PhD Project Advertisement

Project title: Development of a novel platform for targeting animal parasites
Project No: FBS2022-64-Vasudevan-rs
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Project description:

We are seeking a doctoral researcher to carry out PhD research on the development of new anthelminthics to increase the quality of animal welfare n the UK, combining molecular biological, parasitological and bioinformatics techniques.

Infections by intestinal parasites is a global problem that decreases animal health and food production. For example, in the UK, the cost of "wormer" or anthelminthic treatments and the loss of animal productivity for the sheep industry costs £84 million/year. In addition, resistance to most classes of anthelmintics is a growing problem. Therefore, sustainable control of these parasites would involve discovering new classes of anthelmintics. However, identification of drug targets and validation of these drug targets is difficult in parasites because they are difficult to culture due to their need for a host and their complex life cycles.

This project will develop an alternative worm model where we can identify novel classes of drug targets using a mix of data-mining and phenotypic screening of potential candidate proteins. The project will utilize two models: the simple nematode, Caenorhabditis elegans as a "stand-in" for parasitic worms to identify and "pre-screen" nuclear hormone receptor drug targets and a parasitic worm model to test these proteins in related cattle and sheep parasites for their ability to stop proliferation. We will attempt to validate a new class of putative drug candidates - namely the nuclear hormone receptors, which are a large class of proteins in *C.elegans* responsible for reproduction and metabolic regulation. In human, related nuclear hormone receptors are valuable drug targets for diseases such as cancer and metabolic disorders, suggesting that this conserved group of proteins may be good targets for modeling anti-proliferative drugs. Apart from validation of selected nuclear hormone receptors, this project will also give us insight into the functions of these proteins in the worm, where these are largely unknown.

Training opportunities:

This project represents a uniquely diverse training opportunity as the successful applicant will experience and learn various complimentary research techniques including a blend of in-silico analyses and biological experimentation, will use multiple model systems and be exposed to different research environments by joining on this project led by four research groups (Drs Kevei, Vasudevan, Betson and McGuffin) at two locations (University of Reading and University of Surrey). Students will use genetic, molecular, cell biology, bioinformatics and behavioural techniques in their study. The student will be part of a vibrant endocrine, bioinformatics, veterinary network and food science group at the University of Reading and University of Surrey, with an opportunity to get training in teaching pedagogy. Apart from benefiting from a highly

collaborative scheme, the student will also have an opportunity to network with potential overseas collaborators.

The student will undergo practical training in *C. elegans* laboratory techniques such as cultivation, experimental manipulation and genomic engineering in the Kevei laboratory and behavioural scoring and analyses in the Vasudevan laboratory. They will receive training in parasite development assays in the Betson laboratory and in bioinformatics skills in the McGuffin laboratory. In addition, the student will collaborate with the Meade and Johnson laboratories for phylogenetic analyses at UoR .

The student will be enrolled in the mandatory Reading Research Development Programme, which provides a tailored, structured and supported programme of development covering core scientific, some teaching; we will encourage presentation skills through laboratory demonstration. To develop the student's communication skills, they will take part in regular seminar series in the SBS in UoR and in UoS . All supervisors involved in this project are involved in public engagement since we believe that learning to engage beyond academia is an essential skill for graduate students. They will be introduced to the need for removing/decreasing animal numbers from research and will publicize this 3R principle along with science in public engagement activities designed to reach younger students in schools or to the public in events such as Soapbox Science or Pint of Science.

Student profile:

This project is suitable for students with a degree in biology, bioinformatics, animal sciences, parasitology, endocrinology or food science or a closely related science. Students with basic skills in molecular cell biology techniques are eligible; experience in working with *C. elegans* or bioinformatics is an asset but not essential. This proposal is of interest to students who are interested in protein folding, parasite biology or how nuclear hormone receptors modulate reproduction or behaviours that subserve reproduction. Students who like developing tools for pharmacological/toxicology/drug discovery platforms and interacting with industry may also be interested.

References:

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Kevei É, Pokrzywa W, Hoppe T. (2017) Repair or destruction-an intimate liaison between ubiquitin ligases and molecular chaperones in proteostasis. FEBS Lett. 2017 Sep;591(17):2616-2635. doi: 10.1002/1873-3468.12750.

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Funding particulars:

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