A-04 : IMMUNOLOGICAL MECHANISMS FOR THE ACQUISITION OF CLINICAL IMMUNITY TO HUMAN *P.vivax* MALARIA

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We have previously demonstrated that prolong exposure to *P.vivax* malaria as which occurs in adult residents of Kataragama, a malaria endemic region in Sri Lanka confers clinical immunity which manifest as a reduced clinical disease during an acute infection in both extent and degree compared to non-immune patients from Colombo. This clinical immunity we have shown to be distinct from anti-parasite immunity which is also acquired with prolong exposure to malaria. These clinically semi-immune adults had lower blood levels of the cytokine tumour necrosis factor (TNF) and other plasma factor(s) which together inactivate gametocytes compared to clinically non-immunes. This led us to propose that clinical immunity to malaria is achieved by sustaining low plasma cytokine levels. We have demonstrated that one mechanism to achieve such a state was by acquisition of antibodies that neutralize parasite exoantigens that induce cells to produce these cytokines.

In the present study, we present evidence for a second mechanism by means of which adult residents of malaria endemic regions sustain low cytokine levels and thus acquire clinical immunity. This is by down regulation of mononuclear cells which produce these cytokines including TNF. Mononuclear cell responses (production of gametocyte inactivating factors) to bacterial lipopolysacharide (LPS) was studied *in vitro* from clinically semi-immune adults in Kataragama and for comparison a clinically non-immune age matched group, both covalescing from an acute *P.vivax* infection. The ability of cells from clinically semi- immune patients to produce these gametocyte inactivating factors was significantly lower than those of clinically non-immunes, suggesting that this is a second mechanism of acquisition of clinical immunity in humans.