CONCLUSIONS: Animals that showed occurrence of UTIs after elimination of afferents to their bladders subsequently exhibited lower levels of urothelial superoxide production compared to healthy controls. Afferent nerve disruption may impair urothelial function through loss of cellular stress response.

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MP23-05

DEVELOPMENT OF NOVEL KNOCK-IN MICE PROVIDES DIRECT EVIDENCE THAT UROPLAKIN IA IS THE UROTHELIAL RECEPTOR FOR TYPE 1-PILIATED UROPATHOGENIC E. COLI (UPEC)

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INTRODUCTION AND OBJECTIVES: The essential first step for type 1-piliated UPEC to cause urinary tract infection (UTI) is for the FimH adhesin of UPEC to bind to the mannose-bearing receptor on the urothelial surface. Although existing data suggest uroplakin Ia (UPIa) as such a receptor, they are based on in vitro experiments. We created knock-in (KI) mice that express UPIa that is devoid of the mannose glycosylation to assess their susceptibility to UTI.

METHODS: Homologous recombination was done in mouse embryonic stem (ES) cells using a KI vector that replaced the single Asparagine-linked glycosylation site (Asn169) of UPIa with a non-glycosylation site (Gln169). The ES cells were used to produce the KI mice. The single-site mutation, abolishment of Asn-linked glycosylation and biological behavior of UPIa mutant protein were assessed by DNA sequencing, Western blotting, FimH overlay and confocal microscopy. KI and wild-type (WT) mice (female; 8-9 weeks) were transurethrally inoculated with UPEC strains UTI89, NU14 and CFT073. Intracellular UPEC and neutrophil infiltration were determined by gentamicin protection assay and myeloperoxidase assay, respectively.

RESULTS: Loss of Asn-linked glycosylation in uroplakin Ia in KI mice did not affect the biosynthesis, dimerization with UPII, apical translocation of UPIa, urothelial and urinary tract morphology. FimH bound to UPIa from WT mice but not to glycosylation-free UPIa from KI mice. When these two groups of mice were challenged with UPEC, marked differences were observed in bladder colonization, dependent on the size of the inocula. With 10^3 and 10^4 CFU, bladder colonization at 24 h post-inoculation was 20-30 fold less in UPIa KI mice than in WT mice. This trend remained with 10^5 CFU of inoculum, although the difference was less pronounced. With 10^6 and 10^7 CFU inocula, UPIa KI mice and WT mice were equally susceptible to bladder colonization. These results were confirmed by enumeration of intracellular bacteria communities and gentamicin protection assay. The lack of bladder colonization by UPEC at low inocula in UPIa KI mice was also consistent with markedly reduced urothelial infiltration by neutrophils.

CONCLUSIONS: Our data provide the first in vivo evidence demonstrating that under physiologic conditions UPIa is the urothelial receptor for type 1-piliated UPEC. They also suggest that with very large inocula UPEC may exploit non-UPIa receptors at deeper urothelial layers that are normally unavailable. Finally, alteration of UPIa glycosylation may affect host susceptibility to UTIs.

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MP23-06

AN UTILIZATION OF NEXT GENERATION SEQUENCING OF URINE SAMPLES FOR MONITORING OF URINARY TRACT INFECTION IN PATIENTS WITH NEUROGENIC BLADDER

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INTRODUCTION AND OBJECTIVES: The treatment of patients with neurogenic bladder (NGB) associated with chronic urinary retention represents a difficult problem due to the frequent exacerbation of chronic urinary tract infection (UTI). Extensive research has proven microbial identification is not achieved by trying to the microbe using traditional culture technique but by extracting its DNA and matching its unique DNA to a data base with DNA sequence codes for 25,000 microbial species. The purpose of this study was to test a next generation sequencing (NGS) as a novel tool to monitor a status of UTI in patients with NGB.

METHODS: The urine NGS results of 13 patients with NGB associated with chronic urinary retention was analyzed in retrospective study to monitor a level of bacteriuria and fungiuria to prevent a flare-up episodes of chronic UTI. The median age of patients was 45 (range: 25-79). The cohort of patient included a NGB secondary to stroke (4), spina bifida (3), dementia (3), spinal cord injury or surgery (2) and cerebral palsy (1). The urine diversion was performed via clean intermittent catheterization (CIC) (6 cases), indwelling Foley catheter (4), suprapubic tube (2) and Mitrofanoff CIC (1). All urine samples were collected from patients and shipped to MicroGen DX, a US based CLIA certified laboratory. Two methods of molecular microbial diagnostic testing were used : a quantitative real-time PCR test for bacterial and fungal genes with specific assay for presence of antimicrobial drug resistance genes and a comprehensive NGS of all genomic DNA present in the patient specimen which aims to catalog all microbial and fungal pathogens present.

RESULTS: All 13 patients had positive NGS results. The median number of organisms present in each specimen was of 3 species, range (1-9). The majority of patients (10) had a high bacterial load ($>10^7$ microorganisms), 1 - had a moderate load (10^6-10^7 microorganisms), 1- had a low load (10^5 or less microorganisms) and 1- did not have bacteria, only association of 5 fungal species. Resistance genes to different antibiotics detected were found in 9/13 samples and in 6 of them had multidrug resistances genes. The dominant microorganism was found as E. Coli (5 cases), Staph aureus, saprophyticus and hominis (3), Enterobacter hormachei (1), Hemophilus parainfluenzae (1), Pseudomonas aeruginosa (1), Klebsiella oxytoca (1). Two patients had fungal pathogens and one of them in association with bacterial pathogens.

CONCLUSIONS: The treatment of NGB remains a challenging and difficult area in urology practice especially defining an optimal preventive or treatment plan for chronic UTI. This new diagnostic tool such as NGS can provide clinicians with complete information on individual genomic profile of microorganisms for regular monitoring of UTI in order to prevent and treat in targeted manner. A significant number of patients had multidrug (including quinolone) resistant E.Coli, that needs to be readjusted moving from empiric to tailored antibacterial therapy.

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MP23-07

CLINICAL PRACTICE GUIDELINE:UNCOMPLICATED BACTERIAL COMMUNITY ACQUIRED URINARY TRACT INFECTION IN ADULTS—EPIDEMIOLOGY, DIAGNOSIS, TREATMENT, AND PREVENTION

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INTRODUCTION AND OBJECTIVES: Uncomplicated, bacterial, outpatient acquired urinary tract infections are among the most common infections in the outpatient area (prevalence 7.32%). The resistance level of these pathogens has increased considerably in recent years. This S3 guideline therefore contains up-to-date evidence for the rational use of antimicrobial substances, to avoid an inappropriate use of certain antibiotic classes and thus development of resistance. For the first time, recommendations on the prophylaxis of recurrent urinary tract infections are included.

METHODS: The guideline update was conducted by the German Society of Urology. A systematic literature search for the diagnosis, therapy and prevention of uncomplicated urinary tract infections was carried out in the databases Cochrane Library, Medline