

**Stony Brook University
The Graduate School**

Doctoral Defense Announcement

Abstract

Role of Type II Secretion and Type IV Pilus Systems in
the Virulence of Uropathogenic *Escherichia coli*

By

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Type II secretion systems (T2SS) and the evolutionarily related type IV pili (T4P) are important virulence determinants in many Gram-negative bacterial pathogens. However, the roles of T2SS and T4P in the virulence of extraintestinal pathogenic *Escherichia coli* have not been determined. Extraintestinal pathogenic *E. coli* cause a variety of diseases, including urinary tract infections and neonatal meningitis. We investigated the function of T2SS and T4P in the model uropathogenic *E. coli* (UPEC) strains UTI89 and CFT073, which possess T2SS and T4P gene clusters homologous to clusters present in laboratory strains of *E. coli*. In addition, UTI89 contains a second T2SS gene cluster homologous to one present in enterotoxigenic *E. coli* (ETEC) strains that cause diarrhea. We constructed deletion mutations to disable each T2S and T4P system in the UPEC strains, and compared these mutants with their wild type counterparts using tissue culture assays and the CBA/J mouse model of ascending urinary tract infection. No deficiencies were observed with any of the mutants in adherence, invasion or replication in human bladder or kidney cell lines, but UTI89 Δ *hofQ* (T4P) and UTI89 Δ *gspD* (ETEC-T2SS) exhibited approximately 2-fold defects in fluxing out of bladder epithelial cells. In the mouse infection model, each of the knockout mutants was able to establish successful infections in the bladder and kidneys by day one post-infection. However, UTI89 Δ *hofQ* and a CFT073 Δ *hofQ* Δ *yheF* (K12-T2SS) double mutant both exhibited defects in colonizing the kidneys by day seven post-infection. Furthermore, the plasmid-borne copies of *hofQ* and/or *yheF* were able to complement the kidney colonization defect of the deletion mutants. These results establish T4P and potentially also secreted T2SS effectors as virulence determinants of UPEC important for persistence in the urinary tract, particularly in renal tissues.

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