relationship between TNF-α -1031T/C variants and severe malarial anemia (SMA; Hb<6.0g/dL) was investigated in children from a *Plasmodium falciparum* holoendemic transmission area of western Kenya. In this study, children (n=503), matched by age and gender, were enrolled at Siaya District Hospital in western Kenya. Complete hematological counts were obtained with a Beckman Coulter Counter, and Giemsa-stained slides were used to determine parasite densities. TNF-α -1031T/C genotypes were determined using a gene-specific polymerase chain reaction assay, followed by allele-specific restriction enzyme digestion using BbsI. Prevalence of TT and TC genotypes was: 90.1% and 9.9%%, respectively, with allele frequencies of T=0.90 and C=0.10, respectively. In a binary logistic regression model controlling for age, gender, bacteremia, HIV-1 and sickle cell status, polymorphic variability at TNF-α -1031T/C was not associated with severe malarial anemia [SMA, Hb<6.0g/dL; OR: 1.50, 95%CI 0.80-2.81, p=0.209]. Additional analysis based on WHO definition of SMA (Hb<5.0g/dL, with any parasite density) did not show any association with SMA (OR: 0.98, 95%CI 0.49-1.98, p=0.963). These results indicate that polymorphic variability at -1031 in the TNF-α promoter does not appear to be associated with malarial anemia severity in children from this holoendemic region of western Kenya.

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MEASUREMENT OF *PLASMODIUM FALCIPARUM* SEQUESTRATION IN HUMAN TISSUE

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The devastating nature of falciparum malaria is attributed to the ability of *Plasmodium falciparum* to cause infected erythrocytes to adhere to vessel walls. Despite the clinical importance of the sequestered parasite population, there is a lack of available tools to i) quantify parasite load in human biopsied or post-mortem tissues, and ii) distinguish circulating from sequestering parasite populations in these tissues. Our aim has therefore been to evaluate and develop methods for the measurement of these two important parameters. We have conducted this work using diverse tissue types derived from patients of an ongoing autopsy study on fatal pediatric malaria in Blantyre, Malawi. Initial quantification involved the current standard for making these assessments: manual counts of parasites per high power field on H&E stained tissue sections. The limitations of this method include the difficulty in accurately identifying and counting parasites and the inability of obtaining a representative picture of a large and heterogenous tissue. We therefore performed immunohistochemistical staining (IHC) for the detection of Plasmodium lactate dehydrogenase (pLDH), as a more specific method of identifying parasites in the tissue sections. In parallel, we performed ELISA assays for the quantification of pLDH in a tissue homogenate, allowing us to assess parasitemia is a larger section of tissue. In addition, we established a quantitative Real Time PCR (qPCR) assay for the assessment of parasitemia based on parasite genome copies in the tissue homogenate. Importantly, we have also used qPCR to examine the distribution of circulating vs. sequestered parasites through a measurement of stage-specific parasite transcripts. Altogether, we have combined protein and nucleic acid based assays to measure parasitemia and distinguish between circulating and sequestering parasite populations in the human body.

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IDENTIFYING THE COMPONENTS OF INTRAERYTHROCYTIC *PLASMODIUM FALCIPARUM* THAT INTERACT WITH GROWTH-PROMOTING LIPIDS

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Malaria remains a devastating disease, particularly in the tropics. New chemotherapeutic approaches are needed from a better understanding of parasite biology and interaction with the host. Crucial and novel targets for malaria chemotherapy can be found from factors that induce growth of *Plasmodium* spp. and parasite factors interacting with growth-promoting agents. We recently reported on a chemically defined medium formulated with recombinant protein and structurally defined lipids for erythrocytic growth of *P. falciparum*. To determine the chemical actions that underlie growth promotion in the parasite, we identified parasite factors that interacted with the growth promoting lipids detected at the molecular level with a fluorescent analogue of the lipids combined with the LC MS/MS technique. 13 parasite components were confirmed to interact with the agent, including a predominately merozoite surface protein (MSP)-1.

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ANEMIA DURING PREGNANCY AND LOW BIRTH WEIGHT IN AN ENDEMIC MALARIA AREA IN BENIN

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Anemia and malaria are highly prevalent in pregnant women in Benin. We studied the relationship between anemia in pregnant women treated for malaria and low birth weight (LBW) in Benin. A retrospective cohort study was conducted based on data from a randomized controlled trial in a semi-rural area in Benin from July 2005 to April 2008 on intermittent preventive treatment of malaria during pregnancy showing equivalence between sulfadoxine-pyrimethamine and mefloquine. Among the 1601 pregnant women recruited in the trial between 16 and 28 weeks of gestation, 1440 observations have been analyzed including HIV non-infected women. The hemoglobin concentration (Hb) was assessed at least once during pregnancy (at enrolment during the second trimester, at least one month later and/or at delivery) and infant's weight collected at birth. Anemia was defined as severe (Hb < 80 g/l), moderate (Hb ≥ 80 and < 100 g/l), mild (Hb ≥ 100 and < 110 g/l) and no anemia (Hb ≥120 g/l). Gestational age was assessed by the Ballard score in 80% of birth and by the best measure available for others. The proportions of women with severe, moderate, mild and no anemia were 4.1%, 28.8%, 31.2% and 35.9% during the second trimester, 4.1%, 30.2%, 29.8 and 36.0% during the third trimester, and 2.5%, 15.7%, 21.5 and 60.4% at delivery, respectively. The prevalence of LBW was 9.1%. Compared with women without anemia during the third trimester, women with severe anemia during the third trimester were at higher risk of LBW after adjustment for malaria, gravidity, BMI at inclusion, infant sex, maternal age, maternal hypertension, intervention group and number of antenatal care visits (OR=3.4; 95%CI [1.4-8.1]). A dose-response relationship was found between Hb in four categories and LBW (p-trend=0.05; p-trend=0.02 in primigravidae). In conclusion, in the context of malaria prophylaxis and iron/folic acid supplementation during pregnancy, the prevalence of anemia was very high in pregnant women and its severity during the third trimester of pregnancy was associated with a higher risk of LBW.