Gephebase Gene GephelD GP00000207 cyp6g1 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^cyp6g1^#gephebase-summary-title) Main curator Entry Status Martin **Published** PHENOTYPIC CHANGE Trait Category Physiology (https://www.gephebase.org/search-criteria?/and+Trait  ${\it Category="Physiology" \#gephebase-summary-title)}$ Trait Xenobiotic resistance (insecticide) (https://www.gephebase.org/searchcriteria?/and+Trait=^Xenobiotic resistance (insecticide)^#gephebase-summary-title) Trait State in Taxon A Drosophila melanogaster - susceptible - rare allele with no Accord insertion; only reported in some African populations Trait State in Taxon B Drosophila melanogaster - resistant 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 Drosophila melanogaster Drosophila melanogaster  $(https://www.gephebase.org/search-criteria?/and+Taxon\ and\ Synonyms=^Drosophila$ (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Drosophila melanogaster^#gephebase-summary-title) melanogaster^#gephebase-summary-title) Common Name Common Name fruit fly fruit fly Synonyms Synonyms Sophophora melanogaster; fruit fly; Drosophila melanogaster Meigen, 1830; Sophophora Sophophora melanogaster; fruit fly; Drosophila melanogaster Meigen, 1830; Sophophora melanogaster (Meigen, 1830); Drosophila melangaster melanogaster (Meigen, 1830); Drosophila melangaster Rank Rank species species cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda; Insecta; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda; Insecta; Dicondylia; Pterygota; Neoptera; Holometabola; Diptera; Brachycera; Muscomorpha; Dicondylia; Pterygota; Neoptera; Holometabola; Diptera; Brachycera; Muscomorpha; Eremoneura; Cyclorrhapha; Schizophora; Acalyptratae; Ephydroidea; Drosophilidae; Eremoneura; Cyclorrhapha; Schizophora; Acalyptratae; Ephydroidea; Drosophilidae; Drosophilinae; Drosophilini; Drosophila; Sophophora; melanogaster group; melanogaster Drosophilinae; Drosophilini; Drosophila; Sophophora; melanogaster group; melanogaster subgroup subgroup Parent Parent melanogaster subgroup () - (Rank: species subgroup) melanogaster subgroup () - (Rank: species subgroup) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 32351 ) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 32351 ) NCBI Taxonomy ID NCBI Taxonomy ID (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 7227 ) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 7227 ) is Taxon B an Infraspecies? is Taxon A an Infraspecies? No Nο

## **GENOTYPIC CHANGE**

Generic Gene Name UniProtKB Drosophila melanogaster Cyp6g1 Q9V674 (http://www.uniprot.org/uniprot/Q9V674) Synonyms GenebankID or UniProtKB 6g1; an on-WO 03 02 52 23.16; an on-WO 03 02 52 23.17; CG 84 53; Cyp 6-like; cyp 6g1; Cyp 6DQ539136 (https://www.ncbi.nlm.nih.gov/nuccore/DQ539136) CYP6g1; CYP6G1; Cyp6gl; DDT-R; Dmel-Cyp6g1; Dmel\CG8453; RDDT; RI; RI[DDT]; RI[II]; Rst(2)DDT; CYP6-like String 7227.FBpp0087100

Belongs to the cytochrome P450 family.

GO - Molecular Function

Sequence Similarities

GO:0020037 : heme binding (https://www.ebi.ac.uk/QuickGO/term/GO:0020037)

 $(http://string-db.org/newstring\_cgi/show\_network\_section.pl?identifier=7227.FBpp0087100$ 

 $GO:0005506: iron\ ion\ binding\ (https://www.ebi.ac.uk/QuickGO/term/GO:0005506)$ 

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

GO:0046680: response to DDT (https://www.ebi.ac.uk/QuickGO/term/GO:0046680)  $GO:0017085: response \ to \ insecticide \ (https://www.ebi.ac.uk/QuickGO/term/GO:0017085)$ 

GO:0046701: insecticide catabolic process

(https://www.ebi.ac.uk/QuickGO/term/GO:0046701)

GO:0046689 : response to mercury ion

(https://www.ebi.ac.uk/QuickGO/term/GO:0046689) GO:0046683: response to organophosphorus (https://www.ebi.ac.uk/QuickGO/term/GO:0046683)

GO - Cellular Component

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)

Mutation #1

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

Molecular Type

Presumptive Null

Cis-regulatory (https://www.gephebase.org/search-criteria?/and+Molecular Type=^Cis-regulatory^#gephebase-summary-title)

