Harnessing the power of synthetic biology to engineer novel lytic bacteriophages

Supervisory team:
Main supervisor: Dr Tobias Bergmiller (University of Exeter)
Second supervisor: Dr Thomas Gorochowski (University of Bristol)
Dr Ben Temperton (University of Exeter)

Collaborators: Dr Remy Chait (University of Exeter), Dr Vicki Gold (University of Exeter)

Host institution: University of Exeter (Streatham)

Project description:
The ongoing antimicrobial resistance crisis that is going to leave mankind devoid of high-efficacy drugs against bacterial infections has led to a new renaissance of bacteriophage (phage) research. Phages are viruses that predate and kill bacteria. Their narrow-range specificity towards target bacteria, including the critical multi-drug resistant ESKAPE pathogens Acinetobacter baumannii and Klebsiella pneumoniae, makes them much thought-after future therapeutics. Their exceptionally high natural abundance creates a source of new phage variants to tackle emerging bacterial pathogens and phage "building blocks" that can be used to design functionally enhanced synthetic bacteriophages. We are interested in obligatory lytic phages that have very short life cycles, small genomes, and that destroy their bacterial hosts within minutes. They are commonly self-sufficient and self-dependent and likely to be effective across a broad number of hosts. Our aim is to enhance their functionality using synthetic biology tools. Nevertheless, lytic phages are notoriously difficult to work with: genome engineering to construct synthetic phages, and technologies for "rebooting" lytic phages from their in-vitro assembled DNA genomes currently lacks sufficient speed and efficiency. While progress has been made using CRISPR-based genome engineering, phage engineering and rebooting are a serious bottle neck in the endeavour to use phage to tackle the AMR crisis, and more broadly in agriculture and the food industry.

In this interdisciplinary PhD studentship, you will use a range of methods spanning molecular and bacterial genetics, synthetic biology and bioinformatics to devise new phage engineering and rebooting techniques. You will leverage the Exeter-based Citizen Phage Library and create an inventory of modularised phage parts. By using a combination of CRISPR technologies and other DNA "scissors" you will develop new avenues of phage rebooting and breeding, and a suite of novel synthetic bacteriophages that target Gram-negative ESKAPE pathogens. The successful candidate will be supervised by Dr. Tobias Bergmiller (University of Exeter), Dr. Thomas Gorochowski (University of Bristol) and Dr. Ben Temperton (University of Exeter). The supervisory team combines a range of complementary skills such as molecular and synthetic biology, bacterial genetics, bioinformatics and phage biology.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.