## PL 3

# Recognition of Polymorphic Antigens by. the Immune System: Implications for Malaria Vaccine Design

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*Plasmodium falcipamm* malaria is a major cause of death in the tropics. In individuals living in malaria-endemic regions, protective immunity against infection takes many years to develop. Immune responses to various stages of the parasite life-cycle may contribute to this protection and the slow development of protective immunity may reflect the acquisition of specific immunity to many natural parasite variant antigens. Immunity against severe disease may, however, be acquired already after one or two blood-stage infections, supporting a role for strain-transcending immunity in early protection (Gupta et al., 1999).

Widespread and increasing resistance of malaria parasites to antimalarial drugs, development of resistance of *Anopheles* mosquitoes to commonly used insecticides and inadequate infrastructure for delivery of control measures have contributed to persistence and, in many cases, worsening of the malaria problem. This has stimulated research for the development of a malaria vaccine. A variety of malaria vaccine candidate antigens have been identified primarily by protection studies in animal models and by monoclonal antibodies that have parasite growth inhibitory activity *in vitro* (Good et al., 1998). Since individual antigens may comprise both protective and undesirable antigenic determinants, a subunit malaria vaccine may in the end not consist of entire recombinant proteins but may be built of synthetic compounds that mimic individual epitopes. The highly defined nature of such a vaccine will strongly facilitate the evaluation of immune responses. Along these lines, isothermal titration calorimetry and other biophysical techniques are developing into valuable tools for vaccinology, since they allow to quantitatively analyse interactions between antigens and antigen-binding receptors of the adaptive immune system.

Gupta S, Snow RW, Donnelly CA, Marsh K, Newbold C. Immunity to non-cerebral severe malaria is acquired after one or two infections. Nat Med 1999; 5:340-3

Good MF, Kaslow DC, Miller LH. Pathways and strategies for developing a malaria blood-stage vaccine. Annu Rev Immunol 1998;16:57-87