even when the model is adjusted by the Irish risk score. Our data needs to be correlated with a validation cohort to confirm our results.

Source of Funding: none

Infections/Inflammation/Cystic Disease of the Genitourinary Tract: Kidney & Bladder I

Moderated Poster 71

Monday, May 6, 2019 **7:00 AM-9:00 AM**

MP71-01

GENETICALLY DIVERSE UROPATHOGENIC *ESCHERICHIA COLI* ADOPT A COMMON TRANSCRIPTIONAL PROGRAM IN PATIENTS WITH URINARY TRACT INFECTIONS

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INTRODUCTION AND OBJECTIVES: Uropathogenic Escherichia coli (UPEC) is the major causative agent of uncomplicated urinary tract infections (UTIs). UPEC strains carry diverse assortments of virulence factors and a common virulence genotype responsible for urinary tract infection is yet to be defined. We hypothesized that studying patterns of gene expression in patients might identify universal bacterial features that enable uropathogenesis.

METHODS: Using RNA sequencing technology, we examined UPEC gene expression directly in 14 patients presenting with uncomplicated UTI and compared it to the gene expression of identical strains cultured *in vitro* to mid-exponential stage in filter-sterilized human urine.

RESULTS: Here we identify a common transcriptional program shared by genetically diverse UPEC strains isolated from 14 patients with uncomplicated UTIs. Strikingly, the conserved gene expression program in patients is distinct from one observed during *in vitro* urine culture of the identical strains. Moreover, regulatory network analysis reveals that drastic downregulation of key metabolic regulons in all 14 UPEC strains facilitates markedly increased expression of translation and replication machinery.

CONCLUSIONS: Taken together, our study identifies for the first time a common thread underlying UTI and illuminates the molecular underpinnings that likely facilitate the remarkably fast growth rate of UPEC that has been previously observed in infected patients.

Source of Funding: AUA Fellowship, NIH award number R01 DK094777

MP71-02

HYPERMOTILITY OF ESCHERICHIA COLI ISOLATED FROM THE UROTHELIUM OF POSTMENOPAUSAL WOMEN WITH RECURRENT URINARY TRACT INFECTION.

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INTRODUCTION AND OBJECTIVES: Community-acquired urinary tract infections (UTIs) are the most commonly reported infection in adults and have a high rate of recurrence in postmenopausal women (1). In murine models, uropathogenic Escherichia coli (UPEC) invades the bladder urothelium and forms intracellular bacterial reservoirs (IBCs) as a key part of the infection cycle. However, UPEC strains had not been previously isolated from the bladder wall of human RUTI patients (2). The goal of this study was to isolate UPEC strains from bladder wall biopsies of postmenopausal RUTI patients ungergoing cystoscopy with fulguration of trigonitis (CFT) in order to study the virulence factors and adaptations important for effective colonization of the human bladder

METHODS: Following IRB approval, bladder biopsies were obtained from consenting women meeting study criteria for antibiotic-refractory RUTIs who had elected CFT. Biopsies were obtained in the operating room under anesthesia, placed directly in a solution of 100 ug/mL penicillin and gentamicin, and incubated for >2 hours at room temperature to eliminate extracellular bacteria. Tissue was then washed with sterile 1X PBS three times, homogenized, and plated on Chromagar to culture bacteria. UPEC tissue isolates were obtained from two patients. Swim assays in 3% LB agar were performed on two tissue isolates from each patient as well as the lab E. coli strain DH5α as a control. Motility was recorded 24 and 48 hours post-inoculation.

RESULTS: The figure depicts representative swim assay results at 24 and 48 hours post-inoculation for isolates from patients PNK004 (A) and PNK006 (B). All UPEC tissue isolates demonstrated enhanced swimming motility at both 24 and 48 hours post-inoculation compared to the control DH5α E. coli strain.

CONCLUSIONS: Previously, flagella-mediated swimming motility was found to be important for competitive colonization of the murine urinary tract by sepsis isolate CFT073 (3). In this preliminary study, the UPEC tissue isolates from RUTI patients demonstrated enhanced swimming motility compared to DH5α. These findings suggest that flagella-mediated swimming motility may be an important virulence factor for UPEC during human RUTI. Further work is needed to understand the molecular basis of hypermotility in these isolates.

