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## A HOST IMMUNE-CENTRED APPROACH TO UNCOVERING CAUSATION IN CHRONIC UTI

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Urinary tract infections (UTIs) are among the most common bacterial infections. More than half of women will have one UTI in their lifetime, and ~20% will have recurrent infections.1 Understanding UTIs more efficaciously has become a global necessity.2 Recent studies suggest the bladder has a diverse microbiome of mutualists and potential urinary pathogens.3 More recently, researchers have shifted their focus to the host immune system.1 Patients with symptoms of UTI show an increased number of leukocytes in their urine which indicates that the immune system is active and targeting bacteria to prevent or manage disease. Hence, We hypothesised that identifying bacteria being targeted by the immune system could provide insights into the causation of UTIs.

Urine samples were collected from 13 new cUTI patients (attending for first consultation (not-on-treatment)), 16 patients undergoing an extended antibiotic treatment (on-treatment) and 15 healthy controls. Urinary leukocytes were harvested by cell sorting and analysed using 16s rRNA sequencing.

The microbiome-associated leukocyte and epithelial cell, differed greatly between each individual in all groups. These differences indicates that UTI is not simply caused by single 'known' pathogenic bacteria. UTI pathophysiology is more complex, possibly with individual differences in response to microbes, even in the healthy 'normal' microbiome. Understanding these nuances will require longitudinal studies on individuals. We observed the greatest difference in types of bacteria found between the leukocyte and epithelial fractions within the healthy control group. This suggests that, in healthy individuals, the immune system targets pathogens to prevent them from colonising the urinary tract, hence why there is a bigger difference. However, in the not-on-treatment and on-treatment groups, the leukocytes target the pathogens which have colonised the urothelium. Therefore, there is less difference between the fractions in disease. Future studies should concentrate on longitudinal sampling and consider those patients which have successfully completed treatment.

**References:**

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