Effects of Natural Selection and Gene Conversion on the Evolution of Human Glycophorins Coding for MNS Blood Polymorphisms in Malaria-Endemic African Populations

Malaria has been a very strong selection pressure in recent human evolution, particularly in Africa. Of the one million deaths per year due to malaria, more than 90% are in sub-Saharan Africa, a region with high levels of genetic variation and population substructure. However, there have been few studies of nucleotide variation at genetic loci that are relevant to malaria susceptibility across geographically and genetically diverse ethnic groups in Africa. Invasion of erythrocytes by Plasmodium falciparum parasites is central to the pathology of malaria. Glycophorin A (GYPA) and B (GYPB), which determine MN and Ss blood types, are two major receptors that are expressed on erythrocyte surfaces and interact with parasite ligands. We analyzed nucleotide diversity of the glycophorin gene family in 15 African populations with different levels of malaria exposure. High levels of nucleotide diversity and gene conversion were found at these genes. We observed divergent patterns of genetic variation between these duplicated genes and between different extracellular domains of GYPA. Specifically, we identified fixed adaptive changes at exons 3–4 of GYPA. By contrast, we observed an allele frequency spectrum skewed toward a significant excess of intermediate-frequency alleles at GYPA exon 2 in many populations; the degree of spectrum distortion is correlated with malaria exposure, possibly because of the joint effects of gene conversion and balancing selection. We also identified a haplotype causing three amino acid changes in the extracellular domain of glycophorin B. This haplotype might have evolved adaptively in five populations with high exposure to malaria.

General information
State: Published
Organisations: University of Pennsylvania, University of Rome La Sapienza, Museum National d'Histoire Naturelle, University of Khartoum, Muhimbili University of Health and Allied Sciences, Kenya Medical Research Institute, International Biomedical Research in Africa
Pages: 741-754
Publication date: 2011
Peer-reviewed: Yes

Publication information
Journal: American Journal of Human Genetics
Volume: 88
Issue number: 6
ISSN (Print): 0002-9297
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 8.34 SJR 7.45 SNIP 2.428
Web of Science (2017): Impact factor 8.855
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 8.43 SJR 7.504 SNIP 2.536
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 9.71 SJR 8.755 SNIP 3.01
Web of Science (2015): Impact factor 10.794
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 9.66 SJR 8.801 SNIP 3.195
Web of Science (2014): Impact factor 10.931
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): CiteScore 9.58 SJR 7.863 SNIP 3.039
Web of Science (2013): Impact factor 10.987
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes