

Suppression of a novel hematopoietic mediator in children with severe malarial anemia.

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Source

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Abstract

In areas of holoendemic *Plasmodium falciparum* transmission, severe malarial anemia (SMA) is a leading cause of pediatric morbidity and mortality. Although many soluble mediators regulate erythropoiesis, it is unclear how these factors contribute to development of SMA. Investigation of novel genes dysregulated in response to malarial pigment (hemozoin [PfHz]) revealed that stem cell growth factor (SCGF; also called C-type lectin domain family member 11A [CLEC11A]), a hematopoietic growth factor important for development of erythroid and myeloid progenitors, was one of the most differentially expressed genes. Additional experiments with cultured peripheral blood mononuclear cells (PBMCs) demonstrated that PfHz decreased SCGF/CLEC11A transcriptional expression in a time-dependent manner. Circulating SCGF levels were then determined for Kenyan children (n = 90; aged 3 to 36 months) presenting at a rural hospital with various severities of malarial anemia. SCGF levels in circulation (P = 0.001) and in cultured PBMCs (P = 0.004) were suppressed in children with SMA. Circulating SCGF also correlated positively with hemoglobin levels (r = 0.241; P = 0.022) and the reticulocyte production index (RPI) (r = 0.280; P = 0.029). In addition, SCGF was decreased in children with reduced erythropoiesis (RPI of <2) (P < 0.001) and in children with elevated levels of naturally acquired monocytic PfHz (P = 0.019). Thus, phagocytosis of PfHz promotes a decrease in SCGF gene products, which may contribute to reduced erythropoiesis in children with SMA.