Title of PhD project / theme	**Understanding the mechanisms behind the virulence of zoonotic malaria parasite *Plasmodium knowlesi***
Supervisory team	Primary supervisor: Prof. Kiyoshi Kita, TMGH, Nagasaki Univ (kitak@nagasaki-u.ac.jp) Co supervisor: Assist Prof. Robert Moon, LSHTM (Rob.Moon@lshtm.ac.uk) Co supervisor: Prof. Osamu Kaneko, Institute of Tropical Medicine, Nagasaki Univ (okaneko@nagasaki-u.ac.jp)
Brief description of project / theme	*Plasmodium knowlesi* is a zoonotic malaria causing moderate to severe malaria and sometimes mortality cases in Southeast Asia. Autopsy of a fatal knowlesi malaria case has revealed capillary congestion with infected red blood cells (iRBCs) in multiple organs, suggesting a role of cytoadherence in malaria complications. In the case of *P. falciparum*, cytoadhesion of iRBCs to the endothelial cells of the blood vessels is mediated by a molecule called PfEMP1 encoded by a *var* multigene family. To escape from the host immunity, only one PfEMP1 member is expressed among 60 PfEMP1, which occasionally switch to the other member. The *P. knowlesi* genome lacks PfEMP1 ortholog and instead a molecule called *Plasmodium knowlesi* SICAvar has been proposed to mediate cytoadhesion and is potentially responsible for virulence in knowlesi malaria. PkSICAvar is also encoded by a multigene family and the expression is also epigenetically controlled. However, the mechanisms underlying the switching of SICAvar family genes remain unknown. In addition, each SICAvar likely possesses different receptor specificity, as was shown for PfEMP1, however, this has not been shown. Thus, our prime objective is to identify parasite transcriptional factors that control expression of the SICAvar gene. Understanding of such unique mechanism may lead to a discovery of new druggable targets effective against all human infecting species. We set second objective to identify SICAvar member and its human receptor responsible for the cytoadhesion in human. Deciphering of such parasite-host interaction at molecular level would provide critical insights to understand the pathogenecity and virulence of this zoonotic malaria and form a platform of vaccine develop to reduce disease severity.

The role of LSHTM and NU in this collaborative project	Selected student will stay in Nagasaki most of the time and conduct research under active supervision by Prof. Kaneko. The student will visit London occasionally and conduct some experiments under supervision by Prof. Moon, such as genome editing in *P. knowlesi*.
Particular *prior* educational requirements for a student undertaking this project	Basic knowledge of the molecular biology and skills such as PCR is appreciated. Cell culture experience (aseptic technique) is also appreciated, however this is not an absolute necessity.
Skills we expect a student to develop/acquire whilst pursuing this project	Malaria parasite culture techniques, transfection and genome editing techniques (CRISPR/Cas9), and other advanced molecular biological techniques. Analysis of RNAseq expression data. Ability to critically discuss complex ideas based on a deep understanding of malaria cellular and molecular biology.