GEPHE SUMMARY

Gephebase Gene
CYP6P9; CYP6P4 cluster (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^CYP6P9; CYP6P4 cluster^#gephebase-summary-title)

Entry Status
Published

GepheID
GP00000209

Main curator
Martin

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 - sensitive

Trait State in Taxon B
Anopheles funestus - 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
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; Anopheles funestus Giles, 1900

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; 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
62324 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 62324)

is Taxon A an Infraspecies?
No

Taxon B

Latin 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; Anopheles funestus Giles, 1900

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; 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
62324 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 62324)

is Taxon B an Infraspecies?
No

GENOTYPIC CHANGE

Generic Gene Name
-

Synonyms
-

String
-

Sequence Similarities
Belongs to the cytochrome P450 family.

GO - Molecular Function
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:0016705 : oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen (https://www.ebi.ac.uk/QuickGO/term/GO:0016705)

GO - Biological Process
-

UniProtKB Anopheles funestus
Q2YH43 (http://www.uniprot.org/uniprot/Q2YH43)

GenebankID or UniProtKB
AY729661 (https://www.ncbi.nlm.nih.gov/nuccore/AY729661)

GO:0016021 : integral component of membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0016021)

Mutation #1

Presumptive Null

No (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^No^#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

unknown; but 10-30 fold differences in expression levels between phenotypes

Experimental Evidence

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

Main Reference

Two duplicated P450 genes are associated with pyrethroid resistance in Anopheles funestus, a major malaria vector. (2009) (https://pubmed.ncbi.nlm.nih.gov/19196725)

Authors

Wondji CS; Irving H; Morgan J; Lobo NF; Collins FH; Hunt RH; Coetzee M; Hemingway J; Ranson H

Abstract

Pyrethroid resistance in Anopheles funestus is a potential obstacle to malaria control in Africa. Tools are needed to detect resistance in field populations. We have been using a positional cloning approach to identify the major genes conferring pyrethroid resistance in this vector. A quantitative trait locus (QTL) named rp1 explains 87% of the genetic variance in pyrethroid susceptibility in two families from reciprocal crosses between susceptible and resistant strains. Two additional QTLs of minor effect, rp2 and rp3, were also detected. We sequenced a 120-kb BAC clone spanning the rp1 QTL and identified 14 protein-coding genes and one putative pseudogene. Ten of the 14 genes encoded cytochrome P450s, and expression analysis indicated that four of these P450s were differentially expressed between susceptible and resistant strains. Furthermore, two of these genes, CYP6P9 and CYP6P4, which are 25 and 51 times overexpressed in resistant females, are tandemly duplicated in the BAC clone as well as in laboratory and field samples, suggesting that P450 gene duplication could contribute to pyrethroid resistance in An. funestus. Single nucleotide polymorphisms (SNPs) were identified within CYP6P9 and CYP6P4, and genotyping of the progeny of the genetic crosses revealed a maximum penetrance value f(2) = 1, confirming that these SNPs are valid resistance markers in the laboratory strains. This serves as proof of principle that a DNA-based diagnostic test could be designed to trace metabolic resistance in field populations. This will be a major advance for insecticide resistance management in malaria vectors, which requires the early detection of resistance alleles.

Additional References

A cytochrome P450 allele confers pyrethroid resistance on a major African malaria vector, reducing insecticide-treated bednet efficacy. (2019) (https://pubmed.ncbi.nlm.nih.gov/30894503)

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

Site-directed mutagenesis and functional analyses demonstrates that three amino acid changes (Val109Ile, Asp335Glu and Asn384Ser) from the resistant allele of CYP6P9b were key pyrethroid resistance mutations inducing high metabolic efficiency.

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Val	Ile	109

Main Reference

Adaptation by copy number variation increases insecticide resistance in the fall armyworm. (2020) (https://pubmed.ncbi.nlm.nih.gov/33184418)

Authors

Gimenez S; Abdelgaffar H; Goff GL; Hilliou F; Blanco CA; HÃ¤nniger S; Bretaudeau A; Legeai F; NÃ¨gre N; Jurat-Fuentes JL; d'AlenÃ§on E; Nam K

Abstract

Understanding the genetic basis of insecticide resistance is a key topic in agricultural ecology. The adaptive evolution of multi-copy detoxification genes has been interpreted as a cause of insecticide resistance, yet the same pattern can also be generated by the adaptation to host-plant defense toxins. In this study, we tested in the fall armyworm, Spodoptera frugiperda (Lepidoptera: Noctuidae), if adaptation by copy number variation caused insecticide resistance in two geographically distinct populations with different levels of resistance and the two host-plant strains. We observed a significant allelic differentiation of genomic copy number variations between the two geographic populations, but not between host-plant strains. A locus with positively selected copy number variation included a CYP gene cluster. Toxicological tests supported a central role for CYP enzymes in deltamethrin resistance. Our results indicate that copy number variation of detoxification genes might be responsible for insecticide resistance in fall armyworm and that evolutionary forces causing insecticide resistance could be independent of host-plant adaptation.

