PhD Project Advertisement

Project title: Comparative and functional genomics to unveil liver fluke sexual development.
Project No: FBS2023-48-Rinaldi-aq

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Project description:

This project aims at shining light into fundamental biological processes of a foodborne parasite, i.e., a parasite that infects the animal or person by being ingested. The infection of sheep and cattle in UK with the parasitic flatworm *Fasciola hepatica* accounts for livestock industry losses of hundreds of millions of British Pounds per year. Worldwide, the chronic liver infection of livestock with this parasite affects an estimated 700 million animals. Furthermore, it is estimated that at least one fourth of the world livestock population are at risk of infection as they graze at areas where the liver fluke is present. Worryingly, the incidence of human fasciolosis (the human infection with *Fasciola* parasites) has significantly been increasing, and it is now recognised as an emerging zoonotic disease by the World Health Organization. Moreover, the presence of resistant parasites to current drug treatment has been confirmed, leading to a critical animal and human health situation that urgently requires novel drugs and eventually effective vaccines against this pathogen.

The infective stage of the parasite is called metacercaria which is ingested by the animal or human and excysted within the intestine. The newly excysted juveniles (NEJs) burrow through the intestinal wall and migrate eroding the liver tissue while developing. Finally, the worms establish themselves within the biliary ducts and become fertile adult worms; each worm can lay up to 20,000 eggs per day. Both the migration of the juvenile worms in the liver and the establishment of adult worms within the biliary ducts produce inflammation, abdominal pain, anaemia and eventually, without proper treatment, death. A better understanding of the fundamental biology of the parasite has now become critical. Questions like how the parasite interacts with the host (either the infected animal or human), how the infection is established, and how the parasite develops within the host and sexually maturates to start producing and laying eggs are extremely important as they will reveal vulnerabilities of the parasite that can be exploited by developing novel approaches to fight the infection.

Currently, we are living very exciting times, as we have access to novel molecular and functional approaches that can be used to address old questions, like the ones discussed above. The genetic information (i.e., the genome) and data on genes that are active or silence across different developmental stages of the parasite are now available. We started to develop tools to explore the function of individual genes or group of genes during the parasite maturation and interaction with the host. We are experiencing what is called the 'post-genomic era' of this and related parasitic worms, for which cutting-edge technologies can be employed to study the parasite. In this project, we propose to employ cutting-edge molecular and 'omic' approaches (large-scale datasets, e.g. all the genes that are active in a single cell of the parasite, and genome editing) to explore fundamental biological processes that are important or even vital for the parasite to infect the host, migrate and develop into sexually and fertile mature worms. By understanding the process of sexual development in particular, we will find targets to design drugs that ultimately will block the life cycle transmission and reduce the tissue damage associated with the infection.

The student will be trained on exciting computational biology approaches that include gathering large-scale 'omics' data from cells isolated from *Fasciola hepatica* juvenile worms. This technology, called single cell 'omics' will allow the student to reveal molecular factors present in individual cells of the parasite. Thereafter, once key genes involved in the parasite sexual development have been identified, the student will perturb their expression and follow the impact of this genetic

manipulation in the whole parasite. The student will answer questions like; is this particular group of genes important for parasite growth?, what happen when I eliminate the expression of a particular *Fasciola hepatica* gene that is known to be critical in related worm species?, do the reproductive organs disappear after affecting the expression of a gene? Answers to old questions with novel technology is extremely exciting, as novel targets for control would be revealed. In parallel, the student will be developing cross-disciplinary experimental and computational research skills that will be essential for his/her future development as a young researcher.

Training opportunities:

The student will master a wide-range of cellular and molecular methodologies in tandem with computational-based analyses. The student will learn how to work with a extremely relevant parasitic worm not only for UK, but worldwide, and not only for livestock, but for humans. The collaboration between QUB and AU is essential for the student to gain experience on a diverse range of tools, from gene expression manipulation, localisation of proteins and transcripts in the parasite tissues to high-throughput analyses of different phenotypic effects in genetically manipulated parasites. The student will gain experience dissociating parasitic worms into individual cells that will be further sorted and sequenced. Hence, a combination of wet-lab-based approaches and large-scale computational analyses makes this project very attractive. Critically, we will adapt the program of work in case the student has restrictions in moving locations. To ensure no student is disadvantaged by mobility restrictions, if moving location is not feasible, we will facilitate a senior postdoc from the second laboratory visiting the base laboratory to provide the necessary onsite training.

Student profile:

We are looking for a student who has obtained (or predicted to obtain) an upper 2nd class degree in a course relevant to the proposal (biochemistry, parasitology, microbiology, zoology, molecular sciences, animal sciences, veterinary sciences) with evidence of considerable laboratory and/or computational experience and with potential at interview. Advanced technical/practical training (for example through internships, work experience, employed work or hobbies) in parasitology, big data analysis (NGS, images, phenotype screening) or programming/coding will be desirable.

Stipend (Salary):

FoodBioSystems DTP students receive an annual tax free stipend (salary) that is paid in instalments throughout the year. For 2022/23 this will be £17,668 and this 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.

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