

## GEPHE SUMMARY

	Gephebase Gene		GepheID
multidrug resistance protein 2 ( <a href="https://www.gephebase.org/search-criteria?/and+Gene">https://www.gephebase.org/search-criteria?/and+Gene</a> )		GP00001532	
Gephebase="^multidrug resistance protein 2^"#gephebase-summary-title)			Main curator
Published	Entry Status	Prigent	

## PHENOTYPIC CHANGE

	Trait Category		
Physiology ( <a href="https://www.gephebase.org/search-criteria?/and+Trait">https://www.gephebase.org/search-criteria?/and+Trait</a> )			
Category="^Physiology^"#gephebase-summary-title)	Trait		
Xenobiotic resistance (artemisinin) ( <a (artemisinin)^"#gephebase-summary-title"="" ^xenobiotic="" href="https://www.gephebase.org/search-criteria?/and+Trait=" resistance="">https://www.gephebase.org/search-criteria?/and+Trait="^Xenobiotic resistance (artemisinin)^"#gephebase-summary-title</a> )			
	Trait State in Taxon A		
Artemisinin-sensitive Plasmodium with mean parasite clearance half-life of 2.6 hours			
	Trait State in Taxon B		
Artemisinin-resistant Plasmodium with parasite clearance half-life estimated prolongation of 0.54 h			
	Ancestral State		
Taxon A			
	Taxonomic Status		
Intraspecific ( <a href="https://www.gephebase.org/search-criteria?/and+Taxonomic">https://www.gephebase.org/search-criteria?/and+Taxonomic</a> )			
Status="^Intraspecific^"#gephebase-summary-title)			
Taxon A		Taxon B	
	Latin Name		Latin Name
Plasmodium falciparum		Plasmodium falciparum	
( <a ^plasmodium="" falciparum^"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="^Plasmodium falciparum^"#gephebase-summary-title</a> )		( <a ^plasmodium="" falciparum^"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="^Plasmodium falciparum^"#gephebase-summary-title</a> )	
	Common Name		Common Name
malaria parasite P. falciparum		malaria parasite P. falciparum	
	Synonyms		Synonyms
Plasmodium (Laverania) falciparum; malaria parasite P. falciparum		Plasmodium (Laverania) falciparum; malaria parasite P. falciparum	
	Rank		Rank
species		species	
	Lineage		Lineage
cellular organisms; Eukaryota; Alveolata; Apicomplexa; Aconoidasida; Haemosporida; Plasmodiidae; Plasmodium; Plasmodium (Laverania)		cellular organisms; Eukaryota; Alveolata; Apicomplexa; Aconoidasida; Haemosporida; Plasmodiidae; Plasmodium; Plasmodium (Laverania)	
	Parent		Parent
Plasmodium (Laverania) () - (Rank: subgenus)		Plasmodium (Laverania) () - (Rank: subgenus)	
( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=418107">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=418107</a> )		( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=418107">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=418107</a> )	
	NCBI Taxonomy ID		NCBI Taxonomy ID
5833		5833	
( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5833">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5833</a> )		( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5833">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5833</a> )	
	is Taxon A an Intraspecies?		is Taxon B an Intraspecies?
No		No	

## GENOTYPIC CHANGE

	Generic Gene Name		UniProtKB Plasmodium falciparum (isolate 3D7)
PF3D7_1447900		Q8IKZ6 ( <a href="http://www.uniprot.org/uniprot/Q8IKZ6">http://www.uniprot.org/uniprot/Q8IKZ6</a> )	
	Synonyms		GenebankID or UniProtKB
PF3D7_1447900		()	
-	String		
-			
	Sequence Similarities		
-			
	GO - Molecular Function		
GO:0005524 : ATP binding ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0005524">https://www.ebi.ac.uk/QuickGO/term/GO:0005524</a> )			
GO:0042626 : ATPase activity, coupled to transmembrane movement of substances ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0042626">https://www.ebi.ac.uk/QuickGO/term/GO:0042626</a> )			
GO:0008559 : xenobiotic transmembrane transporting ATPase activity ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0008559">https://www.ebi.ac.uk/QuickGO/term/GO:0008559</a> )			
GO:0046872 : metal ion binding ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0046872">https://www.ebi.ac.uk/QuickGO/term/GO:0046872</a> )			
GO:0046873 : metal ion transmembrane transporter activity ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0046873">https://www.ebi.ac.uk/QuickGO/term/GO:0046873</a> )			
	GO - Biological Process		
GO:0006879 : cellular iron ion homeostasis			

(<https://www.ebi.ac.uk/QuickGO/term/GO:0006879>)  
GO:0006855 : drug transmembrane transport  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006855>)

GO - Cellular Component

GO:0016021 : integral component of membrane  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0016021>)  
GO:0005773 : vacuole (<https://www.ebi.ac.uk/QuickGO/term/GO:0005773>)  
GO:0005743 : mitochondrial inner membrane  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0005743>)

Presumptive Null

No (<https://www.gephebase.org/search-criteria?/and+Presumptive Null=^No^#gephebase-summary-title>)

Molecular Type

Coding (<https://www.gephebase.org/search-criteria?/and+Molecular Type=^Coding^#gephebase-summary-title>)

Aberration Type

SNP (<https://www.gephebase.org/search-criteria?/and+Aberration Type=^SNP^#gephebase-summary-title>)

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

p.Thr484Ile

Experimental Evidence

Association Mapping (<https://www.gephebase.org/search-criteria?/and+Experimental Evidence=^Association Mapping^#gephebase-summary-title>)

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

Main Reference

Genetic architecture of artemisinin-resistant *Plasmodium falciparum*. (2015) (<https://pubmed.ncbi.nlm.nih.gov/25599401>)

Authors

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; Phyo AP; Pukrittayakamee S; Chotivanich K; Chuo 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

Abstract

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

Related Genes

6 (apicoplast ribosomal protein S10, chloroquine resistance transporter, ferredoxin, kelch 13, kelch 13 (K13), protein phosphatase) (<https://www.gephebase.org/search-criteria?/or+Taxon ID=^5833^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title>)

Related Haplotypes

No matches found.

## EXTERNAL LINKS

## COMMENTS

