Human genetic factors associated with protection against malaria

Dear Editor,

Today, the knowledge that specific genetic factor variants may contribute to disease resistance in human is becoming well documented.[1] Human genetic factors shield against the malaria point to inherited changes in the deoxyribonucleic acid of human erythrocytes which increase resistance to the disease and eventually increase survival time of the host to genetic change as well as the protection of erythrocytes from invasion by *Plasmodium* parasites or replications within the red cells. These genetic factors (alterations) are most commonly linked to molecules fundamental to erythrocyte function such as enzymes, cytoskeletal proteins, and hemoglobin (Hb) of red cells.[2] Individuals with ovalocytosis (elliptocytosis) have scanty parasitemia of *Plasmodium vivax* and *Plasmodium falciparum* because the elliptical form of erythrocyte resists parasitic invasion (mutation in the gene encoding Band 3 protein).[3] Red blood cell of individuals that lack the Duffy blood group antigens Fy^a and Fy^b also gives a protection and particularly sustained only to homozygotes. These glycophorin protein receptors are needed to *P. vivax* and *Plasmodium knowlesi* to attach and invade the erythrocyte.[4] *Plasmodium* parasites did not grow well in erythrocytes that contain high percentage of Hb peptides $\alpha_2\gamma_2$ (HbF). Accordingly, the newborn babies have protection against malaria parasites, especially the first few months of life.[5] Individuals with certain polymorphisms of human leukocyte antigen (HLA) are also considered to protect against malaria, such as HLA Class I antigen (HLA Bw53) and HLA Class II haplotype (DRB1*13OZ-DQB1*0501). Furthermore, HLA correlations vary depending on the genetic constitution of the polymorphic *Plasmodium* parasites, which change depending on the geographical area.[6] In addition, individuals with sickle cell trait (HbAS) are also protected against the severity of the falciparum malaria (due to changed display of *P. falciparum* erythrocyte membrane protein 1, which is the parasitic major cytoadherence legend and virulence factor on the erythrocyte surface.[7] Furthermore, homozygous Hb C individuals (CC) express a very high protection against malaria in the time that heterozygous (AC) express moderate protection as that seen in glucose-6-phosphate dehydrogenase deficiency (due to the red cell's inability to restore nicotinamide adenine dinucleotide phosphate hydrogen and glutathione, the parasite may be more untenable to the reaction when the parasite breaks down Hb).[9] The degree of parasitemia is lower because the red cells in these conditions are released by the spleen before the parasite is progressed into schizont.[9] Moreover, β (beta)-thalassemia trait also observed to protect against falciparum malaria infection.[10] HbE $^{(\beta 26\ Glu \rightarrow Lys)}$ variant has been present in approximately 70% in South Asia. It also makes the majority of red cells relatively resistant to be invaded by falciparum malaria. This would not shield from uncomplicated malaria infection but may inhibit the development of heavy parasitemia.[11] The severity of pyruvate kinase deficiency and scope of protection against malaria are significantly correlated.[12] The Gerbich (Ge) antigen system is an integrative erythrocyte membrane protein and plays an important functional role in maintaining the red blood cell shape. It also acts as the ligand for the *P. falciparum* erythrocyte-binding protein. Individuals with Ge negativity (rare) are relatively less susceptible to invasion by *P. falciparum*. Such persons have a condition such as elliptocytosis which characterized by an oval- or elliptical-shaped erythrocytes.[13] Rarely, mutations of glycophorin A and B proteins are also known to interpose resistance to *P. falciparum*.[14]

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Conflicts of interest

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References

1. Kaslow RA, McNicholl JM, Hill AV. Genetic Susceptibility to Infectious Diseases. Oxford: Oxford University Press; 2008. p. 107-19.
2. Hedrick PW. Population genetics of malaria resistance in humans. Heredity (Edinb) 2011;107:283-304.
3. Cortés A, Mellombo M, Mgone CS, Beck HP, Reeder JC, Cooke BM, *et al*. Adhesion of *Plasmodium falciparum*-infected red blood cells to CD36 under flow is enhanced by the cerebral malaria-protective trait South-East Asian ovalocytosis. Mol Biochem Parasitol 2005;142:252-7.

4. Ryan JR, Stoute JA, Amon J, Dunton RF, Mtalib R, Koros J, *et al*. Evidence for transmission of *Plasmodium vivax* among a duffy antigen negative population in Western Kenya. Am J Trop Med Hyg 2006;75:575-81.
5. Gitau GM, Eldred JM. Malaria in pregnancy: Clinical, therapeutic and prophylactic considerations. Obstet Gynaecol 2005;7:5-11.
6. Bengtsson BO, Tunlid A. The 1948 international congress of genetics in Sweden: People and politics. Genetics 2010;185:709-15.
7. Cholera R, Brittain NJ, Gillrie MR, Lopera-Mesa TM, Diakité SA, Arie T, *et al*. Impaired cytoadherence of *Plasmodium falciparum*-infected erythrocytes containing sickle hemoglobin. Proc Natl Acad Sci U S A 2008;105:991-6.
8. Nagel RL, Fabry ME, Steinberg MH. The paradox of hemoglobin SC disease. Blood Rev 2003;17:167-78.
9. Tishkoff SA, Verelli BJ. G6PD deficiency and malarial resistance in humans: Insights from evolutionary genetic analysis. In: Dronamraju K, editor. Evolutionary Aspects of Infectious Disease. New York: Cambridge University Press; 2004.
10. Ayi K, Turrini F, Piga A, Arese P. Enhanced phagocytosis of ring-parasitized mutant erythrocytes: A common mechanism that may explain protection against falciparum malaria in sickle trait and beta-thalassemia trait. Blood 2004;104:3364-71.
11. Chotivanich K, Udomsangpetch R, Pattanapanyasat K, Chierakul W, Simpson J, Looareesuwan S, *et al*. Hemoglobin E: A balanced polymorphism protective against high parasitemias and thus severe *P falciparum* malaria. Blood 2002;100:1172-6.
12. Mendes C, Dias F, Figueiredo J, Mora VG, Cano J, de Sousa B, *et al*. Duffy negative antigen is no longer a barrier to *Plasmodium vivax* – Molecular evidences from the African West Coast (Angola and equatorial guinea). PLoS Negl Trop Dis 2011;5:e1192.
13. Ayi K, Min-Oo G, Serghides L, Crockett M, Kirby-Allen M, Quirt I, *et al*. Pyruvate kinase deficiency and malaria. N Engl J Med 2008;358:1805-10.
14. Frodsham AJ, Hill AV. Genetics of infectious diseases. Hum Mol Genet 2004;13:R187-94.

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