD3+CD4+ T cells to the epithelium of the inner foreskin. CCR10 is the cognate receptor for CCL27 that is expressed on T helper 22 (Th22) cells that also express CCR5, making them a possible target for HIV infection. The upregulation of CCL27 and its effect on the inner foreskin may provide a mechanism of why the inner foreskin is a preferential entry site for HIV.

**References**


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