長崎大学
NAGASAKI UNIVERSITY

LONDON
SCHOOL of
HYGIENE
&TROPICAL
MEDICINE

Title of PhD project / theme	**Discovering the genetic drivers of medically important phenotypes in malaria parasites**
Supervisory team	Richard Culleton (NU) Colin Sutherland (LSHTM)
Brief description of project / theme	Malaria parasites exhibit extensive genetic polymorphism between strains. This polymorphism often leads to phenotypic differences between strains of parasites which impact on their pathogenicity to the host. For example, a parasite strain with a fast growth rate may cause more severe disease to the host than strains with slower rates of growth. Identifying the genes that drive such “medically relevant” phenotypes allows the rational design of novel drugs and vaccines to counter malaria. The rodent malaria parasites share significant genotypic and phenotypic homology with the malaria parasites of humans, and have the advantage of being easily studied in both mammalian and insect hosts in the laboratory. We have a large collection of previously uncharacterised subspecies and strains of *Plasmodium yoelii* and *Plasmodium chabaudi*, two of the most commonly used rodent malaria parasite species, that were isolated from thicket rats in Africa in the late 1960s. The main goal of this research project would be the resurrection, cloning and detailed phenotyping of these new strains in both mice and mosquitoes, the identification of medically relevant phenotypic differences between them, and the application of Linkage Group Selection (LGS) to identify the genes that underlie them. LGS involves the production of genetic crosses between strains, and the application of quantitative whole genome sequencing to the cross progeny in the presence and absence of selection to identify genetic drivers (See Abkallo *et al*, Plos Pathogens 13(7): e1006447 2017). Following the identification of interesting genes, orthologues may be identified in the human malaria parasite *Plasmodium falciparum*, and the effects of polymorphisms studied *in vitro* using CRISPR/Cas9 gene editing. The potential scope of this project is large, and the student will have the opportunity to steer the research in the direction of their interest. There will be a large amount of basic biology, genetics and genomics, along with advanced statistical bioinformatics.
Particular *prior* educational requirements for a student undertaking this project	It would be advantageous, although not strictly necessary, for the student to have some experience of working with mice.
Skills we expect a student to develop/acquire whilst pursuing this project	Manipulation and phenotypic characterisation of malaria parasites in vertebrates, invertebrates and in vitro. Genetics, genomics, bioinformatics and molecular biology techniques.