Institute: Institute of Environmental Sciences

Topic: Molecular mechanism of *Wolbachia*-conferred antiviral protection

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Background information:
An antiviral bacterium *Wolbachia* protects insects from viruses. Due to its ability to invade populations and block dengue and Zika viruses in mosquitoes *Wolbachia* is currently on field trials to reduce the burden of these viruses in humans worldwide. Despite considerable investment in developing field strategies and in studies on the molecular basis of *Wolbachia* phenotypes, the mechanism of antiviral protection remains unknown. The reason for this is that we currently cannot directly target *Wolbachia* gene function, genetically manipulate *Wolbachia*, or even culture it outside of host cells. This is an unfortunate state of affairs, as understanding and manipulating *Wolbachia* antiviral function is one of the most under-realised and potent tools for the control of vector-borne disease and for the protection of beneficial agricultural insects from pathogens.
Wolbachia-infected insect cell lines are commonly used in studies on the mechanism of *Wolbachia*-conferred antiviral protection, and they could be useful for validation of involvement of *Wolbachia* genes in protective phenotype. However, there is no data showing that the difference in viral titer between *Wolbachia*-infected and *Wolbachia*-free cells has the same molecular basis as protection in whole insects.

The main question to be addressed in the project:

1. Are cell lines a valid model of *Wolbachia*-conferred antiviral protection?
2. What genes are responsible for *Wolbachia*-conferred antiviral protection?
3. What is the mechanism of *Wolbachia*-conferred antiviral protection?

Information on the methods/description of work:
Successful candidate will characterize cell culture models of *Wolbachia*-conferred antiviral protection and alter cell cycle length to assess *Wolbachia* and virus replication rates. They will analyze the transcriptome of infected cells and compare it to the transcriptome of different insect tissues to discern if the molecular mechanisms of pathogen blocking are the same in these systems. Finally, depending on the results of the previous tasks, the student will confirm involvement of different *Wolbachia* genes in antiviral protection either *in vitro* or *in vivo*.

Additional information (e.g Special requirements from the student) **:**
Interest in host-microbe interactions

Place/name of potential foreign collaborator:
Krzysztof Kus, Oxford University

References (max.3**):**
[1] Teixeira, Luís, Alvaro Ferreira, and Michael Ashburner. 'The Bacterial Symbiont Wolbachia Induces Resistance to RNA Viral Infections in Drosophila Melanogaster.' *PLoS Biology* 6, no. 12 (23 December 2008): e1000002. https://doi.org/10.1371/journal.pbio.1000002.
[2] Chrostek, Ewa, Marta S. P. Marialva, Sara S. Esteves, Lucy A. Weinert, Julien Martinez, Francis M. Jiggins, and Luis Teixeira. 'Wolbachia Variants Induce Differential Protection to Viruses in Drosophila Melanogaster: A Phenotypic and Phylogenomic Analysis.' *PLoS Genetics* 9, no. 12 (12 January 2013): e1003896. https://doi.org/10.1371/journal.pgen.1003896.
[3] Chrostek, Ewa, Gregory D.D. Hurst, and Elizabeth A. McGraw. 'Infectious Diseases: Antiviral Wolbachia Limits Dengue in Malaysia'. *Current Biology* 30, no. 1 (January 2020): R30–32. https://doi.org/10.1016/j.cub.2019.11.046.