NANYANG TECHNOLOGICAL UNIVERSITY

School of Biological Sciences

Reg. No. 200604393R

Research Theme: **Biochemistry & Cell Signaling Transduction**

Research Project Title: **Erythrocyte signalling during Plasmodium falciparum merozoite invasion**

Principal Investigator/Supervisor: **Prof Peter Preiser**

Co-supervisor/ Collaborator(s) (if any): **NA**

Project Description

Malaria remains a huge global health problem. Every year hundreds of millions of people are infected by the parasite resulting in around 500,000 deaths. Plasmodium falciparum is responsible for the most severe from of the disease. Parasite Invasion of the erythrocyte is a tightly regulated and complex process involving a range of parasite derived receptor binding proteins, an actin-myosin motor, proteases and kinases as well as a range of secondary messenger molecules. To date most of our understanding is based on the processes that occur in the merozoite and little is known about the changes in signaling events that happen in the host erythrocyte.

A range of parasite invasion molecules, termed Reticulocyte Binding Protein Homologues (RHs), have been identified to play an active role in host cell recognition and mediate key signaling events in merozoites during invasion. RH5, one member of RHs, appears to have a unique and distinct function. RH5 binds to basigin, a receptor found on erythrocytes and is the only member that is essential for merozoite invasion. However much less is known about the critical function that is mediated by the RH5-basigin interaction. RH5-basigin on its own is able to trigger a specific Ca2+ signal in the erythrocyte and that this leads to similar changes in the phosphorylation of erythrocyte cytoskeleton proteins as observed during merozoite invasion. How the binding of RH5 to basigin leads to an increase in Ca2+ is not yet understood.

We propose that binding of RH5 leads to a conformational or phosphorylation change at the C-terminal domain of basigin which leads to the activation of cAMP or cGMP. The main focus of this project is therefore to investigate the signaling cascade and critical enzymes in the erythrocyte that is activated by merozoite invasion utilizing RH5. Finally, we aim to develop a genetically tractable cell system for the functional validation of essential erythrocyte signaling molecules. Together, this project will provide new and novel insights on how signaling in the erythrocyte is linked to merozoite invasion and may ultimately provide us with new avenues for therapeutic intervention.

Supervisor contact:

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