Polymorphisms in the genes of interleukin 12 and its receptors in association with protection against severe malarial anemia in children residing in western Kenya

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Background

Of the more than 1 million Africans who die from *Plasmodium* infection each year, most are children under five years of age. The majority of these deaths are from severe malarial anemia. P*lasmodium falciparum* has been shown to drive selection of human genetic variants for conferring protection against severe forms of malaria, such as severe malarial anemia (SMA).

Malarial anemia is characterized by the destruction of malaria infected red blood cells and suppression of erythropoiesis. Recent studies in murine models of malarial anemia have demonstrated that interleukin 12 (IL12) significantly boosts erythropoietic responses. Furthermore, several immunological studies conducted in Africa have shown that IL12 production was suppressed in children with SMA compared to asymptomatic children. For these reasons the genes encoding the two IL12 subunits, IL12A and IL12B, and its receptors, IL12RB1 and IL12RB2, are attractive candidate genes for studying SMA.

Methods

In this study, a total of 75 tagging single nucleotide polymorphisms (tagSNPs) covering these four genes were examined. Genotyping was performed with the iPlex MassARRAY technology (Sequenom) in a cohort of 940 children from the Asembo Bay region of western Kenya, an area with intense malaria transmission.

Results

Individuals possessing two copies of IL12A common allele (rs2243140) at 3'UTR showed increased susceptibility to SMA (Hb < 6g/dl and the presence of *P. falciparum* > 10,000/uL) ($p = 0.006$, RR 3.63, 95%CI 1.27-10.38).

Individuals possessing two copies of a rare variant in IL12RB1 (rs429774) appeared to be strongly protected against SMA ($p = 0.00005$, RR 0.18, 95%CI 0.05-0.69).

Conclusion

Identification of genetic polymorphisms that influence human host susceptibility to malaria infection and severe disease outcomes may help us to better understand the immune response to malaria and design novel treatments against severe malarial anemia.