




Immunology of the Female Reproductive Tract

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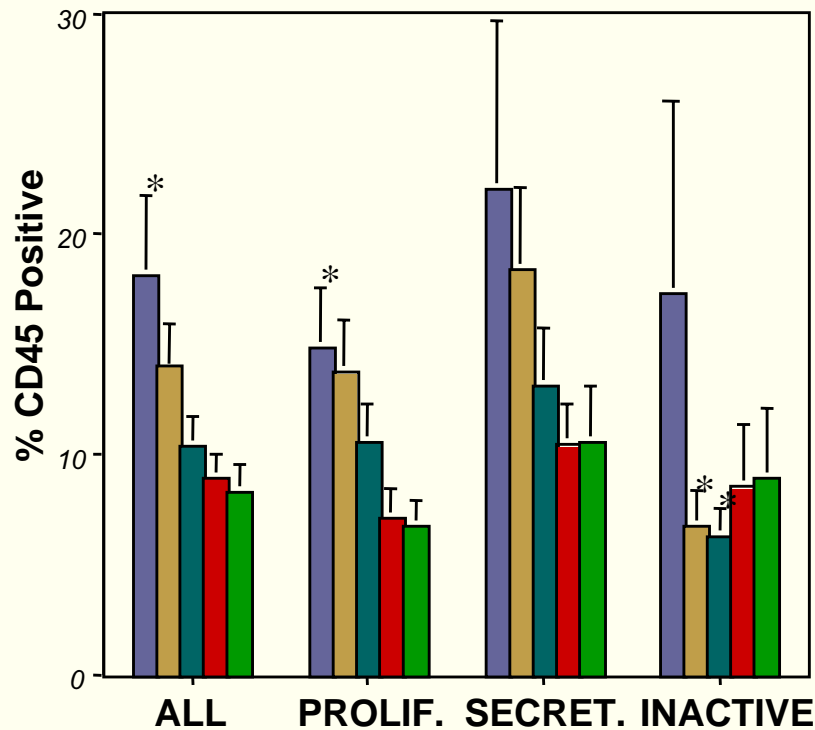


Mucosal Immunity In The Human Female Reproductive Tract

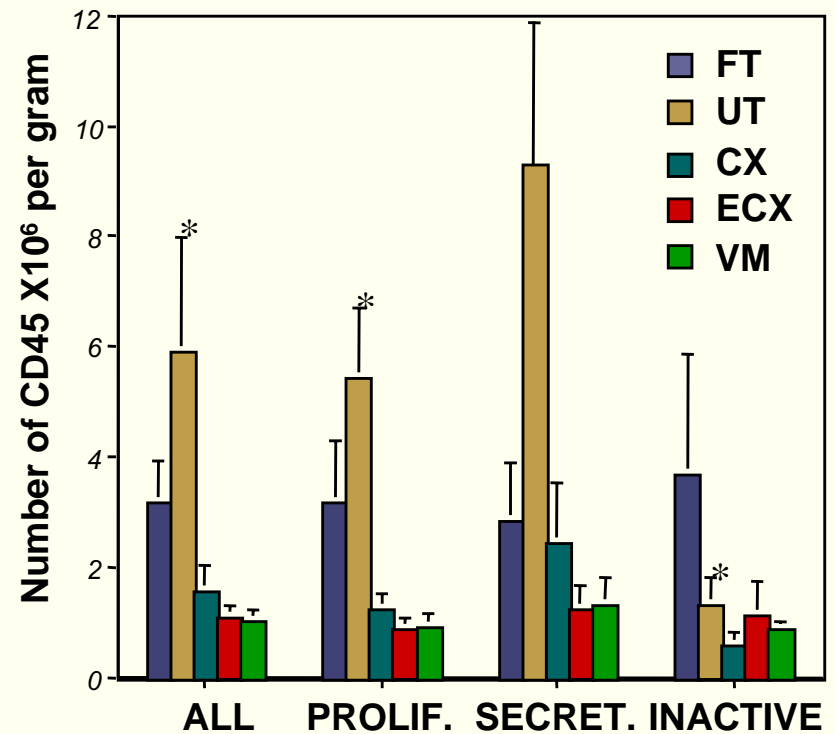
- Immune cells in the female reproductive tract.
 - 1 Antigen presentation by uterine epithelial cells.
 - 1 Localization of HIV receptors and co-receptors in the uterus.
 - 1 Innate Immune responses in the uterus: bactericidal activity and secretory leukocyte protease inhibitor (SLPI) production by epithelial cells.

