

GEPHE SUMMARY

para (kdr) (<a +para+(kdr)+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=">https://www.gephebase.org/search-criteria?/and+Gene Gephebase="+para (kdr)^#gephebase-summary-title)	Gephebase Gene	GP00002446	GepheID
Published	Entry Status	Courtier	Main curator

PHENOTYPIC CHANGE

Physiology (<a +physiology+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Trait+Category=">https://www.gephebase.org/search-criteria?/and+Trait Category="+Physiology^#gephebase-summary-title)	Trait Category
Xenobiotic resistance (insecticide) (<a +xenobiotic+resistance+(insecticide)+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Trait=">https://www.gephebase.org/search-criteria?/and+Trait="+Xenobiotic resistance (insecticide)^#gephebase-summary-title)	Trait
Aedes aegypti	Trait State in Taxon A
Aedes aegypti - resistant from Thailand	Trait State in Taxon B
Taxon A	Ancestral State
Intraspecific (<a +intraspecific+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=">https://www.gephebase.org/search-criteria?/and+Taxonomic Status="+Intraspecific^#gephebase-summary-title)	Taxonomic Status

Taxon A	Latin Name	Taxon B	Latin Name
Aedes aegypti (<a +aedes+aegypti+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="+Aedes aegypti^#gephebase-summary-title)	Aedes aegypti	Aedes aegypti (<a +aedes+aegypti+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="+Aedes aegypti^#gephebase-summary-title)	Aedes aegypti
yellow fever mosquito	Common Name	yellow fever mosquito	Common Name
Stegomyia aegypti; yellow fever mosquito; Aedes aegypti (Linnaeus, 1762)	Synonyms	Stegomyia aegypti; yellow fever mosquito; Aedes aegypti (Linnaeus, 1762)	Synonyms
species	Rank	species	Rank
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda; Insecta; Dicondylia; Pterygota; Neoptera; Holometabola; Diptera; Nematocera; Culicomorpha; Culicoidea; Culicidae; Culicinae; Aedini; Aedes; Stegomyia	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; Culicinae; Aedini; Aedes; Stegomyia	Lineage
Stegomyia () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=53541)	Parent	Stegomyia () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=53541)	Parent
7159 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=7159)	NCBI Taxonomy ID	7159 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=7159)	NCBI Taxonomy ID
No	is Taxon A an Intraspecies?	No	is Taxon B an Intraspecies?

GENOTYPIC CHANGE

para	Generic Gene Name	UniProtKB Drosophila melanogaster
bas; bss; CG9907; Dmel\CG9907; DmNav; DmNav1; DmNa[[v]]; DmNa[[V]]; DmNa[[v]]1; l(1)14Da; l(1)ESH548; lincRNA.S9469; Nav1; Occl; olfD; par; sbl; sbl-1; Shu; Shudderer	Synonyms	GenebankID or UniProtKB
7227.FBpp0303597 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=7227.FBpp0303597)	String	
Belongs to the sodium channel (TC 1.A.1.10) family. Para subfamily.	Sequence Similarities	
GO:0005509 : calcium ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005509)	GO - Molecular Function	
GO:0005244 : voltage-gated ion channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005244)		
GO:0005248 : voltage-gated sodium channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005248)		
GO:0005272 : sodium channel activity		

(<https://www.ebi.ac.uk/QuickGO/term/GO:0005272>)

GO - Biological Process

GO:0045433 : male courtship behavior, veined wing generated song production

(<https://www.ebi.ac.uk/QuickGO/term/GO:0045433>)

GO:0001666 : response to hypoxia (<https://www.ebi.ac.uk/QuickGO/term/GO:0001666>)

GO:0009612 : response to mechanical stimulus

(<https://www.ebi.ac.uk/QuickGO/term/GO:0009612>)

GO:0034765 : regulation of ion transmembrane transport

(<https://www.ebi.ac.uk/QuickGO/term/GO:0034765>)

GO:0035725 : sodium ion transmembrane transport

(<https://www.ebi.ac.uk/QuickGO/term/GO:0035725>)

GO:0007638 : mechanosensory behavior

(<https://www.ebi.ac.uk/QuickGO/term/GO:0007638>)

GO:0060078 : regulation of postsynaptic membrane potential

(<https://www.ebi.ac.uk/QuickGO/term/GO:0060078>)

GO - Cellular Component

GO:0005887 : integral component of plasma membrane

(<https://www.ebi.ac.uk/QuickGO/term/GO:0005887>)

GO:0001518 : voltage-gated sodium channel complex

(<https://www.ebi.ac.uk/QuickGO/term/GO:0001518>)

Mutation #1

Presumptive Null

No ([https://www.gephebase.org/search-criteria?/and+Presumptive Null="No"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Presumptive Null=))

Molecular Type

Coding ([https://www.gephebase.org/search-criteria?/and+Molecular Type="Coding"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Molecular Type=))

Aberration Type

SNP ([https://www.gephebase.org/search-criteria?/and+Aberration Type="SNP"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Aberration Type=))

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

V1016G

Experimental Evidence

Candidate Gene ([https://www.gephebase.org/search-criteria?/and+Experimental Evidence="Candidate Gene"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Experimental Evidence=))

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Val	Gly	1016

Main Reference

Additive effect of knockdown resistance mutations, S989P, V1016G and F1534C, in a heterozygous genotype conferring pyrethroid resistance in *Aedes aegypti* in Thailand. (2016)

(<https://pubmed.ncbi.nlm.nih.gov/27460671>)

Authors

Plernsub S; Saingamsook J; Yanola J; Lumjuan N; Tippawangkosol P; Sukontason K; Walton C; Somboon P

Abstract

Mutation in the voltage-gated sodium channel gene that results in knockdown resistance (kdr), is a major mechanism of pyrethroid resistance in several mosquito species. In *Aedes aegypti*, V1016G (occurring with and without S989P) and F1534C mutations are common and widely distributed throughout Asia. The G1016 allele is known to be associated with resistance to type I and II pyrethroids. The C1534 allele is primarily associated with resistance to type I pyrethroids and is known to be a recessive allele in conferring kdr.

