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Poster abstract submission

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Poster title
Hollow Fiber Infection Model (HFIM): Emulating human pharmacokinetics and pharmacodynamics (PK/PD) in vitro

Poster abstract
The worldwide rise in antimicrobial resistance (AMR) limits our antibiotic armamentarium. Infections associated with antibiotic-resistant bacteria, such as Escherichia coli, may lead to difficult-to-manage urinary tract (UTI), bladder, and lung infections resulting in high morbidity and mortality in patients. Therefore, effective treatment options and robust infection models are needed to guide effective antibiotic therapy.

Traditional AMR susceptibility testing methods, such as minimum inhibitory concentration assays and time-kill studies, provide valuable but limited insights, often failing to translate into in vivo pharmacokinetic (PK) and pharmacodynamic (PD) observations. The Hollow-Fiber Infection Model (HFIM) offers a promising alternative that allows to simulate in vitro drug concentration profiles over time, enabling prolonged studies on bacterial response to antibiotics and the emergence of resistance mechanisms under clinically relevant conditions.

Our efforts as part of the NCCR AntiResist Consortium focus on establishing and optimizing an HFIM system tailored for fluid (UTI, bladder, lung) associated bacterial pathogens, focusing on its application in evaluating antibiotic efficacy and resistance emergence in novel axenic media (e.g. synthetic urine). This work provides an overview of current models used for antimicrobial testing, the principles and advantages of HFIM, and its role in benchmarking novel microfluidic platforms offering better thruput and parallelization options.

As part of the initial validation, we successfully reproduced PK/PD profiles of clinically relevant antibiotics, including levofloxacin and ciprofloxacin, within the HFIM system, demonstrating accurate simulation of antibiotic half-lives and concentration peaks. These preliminary data confirm the capacity of our system to model dynamic antibiotic exposures. Ongoing and future work will focus on studying the effect of other antibiotic therapies and emergence of resistance mechanisms. Moreover, the use of HFIM will also allow us to explore bacterial population dynamics (e.g. transcriptomics) and other omics data to optimize and further benchmark and validate novel miniaturized infection models, such as microfluidics-based HFIM

systems.

Research topic PK/PD