

GEPHE SUMMARY

kelch 13 (K13) (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^kelch 13 (K13)^#gephebase-summary-title)	Gephebase Gene	GP00001388	GephelID
	Entry Status	Courtier	Main curator
Published			

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		
Plasmodium falciparum	Trait State in Taxon B		
Plasmodium falciparum	Ancestral State		
Taxon A	Taxonomic Status		
Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Intraspecific^#gephebase-summary-title)			
	Taxon A	Taxon B	
	Latin Name	Latin Name	
Plasmodium falciparum (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Plasmodium falciparum^#gephebase-summary-title)	Plasmodium falciparum (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Plasmodium falciparum^#gephebase-summary-title)		
malaria parasite P. falciparum	Common Name	Common Name	
Plasmodium (Laverania) falciparum; malaria parasite P. falciparum	Synonyms	Synonyms	
species	Rank	Rank	
cellular organisms; Eukaryota; Alveolata; Apicomplexa; Aconoidasida; Haemosporida; Plasmodiidae; Plasmodium; Plasmodium (Laverania)	Lineage	Lineage	
Plasmodium (Laverania) () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 418107)	Parent	Parent	
5833 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 5833)	NCBI Taxonomy ID	NCBI Taxonomy ID	
No	is Taxon A an Infraspecies?	is Taxon B an Infraspecies?	

GENOTYPIC CHANGE

PF13_0238	Generic Gene Name	UniProtKB Plasmodium falciparum A0A077LQB4 (http://www.uniprot.org/uniprot/A0A077LQB4)	
K13	Synonyms	GenebankID or UniProtKB 0	
-	String		
-	Sequence Similarities		
-	GO - Molecular Function		
-	GO - Biological Process		
GO:0051260 : protein homooligomerization (https://www.ebi.ac.uk/QuickGO/term/GO:0051260)	GO - Cellular Component		
-			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

Nonsynonymous

Molecular Details of the Mutation

M476I

Experimental Evidence

Candidate Gene (<https://www.gephebase.org/search-criteria?/and+Experimental+Evidence=%Candidate+Gene%#gephebase-summary-title>)

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	-	-	-

Main Reference

Drug resistance. K13-propeller mutations confer artemisinin resistance in Plasmodium falciparum clinical isolates. (2015) (<https://pubmed.ncbi.nlm.nih.gov/25502314>)

Authors

Straimer J; Gnädig NF; Witkowski B; Amaratunga C; Duru V; Ramadani AP; Dacheux M; Khim N; Zhang L; Lam S; Gregory PD; Urvoy FD; Mercereau-Puijalon O; Benoit-Vical F; Fairhurst RM; Ménard D; Fidock DA

Abstract

The emergence of artemisinin resistance in Southeast Asia imperils efforts to reduce the global malaria burden. We genetically modified the Plasmodium falciparum K13 locus using zinc-finger nucleases and measured ring-stage survival rates after drug exposure in vitro; these rates correlate with parasite clearance half-lives in artemisinin-treated patients. With isolates from Cambodia, where resistance first emerged, survival rates decreased from 13 to 49% to 0.3 to 2.4% after the removal of K13 mutations. Conversely, survival rates in wild-type parasites increased from ~0.6% to 2 to 29% after the insertion of K13 mutations. These mutations conferred elevated resistance to recent Cambodian isolates compared with that of reference lines, suggesting a contemporary contribution of additional genetic factors. Our data provide a conclusive rationale for worldwide K13-propeller sequencing to identify and eliminate artemisinin-resistant parasites.

Copyright © 2015, American Association for the Advancement of Science.

Additional References

RELATED GEPHE

Related Genes

6 (apicoplast ribosomal protein S10, chloroquine resistance transporter, ferredoxin, kelch 13, multidrug resistance protein 2, protein phosphatase) (<https://www.gephebase.org/search-criteria?/or+Taxon+ID=%5833%27/and+Trait=Xenobiotic+resistance/and+groupHaplotypes=true#gephebase-summary-title>)

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS

@GxG confirmed by in vitro test but effect also depends of genetic background