## GEPHE SUMMARY

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

GepheID
GP00002446

Entry Status
Published

Main curator
Courtier

## 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
Aedes aegypti

Trait State in Taxon B
Aedes aegypti - resistant from Thailand

Ancestral State
Taxon A

Taxonomic Status
Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Intraspecific^#gephebase-summary-title)

### Taxon A

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

Common Name
yellow fever mosquito

Synonyms
Stegomyia aegypti; yellow fever mosquito; Aedes aegypti (Linnaeus, 1762)

Rank
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; Culicinae; Aedini; Aedes; Stegomyia

Parent
Stegomyia () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 53541 )

NCBI Taxonomy ID
7159 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 7159 )

is Taxon A an Infraspecies?
No

### Taxon B

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

Common Name
yellow fever mosquito

Synonyms
Stegomyia aegypti; yellow fever mosquito; Aedes aegypti (Linnaeus, 1762)

Rank
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; Culicinae; Aedini; Aedes; Stegomyia

Parent
Stegomyia () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 53541 )

NCBI Taxonomy ID
7159 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 7159 )

is Taxon B an Infraspecies?
No

## GENOTYPIC CHANGE

Generic Gene Name
para

Synonyms
bas; bss; CG9907; Dmel\CG9907; DmNav; DmNav1; DmNa[[v]]; DmNa[[V]]; DmNa[[v]]1; l(1)14Da; l(1)ESHS48; lincRNA.S9469; Nav1; Ocd; olfD; par; sbl; sbl-1; Shu; Shudderer

String
7227.FBpp0303597 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier= 7227.FBpp0303597 )

Sequence Similarities
Belongs to the sodium channel (TC 1.A.1.10) family. Para subfamily.

GO - Molecular Function
GO:0005509 : calcium ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005509)
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

UniProtKB Drosophila melanogaster
P35500 (http://www.uniprot.org/uniprot/P35500)

GenebankID or UniProtKB
()

(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)

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

V1016G

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 | 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 P989â€‰+â€‰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/P989â€‰+â€‰V/G1016â€‰+â€‰F/F1534 double heterozygous hybrid from the UPK-Râ€‰Ã—â€‰PMD cross was 0.57 (95Â % CI: 0.51-0.63) Î¼gl(-1), which was about 12-fold lower than for UPK-R, 6.98 (6.10-8.04) Î¼gl(-1), and only about 4-fold greater than the susceptible PMD, 0.13 (0.12-0.15) Î¼gl(-1). This resistance returned to 0.08 (0.07-0.09) Î¼gl(-1) on the addition of PBO suggesting that the P989â€‰+â€‰G1016 kdr alleles are recessive. The LC50 of the S/P989â€‰+â€‰V/G1016â€‰+â€‰F/C1534 triple heterozygous hybrid was 3.58 (3.21-3.95) Î¼gl(-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 P989â€‰+â€‰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 P989â€‰+â€‰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) Î¼gl(-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 0.05Â % 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/P989â€‰+â€‰V/G1016â€‰+â€‰F/C1534, 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)

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

S989P

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 | 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

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Additional References

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## RELATED GEPHE

Related Genes

4 (ABCB4, CYP9J26, CYP9M6, resistance to dieldrin) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^7159^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-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^#gephebase-summary-title)

## EXTERNAL LINKS

## COMMENTS

Additive effect of resistance mutations S989P V1016G and F1534C