Institute of Molecular and Cell Biology

A*STAR

SEMINAR ANNOUNCEMENT

DATE: 15 February 2012, Wednesday

TIME / VENUE: 11:00AM @ Level 3, IMCB Seminar Room 3-46, Proteos Building, Biopolis

SPEAKER: Dr. Gavin Wright

TITLE OF SEMINAR: **A systemic extracellular protein interaction screen identifies Basigin as a PfRh5 receptor that is essential for erythrocyte invasion by *Plasmodium falciparum***

Extracellular protein interactions between *Plasmodium falciparum* merozoite ligands and their host receptors on human erythrocytes play a central role in the invasion process but our understanding of merozoite invasion remains incomplete because many of the receptors for parasite ligands are unknown. Several members of the reticulocyte-binding homology (PfRh) family of parasite ligands have been implicated in invasion, but only *PfRh5* has been shown to be essential for parasite blood stage growth.

To identify a receptor for PfRh5, we compiled a protein library that represented the cell surface receptor repertoire of the human erythrocyte and screened it with a recombinant PfRh5 protein using a systematic protein interaction assay called AVEXIS (for AVidity-based EXtracellular protein Interaction Screen). The AVEXIS assay is designed to specifically detect transient protein interactions (half-lives ≤ 0.1s) that are typical of extracellular receptor-ligand interactions. Using this approach, we identified the Ok blood group antigen, Basigin (CD147) as a receptor for PfRh5. We showed that erythrocyte invasion was potently inhibited in a dose-dependent manner by soluble Basigin and could be completely blocked using low (10 μ g/ml) concentrations of anti-basigin monoclonal antibodies. Importantly, these effects were observed across all 15 laboratory-adapted and field strains tested. We also showed that Ok(a^-) erythrocytes, which express a basigin variant that has a weaker binding affinity for PfRh5 or erythrocytes derived from haematopoietic stem cells in which BASIGIN has been knocked down exhibited reduced invasion efficiencies. The discovery of a critical cross-strain dependency on the basigin-PfRh5 receptor-ligand pair for erythrocyte invasion by *P. falciparum* provides a focus for novel anti-malarial therapies.

Host: Prof. Philip Ingham