

GEPHE SUMMARY

ATP2B4 (https://www.gephebase.org/search-criteria?/and+GeneGephebase=^ATP2B4^#gephebase-summary-title)	Gephebase Gene	GP00000127	GepheID
	Entry Status	Martin	Main curator
	Published		

PHENOTYPIC CHANGE

Physiology (https://www.gephebase.org/search-criteria?/and+TraitCategory=^Physiology^#gephebase-summary-title)		Trait Category	
Pathogen resistance (Plasmodium; malaria parasite) (https://www.gephebase.org/search-criteria?/and+Trait=^Pathogen resistance (Plasmodium; malaria parasite)^#gephebase-summary-title)		Trait	
Homo sapiens -Ghana and Gambia		Trait State in Taxon A	
Homo sapiens -Ghana and Gambia		Trait State in Taxon B	
Data not curated		Ancestral State	
Intraspecific (https://www.gephebase.org/search-criteria?/and+TaxonomicStatus=^Intraspecific^#gephebase-summary-title)		Taxonomic Status	
Taxon A		Taxon B	
Homo sapiens (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Homo sapiens^#gephebase-summary-title)		Homo sapiens (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Homo sapiens^#gephebase-summary-title)	
human		human	
human; man; Homo sapiens Linnaeus, 1758; Home sapiens; Homo sampiens; Homo sapeins; Homo sapian; Homo sapians; Homo sapien; Homo sapience; Homo sapiense; Homo sapients; Homo sapines; Homo spaiens; Homo spiens; Humo sapiens		human; man; Homo sapiens Linnaeus, 1758; Home sapiens; Homo sampiens; Homo sapeins; Homo sapian; Homo sapians; Homo sapien; Homo sapience; Homo sapiense; Homo sapients; Homo sapines; Homo spaiens; Homo spiens; Humo sapiens	
species		species	
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Euarchontoglires; Primates; Haplorrhini; Simiiformes; Catarrhini; Hominoidea; Hominidae; Homininae; Homo		cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Euarchontoglires; Primates; Haplorrhini; Simiiformes; Catarrhini; Hominoidea; Hominidae; Homininae; Homo	
Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9605)		Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9605)	
9606 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9606)		9606 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9606)	
No		No	

GENOTYPIC CHANGE

ATP2B4	Generic Gene Name	UniProtKB Homo sapiens
	Synonyms	GenebankID or UniProtKB
	String	
9606.ENSPO0000350310 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPO0000350310)		
Belongs to the cation transport ATPase (P-type) (TC 3.A.3) family. Type IIB subfamily.		
GO - Molecular Function		
GO:0005524 : ATP binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005524)		
GO:0046872 : metal ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0046872)		
GO:0005388 : calcium-transporting ATPase activity		

(<https://www.ebi.ac.uk/QuickGO/term/GO:0005388>)
GO:0005516 : calmodulin binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0005516>)
GO:0050998 : nitric-oxide synthase binding
(<https://www.ebi.ac.uk/QuickGO/term/GO:0050998>)
GO:0036487 : nitric-oxide synthase inhibitor activity
(<https://www.ebi.ac.uk/QuickGO/term/GO:0036487>)
GO:0030165 : PDZ domain binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0030165>)
GO:0019901 : protein kinase binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0019901>)
GO:0030346 : protein phosphatase 2B binding
(<https://www.ebi.ac.uk/QuickGO/term/GO:0030346>)
GO:0097110 : scaffold protein binding
(<https://www.ebi.ac.uk/QuickGO/term/GO:0097110>)

