CEREBAL MALARIA
Malaria eradication – A key area of concern for health
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An estimated 243 million people worldwide are at risk of developing cerebral malaria (CM) (WHO malaria report 2011).One million people, mostly children die from CM each year. Early diagnosis, prompt treatment and disease eradication are fundamental components of the strategy for controlling CM. However, CM is a complex disease and the most common species, P. *falciparum*, has been difficult to eradicate. There are no vaccines available despite many years of effort, and although anti-malarial drug treatment can prevent CM, the time of administration, dosage and type of drug determines the outcome. Rampant drug resistance to commonly used drugs have greatly undermined efforts to control the disease (4). Development of new drugs is not keeping pace (5).These changes have led to a thrust for developing vaccines specifically targeted against CM.

Primary exposure to Plasmodium parasites very early in childhood carries a lower risk of CM, however, a second and subsequent infection carries high risk. This has led to the hypothesis that, CM is predominantly an immune-mediated disease with immunological priming (first encounter with the pathogen) occurring during primary infection and immuno-pathology occurring upon reinfection. The cellular/molecular mechanisms that cause this life-threatening condition are unclear but parasite load is a critical factor that predicts disease in humans (8). In order to understand how parasitic load impacts on the immune system, it is important we use mouse models. Plasmodium berghei ANKA (PbA)-based mouse model of CM provides distinct advantages for studying immune response to parasite as well as for testing efficacy of vaccines *in vivo*. Detailed studies using this model have shown that antibodies taken from immunised mice can adoptively transfer protection to naïve recipients.

A CM vaccine would be expected to particularly protect those who are at risk of developing complications from P. *falciparum* reinfection. A multi-target blood stage vaccine would be expected to have the greatest impact on CM. A blood stage vaccine must be designed with care, taking into consideration the large body of work that implicates host immunity in the pathogenesis of CM. Therefore an ideal approach would be to use a murine model of CM to test the efficacy of vaccine candidates that are known to offer protection against PbA in vitro.

Towards this we have developed an entirely novel brain-imaging model in our laboratory that has the potential to transform malaria research. This model uses 2-Photon Intravital microscopy (2P-IVM) to ‘peek’ into the living brain and visualize in real-time how immune cells and erythrocytes regulate the immunological and pathological events during CM. In this grant application we present

some of these findings and propose an innovative approach using curcumin-encapsulated glycoliposomes for the immunotherapeutic treatment of CM.