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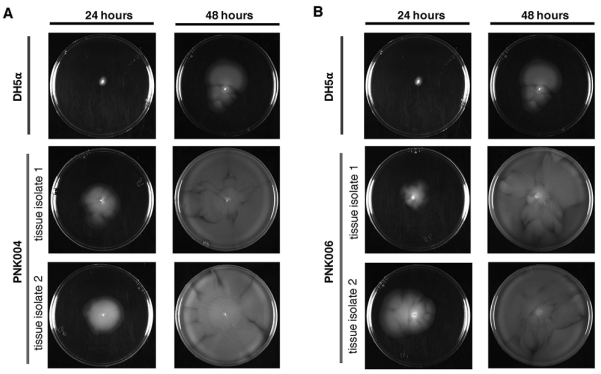

Figure. Agar swim assay results for uropathogenic *E. coli* (UPEC) tissue isolates from cystoscopy with fulguration of trigonitis (CFT) patients PNK004 **(A)** and PNK006 **(B)** are shown. Images were taken at 24 and 48 hours after inoculation at the center of 0.3% agar LB plate with overnight culture. UPEC tissue isolates from CFT patients with recurrent UTI show increased motility when compared to commensal lab strain DH5α.

Source of Funding: None

MP71-03

COMPARISON OF NOVEL DNA-BASED TOOLS FOR BACTERIAL DETECTION IN PATIENTS WITH CHRONIC URINARY TRACT INFECTION (CUTI)

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INTRODUCTION AND OBJECTIVES: The growing rate of culture-negative cases with clinical manifestation of flare-up of cUTI has led to the advent of novel genomic techniques for urinary microbiome identification. The purpose of the study was to evaluate the clinical utility of three of the most frequently used novel techniques compared to traditional urine culture and sensitivity (C&S).

METHODS: A prospective, feasibility, bi-institutional study was performed in 74 patients with cUTI. Urine samples were obtained trough mid-stream catch and shipped to laboratories (lab) for C&S (1st group),

MD lab combining an extended C&S and resistance genes to 12 different antibiotics via polymerase-chain reaction (PCR) (2nd group), Volente Diagnostics (VD) lab (3rd group) and core lab of MicroGenDX (MG) (4th group) using PCR for resistance genes to different antibiotics and Next Generation Sequence (NGS) of entire microbial spectrum. Comparisons were performed for number of pathogens detected in three degrees of concordance such as a complete match (CM), partial match (PM) and mismatch (MM).

RESULTS: Analysis revealed significant difference between the accuracy of C&S versus (vs.) MG. In 19 culture-negative cases the MG detected microbes in 17 patients. In total MG identified a causative bug for UTI in 67 of 69 patients. There was a MM in 34 of 49 patients ($p = .0013$). In contrast, there were 6 cases with PM and 9 with CM. In 16 patients with MM, MG was able to identify bacteria after C&S revealed a low bacterial load. In culture negative cases, VD detected microbes in 5 of cases, but failed to detect bacteria in 4 culture positive cases. There were 39 cases that compared the bacterial detection of VD and MG. MG was able to detect more microorganisms when compared to VD (127 vs. 51; p-value=.000109). There were 5 cases where VD was negative, but MG-positive. From 10 cases comparing C&S and MD in patients MD was able to detect more bacteria compared to C&S. In 18 cases comparing MD with MG, MG was able to detect more bacteria compared to MD (65 vs. 22; p-value = .001055). There were 4 cases where MD cultures were unable to detect bacteria, but MG could. In 14 cases there was no significant difference between the number of bacteria detected between MD and VD.

CONCLUSIONS: Our results indicate that MG provides more accurate data for determining the etiology of cUTI. MG sequencing is superior to C&S, VD and MD in terms of pathogen detection. However, the high sensitivity of MG with detection of few pathogens including commensals should more clearly define the most aggressive one.

Source of Funding: None

MP71-04

PCR BASED URINARY TRACT INFECTION ANALYSIS COMPARED TO TRADITIONAL URINE CULTURE IN IDENTIFYING SIGNIFICANT UROPATHOGENS IN SYMPTOMATIC PATIENTS

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INTRODUCTION AND OBJECTIVES: Urine cultures (UC) have difficulty with polymicrobial infections and fastidious organisms. PCR based molecular testing can rapidly detect and accurately quantify bacterial, viral and fungal organisms. The objective of this study was to evaluate whether PCR is non-inferior to traditional urine culture in detecting organisms, and polymicrobial infections in symptomatic patients.

METHODS: A retrospective review of 582 patients, minimum age of 60, with lower urinary tract symptoms. Traditional UC and PCR molecular urinary tract infection (UTI) testing were run in parallel. Positive UC included one or two organisms and polymicrobial infection was defined as 3 or more organisms. Clinical data were abstracted from the chart.

