Title of PhD project / theme	**Understanding the epigenetic regulation mechanisms of zoonotic malaria parasite *Plasmodium knowlesi***
Supervisory team	**Primary supervisor:** Prof. Kiyoshi Kita, TMGH, Nagasaki Univ. **Co-supervisor:** Assist Prof. Robert Moon, LSHTM **Co-supervisor:** Prof. Osamu Kaneko (Institute of Tropical Medicine, Nagasaki Univ)
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 brain capillary congestion with infected red blood cells (iRBCs), suggesting the possible cerebral 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 each SICAvar is likely to possess different receptor specificity, as was shown for PfEMP1. However, the mechanisms underlying the switching of SICAvar family genes remain unknown. 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. It may also provide a platform to develop a live attenuated vaccine with enhanced antigenicity by suppressing switching mechanism to express all repertories of PkSICAvar on the surface of *P. knowlesi*-iRBCs.
Particular *prior* educational requirements for a student undertaking this project	Basic knowledge of the molecular biology and skills such as PCR and plasmid preparation, and cell culture experience (aseptic technique)
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.