PA-014 CXCL10 GENE PROMOTER POLYMORPHISM – 1447A>G IS ASSOCIATED WITH MALARIA IN GHANAIAN CHILDREN

Felix Botchway, Nana Wilson, Carmen M Dickinson-Copeland, Andrew A. Adjei, Michael Wilson, Jonathan K. Stiles. *Korlebu Teaching Hospital, University of Ghana Medical School, Ghana*

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Background Recent studies indicate that interferon gamma inducible chemokine, CXCL10, is a strong predictor of both human and experimental cerebral malaria. We hypothesised malaria infection is associated with variation in CXCL10 expression. We determined whether polymorphisms in the CXCL10 gene promoter region played a role in the clinical status of malaria patients and addressed the genetic basis of CXCL10 expression during malaria infection.

Methods Basic demographics that may impact our assessments including age, gender, full blood count, sickle cell status and CXCL10 polymorphism were assessed. We assessed a single nucleotide polymorphism in the CXCL10 promoter (–1447A>G [rs4508917]) among 382 malaria and 117 non-malaria subjects using PCR-restriction fragment length polymorphism assay. Adjusted Odds Ratio (AOR) was used to find out if there was any association between CXC10 promoter polymorphism –1447 A>G and susceptibility to malaria.

Results The median age for malaria patients was 4 years and that for non-malaria was14 years. There was significant difference with regards to haemoglobin levels and White cell counts between malaria patients and non-malaria subjects ($p<0.0001$). Individuals with the 21447(A/G) genotype were susceptible to malaria (adjusted odds ratio [AOR]=2.60, 95% CI: 1.51–5.85, $p=0.021$). Additionally, individuals with the 21447(A/G) genotype had significantly higher plasma CXCL10 levels than individuals with the 21447(A/A) genotype. Stratifying patients according to gender, the observed association of malaria with over expression of CXCL10 were more pronounced in females than in male patients (AOR=5.47, 95% CI: 1.34–22.29, $p=0.018$).

Conclusions Polymorphisms in the CXCL10 gene promoter sequence were associated with increased CXCL10 production, which is linked to severity of malaria. These results suggest that the 21447A>G polymorphism in CXCL10 gene promoter could be partly responsible for the reported variation underlying severity of malaria outcomes particularly in females.

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