Leukocytes in The Human Female Reproductive Tract

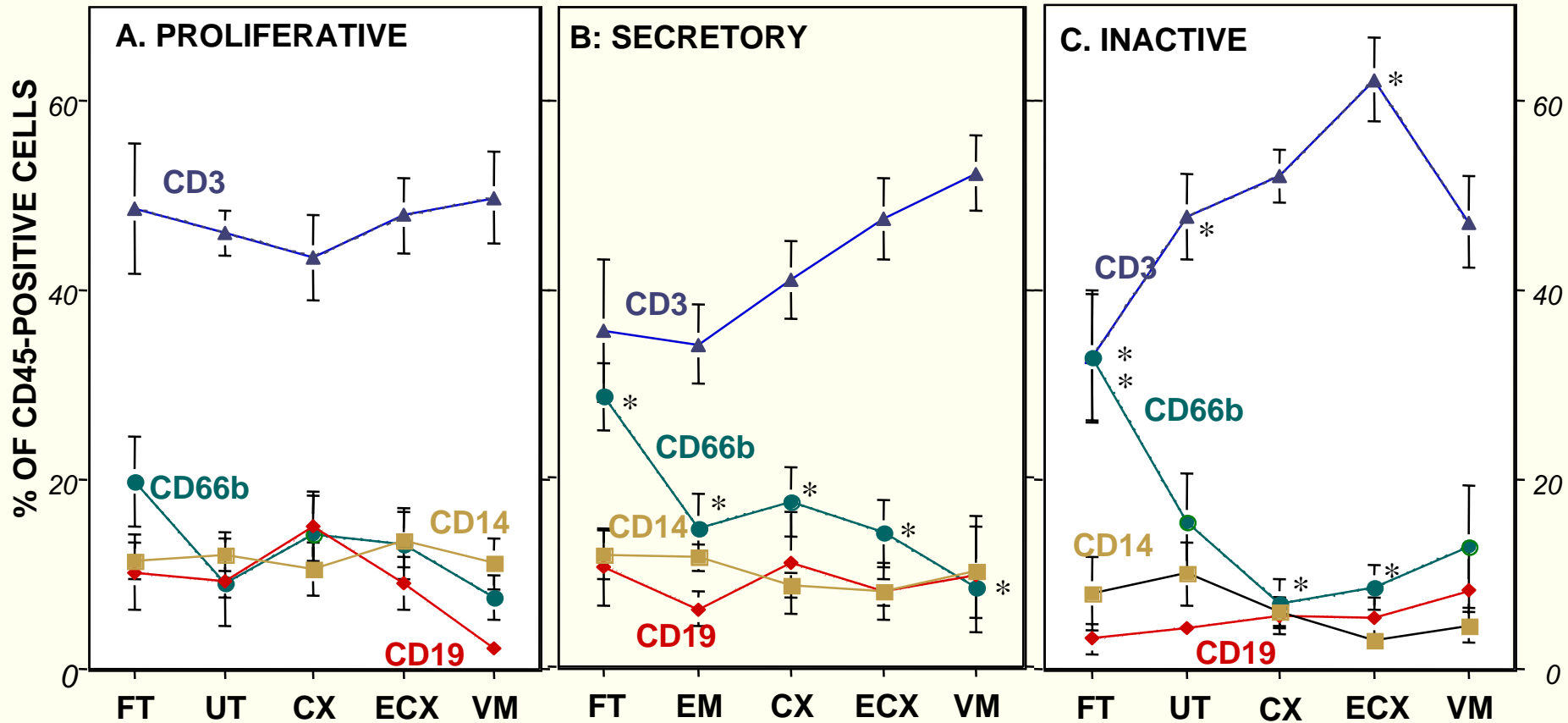
%CD45-POSITIVE CELLS OF TOTAL DISPERSED CELLS



NUMBER OF CD45-POSITIVE CELLS PER GRAM OF TISSUE (x 10⁶)



T Cells (CD3), Neutrophils (Cd66b), B Cells (CD19) and Monocytes (CD14) at Different Stages of the Cycle

