

## GEPHE SUMMARY

**Gephebase Gene**  
kelch 13

**Entry Status**  
Published

**GepheID**  
GP00001523

**Main curator**  
Prigent

## PHENOTYPIC CHANGE

**Trait Category**  
Physiology

**Trait**  
Xenobiotic resistance (artemisinin)

**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 6.67 hours from Vietnam (5 samples)

**Ancestral State**  
Taxon A

**Taxonomic Status**  
Intraspecific

### Taxon A

**Latin Name**  
*Plasmodium falciparum*

**Common Name**  
malaria parasite P. falciparum

**Synonyms**  
Plasmodium (Laverania) falciparum; malaria parasite P. falciparum

**Rank**  
species

**Lineage**  
cellular organisms; Eukaryota; Alveolata; Apicomplexa; Aconoidasida; Haemosporida; Plasmodiidae; Plasmodium; Plasmodium (Laverania)

**Parent**  
Plasmodium (Laverania) () - (Rank: subgenus)

**NCBI Taxonomy ID**  
5833

**is Taxon A an Intraspecies?**  
No

### Taxon B

**Latin Name**  
*Plasmodium falciparum*

**Common Name**  
malaria parasite P. falciparum

**Synonyms**  
Plasmodium (Laverania) falciparum; malaria parasite P. falciparum

**Rank**  
species

**Lineage**  
cellular organisms; Eukaryota; Alveolata; Apicomplexa; Aconoidasida; Haemosporida; Plasmodiidae; Plasmodium; Plasmodium (Laverania)

**Parent**  
Plasmodium (Laverania) () - (Rank: subgenus)

**NCBI Taxonomy ID**  
5833

**is Taxon B an Intraspecies?**  
No

## GENOTYPIC CHANGE

**Generic Gene Name**  
PF3D7\_1343700

**Synonyms**  
PF3D7\_1343700

**String**  
-

**Sequence Similarities**  
-

**GO - Molecular Function**  
-

**GO - Biological Process**  
GO:0042493 : response to drug  
GO:0051260 : protein homooligomerization

**GO - Cellular Component**  
-

**Presumptive Null**  
No

**Molecular Type**

**UniProtKB Plasmodium falciparum (isolate 3D7)**  
Q81DQ2

**GenebankID or UniProtKB**  
KM187892.1

## Coding

### Aberration Type SNP

### SNP Coding Change Nonsynonymous

### Molecular Details of the Mutation V568G affecting the encoded propeller domain

### Experimental Evidence Association Mapping

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

### Main Reference

[Genetic architecture of artemisinin-resistant \*Plasmodium falciparum\*. \(2015\)](#)

### 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)

### Related Haplotypes

19

## COMMENTS