hinder these responses. We have recently addressed this hypothesis using a pre-clinical model of severe malaria and found that the same inflammatory pathways mediating disease syndromes impair T follicular helper cell differentiation and the development of germinal centre (GC) responses required for antibody-mediated control of parasitemia. To further define the impact of inflammation in the induction of protective immunity, the development of GC responses to *P. berghei* ANKA was examined in mice deficient in the pro-inflammatory transcription factor T-bet. Genetic deletion of T-bet significantly improved T follicular helper cell differentiation rates, which translated in enhanced GC and parasite-specific antibody responses to infection. Infection of T-bet$^{fl/fl}$CD23^{Cre} mice, with specific deletion of T-bet in their B cell compartment revealed that antibody production and isotype-switching was also regulated by B-cell-intrinsic expression of T-bet. Moreover, the induction of GC B cells and total plasma cell responses to infection were significantly improved in the absence of T-bet expression specifically in B cells. Thus these data suggest that inflammatory pathways elicited in response to clinical malaria negatively impact the development of long-term humoral immunity not only by inhibiting T cell help for antibody formation but also by directly modulating B cell responses to infection.

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REDUCED *PLASMODIUM* BURDEN IN HUMANS ASSOCIATES WITH CD38+ CD4+ T CELLS DISPLAYING CYTOLYTIC POTENTIAL

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Malaria is associated with complex multi-factorial immune responses, and the exact molecular mechanisms required to control parasite burden remain largely unknown. The recent discipline of systems immunology integrates immunology with molecular and computational sciences to enable comprehensive and quantitative evaluation of human immune responses at a level of detail previously restricted to murine models. We are applying systems immunology approaches to characterize the host response to the *Plasmodium spp* parasite in humans. Using a unique resource of samples from a controlled human malaria infection study, we identified a novel population of CD4$^+$ T cells whose frequency in peripheral blood was inversely correlated with parasite burden following *P. falciparum* infection. These CD4$^+$ T cells expressed the multifunctional ectoenzyme CD38 and had unique features distinguishing them from other CD4$^+$ T cells. Specifically, their phenotype was associated with proliferation, activation and cytotoxic potential as well as significantly impaired production of IFN-γ and other cytokines and reduced basal levels of activated STAT1. A CD38$^+$ CD4$^+$ T cell population with similar features was identified in healthy uninfected individuals, at lower frequency. This is the first report of a population of CD4$^+$ T cells with a cytotoxic phenotype and markedly impaired IFN-γ capacity. The expansion of this population following parasite infection and their ubiquitous presence in humans suggests that they may have a broad role in host-pathogen defense.

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HOST IMMUNITY TO MALARIA INFECTION, ANAEMIA AND SOCIO-ECONOMIC IMPACT AMONG CHILDREN LESS THAN 10 YEARS IN NORTHERN CAMEROON

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Malaria and anaemia are key public-health challenges in Cameroon. However, little has been reported on the interaction between these interconnected health determinants. The present study was designed to investigate the relationship between malaria occurrence, immunity, anaemia and socio-economic impact among under - ten children living in an area of intense seasonal malaria transmission in Northern Cameroon. A Cross- sectional survey was conducted in November 2013, in Pitoa and Mayo-Oulo Health Districts, Northern Cameroon. Total, 368 children aged 6months - 10 years were recruited. Finger-prick blood samples collected were used for haematocrit; immunoglobulin gamma level determination using ELISA; malaria parasite prevalence, specie and density by microscopy; *Plasmodium* DNA extraction from filter paper for PCR. A structured questionnaire was used to assess Socio-economic status.Data analysis was by SPSS 20.Overall prevalence of malaria and anaemia were 32.9% and 20.6% respectively. Globally, 46.4% of the children (95% CI: 41.1 - 51.8) were low anti-malarial Total IgG producers, 36.2% (95% CI: 31.2 - 41.5) low IgG1 producers and 19.8% (95% CI: 15.7- 24.3) were low IgG3 producers. There was no statistically significant (p>0.05) association between immunity and malaria status for all the categories of IgG. The Socio-economic status of the population was poor. Malaria was not the cause of anaemia in the children. Therefore, other factors may have accounted for anaemia. Since no effect of malaria and immunity was observed in the low production of IgGs, the IgG levels observed could not be an indicator of any protection against malaria but may be due to humoral response to malaria infection.Malaria programmes should rapidly scale up on improving the health and immunity status of the anaemic in poor communities.Future studies should focus on finding out the causes of anaemia in malaria - infected children.

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PROFILES OF PFEMP1-SPECIFIC IGG ANTIBODIES FROM BIRTH TO 12 MONTHS OF AGE IN BENINESE INFANTS

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The cytoadherence properties of *Plasmodium falciparum* infected erythrocytes (IE) represent a major contributor to the pathogenesis of malaria through interactions with various endothelial cell surface receptors. These interactions are mediated by members of the highly variable *P. falciparum* erythrocyte membrane protein 1 (PfEMP1) expressed on the IE surface. One particular component of PfEMP1 proteins, the cysteine-rich interdomain region (CIDR), is known to play a very important role in the adhesive interactions between IE and endothelial receptors, making this region a potential vaccine target of interest. Here, we investigated the dynamics of maternally-transferred IgG antibodies targeting the CIDR of a panel of different PfEMP1 proteins, as well as infants' own acquisition of antibodies with the same specificities during the first year of life. We used plasma samples collected longitudinally from the offspring of a cohort of pregnant women who had themselves been followed closely through pregnancy. We show that the levels of all anti-CIDR antibodies quantified declined to the point of disappearing over the 6 first months of life. Antibodies with specificity for the CIDR predicted to adhere to selected receptors (CD36, EPCR) or for the CIDR associated with the unknown phenomen were subsequently acquired by infants between 7-12 months of age, their levels being a function of *P. falciparum* history during infancy. Infected infants developed stronger antibody responses to the CIDR associated with either EPCR binding or unknown compared to uninfected infants. The transcriptional profile of var genes showed no obvious difference between parasites infecting the children before and after 6 months except for some genes of group B var.