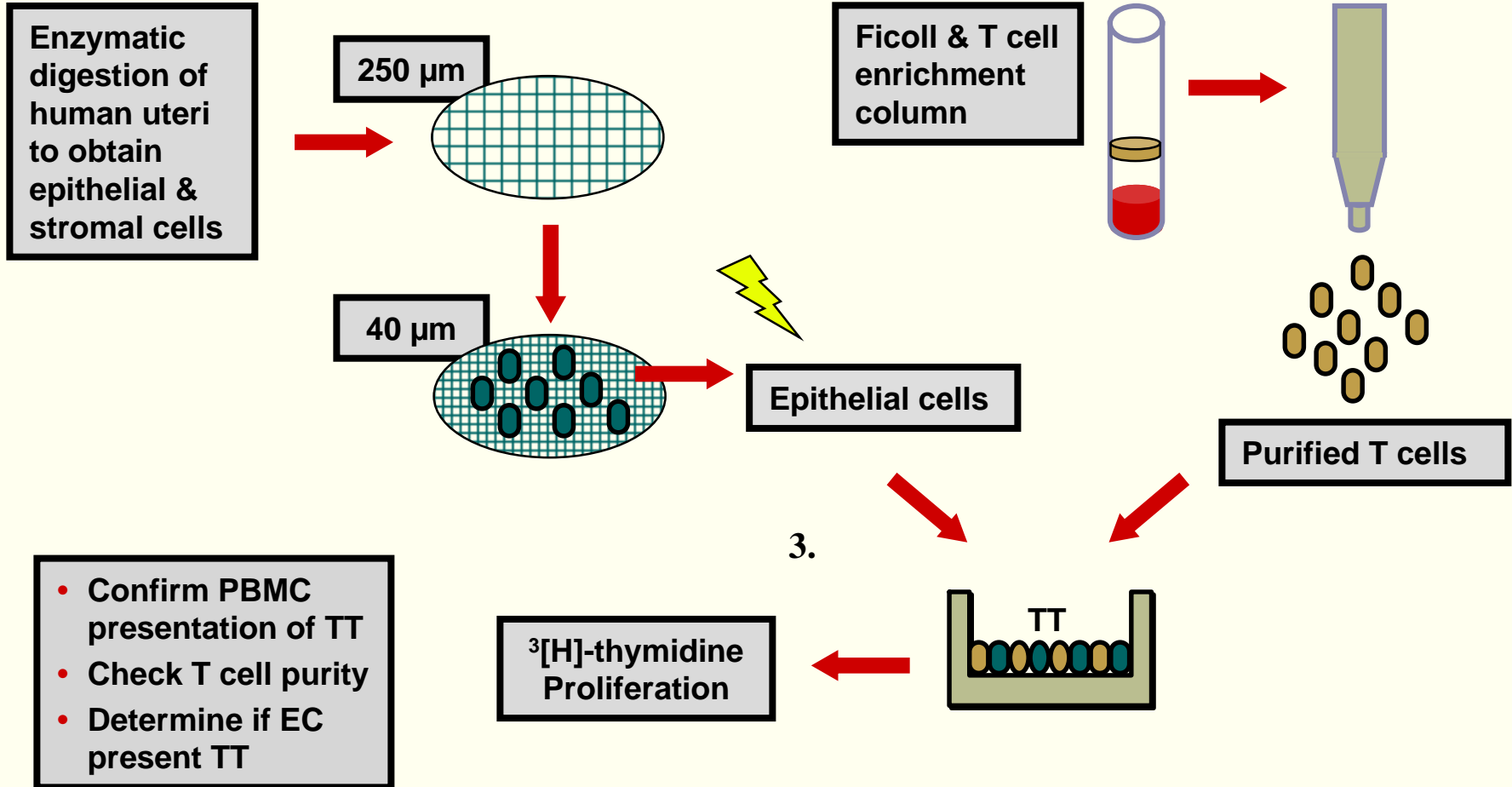


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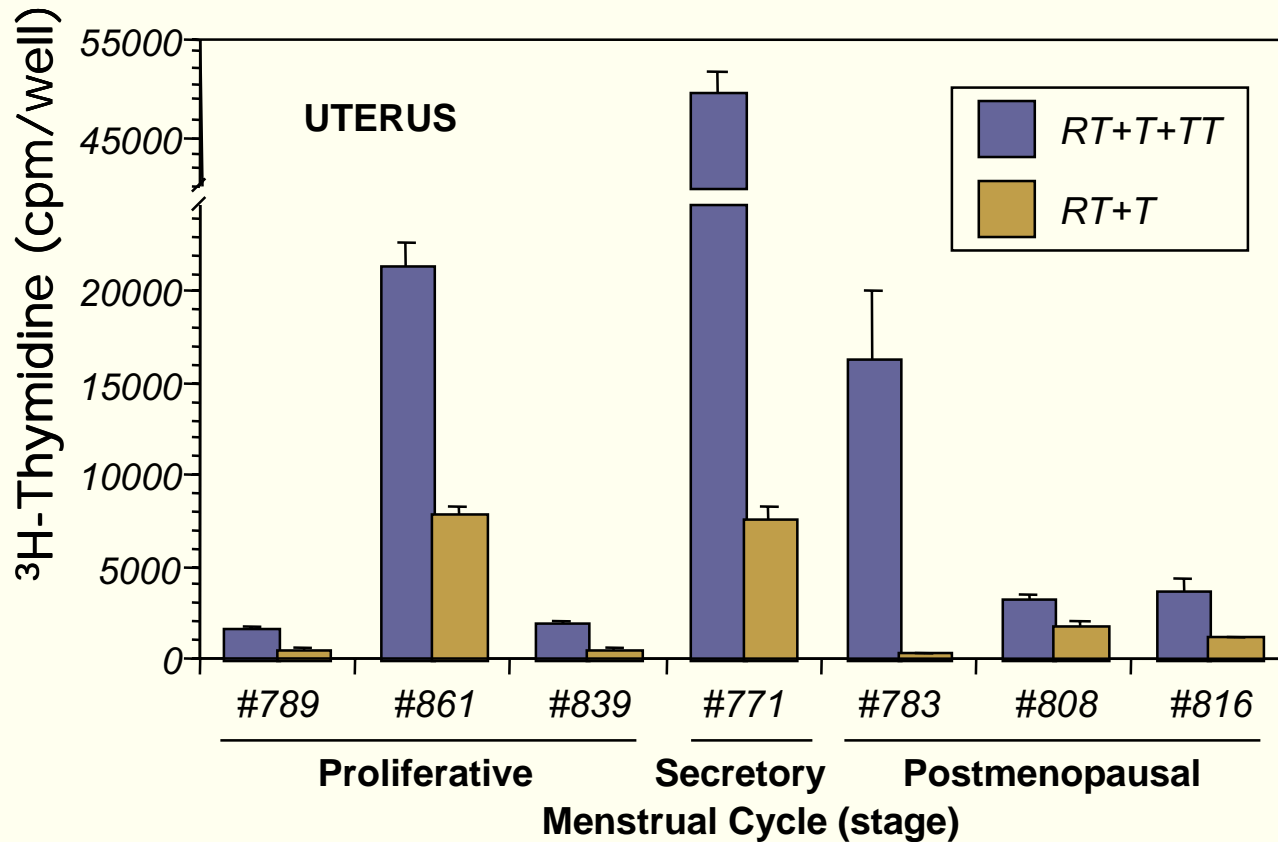
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Experimental Design: Antigen Presentation, Human Studies

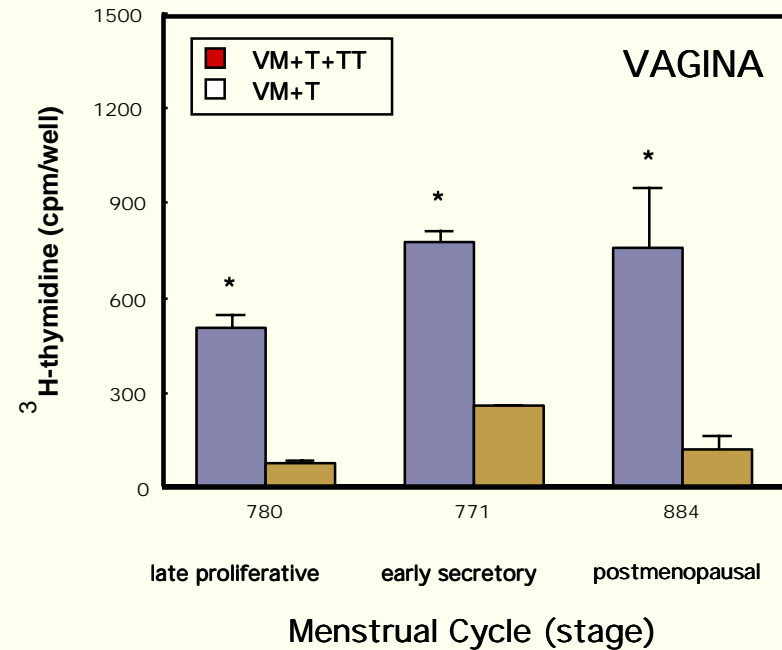
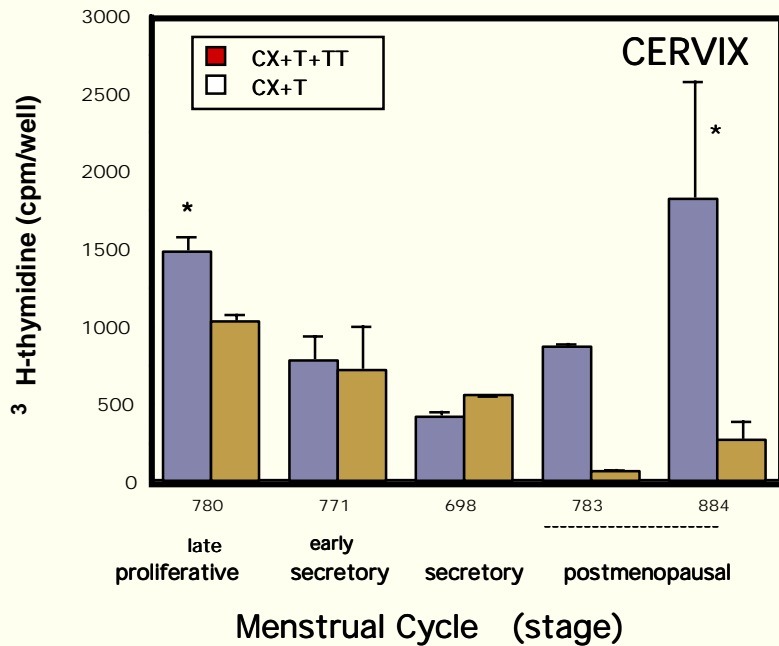
1.



