Control of Malaria-Induced Inflammation in Children is Dependent on Exposure.

Primary exposure to P. falciparum can result in high levels of parasite-infected red blood cells (iRBCs) that promotes systemic inflammation and induces fever, however, repeated exposure in individuals (including children) residing in malaria endemic areas are often asymptomatic with low levels of iRBCs. The authors of this immunological study, tested the hypothesis that initial febrile malaria modulates the immune response in a way that reduces production of pro-inflammatory cytokines and enhances anti-parasite effector mechanisms when re-exposed to P. falciparum. A systems biology analysis was used to analyse peripheral blood mononuclear cells (PBMCs)sampled from healthy children prior to the six-month malaria season as well as seven days after treatment for a primary febrile malaria infection. In vitro stimulation of PBMCs with iRBC showed that before the malaria season, children’s immune cells produced pro-inflammatory cytokines (IL-1beta, IL-6 and IL-8), whilst, following a malarial infection, lower levels of pro-inflammatory cytokines and higher levels of anti-inflammatory cytokines (IL-10, TGF-beta) was observed. It was also observed that mediators involved in phagocytosis and activation of adaptive immunity were upregulated after malaria but not before. The cytokine profile

shift was also accompanied by an increase in P. falciparum-specific CD4+Foxp3- T cells producing IL-10, IFN-gamma and TNFalpha; and interestingly, P. falciparum–inducible IL-10 production was still partially upregulated in children with persistent asymptomatic infections during the dry-season. The authors conclude that re-exposure to P. faciparum in children leads to changes in immunoregulatory responses that downregulates pro-inflammatory cytokine production while enhancing anti-parasite effector mechanisms. This explains the observation that P. falciparum–infected children in endemic areas are often afebrile and tend to control parasite replication.

Portugal, S. et al. 2014. Exposure-Dependent Control of Malaria-Induced Inflammation in Children. *PLOS*.