GEPHE SUMMARY

Gephebase Gene

cyp6d2 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^cyp6d2^#gephebase-summary-title)

Entry Status

Published

GepheID

GP00001984

Main curator

Courtier

PHENOTYPIC CHANGE

Trait Category

Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Physiology^#gephebase-summary-title)

Trait

Xenobiotic resistance (chemotherapeutic agent, camptothecin) (https://www.gephebase.org/search-criteria?/and+Trait=^Xenobiotic resistance (chemotherapeutic agent, camptothecin)^#gephebase-summary-title)

Trait State in Taxon A

Drosophila melanogaster

Trait State in Taxon B

Drosophila melanogaster - more sensitive to camptothecin - no phenotypic effect with the camptothecin analog topotecan or with ionizing radiation

Ancestral State

Taxon A

Taxonomic Status

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

Taxon A

Latin Name

Drosophila melanogaster (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Drosophila melanogaster^#gephebase-summary-title)

Common Name

fruit fly

Synonyms

Sophophora melanogaster; fruit fly; Drosophila melanogaster Meigen, 1830; Sophophora melanogaster (Meigen, 1830); Drosophila melangaster

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda; Insecta; Dicondylia; Pterygota; Neoptera; Holometabola; Diptera; Brachycera; Muscomorpha; Eremoneura; Cyclorrhapha; Schizophora; Acalyptratae; Ephydroidea; Drosophilidae; Drosophilinae; Drosophilini; Drosophila; Sophophora; melanogaster group; melanogaster subgroup

Parent

melanogaster subgroup () - (Rank: species subgroup) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 32351)

NCBI Taxonomy ID

7227 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 7227)

is Taxon A an Infraspecies?

No

Taxon B

Latin Name

Drosophila melanogaster (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Drosophila melanogaster^#gephebase-summary-title)

Common Name

fruit fly

Synonyms

Sophophora melanogaster; fruit fly; Drosophila melanogaster Meigen, 1830; Sophophora melanogaster (Meigen, 1830); Drosophila melangaster

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda; Insecta; Dicondylia; Pterygota; Neoptera; Holometabola; Diptera; Brachycera; Muscomorpha; Eremoneura; Cyclorrhapha; Schizophora; Acalyptratae; Ephydroidea; Drosophilidae; Drosophilinae; Drosophilini; Drosophila; Sophophora; melanogaster group; melanogaster subgroup

Parent

melanogaster subgroup () - (Rank: species subgroup) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 32351)

NCBI Taxonomy ID

7227 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 7227)

is Taxon B an Infraspecies?

No

GENOTYPIC CHANGE

Generic Gene Name

Cyp6g2

Synonyms

6g2; CG8859; Cyp6G2; Dmel\CG8859

String

7227.FBpp0087117 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier= 7227.FBpp0087117)

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)

UniProtKB Drosophila melanogaster

Q9V675 (http://www.uniprot.org/uniprot/Q9V675)

GenebankID or UniProtKB

()

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 - Cellular Component

GO:0005789 : endoplasmic reticulum membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005789)

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

N438T (A22652974C) and N439T (A22652978G) - exact causing mutation(s) not identified - semiquantitative RT-PCR revealed that this mutant produces little to no Cyp6d2 transcript. The mutation is thus also cis-regulatory.

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	-	-	-

Main Reference

Common variants of Drosophila melanogaster Cyp6d2 cause camptothecin sensitivity and synergize with loss of Brca2. (2013) (https://pubmed.ncbi.nlm.nih.gov/23316441)

Authors

Thomas AM; Hui C; South A; McVey M

Abstract

Many chemotherapeutic agents selectively target rapidly dividing cells, including cancer cells, by causing DNA damage that leads to genome instability and cell death. We used Drosophila melanogaster to study how mutations in key DNA repair genes affect an organism's response to chemotherapeutic drugs. In this study, we focused on camptothecin and its derivatives, topotecan and irinotecan, which are type I topoisomerase inhibitors that create DNA double-strand breaks in rapidly dividing cells. Here, we describe two polymorphisms in Drosophila Cyp6d2 that result in extreme sensitivity to camptothecin but not topotecan or irinotecan. We confirmed that the sensitivity was due to mutations in Cyp6d2 by rescuing the defect with a wild-type copy of Cyp6d2. In addition, we showed that combining a cyp6d2 mutation with mutations in Drosophila brca2 results in extreme sensitivity to camptothecin. Given the frequency of the Cyp6d2 polymorphisms in publcly available Drosophila stocks, our study demonstrates the need for caution when interpreting results from drug sensitivity screens in Drosophila and other model organisms. Furthermore, our findings illustrate how genetic background effects can be important when determining the efficacy of chemotherapeutic agents in various DNA repair mutants.

Additional References

RELATED GEPHE

Related Genes

19 (Acetylcholinesterase (Ace-2), alcohol dehydrogenase (Adh), Aldehyde dehydrogenase (Aldh), CG11699, Cyp12d1, Cyp28d1, Cyp28d1-Cyp28d2, cyp6g1, 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)

Related Haplotypes

1 (https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^cyp6d2^/and+Taxon ID=^7227^/or+Gene Gephebase=^cyp6d2^/and+Taxon ID=^7227^#gephebase-summary-title)

EXTERNAL LINKS

COMMENTS

This polymorphism is present in multiple lines - http://flybase.org/reports/FBal0282693 @Cis-RegulatoryInCodingRegion @ProbablyMultiNucleotideMutation