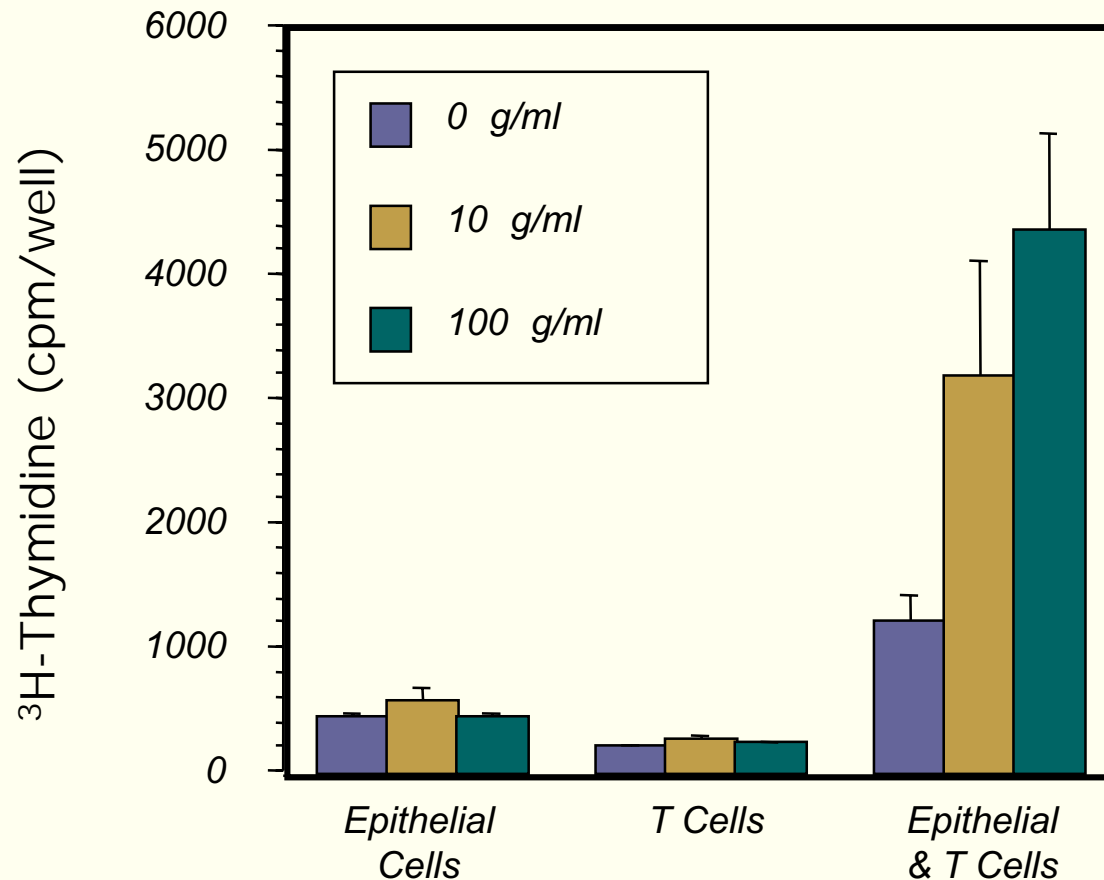
Antigen Presentation by Mixed Uterine Cells to Tetanus Toxoid Primed T Cells



Antigen Presentation By Cervical And Vaginal Cells To Tetanus Toxoid Primed T Cells



