

GEPHE SUMMARY

<p>ferredoxin (https://www.gephebase.org/search-criteria?/and+Gene+Gephebase+^ferredoxin+^#gephebase-summary-title)</p> <p>Published</p>	<p>Gephebase Gene</p> <p>Entry Status</p>	<p>GP00001530</p> <p>Prigent</p>	<p>GepheID</p> <p>Main curator</p>
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PHENOTYPIC CHANGE

<p>Physiology (https://www.gephebase.org/search-criteria?/and+Trait+Category+^Physiology+^#gephebase-summary-title)</p> <p>Xenobiotic resistance (artemisinin) (https://www.gephebase.org/search-criteria?/and+Trait+^Xenobiotic+resistance+(artemisinin)+^#gephebase-summary-title)</p> <p>Artemisinin-sensitive Plasmodium with mean parasite clearance half-life of 2.6 hours</p> <p>Artemisinin-resistant Plasmodium with parasite clearance half-life estimated prolongation of 0.53 h</p> <p>Taxon A</p> <p>Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic+Status+^Intraspecific+^#gephebase-summary-title)</p>	<p>Trait Category</p> <p>Trait</p> <p>Trait State in Taxon A</p> <p>Trait State in Taxon B</p> <p>Ancestral State</p> <p>Taxonomic Status</p>	<p>Taxon A</p> <p>Plasmodium falciparum (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms+^Plasmodium+falciparum+^#gephebase-summary-title)</p> <p>malaria parasite <i>P. falciparum</i></p> <p>Plasmodium (<i>Laverania</i>) <i>falciparum</i>; malaria parasite <i>P. falciparum</i> species</p> <p>cellular organisms; Eukaryota; Alveolata; Apicomplexa; Aconoidasida; Haemosporida; Plasmodiidae; Plasmodium; Plasmodium (<i>Laverania</i>)</p> <p>Plasmodium (<i>Laverania</i>) () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=418107)</p> <p>5833 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5833)</p> <p>is Taxon A an Intraspecies?</p> <p>No</p>	<p>Taxon B</p> <p>Plasmodium falciparum (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms+^Plasmodium+falciparum+^#gephebase-summary-title)</p> <p>malaria parasite <i>P. falciparum</i></p> <p>Plasmodium (<i>Laverania</i>) <i>falciparum</i>; malaria parasite <i>P. falciparum</i> species</p> <p>cellular organisms; Eukaryota; Alveolata; Apicomplexa; Aconoidasida; Haemosporida; Plasmodiidae; Plasmodium; Plasmodium (<i>Laverania</i>)</p> <p>Plasmodium (<i>Laverania</i>) () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=418107)</p> <p>5833 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5833)</p> <p>is Taxon B an Intraspecies?</p> <p>No</p>
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GENOTYPIC CHANGE

<p>PF3D7_1318100</p> <p>PF3D7_1318100</p> <p>-</p> <p>Belongs to the 2Fe2S plant-type ferredoxin family.</p> <p>GO:0046872 : metal ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0046872)</p> <p>GO:0009055 : electron transfer activity (https://www.ebi.ac.uk/QuickGO/term/GO:0009055)</p> <p>GO:0051537 : 2 iron, 2 sulfur cluster binding (https://www.ebi.ac.uk/QuickGO/term/GO:0051537)</p> <p>GO:0055114 : oxidation-reduction process (https://www.ebi.ac.uk/QuickGO/term/GO:0055114)</p> <p>GO:0020011 : apicoplast (https://www.ebi.ac.uk/QuickGO/term/GO:0020011)</p>	<p>Generic Gene Name</p> <p>Synonyms</p> <p>String</p> <p>Sequence Similarities</p> <p>GO - Molecular Function</p> <p>GO - Biological Process</p> <p>GO - Cellular Component</p>	<p>UniProtKB Plasmodium falciparum (isolate 3D7)</p> <p>Q8IED5 (http://www.uniprot.org/uniprot/Q8IED5)</p> <p>GenebankID or UniProtKB</p> <p>Q8IED5</p>
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No (<https://www.gephebase.org/search-criteria?/and+Presumptive Null=^No^#gephebase-summary-title>)

Presumptive Null

Coding (<https://www.gephebase.org/search-criteria?/and+Molecular Type=^Coding^#gephebase-summary-title>)

Molecular Type

SNP (<https://www.gephebase.org/search-criteria?/and+Aberration Type=^SNP^#gephebase-summary-title>)

Aberration Type

Nonsynonymous

SNP Coding Change

p.Asp193Tyr

Molecular Details of the Mutation

Association Mapping (<https://www.gephebase.org/search-criteria?/and+Experimental Evidence=^Association Mapping^#gephebase-summary-title>)

Experimental Evidence

	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; Khantavong 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, 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