We performed crossing experiments using a P989A/G1016 homozygous mutant strain (UPK-R), a C1534 homozygous mutant strain (PMD-R) and a pyrethroid susceptible strain (PMD) to determine the insecticide susceptibility of different genotypic hybrids. Allele-specific PCR methods were used to confirm the genotypes. Metabolic resistance caused by oxidative enzymes and esterase enzymes was ruled out by the addition of piperonyl butoxide (PBO) and bis(4-nitrophenyl)-phosphate, BNPP), respectively.

The median lethal concentration (LC50) of deltamethrin susceptibility of a S/P989A/G1016/F1534 double heterozygous hybrid from the UPK-R-PMD cross was 0.57 (95% CI: 0.51-0.63) µg/l(-1), which was about 12-fold lower than for UPK-R, 6.98 (6.10-8.04) µg/l(-1), and only about 4-fold greater than the susceptible PMD, 0.13 (0.12-0.15) µg/l(-1). This resistance returned to 0.08 (0.07-0.09) µg/l(-1) on the addition of PBO suggesting that the P989A/G1016 kdr alleles are recessive. The LC50 of the S/P989A/G1016/F1534 triple heterozygous hybrid was 3.58 (3.21-3.95) µg/l(-1), which was intermediate between that of the homozygous mutant genotypes, being 2-fold higher than the C1534 homozygote and 2-fold lower than the P989A/G1016 homozygote. These minor differences and the high LC50 values of the triple mutated heterozygote indicate there is some degree of functional equivalence of the P989A/G1016 and C1534 alleles in the heterozygote. Addition of PBO decreased the LC50 values by 2-fold, from 3.58 (3.21-3.95) to 1.52 (1.35-1.73) µg/l(-1), suggesting that oxidase enzymes play a partial role in resistance. The results are consistent with the median lethal time (LT50) of the triple mutated heterozygote against 0.05 µg deltamethrin paper. An adult susceptibility test also revealed that the triple mutated heterozygote was resistant to deltamethrin and permethrin.

The combination of the three kdr alleles in the triple mutated heterozygote, S/P989A/G1016/F1534, confers high resistance to pyrethroids. This heterozygous form is common in *Ae. aegypti* populations throughout Thailand and may have an adverse effect on the efficacy of a mosquito control program using insecticide-based approaches.

Additional References

Pyrethroid resistance in *Aedes aegypti* and *Aedes albopictus*: Important mosquito vectors of human diseases. (2016) (<https://pubmed.ncbi.nlm.nih.gov/27742355>)

Mutation #2

Presumptive Null

No ([https://www.gephebase.org/search-criteria?/and+Presumptive Null="No"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Presumptive Null=))

Molecular Type

Coding ([https://www.gephebase.org/search-criteria?/and+Molecular Type="Coding"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Molecular Type=))

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

Aberration Type

Nonsynonymous

SNP Coding Change

S989P

Molecular Details of the Mutation

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

Experimental Evidence

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Ser	Pro	989

Main Reference

Additive effect of knockdown resistance mutations, S989P, V1016G and F1534C, in a heterozygous genotype conferring pyrethroid resistance in *Aedes aegypti* in Thailand. (2016) (<https://pubmed.ncbi.nlm.nih.gov/27460671>)

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Additional References

Pyrethroid resistance in *Aedes aegypti* and *Aedes albopictus*: Important mosquito vectors of human diseases. (2016) (<https://pubmed.ncbi.nlm.nih.gov/27742355>)

Mutation #3

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

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

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

F1534C

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	Phe	Cys	1534

Main Reference

Additive effect of knockdown resistance mutations, S989P, V1016G and F1534C, in a heterozygous genotype conferring pyrethroid resistance in *Aedes aegypti* in Thailand. (2016) (<https://pubmed.ncbi.nlm.nih.gov/27460671>)

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Additional References

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RELATED GEPHE

Related Genes

4 (ABC4, CYP9J26, CYP9M6, resistance to dieldrin) (<https://www.gephebase.org/search-criteria?/or+Taxon ID=^7159^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gepbase-summary-title>)

Related Haplotypes

7 ([https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^para \(kdr\)^/and+Taxon ID=^7159^/or+Gene Gephebase=^para \(kdr\)^/and+Taxon ID=^7159^#gepbase-summary-title](https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^para (kdr)^/and+Taxon ID=^7159^/or+Gene Gephebase=^para (kdr)^/and+Taxon ID=^7159^#gepbase-summary-title))

EXTERNAL LINKS

COMMENTS

Additive effect of resistance mutations S989P V1016G and F1534C