Emergence of FY*Anull in a Plasmodium vivax-endemic region of Papua New Guinea

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In Papua New Guinea (PNG), numerous blood group polymorphisms and hemoglobinopathies characterize the human population. Human genetic polymorphisms of this nature are common in malarious regions, and all four human malaria parasites are holoendemic below 1500 meters in PNG. At this elevation, a prominent condition characterizing Melanesians is a1-thalassemia. Interestingly, recent epidemiological surveys have demonstrated that a1-thalassemia is associated with increased susceptibility to uncomplicated malaria among young children. It is further proposed that a1-thalassemia may facilitate so-called ‘‘benign’’ *Plasmodium vivax* infection to act later in life as a ‘‘natural vaccine’’ against severe *Plasmodium falciparum* malaria. Here, in a *P. vivax*endemic region of PNG where the resident Abelam-speaking population is characterized by a frequency of a1-thalassemia >0.98, we have discovered the mutation responsible for erythrocyte Duffy antigen-negativity (Fy[a2b2]) on the *FY*A* allele. In this study population there were 23 heterozygous and no homozygous individuals bearing this new allele (allele frequency, 23y1062 5 0.022). Flow cytometric analysis illustrated a 2-fold difference in erythroid-specific Fy-antigen expression between heterozygous (*FY*A*y*FY*A*null) and homozygous (*FY*A*y*FY*A*) individuals, suggesting a gene-dosage effect. In further comparisons, we observed a higher prevalence of *P. vivax* infection in *FY*A*y*FY*A* (83y508 5 0.163) compared with *FY*A*y*FY*A*null (2y23 5 0.087) individuals (odds ratio 5 2.05, 95% confidence interval 5 0.47–8.91). Emergence of *FY*A*null in this population suggests that *P. vivax* is involved in selection of this erythroid polymorphism. This mutation would ultimately compromise a1-thalassemiay*P. vivax*-mediated protection against severe *P. falciparum* malaria.