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Development of a Bladder Organoid Model to study live UPEC infections

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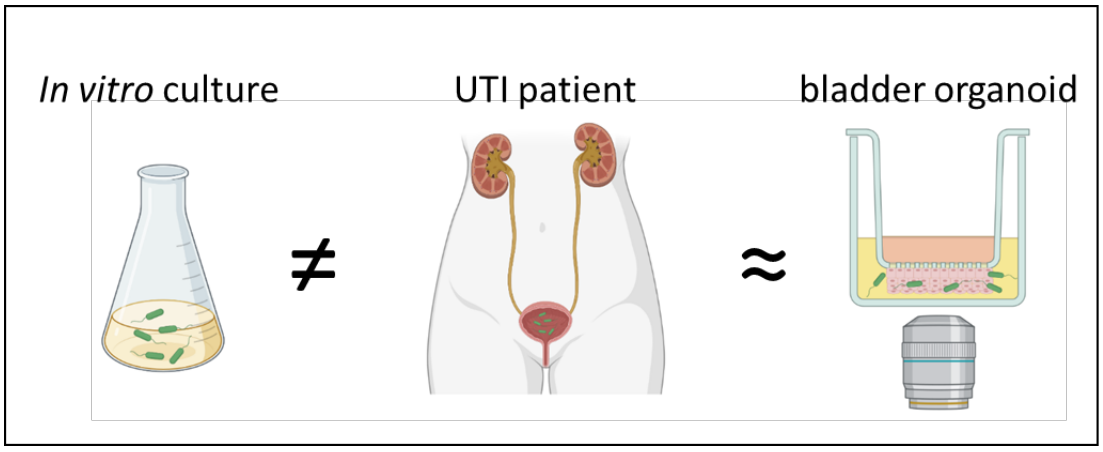
Urinary tract infections (UTIs) are a major cause of hospitalization and morbidity and among the most frequent reason for antibiotic prescription. The primary source of UTIs are **uropathogenic *Escherichia coli* (UPEC)** that are responsible for approximately 80% of UTIs. Besides uncomplicated UTIs which are easily treatable, complicated UTIs account for the majority of general complications during hospitalization and are associated with a high prevalence of **antimicrobial resistance**. Generally, uropathogens ascend from the periurethral area via the urethra to the bladder where they establish an infection. At worst, ascending bacteria can ultimately reach the kidney causing pyelonephritis and increasing the risk of bloodstream infection and sepsis.



To date, nearly all research on bacterial persistence has been done using **conventional *in vitro* cultures** that do not recapitulate the physiology of bacteria in the *in vivo* environment. Furthermore, UPEC have evolved resistance to many antibiotics used to treat UTIs. Consequently, to study antibiotic resilience in UTI and to develop innovative anti-bacterial strategies there is an urgent need for new technologies that enable the **study of UTIs in a patient-like setting**. Therefore, we are developing a 3-dimensional Transwell® bladder organoid model that allows simulation of human bladder infections in a physiological context. In brief, human epithelial bladder cells are grown on Transwell® inserts in inverted orientation until confluence and then differentiated into a stratified tight bladder tissue which shows tolerance towards urine. Furthermore, we developed a microfluidics device which allows us to study UTI at single cell resolution under flow in a live cell setup.