PhD Project Advertisement

Project title: In(ph)inity wars: understanding phages-bacteria evolutionary conflict to design new biocontrol strategies.
Project No: FBS2024-042-Mariano-sq

Lead supervisor: Giuseppina Mariano, Microbial Sciences, University of Surrey

Email: g.mariano@surrey.ac.uk
Co-supervisor/s:
Linda Oyama, Queen's University Belfast
Jai Mehat, University of Surrey
Claudio Avignone, University of Surrey

Project description:

Colibacillosis is a widespread disease in farmed poultry caused by avian pathogenic *Escherichia coli* (APEC)(1). This disease is responsible for multi-million economic losses due to the high mortality of broiler chickens, treatment costs, vaccinations, and feed supplements (2). The continuous (mis)use of antibiotics to control colibacillosis has caused many *E. coli* strains to acquire resistance to multiple antibiotics, increasing the costs and difficulty of treating and controlling colibacillosis in the poultry sector(3). With the human population set to reach 10 billion by 2050, the high mortality caused by colibacillosis in poultry represents a major threat to food security and safety. Antibiotic-resistant *E. coli* can additionally infect humans that come in contact with sick animals, and antibiotic-resistance traits can also be quickly transferred between *E. coli* strains, further exacerbating the threat to humans, animals, and associated ecosystems(2).

Whilst many efforts have focused on developing vaccinations against APEC, their scarce efficacy and ability to target diverse types of pathogenic *E. coli* has created an urgent need for alternative measures of control against APEC(3).

Bacteriophages (aka phages) are specialised viruses of bacteria. Phages can specifically infect and kill bacteria, quickly wiping away a microbial population (4). For this reason, phages/phage cocktails are being considered as alternative therapies for antibiotic-resistant infections in humans and farm animals.

However, recent reports highlighted that bacteria, like humans and plants, have different types of immunity systems, globally known as anti-phage systems. Many of these systems carry similarities with our own innate immunity systems (5).

The wide variety of anti-phage systems found in bacteria is currently one of the main obstacles to overcome to be able to use phage cocktails in clinical settings or as a measure of biocontrol in the poultry sector.

With this project, we will explore several aspects of phage-bacteria interaction, including the role of bacterial immunity systems, when using phage cocktails as a control strategy to reduce the burden of APEC colibacillosis infections.

Milestone 1: Identification of phage types with optimum success rate in killing each pathogenic *E. coli* lineage.

Milestone 2: Identification of novel anti-phage systems in avian-associated *E. coli*.

Milestone 3: Design of probiotic strains to improve avian microbiota health during phage-based treatments

(i)The PhD student will collect >30 diverse coliphages from the environment to supplement our existing collection. Phages' ability to kill pathogenic *E. coli* lineages will be tested to establish phages/phage cocktails combinations that are most efficient. The student will develop an *in vitro* gut model under Dr Mehat's supervision to track the dynamics of co-evolution between mixed populations of *E. coli* lineages and phage cocktails. Lineages that show increased resistance to multiple phage combinations will be prioritised in Milestone 2.

(ii) Using established bioinformatic methods from the Mariano lab (6), the PhD student will identify known and novel anti-phage systems encoded within each E. coli lineage. This analysis will allow to pin-point which anti-phage system can better inhibit the phages/phage cocktails used in Milestone 1.

(iii) We will use the data from the previous task to generate combinations of efficient phage cocktails against pathogenic *E. coli* and generate probiotic *E. coli* strains that carry anti-phage systems that confer resistance to these cocktails. The resistant probiotic strain will maintain a healthy microbiota within the avian gut during phage cocktail treatment, preventing the establishment of other pathogens. We will test our phage-probiotic combinations in our in vitro gut model to ensure that probiotic strains are unable to transfer their anti-phage systems to pathogenic lineages over long periods of co-existence. This will ensure prevention of a new health crisis due to quick transfer of resistance traits between bacterial populations.

Our findings will provide an extensive phage collection that can be employed against pathogenic *E. coli* lineages and provide a powerful strategy that combined phage cocktails and engineered probiotic strains to improve health of poultry.

Training opportunities:

The PhD student will learn advanced molecular biology, microbiology, and genetic skills. Furthermore, the student will be trained in using bioinformatic and comparative genomic-based methods in the Mariano lab. Under the supervision of Dr Jai Mehat, they will have the opportunity to develop a new and innovative gut *in vitro* model, which will be fundamental for the project but will also i) open possibilities for external collaborations for the student and ii) provide the student with a unique skill that will render them highly desirable on the academic, industrial and biomedical job market.

The student will be trained in the investigation of microbial population evolutions through the supervision of Dr Mariano, Dr Oyama and discussion with Dr Mariano's collaborators' network(6). The student will frequently liaise with the supervisory team, providing constant opportunities for training, scientific discussion, and intellectual exchange. Additionally, the student will be encouraged and supported to attend training courses offered by the 'Skillfluence hub' and EMBL-EBI according to any gaps in knowledge or specific skills they want to learn.

Student profile:

Applicants for this studentship will be strongly interested in microbial genetics, molecular biology or comparative genomics; have a passion towards microbiology and a commitment towards delivering scientific excellence and developing new methodologies that will improve human health. A background in molecular biology and/or genetics is desirable.

Additionally, a commitment towards unraveling the complex relationship and the mysteries of how bacteria interact with their viruses(bacteriophages) will be essential.

Stipend (Salary):

FoodBioSystems DTP students receive an annual tax free stipend (salary) that is paid in instalments throughout the year. For 2023/24 this is £18,622 and it will increase slightly each year at rate set by UKRI.

Equality Diversity and Inclusion:

The FoodBioSystems DTP is committed to equality, diversity and inclusion (EDI), to building a doctoral researcher(DR) and staff body that reflects the diversity of society, and to encourage applications from under-represented and disadvantaged groups. Our actions to promote diversity and inclusion are detailed on the FoodBioSystems DTP website.

In accordance with UKRI guidelines, our studentships are offered on a part time basis in addition to full time registration. The minimum registration is 50% FT and the studentship end date will be extended to reflect the part-time registration.

References:

1. S. M. Lutful Kabir, Int J Environ Res Public Health. 7, 89–114 (2010).
2. S. E. Rezatofighi, et al., Frontiers in Veterinary Science. 8 (2021)
3. A. R. Elbestawy et al., Journal of King Saud University - Science. 33, 101353 (2021).
4. A. Abd-El Wahab et al., Front Microbiol. 14, 1136638 (2023).
5. D. Mayo-Muñoz, et al., Cell Reports. 42 (2023)
6. E. Macdonald et al., PLOS Genetics. 19, e1010784 (2023).

For up to date information on funding eligibility, studentship rates and part time registration, please visit the FoodBioSystems website.