Additional References

A cytochrome P450 allele confers pyrethroid resistance on a major African malaria vector, reducing insecticide-treated bednet efficacy. (2019) (https://pubmed.ncbi.nlm.nih.gov/30894503)

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

Site-directed mutagenesis and functional analyses demonstrates that three amino acid changes (Val109Ile, Asp335Glu and Asn384Ser) from the resistant allele of CYP6P9b were key pyrethroid resistance mutations inducing high metabolic efficiency.

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Asp	Glu	335

Main Reference

Adaptation by copy number variation increases insecticide resistance in the fall armyworm. (2020) (https://pubmed.ncbi.nlm.nih.gov/33184418)

Authors

Gimenez S; Abdelgaffar H; Goff GL; Hilliou F; Blanco CA; HÃ¤nniger S; Bretaudeau A; Legeai F; NÃ¨gre N; Jurat-Fuentes JL; d'AlenÃ§on E; Nam K

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Additional References

A cytochrome P450 allele confers pyrethroid resistance on a major African malaria vector, reducing insecticide-treated bednet efficacy. (2019) (https://pubmed.ncbi.nlm.nih.gov/30894503)

Mutation #4

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

Site-directed mutagenesis and functional analyses demonstrates that three amino acid changes (Val109Ile, Asp335Glu and Asn384Ser) from the resistant allele of CYP6P9b were key pyrethroid resistance mutations inducing high metabolic efficiency.

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Asn	Ser	384

Main Reference

Adaptation by copy number variation increases insecticide resistance in the fall armyworm. (2020) (https://pubmed.ncbi.nlm.nih.gov/33184418)

Authors

Gimenez S; Abdelgaffar H; Goff GL; Hilliou F; Blanco CA; HÃ¤nniger S; Bretaudeau A; Legeai F; NÃ¨gre N; Jurat-Fuentes JL; d'AlenÃ§on E; Nam K

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Additional References

A cytochrome P450 allele confers pyrethroid resistance on a major African malaria vector, reducing insecticide-treated bednet efficacy. (2019) (https://pubmed.ncbi.nlm.nih.gov/30894503)
RNAseq-based gene expression profiling of the Anopheles funestus pyrethroid-resistant strain FUMOZ highlights the predominant role of the duplicated CYP6P9a/b cytochrome P450s. (2022) (https://pubmed.ncbi.nlm.nih.gov/34718535)

Mutation #5

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

Recombinant enzymes from CYP6P9a resistant allele metabolize Type I (permethrin and bifenthrin) and Type II (deltamethrin and Î»-cyhalothrin) pyrethroids wherease only very low and non-significant depletions (not more than 20%) are obtained with proteins from the susceptible allele.

Experimental Evidence

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

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

Main Reference

Adaptation by copy number variation increases insecticide resistance in the fall armyworm. (2020) (https://pubmed.ncbi.nlm.nih.gov/33184418)

Authors

Gimenez S; Abdelgaffar H; Goff GL; Hilliou F; Blanco CA; HÃ¤nniger S; Bretaudeau A; Legeai F; NÃ¨gre N; Jurat-Fuentes JL; d'AlenÃ§on E; Nam K

Abstract

Understanding the genetic basis of insecticide resistance is a key topic in agricultural ecology. The adaptive evolution of multi-copy detoxification genes has been interpreted as a cause of insecticide resistance, yet the same pattern can also be generated by the adaptation to host-plant defense toxins. In this study, we tested in the fall armyworm, Spodoptera frugiperda (Lepidoptera: Noctuidae), if adaptation by copy number variation caused insecticide resistance in two geographically distinct populations with different levels of resistance and the two host-plant strains. We observed a significant allelic differentiation of genomic copy number variations between the two geographic populations, but not between host-plant strains. A locus with positively selected copy number variation included a CYP gene cluster. Toxicological tests supported a central role for CYP enzymes in deltamethrin resistance. Our results indicate that copy number variation of detoxification genes might be responsible for insecticide resistance in fall armyworm and that evolutionary forces causing insecticide resistance could be independent of host-plant adaptation.

Additional References

A cytochrome P450 allele confers pyrethroid resistance on a major African malaria vector, reducing insecticide-treated bednet efficacy. (2019) (https://pubmed.ncbi.nlm.nih.gov/30894503)

RELATED GEPHE

Related Genes

3 (CYP6P9 cluster (CYP6P9a and CYP6P9b), GSTe, resistance to dieldrin) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^62324^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS

Cluster of paralogous genes