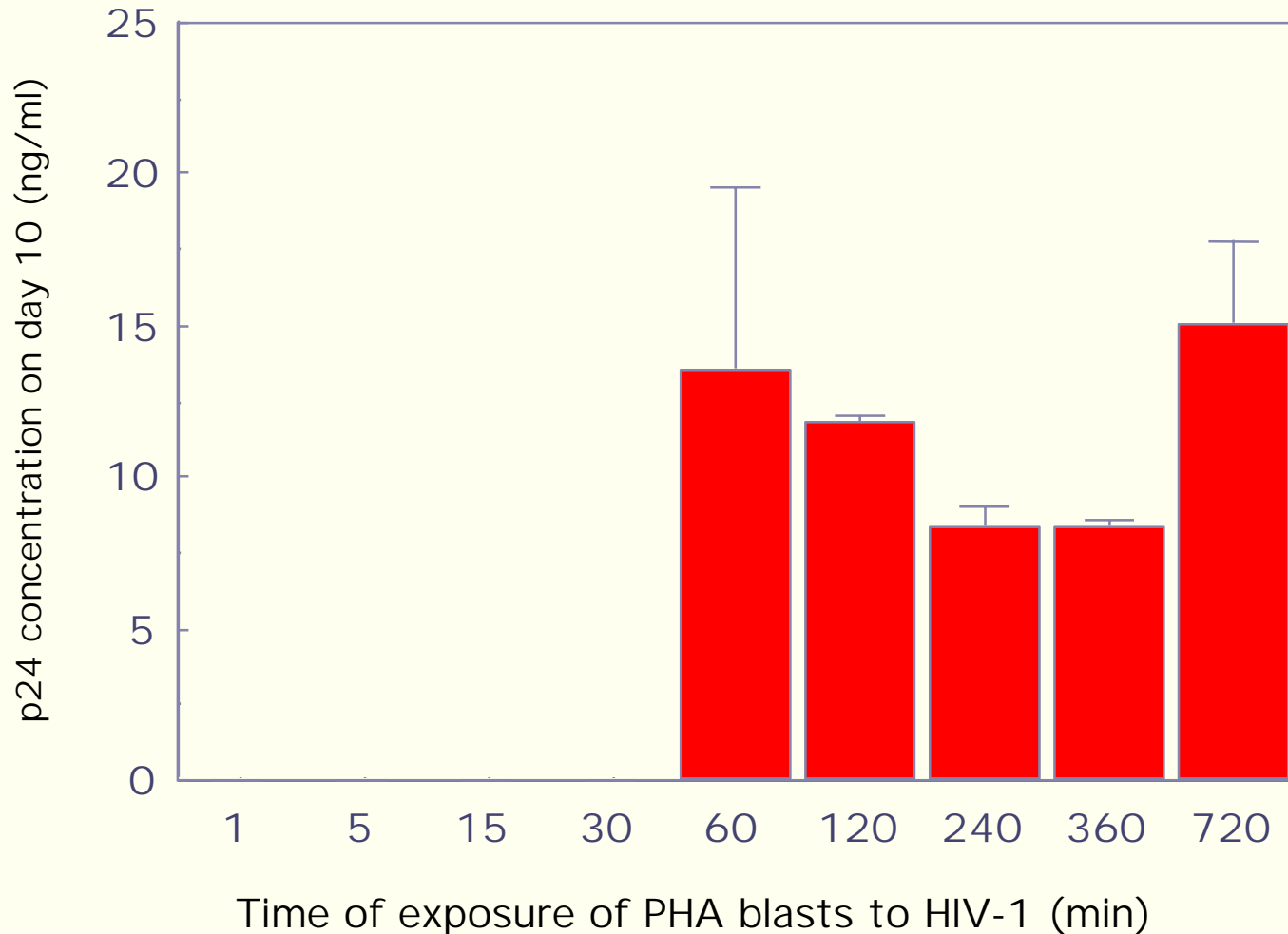
Presentation of Tetanus Toxoid by Uterine Epithelial cells



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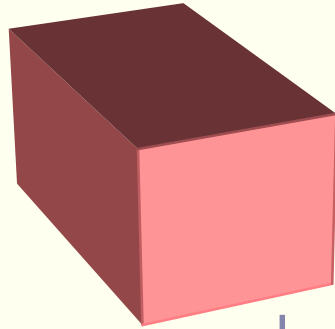
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Time Course of HIV Infectivity of Uterine Epithelial Cells

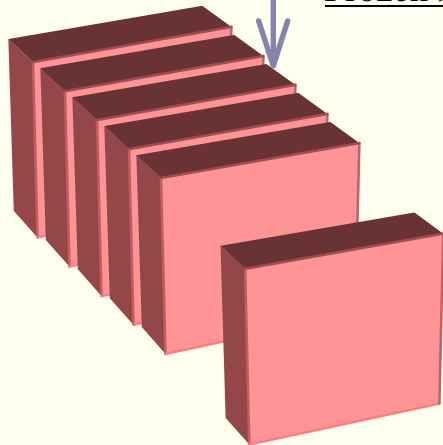


Preparation of Viable Tissue Sections and Confocal Analysis.

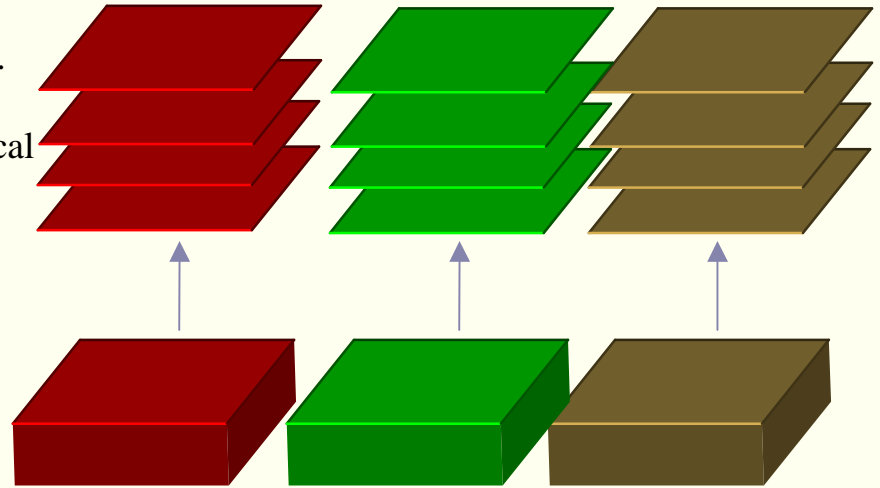
Hysterectomy Tissue.



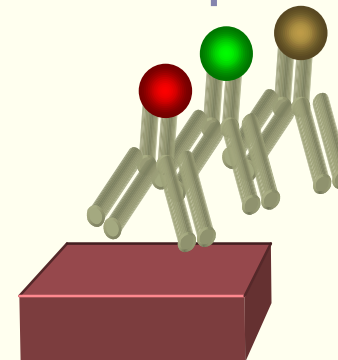
Prepare vibratome or Frozen Sections.



Confocal Analysis.
Simultaneous acquisition of optical sections (minimum thickness 0.7 μ m).



