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Development of a Synthetic Human Urine formulation for the study of UPEC physiology and the development of antibiotics

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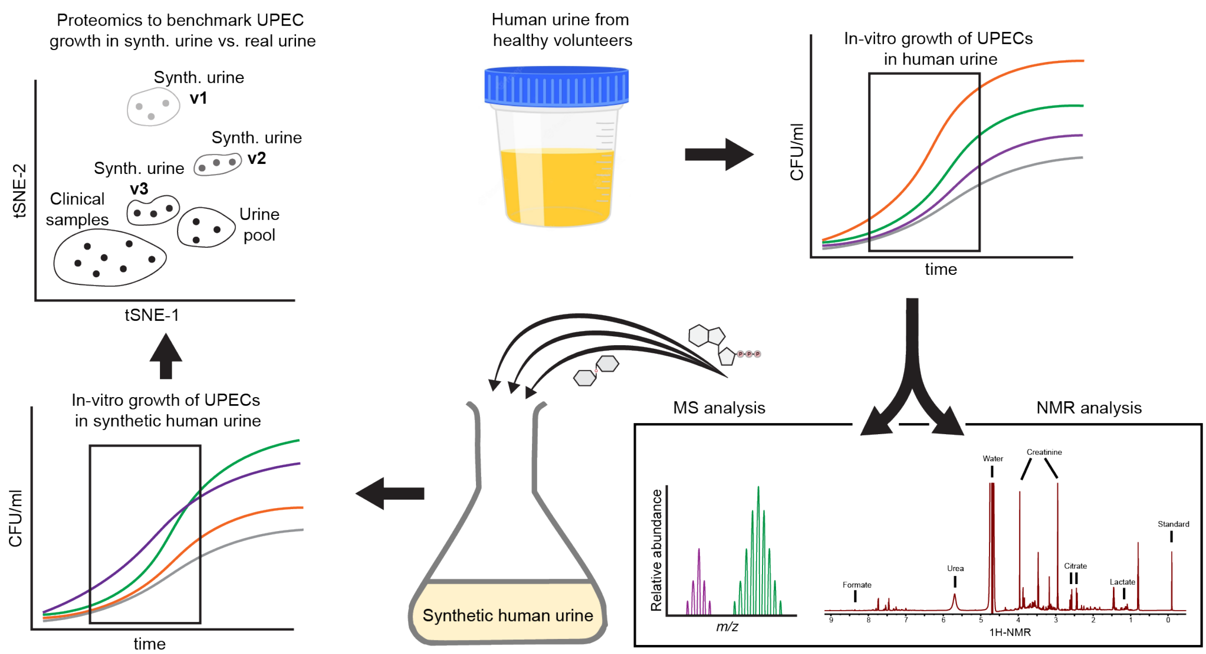
Approximately 150 million people develop a urinary tract infection (UTI) every year and uropathogenic *Escherichia coli* (UPEC) is responsible for more than 75% of these infections. UPEC strains harbor a large variety of virulence factors that contribute to cause the disease and sustain host defenses and antibiotic treatment. Nevertheless, the majority of our knowledge about how antibiotics exhibit their activities is generated from non-pathogenic lab-adapted *E. coli* grown under optimal, nutrient-rich conditions. UPEC strains are metabolically and physiologically adapting to grow in the harsh environment of human urine, which can have dramatic impacts on the susceptibility towards certain antibiotics. Here we aim to create a synthetic human urine formulation in which the metabolic behavior of UPECs is comparable to real human urine.
We apply nuclear magnetic resonance (NMR) and mass spectrometry (MS) to detect the compounds that are consumed by UPECs during growth in human urine and supplement these metabolites to an axenic media with human urine characteristics. These characteristics include, but are not limited to low pH, high osmolality, low carbon availability and the presence of components such as urea, creatinine and uric acid.



We use proteomics to benchmark the cellular program of UPECs during growth in the new synthetic human urine versus growth of UPECs in human urine donated by healthy volunteers. The optimized synthetic human urine will not only be used to better understand the activities of established antibiotics, but it can also be used as a screening medium to directly address the activity of potentially antimicrobial compounds in a standardized human-urine-like environment. Additionally, this artificial human urine composition can be utilized to e.g. examine the processes of bacterial colonization within the urinary tract, study bacterial signaling and signal transduction and provide a convenient in-vitro simulation for investigating the fundamental causes of urinary tract infections in humans.