GO - Biological Process

GO:0006357 : regulation of transcription by RNA polymerase II
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006357>)
GO:0006874 : cellular calcium ion homeostasis
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006874>)
GO:0007283 : spermatogenesis (<https://www.ebi.ac.uk/QuickGO/term/GO:0007283>)
GO:1901660 : calcium ion export (<https://www.ebi.ac.uk/QuickGO/term/GO:1901660>)
GO:0098703 : calcium ion import across plasma membrane
(<https://www.ebi.ac.uk/QuickGO/term/GO:0098703>)
GO:0097553 : calcium ion transmembrane import into cytosol
(<https://www.ebi.ac.uk/QuickGO/term/GO:0097553>)
GO:0070588 : calcium ion transmembrane transport
(<https://www.ebi.ac.uk/QuickGO/term/GO:0070588>)
GO:0071872 : cellular response to epinephrine stimulus
(<https://www.ebi.ac.uk/QuickGO/term/GO:0071872>)
GO:0030317 : flagellated sperm motility
(<https://www.ebi.ac.uk/QuickGO/term/GO:0030317>)
GO:0021766 : hippocampus development
(<https://www.ebi.ac.uk/QuickGO/term/GO:0021766>)
GO:0034220 : ion transmembrane transport
(<https://www.ebi.ac.uk/QuickGO/term/GO:0034220>)
GO:0140199 : negative regulation of adenylate cyclase-activating adrenergic receptor
signaling pathway involved in heart process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0140199>)
GO:1900082 : negative regulation of arginine catabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:1900082>)
GO:0070885 : negative regulation of calcineurin-NFAT signaling cascade
(<https://www.ebi.ac.uk/QuickGO/term/GO:0070885>)
GO:1903243 : negative regulation of cardiac muscle hypertrophy in response to stress
(<https://www.ebi.ac.uk/QuickGO/term/GO:1903243>)
GO:1903249 : negative regulation of citrulline biosynthetic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:1903249>)
GO:0045019 : negative regulation of nitric oxide biosynthetic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0045019>)
GO:0010751 : negative regulation of nitric oxide mediated signal transduction
(<https://www.ebi.ac.uk/QuickGO/term/GO:0010751>)
GO:0051001 : negative regulation of nitric-oxide synthase activity
(<https://www.ebi.ac.uk/QuickGO/term/GO:0051001>)
GO:1902083 : negative regulation of peptidyl-cysteine S-nitrosylation
(<https://www.ebi.ac.uk/QuickGO/term/GO:1902083>)
GO:0098736 : negative regulation of the force of heart contraction
(<https://www.ebi.ac.uk/QuickGO/term/GO:0098736>)
GO:0003407 : neural retina development
(<https://www.ebi.ac.uk/QuickGO/term/GO:0003407>)
GO:2000481 : positive regulation of cAMP-dependent protein kinase activity
(<https://www.ebi.ac.uk/QuickGO/term/GO:2000481>)
GO:0033138 : positive regulation of peptidyl-serine phosphorylation
(<https://www.ebi.ac.uk/QuickGO/term/GO:0033138>)
GO:1903779 : regulation of cardiac conduction
(<https://www.ebi.ac.uk/QuickGO/term/GO:1903779>)
GO:1902806 : regulation of cell cycle G1/S phase transition
(<https://www.ebi.ac.uk/QuickGO/term/GO:1902806>)
GO:0051480 : regulation of cytosolic calcium ion concentration
(<https://www.ebi.ac.uk/QuickGO/term/GO:0051480>)
GO:1902305 : regulation of sodium ion transmembrane transport
(<https://www.ebi.ac.uk/QuickGO/term/GO:1902305>)
GO:0051599 : response to hydrostatic pressure
(<https://www.ebi.ac.uk/QuickGO/term/GO:0051599>)

GO - Cellular Component

GO:0005886 : plasma membrane (<https://www.ebi.ac.uk/QuickGO/term/GO:0005886>)
GO:0016020 : membrane (<https://www.ebi.ac.uk/QuickGO/term/GO:0016020>)
GO:0005887 : integral component of plasma membrane
(<https://www.ebi.ac.uk/QuickGO/term/GO:0005887>)
GO:0098978 : glutamatergic synapse
(<https://www.ebi.ac.uk/QuickGO/term/GO:0098978>)
GO:0032991 : protein-containing complex