Fix and mount



3 Color Immuno-fluorescent staining.
Typically mAbs conjugated to FITC, Cy3 and Cy5

Analysis of CD4, CCR5 and CXCR4 on Viable Tissue Sections by Confocal Analysis

Conclusions

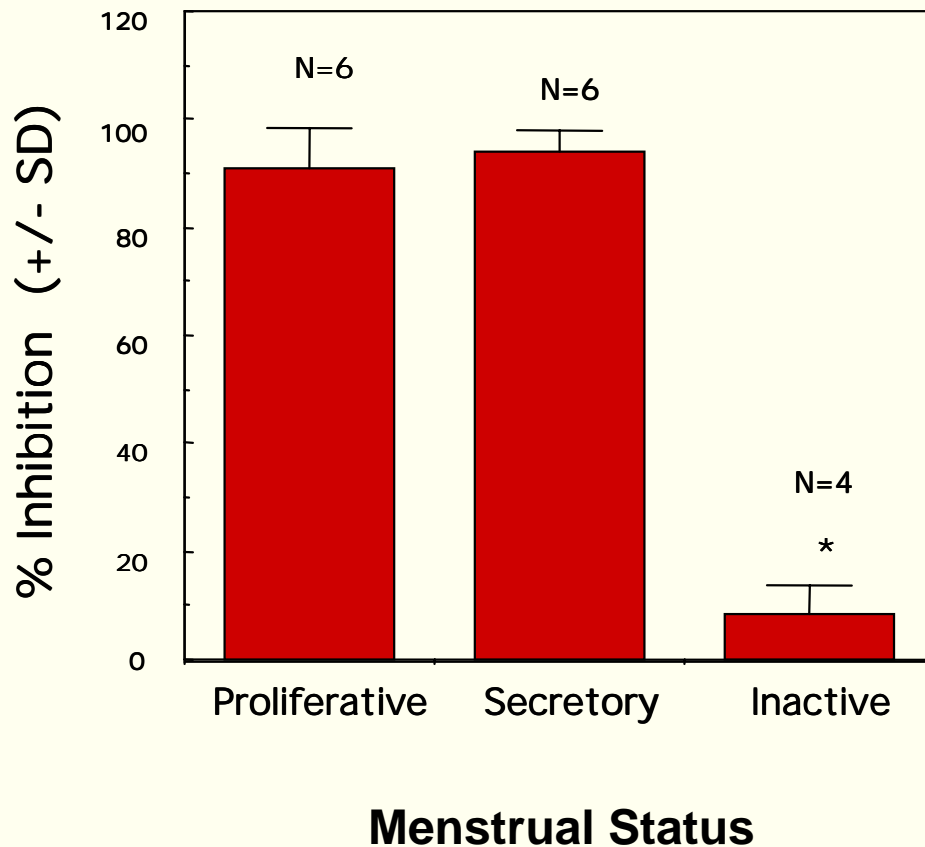
1. Uterine epithelial cells express CD4, CCR5 and CXCR4.
 - Expression of these receptors varies with the stage of the menstrual cycle.
3. These studies suggest that the uterus may be a site of HIV entry.

