Reference: 08/JA

Project Title: Assessing the drive efficacy of components in a Cas9-dependent gene drive system in *Anopheles stephensi*

Supervisors: Dr Joshua Ang, Dr Michelle Anderson, Prof Luke Alphey
Research group: Arthropod Genetics Group

Project Summary: Our lab is interested in developing Cas9-dependent gene drive systems which could lead to suppression of local mosquito vector populations. One example of such a system is the daisy drive[1] with a cargo which disrupts a recessive female fertility gene[2]. The success of the system, however, depends heavily on the ability to express Cas9 at precise location and time in the germline of a developing mosquito. A previously developed drive in *An. stephensi* has shown high fitness cost and high resistant allele formation, both deleterious to the system, due to unintended expression of Cas9[3].

This project will therefore aim to assess the ability of transgenic mosquitoes generated in the lab to cause inheritance bias of the drive element in the germline and the fitness cost conferred by the process. If more time is available after all the lines are assessed, a cage trial will be set up using the most effective transgenic lines to study drive dynamics in a cage population.

Further Details: Depending on progress, the successful student may undertake the following in the duration of the research project:

- microinjection of mosquito embryos to generate transgenic mosquitoes
- mosquito rearing and cage experimental planning
- screening mosquito larvae for expression of fluorescent markers with the Biosorter
- DNA extraction and polymerase chain reaction (PCR)
- design of primers for PCR, Sanger sequencing, and/or cloning
- data analysis with GraphPad/R

References for Suggested Reading:

1. Noble, C. *et al.* Daisy-chain gene drives for the alteration of local populations. *Proc. Natl. Acad. Sci.* **116**, 8275–8282 (2019).
2. Kyrou, K. *et al.* A CRISPR–Cas9 gene drive targeting doublesex causes complete population suppression in caged Anopheles gambiae mosquitoes. *Nat. Biotechnol.* **36**, 1062–1066 (2018).
3. Gantz, V. M. *et al.* Highly efficient Cas9-mediated gene drive for population modification of the malaria vector mosquito Anopheles stephensi. *Proc. Natl. Acad. Sci. U. S. A.* (2015) doi:10.1073/pnas.1521077112.

To Apply:

Please email your CV (no more than two sides of A4) and a covering letter, detailing why you would like to undertake the placement and the knowledge and skills that you will bring to the Institute, to studentship@pirbright.ac.uk.

Closing date to apply: 09.00, 7th February 2022