Ultra-High-Throughput Directed Evolution of Antimicrobials using Droplet Microfluidics

Supervisory team:
Main supervisor: Dr Fabrice Gielen (University of Exeter)
Second supervisor: Dr Stineke van Houte (University of Exeter)
Prof Mike Allen (Plymouth Marine Laboratory; PML)

Collaborators: Prof Yves Briers Other (University of Ghent, Belgium)

Host institution: University of Exeter (Streatham)

Project description:

Antimicrobial resistance has evolved into a major healthcare threat which is further exacerbated by the diminished number of antibiotics in development. Alternatives to antibiotics such as phages and phage endolysins (their lytic enzymes) are being actively researched. This PhD project aims at understanding sequence-function relationships for endolysin activity and unravel the rules for successful bacteriolysis, developing novel high-throughput assays for the directed evolution of bacteriophage endolysins, enzymes capable of killing host bacteria from outside.

In this project, we will combine cutting-edge high-throughput screening technologies in microfluidic droplets with protein engineering to create an endolysin evolution platform. Microdroplet technology has already shown enormous potential for enzyme evolution and the exploration of sequence space at high-throughput and low cost. Each droplet, whose volume typically ranges from femto to nanoliter scale represents a single reaction in which individual enzymes are confined. By encapsulating a single gene corresponding to a single enzyme variant, large gene libraries can be screened in a time and resource efficient manner. FG's group is developing label-free technology platforms for the high-throughput analysis of bacteria-phage interactions and this project builds on this high-profile work [1]. During this studentship, you will be developing/furthering skills across many fields from microfluidic fabrication, building and operation of complex optical setups, protein engineering, biophysics, gene expression and microbiology.

In summary, this is an experimental project to develop novel high-throughput functional assays that can identify novel bacteriolytic enzymes. You will be based in the newly-built Living Systems Institute which brings together scientists from different disciplines and host cutting-edge equipment. This PhD studentship will also allow you to take advantage of the expertise available in Physics, Biosciences, the Environment and Sustainability Institute at Exeter and Plymouth Marine Laboratory to shine new light on endolysin evolution.

The supervision team is composed of Dr. Fabrice Gielen (Living Systems Institute, Exeter), Dr. Stineke van Houte (Environment and Sustainability Institute, Penryn) and Prof. Mike Allen (Plymouth Marine Laboratory) who have complementary expertise on the subject. [1] Gielen et al. PNAS (2016).