PhD Project Advertisement

Project title: Understanding fluke evolutionary biology: Finding new ways to sustainably monitor, predict and assess the biological impact of parasite adaptation and regulatory mechanisms

Project No: FBS2024-084-Daramola-sq

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Project description:

Background

Flukes are group of parasitic flatworms that cause disease in livestock animals and humans. These trematodes have complex life cycles, and cause significant economic losses to infected hosts. For example, liver flukes - Fasciola hepatica and Fasciola gigantica - are the cause of fasciolosis, a neglected tropical disease. Infections caused by these parasites can spread to humans and it is estimated that the disease cost the UK cattle industry at least £23 million annually. Unfortunately, there is currently no commercially available vaccine against the disease.

Problem

Triclabendazole, a dewormer is the drug of choice in controlling the parasite, however overreliance on the drug has led to increase in drug resistance worldwide. Fasciola parasites are genetically diverse, can influence host immune systems, and adapt rapidly to ensure parasite survival across all its life stages. To control the parasite, there is need to understand its biology, its adaptation mechanisms in the host and environment, identify new drug targets, and unlock parasite regulatory mechanisms. Up until now, knowledge on fluke regulatory mechanisms has been limited due to various reasons, such as complexity and poor structural and functional annotation of these regions in the liver fluke genome.

Work Plan

Previous efforts have produced the genomic sequence of the parasite, and this dataset has provided insight into structural and functional mechanisms in the parasite. Despite this, less is known about how these liver flukes can rapidly evolve to evade drugs and host immune system. An understanding of gene regulatory mechanisms will enable us to appreciate how the parasite adapts rapidly. In this project the student will undertake a comparative genomic evolutionary analysis of liver fluke and other trematode (such as Fasciolopsis buski – intestine fluke, Calicophoron daubneyi – rumen fluke, Paragonimus westermani – lung fluke, Schistosoma mansoni – blood fluke, etc.) regulatory genes and other known key genes associated with drug resistance. This will enable us to predict promising drug targets to focus on. We will use available sequence data from these trematodes to improve understanding of fluke biology, crucial proteins, and drug resistance mechanisms in the parasite.

In addition to investigate genetic diversity of fluke populations across the UK, the student will generate and assembling high quality parasite genomic sequences from liver fluke. In order to address the poor genomic structural and functional annotation of fluke liver fluke regulatory mechanisms, the student will leverage on new and existing data on various databases (such as Wormbase Parasite) to develop a user-friendly

bioinformatics tool to improve the annotations and to analyse liver fluke gene regulatory mechanisms.

Training opportunities:

This project has a laboratory and bioinformatics component, thus presents a good training opportunity for prospective student. The student will diverse experience in molecular biology, evolutionary biology, parasitology, and other generic research methods. We will provide bioinformatics training depending on students' level of experience; training will include genome assembly and analysis, phylogenetic analysis, programming skills in R and python, and the use of linux computing for omic data analysis. A significant component of the project will involve extensive use of high-performance computing clusters, and an opportunity for some hybrid work while acquiring skills valuable to develop as a researcher upon completion of the doctoral training.

We will also encourage student to develop research writing and communication skills, via conference attendance, research presentations, and supervisory training in academic scientific communication. There will be opportunity for student to work and engage with our diverse research team at Surrey and Belfast via seminar presentations. There will be budget to attend and present at conferences, undertake short courses to improve skills, and an opportunity to visit the co-supervisor laboratory if needed to work together.

Student profile:

This project would be suitable for students with background in a course relevant to the project (parasitology, veterinary sciences, molecular genetics, biological sciences, computational biology) with evidence of laboratory and bioinformatics experience. The project will have a significant big data analysis component and so intermediate coding experience and some 'omic data analysis experience is desirable. Demonstrated experience in working with parasites or other pathogens coupled with data analysis is also desirable. Students interested in parasite biology, evolutionary biology and drug discovery platforms are also encouraged to apply. Additional training will be provided.

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:

https://doi.org/10.1371/journal.ppat.1011081
https://doi.org/10.1186/s13059-015-0632-2

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