Yeaman et al. Unpublished observations

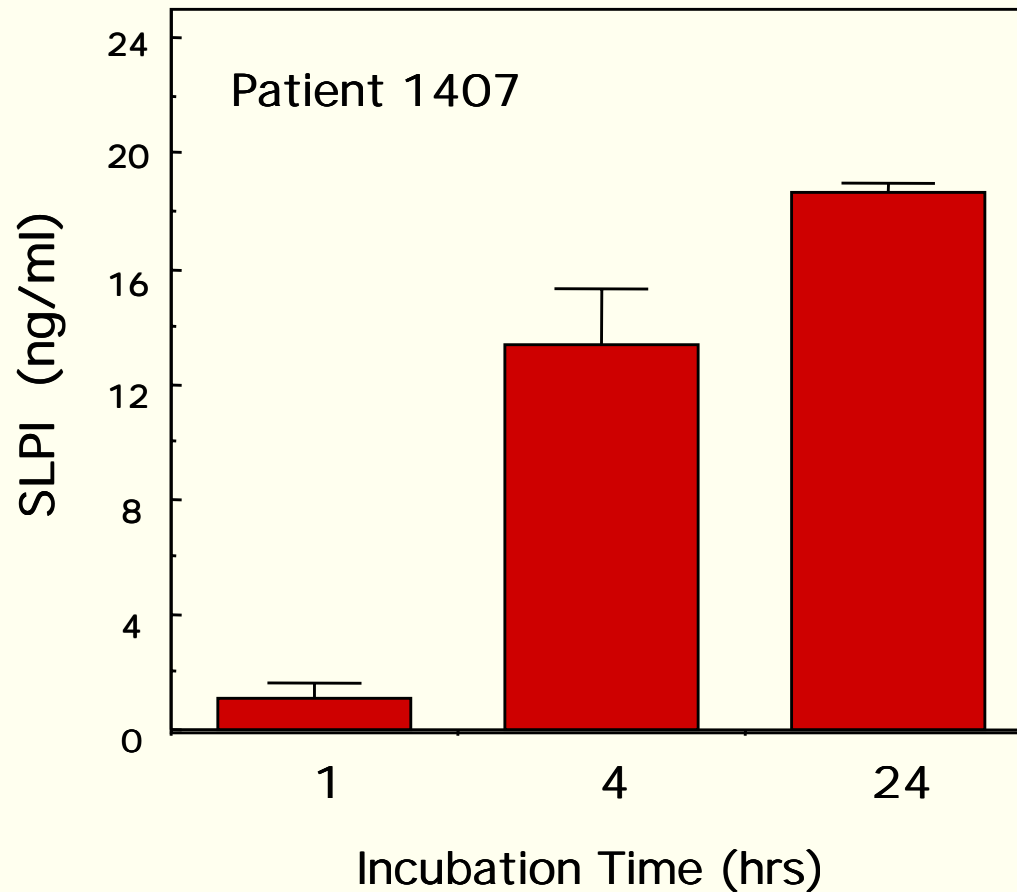
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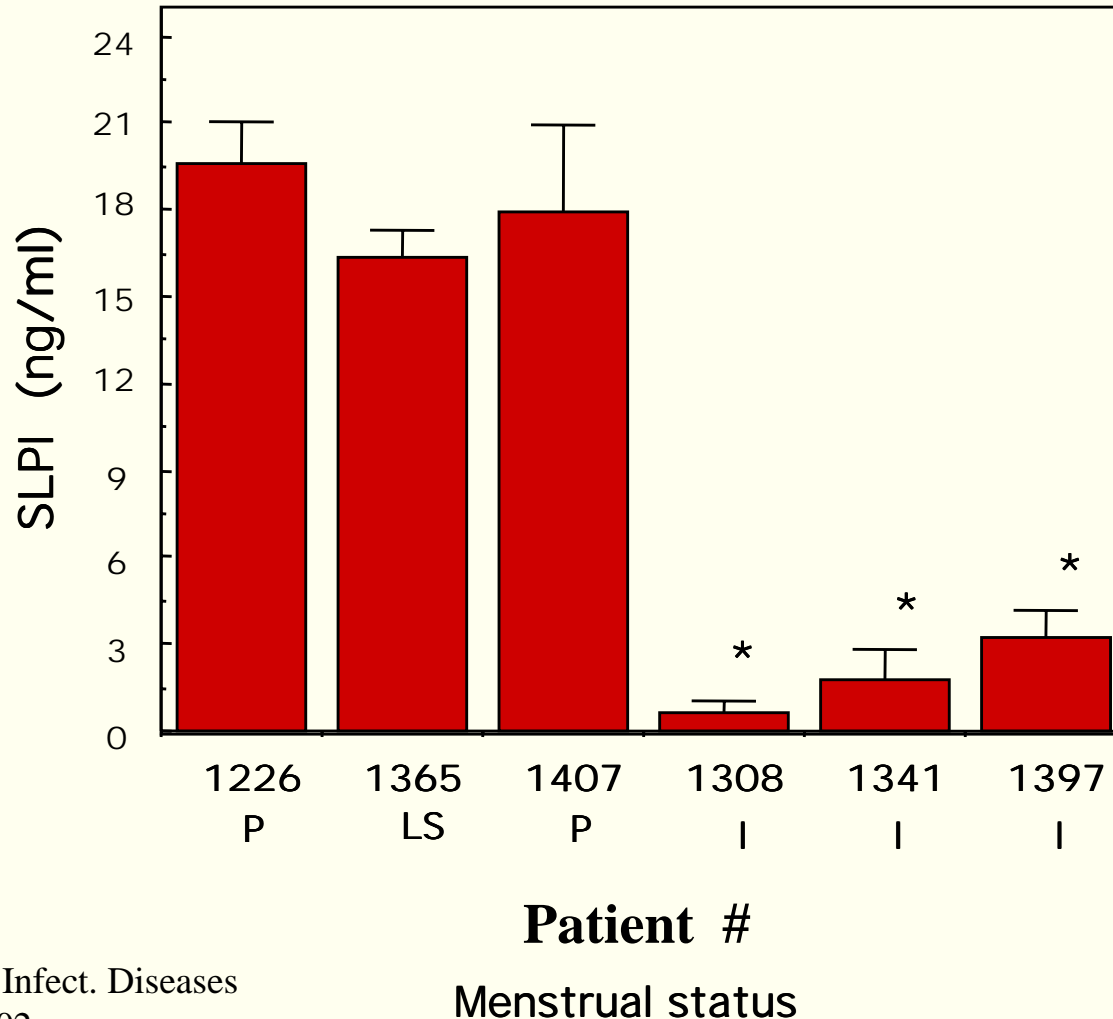
Effect of Menstrual Cycle Stage and Menopause on Anti-bacterial Activity by Human Uterine Epithelial Cells



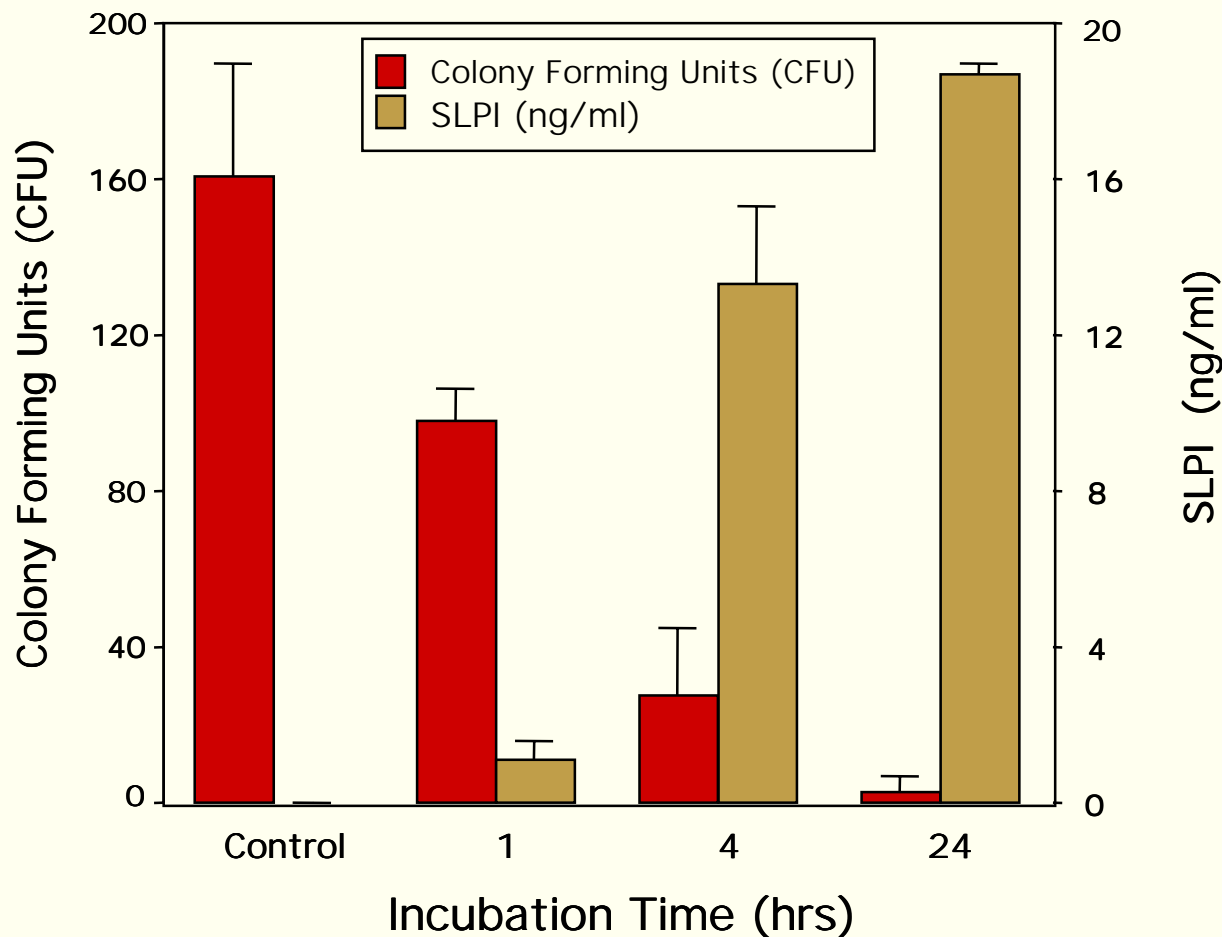
SLPI Concentrations in Apical rinses of Uterine Epithelial Cells



