

GEPHE SUMMARY

	Gephebase Gene	GepheID
CYP6P9 cluster (CYP6P9a and CYP6P9b) (https://www.gephebase.org/search-criteria?/and+Gene=Gephebase=CYP6P9+cluster+(CYP6P9a+and+CYP6P9b)^#gephebase-summary-title)	GP00000208	
	Martin	Main curator
Published	Entry Status	

PHENOTYPIC CHANGE

	Trait Category		
Physiology (https://www.gephebase.org/search-criteria?/and+Trait=Category=Physiology^#gephebase-summary-title)	Trait		
Xenobiotic resistance (insecticide) (https://www.gephebase.org/search-criteria?/and+Trait=Xenobiotic+resistance+(insecticide)^#gephebase-summary-title)	Trait State in Taxon A		
Anopheles funestus - Southern Africa - sensitive to pyrethroids	Trait State in Taxon B		
Anopheles funestus - Southern Africa - resistant to pyrethroids	Ancestral State		
Taxon A	Taxonomic Status	Taxon B	
Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=Intraspecific^#gephebase-summary-title)			
Taxon A	Latin Name	Taxon B	Latin Name
Anopheles funestus (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=Anopheles+funestus^#gephebase-summary-title)	Common Name	Anopheles funestus (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=Anopheles+funestus^#gephebase-summary-title)	Common Name
African malaria mosquito	Synonyms	African malaria mosquito	Synonyms
African malaria mosquito; Anopheles funestus Giles, 1900	Rank	African malaria mosquito; Anopheles funestus Giles, 1900	Rank
species	Lineage	species	Lineage
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda; Insecta; Dicondylia; Pterygota; Neoptera; Holometabola; Diptera; Nematocera; Culicomorpha; Culicoidea; Culicidae; Anophelinae; Anopheles; Cellia; Myzomyia; funestus group; funestus subgroup	Parent	cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda; Insecta; Dicondylia; Pterygota; Neoptera; Holometabola; Diptera; Nematocera; Culicomorpha; Culicoidea; Culicidae; Anophelinae; Anopheles; Cellia; Myzomyia; funestus group; funestus subgroup	Parent
funestus subgroup () - (Rank: species subgroup) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=62323)	NCBI Taxonomy ID	funestus subgroup () - (Rank: species subgroup) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=62323)	NCBI Taxonomy ID
62324 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=62324)	is Taxon A an Intraspecies?	62324 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=62324)	is Taxon B an Intraspecies?
No		No	

GENOTYPIC CHANGE

	Generic Gene Name	UniProtKB Homo sapiens
CYP2C9	Synonyms	P11712 (http://www.uniprot.org/uniprot/P11712)
CPC9; CYP2C; CYP2C10; CYP11C9; P45011C9	String	GenebankID or UniProtKB
9606.ENSPP00000260682 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPP00000260682)	Sequence Similarities	ACA42438 (https://www.ncbi.nlm.nih.gov/nuccore/ACA42438)
Belongs to the cytochrome P450 family.	GO - Molecular Function	
GO:0016491 : oxidoreductase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0016491)		
GO:0020037 : heme binding (https://www.ebi.ac.uk/QuickGO/term/GO:0020037)		
GO:0005506 : iron ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005506)		
GO:0004497 : monooxygenase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0004497)		

GO:0034875 : caffeine oxidase activity
(<https://www.ebi.ac.uk/QuickGO/term/GO:0034875>)
GO:0016712 : oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, reduced flavin or flavoprotein as one donor, and incorporation of one atom of oxygen (<https://www.ebi.ac.uk/QuickGO/term/GO:0016712>)
GO:0008392 : arachidonic acid epoxygenase activity
(<https://www.ebi.ac.uk/QuickGO/term/GO:0008392>)
GO:0008144 : drug binding (<https://www.ebi.ac.uk/QuickGO/term/GO:0008144>)
GO:0008395 : steroid hydroxylase activity
(<https://www.ebi.ac.uk/QuickGO/term/GO:0008395>)

