Mal018- **Mutations in *SOD-1* gene are associated with different protein expression and susceptibility to malaria.**

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Introduction: During malaria, intense inflammation results in oxidative stress, and superoxide anions are the main reactive oxygen species produced. Cu/Zn superoxide dismutase (SOD1) is a key enzyme that, in together with catalase and glutathione peroxidase, scavenges superoxide anions and protects cells from oxidative damage. We have previously shown that SOD1 plasma levels are elevated in vivax malaria and that this enzyme can be used as a reliable biomarker for severe disease. Here, we test whether mutations in *SOD1* gene (exon 1) and a Single Nucleotide Polymorphism (SNP) -308 (G>A) in the *TNFalpha* gene are associated with susceptibility to vivax malaria. **Material and Methods:** We studied 124 subjects, including 49 with symptomatic vivax malaria, 43 with asymptomatic vivax malaria and 32 uninfected individuals from the Brazilian Amazon. The first exon of *SOD-1* and *TNF-alpha* -308 (G>A) SNP were amplified by PCR. *SOD1* PCR products were sequenced on an ABI Prism 3100 automated DNA sequencer and *TNF-alpha* SNP were analyzed by NcoI restriction enzyme. SOD1 and TNF-alpha plasma levels were measured by ELISA and Cytometric Bead Array respectively. **Results:** SOD1 and TNF-alpha plasma levels were increased in symptomatic malaria (44.73±31.35ng/mL and 39.07±30.25pg/mL, respectively) when compared with asymptomatic (8.49±5.82ng/mL and 5.88±10.27 pg/mL, respectively) and uninfected individuals (6.99±7.42ng/mL and 6.35±19.97pg/mL, respectively) (P<0.0001 for each comparison). We did not find any association between the *TNF-alpha* -308 (G>A) SNP and susceptibility to malaria (p=0.7446) and the TNF-alpha plasma levels were not significantly different between the subjects homozygous wild-type (GG), mutant homozygous (AA) and heterozygous (GA) (p=0.6892). We found 8 novel SNPs from *SOD1* gene in 6 individuals, 4 with symptomatic malaria and 2 uninfected. The patient with the -5217 (G>T; stop codon) SNP was symptomatic and had the highest SOD1 plasma level when compared with all individuals analyzed (125.9ng/mL). Furthermore, an individual with two SNPs side by side (-5206 A>T, -5207 A>T; Gln>Leu) was symptomatic and had also a high systemic concentration of SOD-1 (95.4ng/mL). In contrast, a patient presenting with three different SNPs (-5207 A>T Gln>His; -5210 T>C Arg>Gli; -5211 C>G Arg>Gli) was also symptomatic but had undetectable levels of SOD1. **Main Conclusions:** This is the first study to describe functional SNPs in the *SOD1* gene among subjects with *vivax malaria*. Our findings argue that single mutations in *SOD1* gene are associated with differences in the plasma levels of this enzyme and may influence the malaria clinical outcome. These results are preliminary and we are currently performing experiments to increase the sample and to screen for polymorphisms in other exons (a total of five) of SOD1. **E-mail:** manoel.barral@gmail.com