RBC. Rabbit serum antibodies specific for PfEMP1, an immunodominant *P. falciparum* variant antigen at the surface of infected RBC, induced selective lysis of infected RBC by NK cells. Plasma from malaria-immune individuals also triggered selective NK-mediated ADCC of infected RBCs. Granzyme B, a serine protease released by cytotoxic lymphocytes, is a key effector of target cell death. Granzyme B activity was detected in infected RBCs during NK-mediated ADCC using a granzyme B reporter in live cells. Furthermore, the general serine protease inhibitor DCI blocked RBC lysis. These results suggest that granzymes contribute to NK-mediated cytotoxicity towards infected RBCs. Using time-lapse imaging, dynamics of granzyme B delivery into infected RBC and subsequent outcome will be analyzed. Furthermore, NK-mediated ADCC triggered by antibodies from malaria-immune individuals inhibited *Plasmodium falciparum* growth, as determined by the re-invasion of fresh, uninfected RBC. Therefore, primary human NK cells have the potential to limit the growth of blood-stage *P. falciparum* through specific ADCC-mediated lysis of infected RBC.

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TRANSPLACENTAL TRANSFER OF MATERNAL MALARIA-SPECIFIC IGG3 IS ALTERED BY A POLYMORPHISM IN THE BINDING DOMAIN TO FCRN

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Transfer of protective maternal IgG to the fetus occurs by active transport via the Fc Receptor (FcRN) on the syncytiotrophoblast cells of the placenta, contributing to antibody-mediated protection against malaria in early infancy. IgG1 and IgG3 subclasses are the most efficiently transported antibodies. Although IgG1 subclasses dominate the immune response to many pathogens, robust malaria-specific IgG3 often occurs to many malaria proteins and have been strongly correlated with protection against clinical malaria as it is the case for the Merozoite Surface Protein 2. Interestingly IgG3 subclass is the only IgG subclass to contain a single amino acid polymorphism R435H, localized on the Fc fragment of the heavy chain, that affects the *in vitro* IgG3 binding of IgG3 to FcRN *in vitro*. Indeed, the R435 proteoform is associated with a reduced binding). Based on a cohort of mother-newborn pairs from a malaria endemic area of Benin (N=527), where the R435 allele frequency is 80%), we show for several asexual blood stage antigens a reduced efficiency of the transplacental transfer of malaria-specific IgG3 relative to IgG1 to the same blood stage antigen (MSP1, MSP2-3D7, MSP2-FC27, MSP3, Apical Membrane Antigen 1, Glutamate-Rich Protein region R0 and R2). This impaired transport is associated with the R435H polymorphism (p=0.01) after adjustment on for malaria exposure, and *P. falciparum* placental malaria infection. Thus transplacental transfer of malaria-specific IgG3 can be impaired by an individual polymorphism in the binding domain of the Fc fragment to the FcRN and may affect the efficacy by which of newborns acquire sufficient levels of protective antibodies to combat malaria.

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EVALUATING THE ANTIMALARIAL ANTIBODY RESPONSE TO SEVERE *PLASMODIUM FALCIPARUM* MALARIA IN UGANDAN CHILDREN: A CASE-CONTROL STUDY

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Severe malaria remains a leading cause of morbidity and mortality worldwide. The brunt of the disease is borne by children in the sub-Saharan region where *Plasmodium falciparum* is endemic. This sub-population is at a higher risk of developing severe disease because it is only beginning to develop immunity to the disease. Epidemiologic studies have established that individuals in endemic areas acquire immunity through repeated exposure over many years, but this is not fully protective. We conducted a prospective study in Uganda, a malaria endemic area, to evaluate the antibody responses to several well characterized sporozoite and merozoite *P. falciparum* antigens. The study enrolled 711 children and followed them for a year with data collection completed every 6 months. We compared antibody responses in 498 children diagnosed with severe malaria, in the form cerebral malaria or severe anemia due to malaria, to that in 213 healthy controls matched for age and place of residence. Preliminary data indicate that, at enrollment, children with severe malaria had significantly higher antibody levels to CSP, EBA-140, EBA-175, EBA-181, MSP-2, MSP-3 and SERA5 antigens (all $p < 0.0001$) with no diminution of statistical significance following Bonferroni adjustment for multiple comparisons. Data analysis, including evaluation of response to 5 unique PfEMP1 antigens, is ongoing.

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TESTING ANTIGEN INTERFERENCE ON A MULTIPLEX PLATFORM FOR MALARIA VACCINE RESEARCH

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The enzyme-linked immunosorbent assay (ELISA) is a technique, commonly used to measure antibody responses in serum or plasma samples. A traditional limitation of this technique is that, individual testing is required for every antigen against which samples are evaluated. With the introduction of multiplex detection assays, such as the one developed by the Luminex Corporation (Austin, Texas), more than one analyte can now be measured simultaneously. Such assays use fluorescent coded microspheres to which individual antigens or antibodies are covalently linked. The luminescence generated from each microsphere is used to quantify the amount of antigen/antibody present in a given test sample. This technique is currently being used for the multiplex detection of malaria antibodies in serum/plasma samples.The expanded capabilities of multiplex assays bring their own inherent challenges secondary to the potential for unintended protein- protein interactions. Such interactions may alter the measurable antigen concentrations or the antibody binding affinity, leading to antibody interference, higher background signals and decreased assay sensitivity. It is thus crucial to identify any interferences that may occur in assays, in order to provide acceptable ranges for each of the multiplexed antigens in the given test serum.We tested for the interference of different malarial antigens on a Luminex multiplex platform. Recombinant full length CSP, peptides of (NANP)6 antigen and Pf16, three antigens known to impact immunity in malaria, were used. These antigens were tested in various combinations of up to four antigens