

GEPHE SUMMARY

	Gephebase Gene		GepheID
kelch 13 (<a +kelch+13+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=">https://www.gephebase.org/search-criteria?/and+Gene+Gephebase="+kelch+13+"#gephebase-summary-title)	GP00001525		
	Entry Status	Prigent	Main curator
Published			

PHENOTYPIC CHANGE

	Trait Category		
Physiology (<a +physiology+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Trait+Category=">https://www.gephebase.org/search-criteria?/and+Trait+Category="+Physiology+"#gephebase-summary-title)			
	Trait		
Xenobiotic resistance (artemisinin) (<a +xenobiotic+resistance+(artemisinin)+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Trait=">https://www.gephebase.org/search-criteria?/and+Trait="+Xenobiotic+resistance+(artemisinin)+"#gephebase-summary-title)			
	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 mean parasite clearance half-life of 6.72 hours from Myanmar (11 samples) Thailand (21 samples) Cambodia (241 samples) and Vietnam (9 samples)			
	Ancestral State		
Taxon A			
	Taxonomic Status		
Intraspecific (<a +intraspecific+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=">https://www.gephebase.org/search-criteria?/and+Taxonomic+Status="+Intraspecific+"#gephebase-summary-title)			
Taxon A		Taxon B	
	Latin Name		Latin Name
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)		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)	
	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) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=418107)		Plasmodium (Laverania) () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=418107)	
	NCBI Taxonomy ID		NCBI Taxonomy ID
5833 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5833)		5833 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5833)	
	is Taxon A an Intraspecies?		is Taxon B an Intraspecies?
No		No	

GENOTYPIC CHANGE

	Generic Gene Name		UniProtKB Plasmodium falciparum (isolate 3D7)
PF3D7_1343700		Q8IDQ2 (http://www.uniprot.org/uniprot/Q8IDQ2)	
	Synonyms		GenebankID or UniProtKB
PF3D7_1343700		KM187892.1 (https://www.ncbi.nlm.nih.gov/nuccore/KM187892.1)	
	String		
-			
	Sequence Similarities		
-			
	GO - Molecular Function		
-			
	GO - Biological Process		
GO:0042493 : response to drug (https://www.ebi.ac.uk/QuickGO/term/GO:0042493)			
GO:0051260 : protein homooligomerization (https://www.ebi.ac.uk/QuickGO/term/GO:0051260)			
	GO - Cellular Component		
-			
			Presumptive Null
No (<a +no+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Presumptive+Null=">https://www.gephebase.org/search-criteria?/and+Presumptive+Null="+No+"#gephebase-summary-title)			

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.Cys580Tyr affecting the encoded propeller domain

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	-	-	-

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

Main Reference

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; 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

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

6 (apicoplast ribosomal protein S10, chloroquine resistance transporter, ferredoxin, kelch 13 (K13), multidrug resistance protein 2, protein phosphatase) (<https://www.gephebase.org/search-criteria?/or+Taxon+ID=~5833^/and+Trait=Xenobiotic+resistance/and+groupHaplotypes=true#gephebase-summary-title>)

Related Genes

19 (<https://www.gephebase.org/search-criteria?/or+Gene+Gephebase=~kelch+13^/and+Taxon+ID=~5833^/or+Gene+Gephebase=~kelch+13^/and+Taxon+ID=~5833^#gephebase-summary-title>)

Related Haplotypes

EXTERNAL LINKS

COMMENTS

k13-C580Y the most widespread resistance allele has originated independently in multiple locations