

HUMAN TNF ALPHA AND TNF BETA ALLELES AS HEREDITY COMPONENTS ASSOCIATED WITH THE FEVER OF *PLASMODIUM FALCIPARUM* MALARIA.

Human host genetic factors are thought to play a major role in determining the outcome of malarial disease. It was also evident from a previous study that there was a heritable component to fever responses with *P. falciparum* malarial disease in a Sri Lankan population. Moreover, involvement of TNF genes as fever generating factors in malarial disease have been described elsewhere. In this study, associations between the heritable component of fever and TNF alpha and beta genotypes/ alleles (with respect to alleles 1 and 2 of TNF alpha and beta genes) were investigated in the same Sri Lankan population. 300 individuals who had malaria infections as tested in the previous study, of whom 150 had high and 150 had low genetic value (GV) (estimation of heritability for fever responses among tested individuals) for the fever responses, were subjected to TNF alpha and beta genotyping in this study.

The genotyping was done by PCR and oligonucleotide probing. The results showed that the proportion of carriers of only the TNF alpha 1,2 genotype (compared to TNF alpha 1,1 and TNF alpha 2,2 genotypes) was significantly higher in the high GV group than in the low GV group ($p=0.003$). No such association was however found for any of the TNF beta genotypes (TNF beta 1,1, TNFbeta1,2 and TNF beta 2,2). Further, there was a more significantly higher proportion of carriers of the combination of the TNF alpha1,2 genotype together with TNF beta 2 allele (compared to TNF beta 1 allele) in the high GV category compared to the low GV category ($p=0.001$) (compared to all other genotype/allele combinations tested). These results suggest the involvements of specific TNF alpha and beta genotypes/alleles operating as heritable components in fever responses in *P. falciparum* malaria.