

GEPHE SUMMARY

<p>cyp6d2 (https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=cyp6d2#gephebase-summary-title)</p> <p>Published</p>	<p>Gephebase Gene</p> <p>Entry Status</p>	<p>GP00001984</p> <p>Courtier</p>	<p>GepheID</p> <p>Main curator</p>
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PHENOTYPIC CHANGE

<p>Physiology (https://www.gephebase.org/search-criteria?/and+Trait+Category=Physiology#gephebase-summary-title)</p> <p>Xenobiotic resistance (chemotherapeutic agent, camptothecin) (https://www.gephebase.org/search-criteria?/and+Trait=Xenobiotic+resistance(chemotherapeutic+agent,+camptothecin)#gephebase-summary-title)</p> <p>Drosophila melanogaster</p> <p>Drosophila melanogaster - more sensitive to camptothecin - no phenotypic effect with the camptothecin analog topotecan or with ionizing radiation</p> <p>Taxon A</p> <p>Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=Intraspecific#gephebase-summary-title)</p>	<p>Trait Category</p> <p>Trait</p> <p>Trait State in Taxon A</p> <p>Trait State in Taxon B</p> <p>Ancestral State</p> <p>Taxonomic Status</p>	<p>Drosophila melanogaster</p> <p>Drosophila melanogaster</p> <p>fruit fly</p> <p>Sophophora melanogaster; fruit fly; Drosophila melanogaster Meigen, 1830; Sophophora melanogaster (Meigen, 1830); Drosophila melangaster</p> <p>species</p> <p>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; Acalyptera; Ephydroidea; Drosophilidae; Drosophilinae; Drosophilini; Drosophila; Sophophora; melanogaster group; melanogaster subgroup</p> <p>melanogaster subgroup () - (Rank: species subgroup) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=32351)</p> <p>7227 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=7227)</p> <p>No is Taxon A an Intraspecies?</p>	<p>Taxon A</p> <p>Latin Name</p> <p>Common Name</p> <p>Synonyms</p> <p>Rank</p> <p>Lineage</p> <p>Parent</p> <p>NCBI Taxonomy ID</p>	<p>Drosophila melanogaster</p> <p>Drosophila melanogaster</p> <p>fruit fly</p> <p>Sophophora melanogaster; fruit fly; Drosophila melanogaster Meigen, 1830; Sophophora melanogaster (Meigen, 1830); Drosophila melangaster</p> <p>species</p> <p>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; Acalyptera; Ephydroidea; Drosophilidae; Drosophilinae; Drosophilini; Drosophila; Sophophora; melanogaster group; melanogaster subgroup</p> <p>melanogaster subgroup () - (Rank: species subgroup) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=32351)</p> <p>7227 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=7227)</p> <p>No is Taxon B an Intraspecies?</p>	<p>Taxon B</p> <p>Latin Name</p> <p>Common Name</p> <p>Synonyms</p> <p>Rank</p> <p>Lineage</p> <p>Parent</p> <p>NCBI Taxonomy ID</p>
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GENOTYPIC CHANGE

<p>Cyp6g2</p> <p>6g2; CG8859; Cyp6G2; Dmel\CG8859</p> <p>7227.FBpp0087117 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=7227.FBpp0087117)</p> <p>Belongs to the cytochrome P450 family.</p> <p>GO:0020037 : heme binding (https://www.ebi.ac.uk/QuickGO/term/GO:0020037)</p> <p>GO:0005506 : iron ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005506)</p>	<p>Generic Gene Name</p> <p>Synonyms</p> <p>String</p> <p>Sequence Similarities</p> <p>GO - Molecular Function</p>	<p>Q9V675 (http://www.uniprot.org/uniprot/Q9V675)</p> <p>()</p>	<p>UniProtKB Drosophila melanogaster</p> <p>GenebankID or UniProtKB</p>
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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 publicly 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>

