A Uropathogenic *E. coli* UTI89 model of prostatic inflammation and collagen accumulation for use in studying aberrant collagen production in the prostate

Background: Bacterial infection is one known etiology of prostatic inflammation. Prostatic inflammation is associated with prostatic collagen accumulation and both are linked to progressive lower urinary tract symptoms in men. We characterized a model of prostatic inflammation utilizing transurethral instillations of uropathogenic *E. coli* UTI89 (UPEC UTI89) in C57BL/6J male mice with the goal of determining the optimal instillation conditions, understanding the impact of instillation conditions on urinary physiology, and identifying ideal prostatic lobes and collagen 1a1 (COL1A1) producing prostatic cell types for further analysis.

Methods: Transurethral instillation of 50, 100, 200, or 500µL of green tissue dye to determine fluid distribution (n=3 per volume). Transurethral instillation of sterile PBS, and UPEC UTI89 in sterile PBS with optical density (OD) of 0.2, 0.4, and 0.8 to collect prostate lobes and determine UPEC UTI89 distribution (n=2-5 per OD). Transurethral instillation of 50µL OD 0.35 UPEC UTI89 or 100µL OD 0.7 UPEC UTI89 to compare instillation conditions (n= 8-12 per condition). Sterile PBS instillation of equal volume were used as controls (n=8-12 per group). Spontaneous void spot assay and cystometry were used to assess changes in urinary function. Picrosirius red staining was used to assess collagen accumulation and ProCOL1A1 immunostaining in combination with smooth muscle actin (ACTA2) and protein tyrosine phosphatase, receptor type C (PTPRC also known as CD45) immunostaining was used to determine COL1A1 producing cell types.

Results: A 50 µL instillation volume distributes exclusively to bladder, 100 and 200 µL volumes distribute to bladder and prostate, and a 500 µL volume distributes to bladder, prostate and ureter. A threshold OD of 0.4 UPEC UTI89 in the instillation fluid is necessary for significant ($p < 0.05$) prostate colonization. UPEC UTI89 infection results in a low frequency, high volume spontaneous voiding pattern. This phenotype is due to exposure to UPEC UTI89, not catheterization alone. Prostate inflammation is isolated to the dorsal prostate and is accompanied by increased collagen density. This is partnered with increased density of PTPRC+, ProCOL1A1+ co-positive cells and decreased density of ACTA2+, ProCOL1A1+ co-positive cells.

Conclusions: Overall, we determined that this model is effective in altering urinary phenotype and producing prostatic inflammation and collagen accumulation in mice.