GEPHE SUMMARY

Gephebase Gene
kelch 13 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^kelch 13^#gephebase-summary-title)

GepheID
GP00001515

Entry Status
Published

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 mean parasite clearance half-life of 6.13 hours from Thailand (1 sample) and Cambodia (2 samples)

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
PF3D7_1343700

Synonyms
PF3D7_1343700

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
-

UniProtKB Plasmodium falciparum (isolate 3D7)
Q8IDQ2 (http://www.uniprot.org/uniprot/Q8IDQ2)

GenebankID or UniProtKB
KM187892.1 (https://www.ncbi.nlm.nih.gov/nuccore/KM187892.1)

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

A481V 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	-	-	-

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