Aberration Type

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

Insertion Size

100-999 bp

Molecular Details of the Mutation

Insertion of 491 base pairs presenting homology to the long terminal repeat of an Accord transposable element 291bp upstream of the Cyp6g1 transcription start site

Experimental Evidence

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

Main Reference

Cis-regulatory elements in the Accord retrotransposon result in tissue-specific expression of the Drosophila melanogaster insecticide resistance gene Cyp6g1. (2007) (https://pubmed.ncbi.nlm.nih.gov/17179088)

Authors

Chung H; Bogwitz MR; McCart C; Andrianopoulos A; Ffrench-Constant RH; Batterham P; Daborn PJ

Abstract

Transposable elements are a major mutation source and powerful agents of adaptive change. Some transposable element insertions in genomes increase to a high frequency because of the selective advantage the mutant phenotype provides. Cyp6g1-mediated insecticide resistance in Drosophila melanogaster is due to the upregulation of the cytochrome P450 gene Cyp6g1, leading to the resistance to a variety of insecticide classes. The upregulation of Cyp6g1 is correlated with the presence of the long terminal repeat (LTR) of an Accord retrotransposon inserted 291bp upstream of the Cyp6g1 transcription start site. This resistant allele (DDT-R) is currently at a high frequency in D. melanogaster populations around the world. Here, we characterize the spatial expression of Cyp6g1 in insecticide-resistant and -susceptible strains. We show that the Accord LTR insertion is indeed the resistance-associated mutation and demonstrate that the Accord LTR carries regulatory sequences that increase the expression of Cyp6g1 in tissues important for detoxification, the midgut, Malpighian tubules, and the fat body. This study provides a significant example of how changes in tissue-specific gene expression caused by transposable-element insertions can contribute to adaptation.

Additional References

Mutation #2

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

Gene Amplification (https://www.gephebase.org/search-criteria?/and+Molecular Type=^Gene Amplification^#gephebase-summary-title)

Molecular Type

 $Insertion \ (https://www.gephebase.org/search-criteria?/and+Aberration \ Type=^lnsertion^{\#gephebase-summary-title})$ 

Aberration Type Insertion Size

1-10 kb

Molecular Details of the Mutation

duplication of the Cyp6g1 locus with insertion of the Accord element in both promoters (allele AA)

Experimental Evidence

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

Main Reference

Copy number variation and transposable elements feature in recent, ongoing adaptation at the Cyp6g1 locus. (2010) (https://pubmed.ncbi.nlm.nih.gov/20585622)

Authors

 $Schmidt\ JM;\ Good\ RT;\ Appleton\ B;\ Sherrard\ J;\ Raymant\ GC;\ Bogwitz\ MR;\ Martin\ J;\ Daborn\ PJ;\ Goddard\ ME;\ Batterham\ P;\ Robin\ C$ 

The increased transcription of the Cyp6g1 gene of Drosophila melanogaster, and consequent resistance to insecticides such as DDT, is a widely cited example of adaptation mediated by cis-regulatory change. A fragment of an Accord transposable element inserted upstream of the Cyp6g1 gene is causally associated with resistance and has spread to high frequencies in populations around the world since the 1940s. Here we report the existence of a natural allelic series at this locus of D. melanogaster, involving copy number variation of Cyp6g1, and two additional transposable element insertions (a P and an HMS-Beagle). We provide evidence that this genetic variation underpins phenotypic variation, as the more derived the allele, the greater the level of DDT resistance. Tracking the spatial and temporal patterns of allele frequency changes indicates that the multiple steps of the allelic series are adaptive. Further, a DDT association study shows that the most resistant allele, Cyp6g1-[BP], is greatly enriched in the top 5% of the phenotypic distribution and accounts for approximately 16% of the underlying phenotypic variation in resistance to DDT. In contrast, copy number variation for another candidate resistance gene, Cyp12d1, is not associated with resistance. Thus the Cyp6g1 locus is a major contributor to DDT resistance in field populations, and evolution at this locus features multiple adaptive steps occurring in rapid succession.

Additional References

Mutation #3

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

Presumptive Null

Molecular Type

 $Insertion \ (https://www.gephebase.org/search-criteria?/and+Aberration \ Type=^lnsertion^\#gephebase-summary-title)$ 

 $Cis-regulatory \ (https://www.gephebase.org/search-criteria?/and+Molecular\ Type=^Cis-regulatory^\#gephebase-summary-title)$ 

Aberration Type

Insertion Size

1-10 kb

Molecular Details of the Mutation

insertion of a HMS-Beagle element in one of the two Accord element (allele AB derived from allele AA)

Experimental Evidence

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

Main Reference

Copy number variation and transposable elements feature in recent, ongoing adaptation at the Cyp6q1 locus. (2010) (https://pubmed.ncbi.nlm.nih.gov/20585622)

