

GEPHE SUMMARY

Gephebase Gene

kelch 13

Entry Status

Published

GepheID

GP00001524

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 6.85 hours from Myanmar (6 samples) and Thailand (1 sample)

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 P574L 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