**Invasion Of Vaginal Epithelial Cells By Uropathogenic Escherichia coli**

**Abstract**

Uropathogenic Escherichia coli (UPEC) is the primary causative agent of urinary tract infections (UTIs) and account for the majority of antibiotic prescriptions. The rise of multidrug resistant UPEC strains limits UTI treatment options, leading to more severe outcomes. In this light, outlining factors that allow for UPEC to reside within human reservoirs that contribute to recurrent UTIs (rUTIs) is of importance. Due to the shorter urethral length and personal distance, UTIs predominately occur in women. Several studies demonstrate vaginal colonization by UPEC precedes UTI, and the vagina is a likely reservoir for recurrent infections. Approximately 30-50% of women, experience recurrent UTIs (rUTIs) which originate from either: 1) the re-emergence of UPEC that invaded the bladder urothelium and form quiescent intracellular reservoirs, thus evading antibiotic treatment or 2) the re-accession of UPEC from the intestinal reservoir across the perineum, vaginal introitus, and to the urethra. Previous studies have demonstrated that prior to UTI, UPEC adheres to vaginal epithelial cells (VECs). However, the full extent to which UPEC interact with epithelial cells, as it transverses the perineal space, remains largely unknown in both human models and women with acute or chronic UTIs. We have begun to assess the full extent to which UPEC colonizes the vaginal epithelium. Here, we show prototypical and clinical UPEC isolates adhere to VECs. Additionally, we find that UPEC invades VECs in an cell line model, acute and chronic murine UTI models. We also show that clinical strains are isolated from women with a history of rUTIs. Our results demonstrate that UPEC invades VECs where it may reside safely from neutrophils, antibiotics, and away from the competition of the host's microbiota. We propose that UPEC invasion of VECs may serve as vaginal intracellular communities (VICs) that reseed the occurrence of rUTI in women.

**Background**

**UPEC invades vaginal epithelial cells during colonization of the reproductive tract in acute and chronic murine UTI models.**

UPEC invades vaginal epithelial cells (VECs) during colonization of the reproductive tract in acute and chronic murine UTI models. In Fig. 3, human vaginal epithelial cells (HVECs) were transuretherally inoculated with a strain of UPEC at the indicated MOI. VECs were immunostained with antibodies to cytokeratin 13 (green) and Lysotracker Red (red). Images were acquired by confocal microscopy. The total number of bacteria within the VEC was determined by gentamicin-based invasion assay with UTI89 at a MOI of 50:1. **Fig. 4** shows the colonization of human vaginas with UPEC from women with a history of rUTIs. In vitro, UTIs were transuretherally inoculated with UTI89 at the indicated MOI. VECs were immunostained with antibodies to cytokeratin 13 (green) and Lysotracker Red (red). Images were acquired by confocal microscopy. The total number of bacteria within the VEC was determined by gentamicin-based invasion assay with UTI89 at a MOI of 50:1. **Fig. 5** shows the colonization of murine vaginas with UPEC from women with a history of rUTIs. In vitro, UTIs were transuretherally inoculated with UTI89 at the indicated MOI. VECs were immunostained with antibodies to cytokeratin 13 (green) and Lysotracker Red (red). Images were acquired by confocal microscopy. The total number of bacteria within the VEC was determined by gentamicin-based invasion assay with UTI89 at a MOI of 50:1.

**Hypothesis**

**UPEC invades vaginal epithelial cells during the course of colonizing the vaginal lumen.**

**Methods**

**Gentamicin-based Protection Assay:**

**Results**

**Conclusions**

1. **UPEC invades vaginal epithelial cells.**

2. **UPEC invades vaginal epithelial cells through a zipper-like mechanism.**

3. **UPEC persists in vaginal epithelial cell cultures with women with rUTIs.**

**References:**