

## GEPHE SUMMARY

|  |                |            |              |
|--|----------------|------------|--------------|
|  | Gephebase Gene |            | GepheID      |
| kelch 13 ( <a href="https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=^kelch+13^#gepbase-summary-title">https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=^kelch+13^#gepbase-summary-title</a> ) |                | GP00001510 |              |
|  | Entry Status   | Prigent    | Main curator |
| Published  |                |            |              |

## PHENOTYPIC CHANGE

|   |                             |  |                             |
|---|-----------------------------|--|-----------------------------|
|   | Trait Category              |  |                             |
| Physiology ( <a href="https://www.gephebase.org/search-criteria?/and+Trait+Category=^Physiology^#gepbase-summary-title">https://www.gephebase.org/search-criteria?/and+Trait+Category=^Physiology^#gepbase-summary-title</a> )  |                             |  |                             |
|   | Trait                       |  |                             |
| Xenobiotic resistance (artemisinin) ( <a href="https://www.gephebase.org/search-criteria?/and+Trait=^Xenobiotic+resistance+(artemisinin)^#gepbase-summary-title">https://www.gephebase.org/search-criteria?/and+Trait=^Xenobiotic+resistance+(artemisinin)^#gepbase-summary-title</a> ) |                             |  |                             |
|   | 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 ( <a href="https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=^Intraspecific^#gepbase-summary-title">https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=^Intraspecific^#gepbase-summary-title</a> )   |                             |  |                             |
| Taxon A   |                             | Taxon B  |                             |
|   | Latin Name                  |  | Latin Name                  |
| Plasmodium falciparum<br>( <a href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Plasmodium+falciparum^#gepbase-summary-title">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Plasmodium+falciparum^#gepbase-summary-title</a> )              |                             | Plasmodium falciparum<br>( <a href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Plasmodium+falciparum^#gepbase-summary-title">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Plasmodium+falciparum^#gepbase-summary-title</a> ) |                             |
|   | Common Name                 |  | Common Name                 |
| malaria parasite P. falciparum  |                             | malaria parasite P. falciparum   |                             |
|   | Synonyms                    |  | Synonyms                    |
| Plasmodium (Laverania) falciparum; malaria parasite P. falciparum   |                             | Plasmodium (Laverania) falciparum; malaria parasite P. falciparum  |                             |
|   | Rank                        |  | Rank                        |
| species   |                             | species  |                             |
|   | Lineage                     |  | Lineage                     |
| cellular organisms; Eukaryota; Alveolata; Apicomplexa; Aconoidasida; Haemosporida; Plasmodiidae; Plasmodium; Plasmodium (Laverania)   |                             | cellular organisms; Eukaryota; Alveolata; Apicomplexa; Aconoidasida; Haemosporida; Plasmodiidae; Plasmodium; Plasmodium (Laverania)  |                             |
|   | Parent                      |  | Parent                      |
| Plasmodium (Laverania) () - (Rank: subgenus)<br>( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=418107">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=418107</a> )   |                             | Plasmodium (Laverania) () - (Rank: subgenus)<br>( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=418107">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=418107</a> )  |                             |
|   | NCBI Taxonomy ID            |  | NCBI Taxonomy ID            |
| 5833<br>( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5833">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5833</a> )   |                             | 5833<br>( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5833">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5833</a> )  |                             |
|   | is Taxon A an Intraspecies? |  | is Taxon B an Intraspecies? |
| No  |                             | No   |                             |

## GENOTYPIC CHANGE

|  |                         |  |   |
|--|-------------------------|--|---|
|  | Generic Gene Name       |  | UniProtKB Plasmodium falciparum (isolate 3D7) |
| PF3D7_1343700  |                         | Q8IDQ2 ( <a href="http://www.uniprot.org/uniprot/Q8IDQ2">http://www.uniprot.org/uniprot/Q8IDQ2</a> )                               |   |
|  | Synonyms                |  | GenebankID or UniProtKB                       |
| PF3D7_1343700  |                         | KM187892.1 ( <a href="https://www.ncbi.nlm.nih.gov/nucleotide/KM187892.1">https://www.ncbi.nlm.nih.gov/nucleotide/KM187892.1</a> ) |   |
| -  | String                  |  |   |
| -  | Sequence Similarities   |  |   |
| -  | GO - Molecular Function |  |   |
| -  | GO - Biological Process |  |   |
| GO:0042493 : response to drug ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0042493">https://www.ebi.ac.uk/QuickGO/term/GO:0042493</a> )  |                         |  |   |
| GO:0051260 : protein homooligomerization<br>( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0051260">https://www.ebi.ac.uk/QuickGO/term/GO:0051260</a> )  |                         |  |   |
|  | GO - Cellular Component |  |   |
| -  |                         |  |   |
|  |                         |  | Presumptive Null                              |
| No ( <a href="https://www.gephebase.org/search-criteria?/and+Presumptive+Null=^No^#gepbase-summary-title">https://www.gephebase.org/search-criteria?/and+Presumptive+Null=^No^#gepbase-summary-title</a> ) |                         |  | 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

D353Y affecting the BTB/POZ 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; Chhor 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