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Malaria risk reduced by genetic predisposition for cell suicide

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A human genetic variant associated with an almost 30 percent reduced risk of developing severe malaria has been identified. Scientists from the Bernhard Nocht Institute for Tropical Medicine (BNITM), Hamburg, and Kumasi University, Ghana, reveal that a variant at the FAS locus can prevent an excessive and potentially hazardous immune response in infected children. The study appears in the open-access journal *PLoS Genetics* on May 19.

Severe malaria is a major public health burden in Sub-Saharan Africa, where approximately one million individuals die each year as a result of infection with Plasmodium falciparum. Whereas adults in endemic areas develop some resistance to malaria, preventing severe complications, children under the age of five years can develop life-threatening forms of the disease. To date, the molecular mechanisms causing these manifestations are poorly understood.

FAS encodes for CD95, a molecule critically involved in the programmed death of some white blood cells. This candidate gene study, including more than 6,000 child subjects, details how a single nucleotide variant of FAS predisposes its carriers to a higher number of immune cells prone to suicide. These findings indicate that a genetic predisposition to an increased expression of CD95 may help to protect from severe malaria, possibly by rendering a type of white blood cell more susceptible to programmed cell death.

Kathrin Schuldt, co-author, said, "We believe that our study will help to

unravel the mechanisms causing the fatal forms of malaria."

More information: Schuldt K, Kretz CC, Timmann C, Sievertsen J, Ehmen C, et al. (2011) A 2436C.A Polymorphism in the Human FAS Gene Promoter Associated with Severe Childhood Malaria. PLoS Genet 7(5): e1002066. doi:10.1371/journal.pgen.1002066