

Gephebase Gene	GepheID
kelch 13 (https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=~kelch+13^#gephebase-summary-title)	GP00001511
Entry Status	Prigent
Published	Main curator

Trait Category	Trait	Trait State in Taxon A	Trait State in Taxon B	Ancestral State	Taxonomic Status
Physiology (https://www.gephebase.org/search-criteria?/and+TraitCategory=~Physiology^#gephebase-summary-title)					
Xenobiotic resistance (artemisinin) (https://www.gephebase.org/search-criteria?/and+Trait=~Xenobiotic resistance (artemisinin)^#gephebase-summary-title)		Artemisinin-sensitive Plasmodium with mean parasite clearance half-life of 2.6 hours	Artemisinin-resistant Plasmodium with mean parasite clearance half-life of 6.34 hours from Myanmar (5 samples) and Thailand (6 samples)		Intraspecific (https://www.gephebase.org/search-criteria?/and+TaxonomicStatus=~Intraspecific^#gephebase-summary-title)

GENOTYPIC CHANGE

PF3D7_1343700	Generic Gene Name	UniProtKB Plasmodium falciparum (isolate 3D7)
	Synonyms	Q8IDQ2 (http://www.uniprot.org/uniprot/Q8IDQ2)
PF3D7_1343700	String	GenebankID or UniProtKB KM187892.1 (https://www.ncbi.nlm.nih.gov/nuccore/KM187892.1)
-	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)	
		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

P441L affecting the BTB/POZ 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	-	-	-

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; 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

Related Genes

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 Haplotypes

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>)

EXTERNAL LINKS

COMMENTS