DYNAMICS OF IMMUNOLOGICAL MEMORY TO *PLASMODIUM FALCIPARUM* INFECTION

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Background

Plasmodium falciparum (*Pf*) malaria remains an important cause of morbidity and mortality in sub-Saharan Africa particularly among children under 5 years of age and pregnant women. In Ghana, malaria alone accounts for about 33% of all deaths in children under 5 years of age. Malaria deaths may be averted if an efficacious vaccine that can offer long term protection against the disease was available. However, such a vaccine is currently non-existent primarily due to lack of understanding of the dynamics of immunological memory in *Pf* infection. Protection offered by the world's leading malaria vaccine candidate, RTS,S/AS01, showed an efficacy decline from 50% to 36% within a 4 year period, suggesting a waning immunological memory to drive an effective secondary immune response. B cells are the primary custodians of immunological memory capable of developing into antibody producing cells (plasma cells) to mount an immune response against invading pathogens. However, the impact of *Pf* infection on their activity remains unclear. It is also yet to be shown if immunological memory to antigens expressed in different stages of *Pf* life cycle are acquired and maintained in a similar manner. In our study, we used a 1 year longitudinal clinical, parasitological, antigen specific antibody and B cell frequency as well as B cell immuno-phenotyping data to elucidate the dynamics of immunological memory in *Plasmodium falciparum* infection.

Methodology

A total of 40 Ghanaian adult male and non-pregnant female volunteers (aged 18 – 49 years old) were enrolled among the staff at Noguchi Memorial Institute for Medical Research, Legon, Ghana after obtaining informed consent. About 20 ml blood was obtained from each participant at quarterly intervals across two malaria transmission seasons (1 year). Plasma IgG levels against candidate malaria vaccine antigens (AMA1, GLURP-R0 and R2, MSP3, CSP and LSA) was measured using the Afro Immuno Assay ELISA protocol. B cell subpopulation immuno-phenotyping was also performed by multi-parameter flow cytometry analysis of cell stained with APC-CD10, PE-CD19, PerCP Cy5.5-CD21 and FITC-CD27 to identify immature, naive, classical memory, atypical memory and activated B cells as well as plasma cells. Malaria antigen specific memory B-cell phenotyping was also performed by ELISPOT and using culture supernatants for ELISA.

Results

Our results showed a significant decline in memory B cell responses against all the P*f* specific antigens and the whole parasite at the schizont stage over the 1-year period and showed significant relationship with seasonality. We also observed significant differences in the levels of B cell subpopulations in relation to P*f* infection across the different transmission seasons. The relationship between malaria specific B cell subpopulations and IgG antibodies against the specific P*f* antigens and the whole parasite was significantly different between the various antigens across the period and against seasonality.

Conclusion

We believe that the results from this study will provide fundamental data on the subtleties of immunological memory to malaria in an endemic population which will inform vaccine design and implementation strategies that will ultimately provide long lasting protection against the disease.