GEPHE SUMMARY

Gephebase Gene

chloroquine resistance transporter (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^chloroquine resistance transporter^#gephebase-summary-title)

Entry Status

Published

GepheID

GP00001533

Main curator

Prigent

PHENOTYPIC CHANGE

Trait Category

Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Physiology^#gephebase-summary-title)

Trait

Xenobiotic resistance (artemisinin) (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 parasite clearance half-life estimated prolongation of 0.47 h

Ancestral State

Taxon A

Taxonomic Status

Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Intraspecific^#gephebase-summary-title)

Taxon A

Latin Name

Plasmodium falciparum (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Plasmodium falciparum^#gephebase-summary-title)

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) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 418107)

NCBI Taxonomy ID

5833 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 5833)

is Taxon A an Infraspecies?

No

Taxon B

Latin Name

Plasmodium falciparum (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Plasmodium falciparum^#gephebase-summary-title)

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) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 418107)

NCBI Taxonomy ID

5833 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 5833)

is Taxon B an Infraspecies?

No

GENOTYPIC CHANGE

Generic Gene Name

CRT

Synonyms

-

String

-

Sequence Similarities

Belongs to the CRT-like transporter family.

GO - Molecular Function

GO:0015238 : drug transmembrane transporter activity (https://www.ebi.ac.uk/QuickGO/term/GO:0015238)

GO - Biological Process

-

GO - Cellular Component

GO:0016021 : integral component of membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0016021)
GO:0005774 : vacuolar membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005774)

UniProtKB Plasmodium falciparum

Q9N623 (http://www.uniprot.org/uniprot/Q9N623)

GenebankID or UniProtKB

()

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.Ile356Thr

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, ferredoxin, kelch 13, 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

No matches found.

EXTERNAL LINKS

COMMENTS