

Project Details	
Project Code	MRCIAR25Ba Hunt
Title	Environmental and genetic determinants of transmission by a parasitic nematode
Research Theme	Infection, Immunity, Antimicrobial Resistance & Repair
Summary	The parasitic nematode <i>Strongyloides</i> infects >600 million people and is transmitted between hosts through a larval stage in the soil. We know little about <i>Strongyloides</i> transmission including what environmental factors determine transmission success. This project aims to investigate the following questions: (i) under what conditions and for how long can parasites survive outside of the host? (ii) what environmental factors such as temperature and humidity are important for transmission, and (iii) are parasites with specific genotypes better equipped to survive and transmit under adverse conditions? This project will span lab-work, fieldwork and computational analyses.
Description	<p><i>Strongyloides stercoralis</i> is a gastrointestinal parasitic nematode that infects &gt;600 million people globally causing a range of symptoms including intestinal, lung and skin complaints. In some cases e.g. where the patient is treated with immunosuppressants, a hyperinfection can occur which is usually fatal. The aim of this project is to identify and understand the factors that are important for <i>Strongyloides</i> transmission, with the view of identifying potential applications of this information to reduce transmission in regions where <i>Strongyloides</i> is endemic. The specific objectives of this project are to investigate the following questions: (i) under what conditions and for how long can parasites survive outside of the host?, (ii) what environmental factors such as temperature and humidity are important for transmission?, (iii) are parasites with specific genotypes better equipped to survive and transmit under adverse conditions? Although collectively soil-transmitted helminth (STHs) such as <i>Strongyloides</i> have a disease burden greater than that of malaria or HIV/AIDS (WHO estimates the STHs have a disease burden of 5 million DALYs - disability-adjusted life years), we know very little, and in some cases nothing, about (i) the environmental conditions, and (ii) genetic background of parasites, associated with successful transmission between hosts. Better understanding transmission dynamics of these parasites could directly lead to improved strategies to prevent transmission and thus the associated disease they cause.</p> <p>This project will take complementary approaches including working with patients infected with <i>Strongyloides</i>, and using a laboratory model of <i>Strongyloides</i> infection to test hypotheses about transmission. The project is interdisciplinary and encompasses fieldwork, lab-based work (molecular biology/ genetics and in vivo work) and bioinformatics. Depending on the students interests, the project can be weighted differently in these aspects. Three specific aims have been outlined for this project, but the student will have the opportunity to drive the project in a specific direction depending on their interests and the results attained as the project progresses. The balance between aims (1), (2) and (3) can vary depending on the students' interests. For example, if they take more of an interest in lab-based aspects of the projects and developing the in vivo model then they can focus more on lab-work, and</p>

they can spend more time on field-based project if they are interested in working in the field and with human parasite data. There is also opportunity for the student to take this project in a different but relevant direction based on interests that develop during the prep period or results that are attained during the project. Full training will be provided for all aspects of the project.

**Laboratory work:** We will use an established in vivo laboratory model of Strongyloides parasite infection. Faecal samples from laboratory animals will be maintained under different environmental conditions including a range of temperatures, humidity and soil substrates. These will be maintained under diurnal-nocturnal regimes to mimic real world environments. The portion of eggs that develop into infective larvae (the life cycles stage that infects a new host), the success rate of larvae developing to an adult parasite (the life cycle stage that causes disease in the intestine) and survival time of an egg or larval stage outside of the host will be measured under different conditions. This in vivo method will enable hypotheses about environmental conditions e.g. from the fieldwork component of the project or from literature reviews, to be tested under controlled conditions.

**Fieldwork:** The student will have opportunity to work with collaborators in Southeast Asia in regions where Strongyloides parasites are endemic and up to 40% of some populations are infected with Strongyloides. Parasites will be collected directly from stool samples from volunteers (volunteer networks have been established by our collaborators in these regions) and from the soil. Samples will be collected at different seasons and at different locations alongside information on environmental conditions. This work will enable us to identify if there are seasonal variations in transmission rates and improve our understanding of when people are most at risk of infection. Furthermore, from the results of this work we can carry out hypothesis-driven experimental work in the laboratory.

**Bioinformatics:** From both laboratory-based experiments and fieldwork parasite samples will be collected directly from the host and from the external environment. We will sequence the genomes of these parasites and identify genomics features e.g. 'parasitism islands' where regions of the genome are enriched for parasitism-associated genes or SNPs, and carry out genome-wide associated studies (GWAS) to identify genomic and genetic features directly associated with successful transmission. Laboratory experiments, described above, will also identify which conditions are most favourable for transmission and we will use comparative analyses of genomes to identify if particular genetic backgrounds are more successful at infecting a host under adverse conditions.

#### Supervisory Team

##### Lead Supervisor

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