

GEPHE SUMMARY

	Gephebase Gene	GephelD
chloroquine resistance transporter (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^chloroquine resistance transporter^#gephebase-summary-title)	GP00001533	Main curator
	Entry Status	Prigent
Published		

PHENOTYPIC CHANGE

	Trait Category
Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Physiology^#gephebase-summary-title)	
Xenobiotic resistance (artemisinin) (https://www.gephebase.org/search-criteria?/and+Trait Xenobiotic resistance (artemisinin)^#gephebase-summary-title)	Trait
Artemisinin-sensitive Plasmodium with mean parasite clearance half-life of 2.6 hours	Trait State in Taxon A
Artemisinin-resistant Plasmodium with parasite clearance half-life estimated prolongation of 0.47 h	Trait State in Taxon B
	Ancestral State
Taxon A	Taxonomic Status
Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Intraspecific^#gephebase-summary-title)	

Taxon A		Taxon B	
	Latin Name		Latin Name
Plasmodium falciparum (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Plasmodium+falciparum^#gephebase-summary-title)		Plasmodium falciparum (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Plasmodium+falciparum^#gephebase-summary-title)	
malaria parasite P. falciparum	Common Name	malaria parasite P. falciparum	Common Name
Plasmodium (Laverania) falciparum; malaria parasite P. falciparum	Synonyms	Plasmodium (Laverania) falciparum; malaria parasite P. falciparum	Synonyms
species	Rank	species	Rank
	Lineage		Lineage
cellular organisms; Eukaryota; Alveolata; Apicomplexa; Aconoidasida; Haemosporida; Plasmodiidae; Plasmodium; Plasmodium (Laverania)		cellular organisms; Eukaryota; Alveolata; Apicomplexa; Aconoidasida; Haemosporida; Plasmodiidae; Plasmodium; Plasmodium (Laverania)	
Plasmodium (Laverania) () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=418107)	Parent	Plasmodium (Laverania) () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=418107)	Parent
5833 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5833)	NCBI Taxonomy ID	5833 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5833)	NCBI Taxonomy ID
No	is Taxon A an Infraspecies?	No	is Taxon B an Infraspecies?

GENOTYPIC CHANGE

CRT	Generic Gene Name	UniProtKB Plasmodium falciparum
-	Synonyms	GenebankID or UniProtKB
-	String	
Belongs to the CRT-like transporter family.	Sequence Similarities	
GO:0015238 : drug transmembrane transporter activity (https://www.ebi.ac.uk/QuickGO/term/GO:0015238)	GO - Molecular Function	
-	GO - Biological Process	
GO:0016021 : integral component of membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0016021)	GO - Cellular Component	
GO:0005774 : vacuolar membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005774)		Presumptive Null
No (https://www.gephebase.org/search-criteria?/and+Presumptive+Null=^No^#gephebase-summary-title)		

Coding (https://www.gephebase.org/search-criteria?/and+Molecular Type=%5BCoding%5D#gephebase-summary-title)	Molecular Type
SNP (https://www.gephebase.org/search-criteria?/and+Aberration Type=%5BSNP%5D#gephebase-summary-title)	Aberration Type
Nonsynonymous	SNP Coding Change
p.Ile356Thr	Molecular Details of the Mutation
Association Mapping (https://www.gephebase.org/search-criteria?/and+Experimental Evidence=%5BAssociation Mapping%5D#gephebase-summary-title)	Experimental Evidence

Taxon A	Taxon B	Position
Codon	-	-
Amino-acid	-	-

Genetic architecture of artemisinin-resistant Plasmodium falciparum. (2015) (https://pubmed.ncbi.nlm.nih.gov/25599401)	Main Reference
Miotto O; Amato R; Ashley EA; MacInnis B; Almagro-Garcia J; Amaratunga C; Lim P; Mead D; Oyola SO; Dhorda M; Imwong M; Woodrow C; Manske M; Stalker J; Drury E; Campino S; Amenga-Etego L; Thanh TN; Tran HT; Ringwald P; Bethell D; Nosten F; Phy AP; Pukrittayakamee S; Chotivanich K; Chuor CM; Nguon C; Suon S; Sreng S; Newton PN; Mayxay M; Khanthavong M; Hongvanthong B; Htut Y; Han KT; Kyaw MP; Faiz MA; Fanello CI; Onyamboko M; Mokuolu OA; Jacob CG; Takala-Harrison S; Plowe CV; Day NP; Dondorp AM; Spencer CC; McVean G; Fairhurst RM; White NJ; Kwiatkowski DP	Authors

We report a large multicenter genome-wide association study of *Plasmodium falciparum* resistance to artemisinin, the frontline antimalarial drug. Across 15 locations in Southeast Asia, we identified at least 20 mutations in kelch13 (PF3D7_1343700) affecting the encoded propeller and BTB/POZ domains, which were associated with a slow parasite clearance rate after treatment with artemisinin derivatives. Nonsynonymous polymorphisms in fd (ferredoxin), arps10 (apicoplast ribosomal protein S10), mdr2 (multidrug resistance protein 2) and crt (chloroquine resistance transporter) also showed strong associations with artemisinin resistance. Analysis of the fine structure of the parasite population showed that the fd, arps10, mdr2 and crt polymorphisms are markers of a genetic background on which kelch13 mutations are particularly likely to arise and that they correlate with the contemporary geographical boundaries and population frequencies of artemisinin resistance. These findings indicate that the risk of new resistance-causing mutations emerging is determined by specific predisposing genetic factors in the underlying parasite population.

[Additional References](#)

RELATED GEPHE

6 (apicoplast ribosomal protein S10, ferredoxin, kelch 13, kelch 13 (K13), multidrug resistance protein 2, protein phosphatase) (https://www.gephebase.org/search-criteria?/or+TaxonID=%5B5833%5D/and+Trait=Xenobiotic+resistance/and+groupHaplotypes=true#gephebase-summary-title)	Related Genes
No matches found.	Related Haplotypes

EXTERNAL LINKS

COMMENTS