Polymorphic variability in the interleukin (IL)-1beta promoter conditions susceptibility to severe malarial anemia and functional changes in IL-1beta production.

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Abstract

Interleukin (IL)-1beta is a cytokine released as part of the innate immune response to Plasmodium falciparum. Because the role played by IL-1beta polymorphic variability in conditioning the immunopathogenesis of severe malarial anemia (SMA) remains undefined, relationships between IL-1beta promoter variants (-31C/T and -511A/G), SMA (hemoglobin [Hb] level <6.0 g/dL), and circulating IL-1beta levels were investigated in children with parasitemia (n= 566) from western Kenya. The IL-1beta promoter haplotype -31C/-511A (CA) was associated with increased risk of SMA (Hb level <6.0 g/dL; odds ratio [OR], 1.98 [95% confidence interval {CI}, 1.55-2.27; P < .05) and reduced circulating IL-1beta levels (p <.05). The TA (-31T/-511A) haplotype was nonsignificantly associated with protection against SMA (OR, 0.52 [95% CI 0.18-1.16]; p =.11) and elevated IL-1beta production ( p<.05). Compared with the non-SMA group, children with SMA had significantly lower IL-1beta levels and nonsignificant elevations in both IL-1 receptor antagonist (IL-1Ra) and the ratio of IL-1Ra to IL-1beta. The results presented demonstrate that variation in IL-1beta promoter conditions susceptibility to SMA and functional changes in circulating IL-1beta levels.