

GEPHE SUMMARY

	Gephebase Gene	GephelD
GSTE1-E10 cluster (#gephebase-summary-title)	GP00000419	
	Entry Status	Main curator
Published	Martin	

PHENOTYPIC CHANGE

	Trait Category	
Physiology (#gephebase-summary-title)	Trait	
Xenobiotic resistance (drug) (https://www.gephebase.org/search-criteria/?and+Trait=%Xenobiotic+resistance+(drug) #gephebase-summary-title)	Trait State in Taxon A	
Drosophila melanogaster DSRP	Trait State in Taxon B	
Drosophila melanogaster DSRP	Ancestral State	
Data not curated	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 (#gephebase-summary-title))	Drosophila melanogaster (#gephebase-summary-title))	
fruit fly	Common Name	Common Name
Sophophora melanogaster; fruit fly; Drosophila melanogaster Meigen, 1830; Sophophora melanogaster (Meigen, 1830); Drosophila melanogaster	Synonyms	Synonyms
species	Rank	Rank
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; Ephydriodea; Drosophilidae; Drosophilinae; Drosophilini; Drosophila; Sophophora; melanogaster group; melanogaster subgroup	Lineage	Lineage
melanogaster subgroup () - (Rank: species subgroup) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=32351)	Parent	Parent
7227 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=7227)	NCBI Taxonomy ID	NCBI Taxonomy ID
No	is Taxon A an Infraspecies?	is Taxon B an Infraspecies?

GENOTYPIC CHANGE

	Generic Gene Name	UniProtKB Drosophila melanogaster
GstE1		
CG5164; CT16545; Dmel\CG5164; DmGST-3; DmGSTE1; DmGSTE1-1; gst-3; Gst-3; GST-3; GST-E1; Gst-theta 55F; Gst3; GST3; Gst55F; gste1; gstE1; GSTE1; Dmel_LCG5164	Synonyms	GenebankID or UniProtKB
7227.FBpp0085850 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=7227.FBpp0085850)	String	
-	Sequence Similarities	
GO:0004364 : glutathione transferase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0004364)	GO - Molecular Function	
		GO - Biological Process

GO:0006749 : glutathione metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006749>)
GO:0009408 : response to heat (<https://www.ebi.ac.uk/QuickGO/term/GO:0009408>)
GO:0006979 : response to oxidative stress
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006979>)

GO - Cellular Component

GO:0005737 : cytoplasm (<https://www.ebi.ac.uk/QuickGO/term/GO:0005737>)

Presumptive Null

Unknown (<https://www.gephebase.org/search-criteria?/and+Presumptive+Null=^Unknown^#gephebase-summary-title>)

Molecular Type

Unknown (<https://www.gephebase.org/search-criteria?/and+Molecular+Type=^Unknown^#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

Experimental Evidence

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

Main Reference

The genetic architecture of methotrexate toxicity is similar in *Drosophila melanogaster* and humans. (2013) (<https://pubmed.ncbi.nlm.nih.gov/23733889>)

Authors

Kislukhin G; King EG; Walters KN; Macdonald SJ; Long AD

Abstract

The severity of the toxic side effects of chemotherapy varies among patients, and much of this variation is likely genetically based. Here, we use the model system *Drosophila melanogaster* to genetically dissect the toxicity of methotrexate (MTX), a drug used primarily to treat childhood acute lymphoblastic leukemia and rheumatoid arthritis. We use the *Drosophila* Synthetic Population Resource, a panel of recombinant inbred lines derived from a multiparent advanced intercross, and quantify MTX toxicity as a reduction in female fecundity. We identify three quantitative trait loci (QTL) affecting MTX toxicity: two colocalize with the fly orthologs of human genes believed to mediate MTX toxicity and one is a novel MTX toxicity gene with a human ortholog. A fourth suggestive QTL spans a centromere. Local single-marker association scans of candidate gene exons fail to implicate amino acid variants as the causative single-nucleotide polymorphisms, and we therefore hypothesize the causative variation is regulatory. In addition, the effects at our mapped QTL do not conform to a simple biallelic pattern, suggesting multiple causative factors underlie the QTL mapping results. Consistent with this observation, no single single-nucleotide polymorphism located in or near a candidate gene can explain the QTL mapping signal. Overall, our results validate *D. melanogaster* as a model for uncovering the genetic basis of chemotoxicity and suggest the genetic basis of MTX toxicity is due to a handful of genes each harboring multiple segregating regulatory factors.

Additional References

RELATED GEPHE

Related Genes

19 (Acetylcholinesterase (Ace-2), alcohol dehydrogenase (Adh), Aldehyde dehydrogenase (Aldh), CG11699, Cyp12d1, Cyp28d1, Cyp28d1-Cyp28d2, cyp6d2, cyp6g1, glutamate-gated chloride channel (GluCl), GSS (glutathione synthetase), 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

No matches found.

EXTERNAL LINKS

COMMENTS

Gene cluster