Authors

Schmidt JM; Good RT; Appleton B; Sherrard J; Raymant GC; Bogwitz MR; Martin J; Daborn PJ; Goddard ME; Batterham P; Robin C

**Abstract** 

The increased transcription of the Cyp6g1 gene of Drosophila melanogaster, and consequent resistance to insecticides such as DDT, is a widely cited example of adaptation mediated by cis-regulatory change. A fragment of an Accord transposable element inserted upstream of the Cyp6g1 gene is causally associated with resistance and has spread to high frequencies in populations around the world since the 1940s. Here we report the existence of a natural allelic series at this locus of D. melanogaster, involving copy number variation of Cyp6g1, and two additional transposable element insertions (a P and an HMS-Beagle). We provide evidence that this genetic variation underpins phenotypic variation, as the more derived the allele, the greater the level of DDT resistance. Tracking the spatial and temporal patterns of allele frequency changes indicates that the multiple steps of the allelic series are adaptive. Further, a DDT association study shows that the most resistant allele, Cyp6g1-[BP], is greatly enriched in the top 5% of the phenotypic distribution and accounts for approximately 16% of the underlying phenotypic variation in resistance to DDT. In contrast, copy number variation for another candidate resistance gene, Cyp12d1, is not associated with resistance. Thus the Cyp6g1 locus is a major contributor to DDT resistance in field populations, and evolution at this locus features multiple adaptive steps occurring in rapid succession.

Additional References

Mutation #4

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

Presumptive Null

 $Cis-regulatory \ (https://www.gephebase.org/search-criteria?/and+Molecular\ Type=^Cis-regulatory^\#gephebase-summary-title)$ 

Molecular Type

 $Insertion \ (https://www.gephebase.org/search-criteria?/and+Aberration \ Type=`lnsertion`\#gephebase-summary-title)$ 

Aberration Type

Insertion Size

1-10 kb

Molecular Details of the Mutation

insertion of a P element in one of the two Cyp6g1 copies (allele BP derived from allele AB). Allele BP contains two copies of Cyp6g1 both with the Accord insertion,; one of the Accord contains the HMS-Beagle element and the other the P-element.

Experimental Evidence

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

Main Reference

Copy number variation and transposable elements feature in recent, ongoing adaptation at the Cyp6g1 locus. (2010) (https://pubmed.ncbi.nlm.nih.gov/20585622)

Authors

Schmidt JM; Good RT; Appleton B; Sherrard J; Raymant GC; Bogwitz MR; Martin J; Daborn PJ; Goddard ME; Batterham P; Robin C

Abstract

The increased transcription of the Cyp6g1 gene of Drosophila melanogaster, and consequent resistance to insecticides such as DDT, is a widely cited example of adaptation mediated by cis-regulatory change. A fragment of an Accord transposable element inserted upstream of the Cyp6g1 gene is causally associated with resistance and has spread to high frequencies in populations around the world since the 1940s. Here we report the existence of a natural allelic series at this locus of D. melanogaster, involving copy number variation of Cyp6g1, and two additional transposable element insertions (a P and an HMS-Beagle). We provide evidence that this genetic variation underpins phenotypic variation, as the more derived the allele, the greater the level of DDT resistance. Tracking the spatial and temporal patterns of allele frequency changes indicates that the multiple steps of the allelic series are adaptive. Further, a DDT association study shows that the most resistant allele, Cyp6g1-[BP], is greatly enriched in the top 5% of the phenotypic distribution and accounts for approximately 16% of the underlying phenotypic variation in resistance to DDT. In contrast, copy number variation for another candidate resistance gene, Cyp12d1, is not associated with resistance. Thus the Cyp6g1 locus is a major contributor to DDT resistance in field populations, and evolution at this locus features multiple adaptive steps occurring in rapid succession.

Additional References

## **RELATED GEPHE**

Related Genes

19 (Acetylcholinesterase (Ace-2), alcohol dehydrogenase (Adh), Aldehyde dehydrogenase (Aldh), CG11699, Cyp12d1, Cyp28d1, Cyp28d1, Cyp28d2, cyp6d2, glutamate-gated chloride channel (GluCl), GSS (glutathione synthetase), GSTE1-E10 cluster, kin of irre (kire), para (kdr), PHGPx, resistance to dieldrin, RnrS, SOD1, Ugt86Dd, CHKov1) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^7227^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title)

No matches found.

Related Haplotypes

## COMMENTS

@TE @SuccessiveMutations @SelectiveSweep - http://flybase.org/reports/FBal0014805