PhD Studentship: Engineering genetic systems for control of Anopheles stephensi

Closing date: 27.09.19
Anticipated Start Date: January 2020
Duration: 3.5 years
Project Ref: 2019-21 LA

Eligibility:

- This studentship is open to science graduates (with, or who anticipate obtaining, at least a **2.1 or equivalent, in a relevant biological subject in their undergraduate degree, or a Masters degree - subject to university regulations)**. Other first degrees, e.g. veterinary science, will be considered. You should be looking for a challenging, interdisciplinary research training environment and have an active interest in the control of infectious diseases.
- This is a **fully-funded studentship open to UK, EU and international students.**
- Students without English as a first language must provide evidence that they meet the English language requirement, e.g. with an IELTS score of 7.0 and no less than 6.5 in any of the subsections.

Supervision:

Principal Supervisors: Prof Luke Alphey (The Pirbright Institute), Dr Rob Noad (Royal Veterinary College)
Co-Supervisors: Michelle Anderson (The Pirbright Institute)

Project Details:

A PhD studentship is available to a highly motivated student interested in the genetic control of mosquitoes.

New tools are required for improved malaria control or elimination. The development of CRISPR-based systems has led to a resurgence of interest in "gene drive" methods. Gene drives bias inheritance in their favour and can thereby, in principle, persist and even increase in allele frequency in wild populations despite not conferring an individual fitness benefit. However, simple CRISPR/Cas9-based designs may spread through entire species, which is unlikely to be desirable in all cases. Instead, we seek to develop alternative gene drive designs allowing intervention in one population with minimal impact on nearby non-target populations of the same species. The student will focus on the development of such population-level drive systems in the mosquito *Anopheles stephensi*, an important malaria vector that is also relatively amenable to genetic studies.

The 'daisy drive' concept provides an elegant conceptual method for limiting both spatial spread and temporal persistence of CRISPR/Cas designs. The daisy drive is a multi-component 'split drive' system, in which each element drives ('homes') only in the presence of the previous element in the chain. However, the first element of the chain does not drive, so forming a 'licensing factor' or 'tether' for the whole system, limiting its geographic spread.

Key to homing drives is controlling the 'homing'. It is crucial for many designs that this occurs only where intended, which is premeiotic germline cells, and not elsewhere, e.g. embryos via maternal deposition, somatic cells, etc. Expression elsewhere can have severely negative consequences on fitness, resistance and other aspects of drive performance.

The student will develop methods to control expression of Cas9, building on our prior experience of development of engineered sterile males, which have successfully entered field use. We take a synthetic biology approach, using rational design and standardised, characterised parts and modules to the extent possible, though recognizing also than the degree of characterisation available is less than in some microbial systems. The Pirbright Arthropod Genetics Group has several related gene drive and genetic control projects ongoing, with about 24 research staff; world-leading expertise and resources are available.

References for Background Reading:

- Alphey, L. (2014). "Genetic Control of Mosquitoes." Annual Review of Entomology 59: 205-224
- Noble, C., et al. (2019). "Daisy-chain gene drives for the alteration of local populations." Proceedings of the National Academy of Science (USA) 116: 8275-8282.

Registration, Training and Funding:

This is a Pirbright Institute/RVC fully funded project. The student will be mainly based at The Pirbright Institute and registered with the RVC, with regular visits to the university to undertake research and training as required. Eligible students will receive a minimum annual stipend of £15,009 and a small cost-of living top-up; university registration fees will be paid. A full range of research and transferrable skills training will be made available to the student as appropriate.

Applications:

Details of how to apply can be found here: How to apply

Essential documents:

- Application Form
- CV
- Two references sent directly by your referees

Please email your application to studentship@pirbright.ac.uk by the closing date noted above.