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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

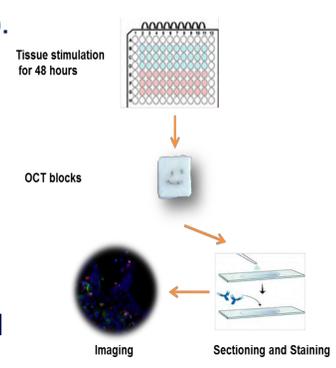
Previous studies have shown that the **inner foreskin** is more susceptible to HIV infection. This has been postulated to be due to the higher density of **HIV target cells (CD4+ T cells)** in the inner foreskin and increased inflammatory markers in the tissue compared to the outer foreskin and the glans 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:

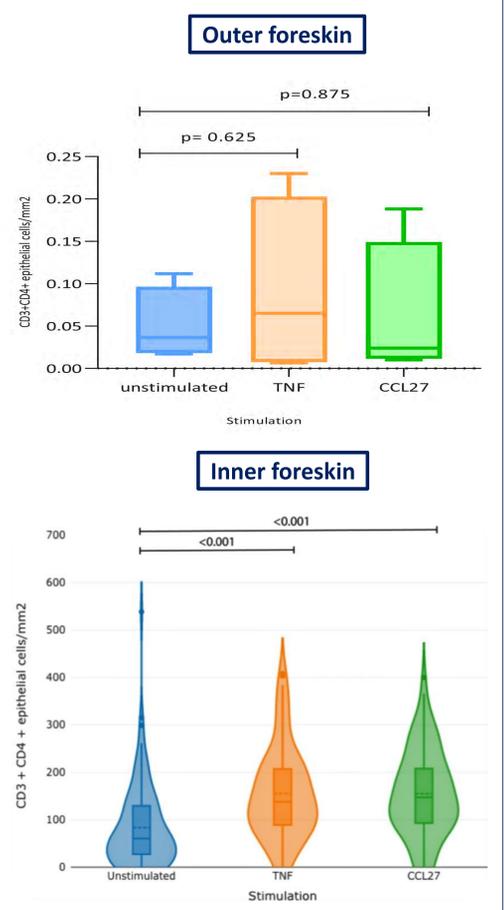
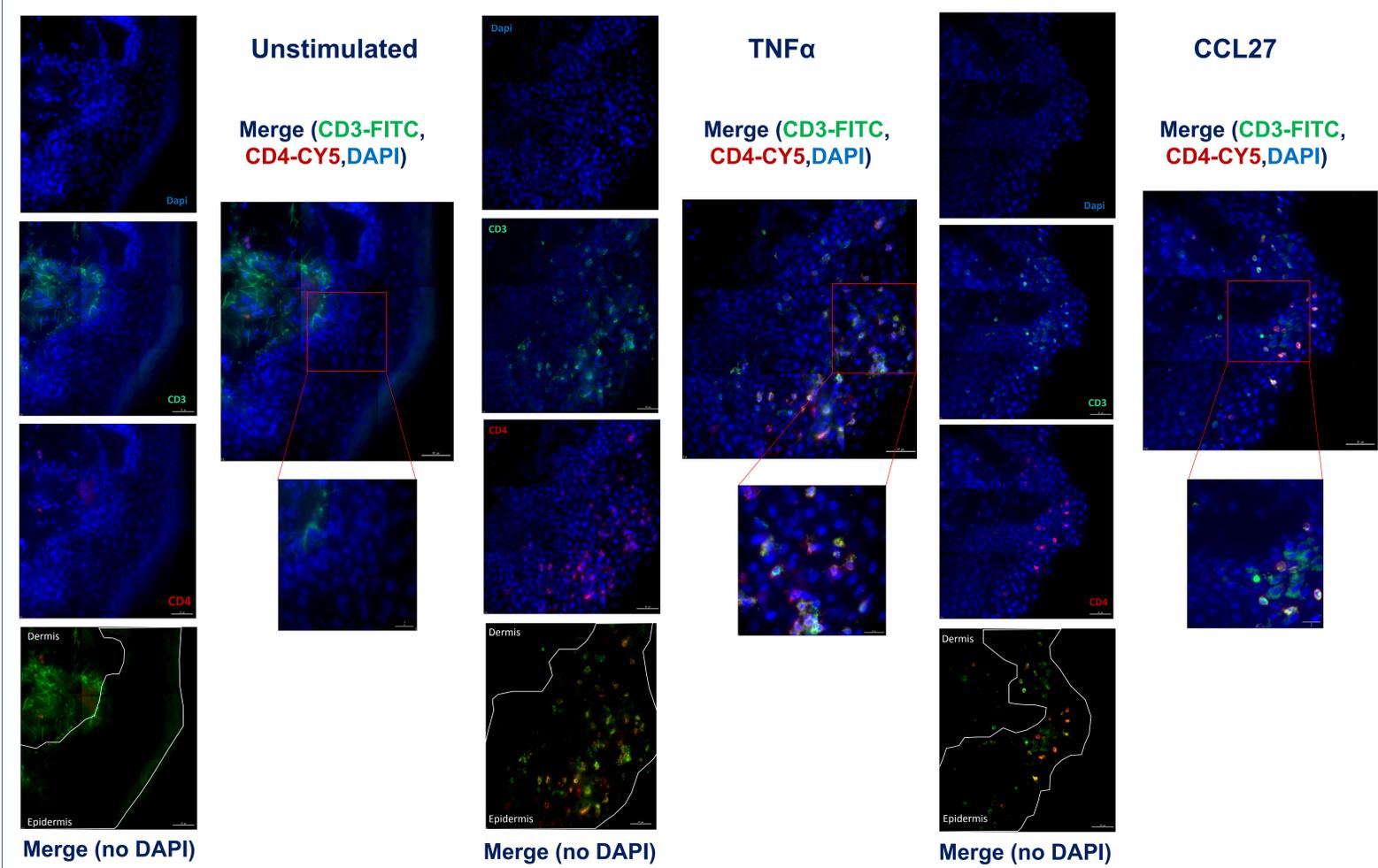
- complete R10 media (unstimulated).
- TNFα (100ng/ml) in R10 media (+ve control).
- CCL27 (400ng/ml) in R10 media.

Explants stained for **CD3-FITC**, **CD4-CY5** 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** (q<0.001) increase in CD3+CD4+ T cell numbers in the epithelium after stimulation with TNFα (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 TNFα, 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

1- Homey, B. et al. Cutting edge: the orphan chemokine receptor G protein-coupled receptor-2 (GPR-2, CCR10) binds the skin-associated chemokine CCL27 (CTACK/ALP/ILC). J. Immunol. 164, 3465–3470 (2000).

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