GEPHE SUMMARY

Gephebase Gene
kelch 13

GephelD
GP00001510

Entry Status
Published

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 7.70 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 Infraspecies?
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 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
GO:0051260 : protein homooligomerization

GO - Cellular Component
-

Presumptive Null
No

Molecular Type

UniProtKB Plasmodium falciparum (isolate 3D7)
Q8IDQ2

GenebankID or UniProtKB
KM187892.1

Coding

Aberration Type
SNP

SNP Coding Change
Nonsynonymous

Molecular Details of the Mutation
D353Y affecting the BTB/POZ 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