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.

2. Localization of HIV receptors and co-receptors in the uterus.

3. 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

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

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Experimental Design: Antigen Presentation, Human Studies

1. Enzymatic digestion of human uteri to obtain epithelial & stromal cells

2. Ficoll & T cell enrichment column

3. Ficoll & T cell enrichment column

- Confirm PBMC presentation of TT
- Check T cell purity
- Determine if EC present TT

$\text{TT}$

$\text{3[H]-thymidine Proliferation}$

$\text{Purified T cells}$

$\text{Epithelial cells}$

$\text{250 \mu m}$

$\text{40 \mu m}$
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

Wallace, P.K., Yeaman, G.R., Kristy Johnson, K., Collins, J.E., Guyre, P.M. and Wira, C.R.
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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 µm).

Fix and mount

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 Unpublished observations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