(<https://www.ebi.ac.uk/QuickGO/term/GO:0032991>)
GO:0016323 : basolateral plasma membrane
(<https://www.ebi.ac.uk/QuickGO/term/GO:0016323>)
GO:0005901 : caveola (<https://www.ebi.ac.uk/QuickGO/term/GO:0005901>)
GO:0099059 : integral component of presynaptic active zone membrane
(<https://www.ebi.ac.uk/QuickGO/term/GO:0099059>)
GO:0043005 : neuron projection (<https://www.ebi.ac.uk/QuickGO/term/GO:0043005>)
GO:0036126 : sperm flagellum (<https://www.ebi.ac.uk/QuickGO/term/GO:0036126>)
GO:0097228 : sperm principal piece (<https://www.ebi.ac.uk/QuickGO/term/GO:0097228>)
GO:0030315 : T-tubule (<https://www.ebi.ac.uk/QuickGO/term/GO:0030315>)
GO:0030018 : Z disc (<https://www.ebi.ac.uk/QuickGO/term/GO:0030018>)

	Presumptive Null
Unknown (https://www.gephebase.org/search-criteria?/and+Presumptive Null=~Unknown~#gephebase-summary-title)	
	Molecular Type
Unknown (https://www.gephebase.org/search-criteria?/and+Molecular Type=~Unknown~#gephebase-summary-title)	
	Aberration Type
Unknown (https://www.gephebase.org/search-criteria?/and+Aberration Type=~Unknown~#gephebase-summary-title)	
	Molecular Details of the Mutation
unknown	
	Experimental Evidence
Association Mapping (https://www.gephebase.org/search-criteria?/and+Experimental Evidence=~Association Mapping~#gephebase-summary-title)	
	Main Reference
Genome-wide association study indicates two novel resistance loci for severe malaria. (2012) (https://pubmed.ncbi.nlm.nih.gov/22895189)	

Authors
Timmann C; Thye T; Vens M; Evans J; May J; Ehmen C; Sievertsen J; Muntau B; Ruge G; Loag W; Ansong D; Antwi S; Asafo-Adjei E; Nguah SB; Kwakye KO; Akoto AO; Sylverken J; Brendel M; Schuldt K; Loley C; Franke A; Meyer CG; Agbenyega T; Ziegler A; Horstmann RD

Abstract
Malaria causes approximately one million fatalities per year, mostly among African children. Although highlighted by the strong protective effect of the sickle-cell trait, the full impact of human genetics on resistance to the disease remains largely unexplored. Genome-wide association (GWA) studies are designed to unravel relevant genetic variants comprehensively; however, in malaria, as in other infectious diseases, these studies have been only partly successful. Here we identify two previously unknown loci associated with severe falciparum malaria in patients and controls from Ghana, West Africa. We applied the GWA approach to the diverse clinical syndromes of severe falciparum malaria, thereby targeting human genetic variants influencing any step in the complex pathogenesis of the disease. One of the loci was identified on chromosome 1q32 within the ATP2B4 gene, which encodes the main calcium pump of erythrocytes, the host cells of the pathogenic stage of malaria parasites. The second was indicated by an intergenic single nucleotide polymorphism on chromosome 16q22.2, possibly linked to a neighbouring gene encoding the tight-junction protein MARVELD3. The protein is expressed on endothelial cells and might therefore have a role in microvascular damage caused by endothelial adherence of parasitized erythrocytes. We also confirmed previous reports on protective effects of the sickle-cell trait and blood group O. Our findings underline the potential of the GWA approach to provide candidates for the development of control measures against infectious diseases in humans.

Additional References

RELATED GEPHE

	Related Genes
10 (CCL3L1, Duffy, Glucose-6-phosphate dehydrogenase (G6PD), Glycophorin GYPA-GYPB-GYPE cluster, hemoglobin; HBB, HLA-DRB1, Human Leukocyte Antigen-B (HLA-B), MARVELD3, SIGLEC13, SIGLEC17P (pseudogene)) (https://www.gephebase.org/search-criteria?/or+Taxon ID=~9606~/and+Trait=Pathogen resistance/and+groupHaplotypes=true#gephebase-summary-title)	
	Related Haplotypes
No matches found.	

EXTERNAL LINKS

COMMENTS