GEPHE SUMMARY

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

GepheID
GP00001484

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

Trait State in Taxon A
Malaria parasite - sensitive

Trait State in Taxon B
Malaria parasite - resistant

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

Common Name
malaria parasite P. vivax

Synonyms
Haemamoeba vivax; malaria parasite P. vivax

Rank
species

Lineage
cellular organisms; Eukaryota; Alveolata; Apicomplexa; Aconoidasida; Haemosporida; Plasmodiidae; Plasmodium; Plasmodium (Plasmodium)

Parent
Plasmodium (Plasmodium) () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 418103)

NCBI Taxonomy ID
5855 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 5855)

is Taxon A an Infraspecies?
No

Taxon B

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

Common Name
malaria parasite P. vivax

Synonyms
Haemamoeba vivax; malaria parasite P. vivax

Rank
species

Lineage
cellular organisms; Eukaryota; Alveolata; Apicomplexa; Aconoidasida; Haemosporida; Plasmodiidae; Plasmodium; Plasmodium (Plasmodium)

Parent
Plasmodium (Plasmodium) () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 418103)

NCBI Taxonomy ID
5855 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 5855)

is Taxon B an Infraspecies?
No

GENOTYPIC CHANGE

Generic Gene Name
DHFR

Synonyms
DYR; DHFRP1

String
9606.ENSP00000396308 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000396308)

Sequence Similarities
Belongs to the dihydrofolate reductase family.

GO - Molecular Function
GO:0003729 : mRNA binding (https://www.ebi.ac.uk/QuickGO/term/GO:0003729)
GO:0008144 : drug binding (https://www.ebi.ac.uk/QuickGO/term/GO:0008144)
GO:0050661 : NADP binding (https://www.ebi.ac.uk/QuickGO/term/GO:0050661)
GO:0000900 : translation repressor activity, mRNA regulatory element binding (https://www.ebi.ac.uk/QuickGO/term/GO:0000900)
GO:0004146 : dihydrofolate reductase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0004146)
GO:0033560 : folate reductase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0033560)

UniProtKB Homo sapiens
P00374 (http://www.uniprot.org/uniprot/P00374)

GenebankID or UniProtKB
JN794515.1 (https://www.ncbi.nlm.nih.gov/nuccore/JN794515.1)

GO:0005542 : folic acid binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005542)
GO:0051870 : methotrexate binding (https://www.ebi.ac.uk/QuickGO/term/GO:0051870)
GO:0070402 : NADPH binding (https://www.ebi.ac.uk/QuickGO/term/GO:0070402)
GO:1990825 : sequence-specific mRNA binding
(https://www.ebi.ac.uk/QuickGO/term/GO:1990825)

GO - Biological Process

GO:0055114 : oxidation-reduction process
(https://www.ebi.ac.uk/QuickGO/term/GO:0055114)
GO:0051000 : positive regulation of nitric-oxide synthase activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0051000)
GO:0017148 : negative regulation of translation
(https://www.ebi.ac.uk/QuickGO/term/GO:0017148)
GO:0031103 : axon regeneration (https://www.ebi.ac.uk/QuickGO/term/GO:0031103)
GO:0046452 : dihydrofolate metabolic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0046452)
GO:0046655 : folic acid metabolic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0046655)
GO:0006730 : one-carbon metabolic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0006730)
GO:2000121 : regulation of removal of superoxide radicals
(https://www.ebi.ac.uk/QuickGO/term/GO:2000121)
GO:0000083 : regulation of transcription involved in G1/S transition of mitotic cell cycle
(https://www.ebi.ac.uk/QuickGO/term/GO:0000083)
GO:0031427 : response to methotrexate
(https://www.ebi.ac.uk/QuickGO/term/GO:0031427)
GO:0006729 : tetrahydrobiopterin biosynthetic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0006729)
GO:0046654 : tetrahydrofolate biosynthetic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0046654)
GO:0046653 : tetrahydrofolate metabolic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0046653)

GO - Cellular Component

GO:0005829 : cytosol (https://www.ebi.ac.uk/QuickGO/term/GO:0005829)
GO:0005739 : mitochondrion (https://www.ebi.ac.uk/QuickGO/term/GO:0005739)

Presumptive Null

Unknown (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^Unknown^#gephebase-summary-title)

Molecular Type

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

Aberration Type

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

Molecular Details of the Mutation

unknown

Experimental Evidence

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

Main Reference

Genomic analysis of local variation and recent evolution in Plasmodium vivax. (2016) (https://pubmed.ncbi.nlm.nih.gov/27348299)

Authors

Pearson RD; Amato R; Auburn S; Miotto O; Almagro-Garcia J; Amaratunga C; Suon S; Mao S; Noviyanti R; Trimarsanto H; Marfurt J; Anstey NM; William T; Boni MF; Dolecek C; Hien TT; White NJ; Michon P; Siba P; Tavul L; Harrison G; Barry A; Mueller I; Ferreira MU; Karunaweera N; Randrianarivelojosia M; Gao Q; Hubbart C; Hart L; Jeffery B; Drury E; Mead D; Kekre M; Campino S; Manske M; Cornelius VJ; MacInnis B; Rockett KA; Miles A; Rayner JC; Fairhurst RM; Nosten F; Price RN; Kwiatkowski DP

Abstract

The widespread distribution and relapsing nature of Plasmodium vivax infection present major challenges for the elimination of malaria. To characterize the genetic diversity of this parasite in individual infections and across the population, we performed deep genome sequencing of >200 clinical samples collected across the Asia-Pacific region and analyzed data on >300,000 SNPs and nine regions of the genome with large copy number variations. Individual infections showed complex patterns of genetic structure, with variation not only in the number of dominant clones but also in their level of relatedness and inbreeding. At the population level, we observed strong signals of recent evolutionary selection both in known drug resistance genes and at new loci, and these varied markedly between geographical locations. These findings demonstrate a dynamic landscape of local evolutionary adaptation in the parasite population and provide a foundation for genomic surveillance to guide effective strategies for control and elimination of P. vivax.

Additional References

RELATED GEPHE

Related Genes

5 (ABC transporter pvmrp1, Dihydropteroate synthase (pvdhps), Multidrug resistance protein 1 (pvmdr1), PVX_084940, PVX_101445) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^5855^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS

With strong evidence of recent selection in western Thailand. The signal of selection encompasses multiple genes such that we cannot be certain of the specific gene under selection. A noteworthy candidate also observed in selective sweeps in South America