GO - Biological Process

GO:0055114 : oxidation-reduction process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0055114>)
GO:0042737 : drug catabolic process (<https://www.ebi.ac.uk/QuickGO/term/GO:0042737>)
GO:0017144 : drug metabolic process (<https://www.ebi.ac.uk/QuickGO/term/GO:0017144>)
GO:0019373 : epoxygenase P450 pathway
(<https://www.ebi.ac.uk/QuickGO/term/GO:0019373>)
GO:0042738 : exogenous drug catabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0042738>)
GO:0042759 : long-chain fatty acid biosynthetic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0042759>)
GO:0032787 : monocarboxylic acid metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0032787>)
GO:0016098 : monoterpene metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0016098>)
GO:0097267 : omega-hydroxylase P450 pathway
(<https://www.ebi.ac.uk/QuickGO/term/GO:0097267>)
GO:0070989 : oxidative demethylation
(<https://www.ebi.ac.uk/QuickGO/term/GO:0070989>)
GO:0006805 : xenobiotic metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006805>)
GO:0043603 : cellular amide metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0043603>)
GO:0006082 : organic acid metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006082>)
GO:0008202 : steroid metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0008202>)
GO:0019627 : urea metabolic process (<https://www.ebi.ac.uk/QuickGO/term/GO:0019627>)

GO - Cellular Component

GO:0005737 : cytoplasm (<https://www.ebi.ac.uk/QuickGO/term/GO:0005737>)
GO:0043231 : intracellular membrane-bounded organelle
(<https://www.ebi.ac.uk/QuickGO/term/GO:0043231>)
GO:0005789 : endoplasmic reticulum membrane
(<https://www.ebi.ac.uk/QuickGO/term/GO:0005789>)
GO:0031090 : organelle membrane (<https://www.ebi.ac.uk/QuickGO/term/GO:0031090>)

	Presumptive Null
Unknown (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^Unknown^#gephebase-summary-title)	
	Molecular Type
Cis-regulatory (https://www.gephebase.org/search-criteria?/and+Molecular Type=^Cis-regulatory^#gephebase-summary-title)	
	Aberration Type
Unknown (https://www.gephebase.org/search-criteria?/and+Aberration Type=^Unknown^#gephebase-summary-title)	
	Molecular Details of the Mutation
Cis-regulatory variation in CYP6P9b gene	
	Experimental Evidence
Candidate Gene (https://www.gephebase.org/search-criteria?/and+Experimental Evidence=^Candidate Gene^#gephebase-summary-title)	
	Main Reference
Directionally selected cytochrome P450 alleles are driving the spread of pyrethroid resistance in the major malaria vector Anopheles funestus. (2013) (https://pubmed.ncbi.nlm.nih.gov/23248325)	
	Authors
Riveron JM; Irving H; Ndula M; Barnes KG; Ibrahim SS; Paine MJ; Wondji CS	

Abstract

Pyrethroid insecticides are critical for malaria control in Africa. However, resistance to this insecticide class in the malaria vector *Anopheles funestus* is spreading rapidly across Africa, threatening the success of ongoing and future malaria control programs. The underlying resistance mechanisms driving the spread of this resistance in wild populations remain largely unknown. Here, we show that increased expression of two tandemly duplicated P450 genes, CYP6P9a and CYP6P9b, is the main mechanism driving pyrethroid resistance in Malawi and Mozambique, two southern African countries where this insecticide class forms the mainstay of malaria control. Genome-wide transcription analysis using microarray and quantitative RT-PCR consistently revealed that CYP6P9a and CYP6P9b are the two genes most highly overexpressed (>50-fold; $q < 0.01$) in permethrin-resistant mosquitoes. Transgenic expression of CYP6P9a and CYP6P9b in *Drosophila melanogaster* demonstrated that elevated expression of either of these genes confers resistance to both type I (permethrin) and type II (deltamethrin) pyrethroids. Functional characterization of recombinant CYP6P9b confirmed that this protein metabolized both type I (permethrin and bifenthrin) and type II (deltamethrin and Lambda-cyhalothrin) pyrethroids but not DDT. Variability analysis identified that a single allele of each of these genes is predominantly associated with pyrethroid resistance in field populations from both countries, which is suggestive of a single origin of this resistance that has since spread across the region. Urgent resistance management strategies should be implemented in this region to limit a further spread of this resistance and minimize its impact on the success of ongoing malaria control programs.

Additional References

Cis-regulatory CYP6P9b P450 variants associated with loss of insecticide-treated bed net efficacy against *Anopheles funestus*. (2019) (<https://pubmed.ncbi.nlm.nih.gov/31604938>)

3 (CYP6P9; CYP6P4 cluster, GSTe, resistance to dieldrin) (<https://www.gephebase.org/search-criteria?/or+Taxon ID=^62324^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title>)

No matches found.

EXTERNAL LINKS

COMMENTS