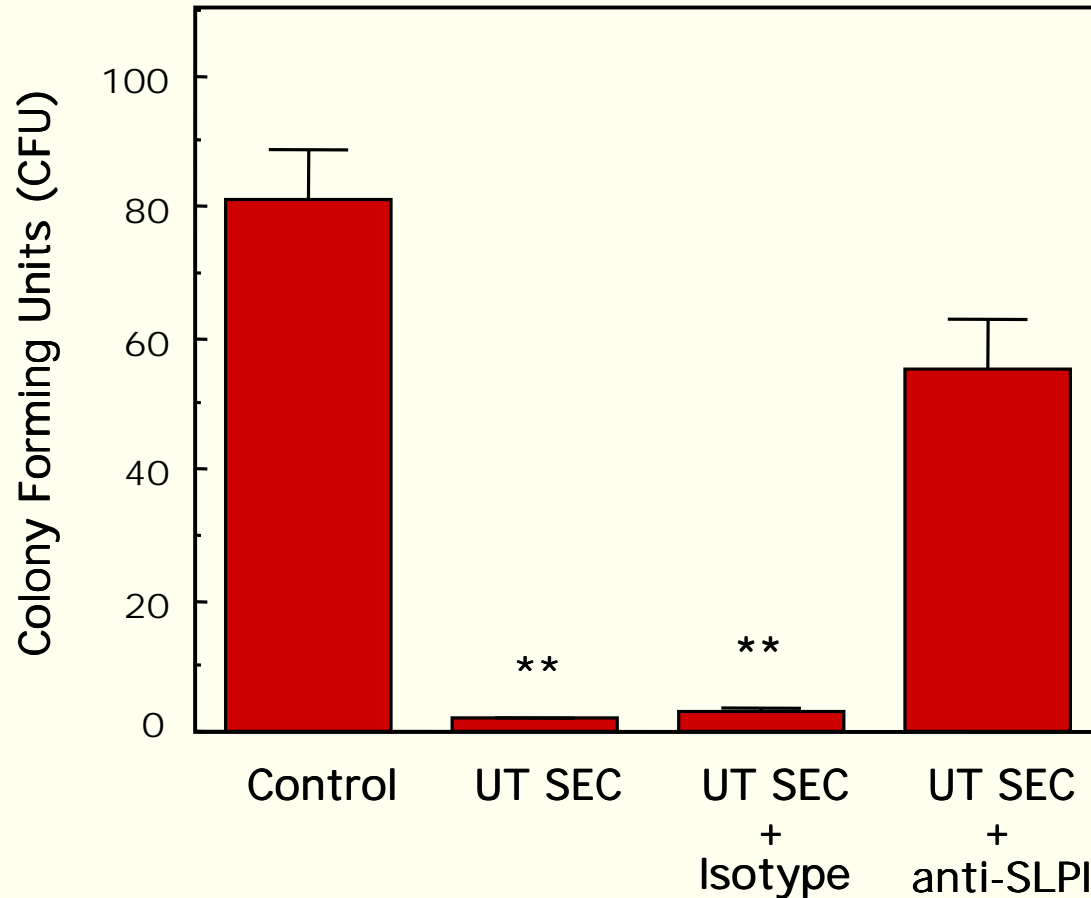
SLPI Concentrations in Water Rinses of Uterine Epithelial Cell Monolayers



Correlation Between Anti-bacterial Activity and SLPI Production by Human Uterine Epithelial Cells in Culture



Neutralization of *S. Aureus* Anti-Bactericidal Activity in Uterine Epithelial Cell Apical Secretions by anti-human SLPI Antibody



Conclusions

- The female reproductive tract (FRT) contains a full spectrum of immune cells.
- Antigen presenting cells in the uterus, cervix and vagina are able to present antigen. Epithelial cells are able to present antigen to autologous T cells.
- Uterine epithelial cells express CD4, CCR5 and CXCR4. Expression of these receptors varies with the stage of the menstrual cycle. These studies suggest that the uterus may be a site of HIV entry.
- Uterine epithelial cells produce SLPI, which appears to be under hormonal control, to protect pre-menopausal women from potential bacterial pathogens.
- Overall, these studies demonstrate that immune cell function in the FRT varies with stage of the menstrual cycle and menopause.

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