

Haplotypes of IL-10 promoter variants are associated with susceptibility to severe malarial anemia and functional changes in IL-10 production.

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Source

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Abstract

Plasmodium falciparum malaria is one of the leading global causes of morbidity and mortality with African children bearing the highest disease burden. Among the various severe disease sequelae common to *falciparum* malaria, severe malarial anemia (SMA) in pediatric populations accounts for the greatest degree of mortality. Although the patho-physiological basis of SMA remains unclear, dysregulation in inflammatory mediators, such as interleukin (IL)-10, appear to play an important role in determining disease outcomes. Since polymorphic variability in innate immune response genes conditions susceptibility to malaria, the relationship between common IL-10 promoter variants (-1,082A/G, -819T/C, and -592A/C), SMA (Hb < 6.0 g/dL), and circulating inflammatory mediator levels (i.e., IL-10, TNF-alpha, IL-6 and IL-12) were investigated in parasitemic Kenyan children (n = 375) in a holoendemic *P. falciparum* transmission area. Multivariate logistic regression analyses demonstrated that the -1,082G/-819C/-592C (GCC) haplotype was associated with protection against SMA (OR; 0.68, 95% CI, 0.43-1.05; P = 0.044) and increased IL-10 production (P = 0.029). Although none of the other haplotypes were significantly associated with susceptibility to SMA, individuals with the -1,082A/-819T/-592A (ATA) haplotype had an increased risk of SMA and reduced circulating IL-10 levels (P = 0.042). Additional results revealed that the IL-10:TNF-alpha ratio was higher in the GCC group (P = 0.024) and lower in individuals with the ATA haplotype (P = 0.034), while the IL-10:IL-12 ratio was higher in ATA haplotype (P = 0.006). Results presented here demonstrate that common IL-10 promoter haplotypes condition susceptibility to SMA and functional changes in circulating IL-10, TNF-alpha, and IL-12 levels in children with *falciparum* malaria.