Distilling bacteriophage-host webs: methods to characterise and combine phages for agricultural biocontrol

Supervisory team:
Main supervisor: Dr Remy Chait (University of Exeter)
Second supervisor: Dr Cedric Berger (Cardiff University)
Prof Ben Temperton (University of Exeter)

Collaborators: Dr Fabrizio Costa (University of Exeter), Prof Eshwar Mahenthiralingam (Cardiff University), Dr Rebecca Weiser (Cardiff University)

Host institution: University of Exeter (Streatham)

Project description:
A web of interactions between 10^30 bacteria and 10^31 bacterial viruses (phages), by far the most numerous lifeforms on Earth, shapes global chemical cycles and impacts health from individual animals through ecosystems. While phages are a central natural feature of our world (e.g., lysing 20-40% of oceanic bacteria daily and affecting oxygen production and nutrient cycles), interest is growing in their practical use as agricultural biocontrol agents to reduce antibiotic dependence and keep antibiotic-resistant pathogens in check. In this context, phages targeting bacterial pathogens could improve plant and animal health, reduce losses, relieve agricultural selection for antibiotic resistance and curtail transmission of food-borne bacterial pathogens (e.g. E.coli, Listeria, Salmonella) to humans.

Attractively, phages are non-toxic, naturally-derived, surgically targeted to specific hosts, and self-multiplying at the site of infection. However, narrow host ranges and sparse knowledge of phage infection and resistance dynamics present crucial challenges to efficiently isolating and combining phages into cocktails to optimally control target pathogens. The University of Exeter's Citizen Phage Library (CPL) was established to provide safe bacteriophage treatments to clinicians to treat otherwise intractable bacterial infections. Recently, Exeter's Chait and Temperton labs and Institute for Data Science and Artificial Intelligence (IDSAI) embarked on a multidisciplinary effort to improve this pipeline through by richly characterising infections of pathogens by CPL phages, and using these data to prioritise and combine the phages into optimised treatment cocktails. This project will extend this work by focusing on common cattle-borne enteropathogenic Escherichia coli (EPEC) for which monitoring and control is required to prevent infection of humans. The student will refine and automate the new methods to characterise existing CPL phages (and additional isolates) targeting EPEC and related strains, and will predict optimal combination treatments. They will use in-vitro assays (and potentially rodent infection model) in the Berger lab (Cardiff) to resolve the properties of these phage cocktails critical to practical use, (e.g., efficacy, phage induction, emergence of resistance). This work will inform how deeply characterised phage-host interactions can guide optimal phage treatments of important agricultural pathogens.

This project is multidisciplinary. The student will work with the supervisory team and collaborators on all aspects of instrument, assay, and analytic pathway development as well as on the microbiological systems. Prior experience with coding, machine learning, image analysis, and microbiology are welcome. Due to work with agricultural pathogens that can infect humans, immunocompromised individuals should consult the supervisory team prior to application.

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.