RESULTS: 582 patients, mean age 77 (60-95), with clinical UTI had UC between March and July 2018. 347 (60%) were male and 235 (40%) female. Clinical symptoms included dysuria (38%), incontinence (33%), urine cloudy / odor (23%) and pain / discomfort (7%). PCR was positive in 56% and culture positive in 37%, Table. Agreement between PCR and UC for positive UC was 90%, exceeding the non-inferiority threshold ($p=0.03$). PCR detected 85 polymicrobial infections compared to 13 on UC. The most common organisms by PCR were Actinobaculum schaalii (n=89, 15%), Viridians group strep (n=89, 15%), and Aerococcus urinae (n=81, 14%), urinary pathogens that were rarely isolated in UC (n=0, 0%; n=14, 2% and n=3, 0.5%). The two most common bacterial organisms on UC in men and women were E Coli and enterococcus but on PCR these two were the 3rd and 6th most common in women and the 2nd and 3rd most common in men. Importantly, PCR also detected more E Coli and enterococcus infections in both men and women than UC. Non-bacterial organisms were detected in 126/582 (21.6%), yeast = 10 (1.7%) and virus = 117 (20.1%) with JC virus (n=92, 15.8%) being the 2nd most common organism identified.

CONCLUSIONS: PCR based UTI analysis is non-inferior in detecting bacterial infections to UC, detecting around 50% additional positive infections, more polymicrobial infections and viral genome in one fifth of cultures. The accuracy of PCR UTI testing over UC may significantly improve patient care.

Patients with Cystitis/UTI (N=582)				
	PCR Positive	PCR Negative	Total	
Culture Positive	196 (33.7%)	21 (3.6%)	217 (37.3%)	
Culture Negative	130 (22.3%)	235 (40.4%)	365 (62.7%)	
Total	326 (56.0%)	256 (44.0%)	582	
	PCR ≥ 3 organisms	PCR 1-2 organisms	PCR Negative	Total
Culture ≥ 3 organisms	6 (1.0%)	5 (0.9%)	2 (0.3%)	13 (2.2%)
Culture 1-2 organisms	46 (7.9%)	139 (23.9%)	19 (3.3%)	204 (35.1%)
Culture Negative	33 (5.7%)	97 (16.7%)	235 (40.4%)	365 (62.7%)
Total	85 (14.6%)	241 (41.5%)	256 (44.0%)	582 (100.0%)

Source of Funding: Pathnostics

MP71-05

PHOSPHORYLATION OF CREB IN DORSAL ROOT GANGLIA AFTER UROPATHOGENIC ESCHERICHIA COLI INFECTION IN RAT URINARY BLADDER

Taesoo Choi, Sung Tae Cho, Koo Han Yoo, Dong-Gi Lee, Gyeong Eun Min, Seung Hyun Jeon, Hyung-Lae Lee, Seoul, Korea, Republic of*

INTRODUCTION AND OBJECTIVES: Bladder stimulation induces up-regulation of neurotrophins which may contribute to voiding reflex. Elevated levels of neurotrophins have been detected in the urine and urothelium of individuals with interstitial cystitis. Phlogogenic bacterial infection involving the bladder can also be a stimulant to activation of its system resulting in pathological state. Phosphorylated responsive element of binding protein (p-CREB) is an important transcriptional factor in the neurotrophin signaling pathway. In vitro studies demonstrated that activation of downstream intracellular signaling molecules, especially transcription factors including CREB are important steps in neurotrophin-signaling cascades. One study reported that p-CREB was up-regulated in afferent neuron of rat DRG (dorsal root ganglia) by chemical induced cystitis. The aim of our study was to examine the change of p-CREB in rat DRG after repeated uropathogenic Escherichia coli (UPEC) infection of rat bladder.

METHODS: The involvement of CREB signaling in acute and chronic E.coli infection was characterized by measuring p-CREB using a specific antibody. Adult female Sprague-Dawley rats weighing 280 ± 20g were prepared in this study. Total 19 rats were induced into acute E.coli infection (n=7) or into chronic E.coli infection (n=6) or control (n=6). After control or E.coli infection, all animals were anesthetized with sodium pentobarbital (50mg/kg, intraperitoneal) and then perfused with 0.05M phosphate-buffered saline (PBS), followed by 4% paraformaldehyde. After perfusion, the spinal cord and DRG were quickly removed and post-fixed for 6 hours. In DRG from control and acute/chronic cystitis rats, p-CREB cell profiles were counted in 6-10 sections of each DRG. For p-CREB immunoreactivity, DRG cells exhibiting intense nuclear staining were considered positively stained. The cell profiles of p-CREB immunoreactivity in each DRG section were presented as mean ± standard deviations (SD) of the mean. All data were assessed using an ANOVA test for comparison among groups.

RESULTS: In all groups, p-CREB immunoreactivity was observed in relatively small-diameter cell profiles with nuclear staining or nuclear & cytoplasmic staining in the DRGs (L1-L6, S1). p-CREB-