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Poster abstract submission

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Poster title
Microdroplet arrays for directed evolution and high-throughput screening of antimicrobial peptides

Poster abstract

Bacterial resistance to common antibiotics has become a worldwide threat, requiring novel compound development. Here, antimicrobial peptides (AMPs) have been identified as promising candidates. Naturally occurring AMPs must be enhanced in their bactericidal capabilities to become clinically viable, either by rational design, computational prediction, or directed evolution. Conventional droplet microfluidics has been established as a platform for directed evolution, as it enables high-throughput and phenotype-genotype linkage via compartmentalization. However, it has the drawback that droplets cannot be accessed easily, and the entire process, including the final AMP screening against bacteria, becomes highly laborious.
The goal of this project is to generate and identify effective AMPs using an open droplet microfluidic system. For this, up to 100’000 accessible nanoliter droplets are created and deposited on a patterned surface, which can be observed via (fluorescence) microscopy, recovered, or subjected to MALDI MS. This platform, so-called microdroplet arrays, initially enables (combinatorial) screening of bulk AMPs and/or small molecule drug libraries.
Furthermore, distributing randomized AMP-encoding DNA libraries to the droplets, followed by on-array cell-free protein synthesis, will enable screening of thousands of individual AMP mutants against bacteria. After each screening, the AMP amino acid sequence in droplets of interest will be elucidated via droplet recovery and DNA sequencing or on-array MALDI-MS/MS, leading to the next directed evolution round. Ultimately, this project aims to develop a more efficient workflow for the directed evolution of AMPs and to identify improved ones to contribute to the fight against globally rising antimicrobial resistance.

Research topic Biological therapeutics