One of the major limitations in the control of malaria either through vaccine development or use of insecticide-treated bed nets (ITBN) has been the lack of in vitro protection correlates and understanding of what constitutes immunity to malaria. Furthermore, ITBN intervention, as well as the infection with human immunodeficiency virus (HIV) prevalent in most malaria endemic areas, may interfere with the development of protective immunity.

This study was designed to answer some of these questions. IFN-γ was characterized and lymphoproliferative responses to previously defined CD8+ CTL epitopes from 6 pre-erythrocytic stage antigens in 107 children aged 6 months to 2 years from a community based birth cohort in western Kenya were determined. The antigens studied included liver stage antigen (LSA) - 1, LSA-3, thrombospondin related adhesive protein (TRAP), exported protein-1 (EXP-1), circumsporozoite protein (CSP) and Pfs16. The results of this study showed that IFN-γ-positive responders, suggesting that IFN-γ immune responses to these pre-erythrocytic antigens were associated with improved haemoglobin levels (P=0.002). Children who responded by lymphoproliferation had a significantly longer time to first documented malaria parasitaemia after birth (P=0.007).

To assess the effect of ITBN intervention on the immune responses of children less than 5 years old living in a malaria endemic area of western Kenya, 216 children (106 children using ITBN and 110 not using ITBN (controls) were involved in this study. IFN-γ and lymphoproliferative responses to the 6 pre-erythrocytic stage antigens were assessed in a similar way as the first part of this study. There was no relationship between these responses, haemoglobin levels and bed net use. The prevalence and density of *P. falciparum* infection at the time of sample collection was significantly lower in the ITBN users compared to the controls (P=0.027 and P=0.044, respectively).

In determining the nature of the naturally acquired immunity to malaria, immune parameters including HLA-DR, Fas, and cytokine production were compared between immune adults and non-immune children, HIV-infected and non-infected adults; and HIV-infected and non-infected children, to determine the effect of HIV infection on the expression of the immune markers on the memory T cells. It was observed that the un-infected adults had high frequencies of activated memory T cells compared to the un-infected children. Similarly, these un-infected adults had high frequencies of B cells expressing costimulatory molecules CD80, memory T cells expressing CD28 and CD154, memory TG cells and CD3+T cells expressing Fas compared to the children. The cytokine pattern in the adults was a dominant IFN-γ/IL-2 type. HIV infection in the adults induced significantly high activation of the CD3+ and memory T cells compared to the un-infected adults. It also induced significant expression of Fas and CD152 on memory T cells, and CD86 and CD 80 on B cells compared to the un-infected adults. The cytokine profile was IFN-γ with impaired IL-2. In children the effect of HIV infection was greatest, resulting in increased activation and memory T cells, increased expression of CD80 and CD86 on B cells, and Fas expression. Cytokine profile was an enhanced IFN-γ/IL-2/IL-4 type.

These results suggest that the immune adults have a different immune constitution compared with the malaria non-immune children. These patterns are affected by HIV infection, more so in the children. It is therefore critical that the role of these molecules in malaria-specific immunity be determined for the rational development of malaria vaccines.