

GEPHE SUMMARY

Gephebase Gene		GepheID
AMPD1 (=CG32626) (<a +cg32626+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=">https://www.gephebase.org/search-criteria?/and+Gene+Gephebase="+CG32626+"#gephebase-summary-title)	GP00000083	Main curator
Published	Entry Status	Martin

PHENOTYPIC CHANGE

Trait Category		Trait Category	
Physiology (<a +physiology+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Trait+Category=">https://www.gephebase.org/search-criteria?/and+Trait+Category="+Physiology+"#gephebase-summary-title)		Physiology (<a +physiology+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Trait+Category=">https://www.gephebase.org/search-criteria?/and+Trait+Category="+Physiology+"#gephebase-summary-title)	
Drug resistance (<a +drug+resistance+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Trait=">https://www.gephebase.org/search-criteria?/and+Trait="+Drug+resistance+"#gephebase-summary-title)		Drug resistance (<a +drug+resistance+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Trait=">https://www.gephebase.org/search-criteria?/and+Trait="+Drug+resistance+"#gephebase-summary-title)	
Drosophila melanogaster DSRP		Drosophila melanogaster DSRP	
Drosophila melanogaster DSRP		Drosophila melanogaster DSRP	
Data not curated		Data not curated	
Intraspecific (<a +intraspecific+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=">https://www.gephebase.org/search-criteria?/and+Taxonomic+Status="+Intraspecific+"#gephebase-summary-title)		Intraspecific (<a +intraspecific+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=">https://www.gephebase.org/search-criteria?/and+Taxonomic+Status="+Intraspecific+"#gephebase-summary-title)	
Taxon A		Taxon B	
Drosophila melanogaster (<a +drosophila+melanogaster+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms="+Drosophila+melanogaster+"#gephebase-summary-title)		Drosophila melanogaster (<a +drosophila+melanogaster+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms="+Drosophila+melanogaster+"#gephebase-summary-title)	
fruit fly		fruit fly	
Sophophora melanogaster; fruit fly; Drosophila melanogaster Meigen, 1830; Sophophora melanogaster (Meigen, 1830); Drosophila melangaster		Sophophora melanogaster; fruit fly; Drosophila melanogaster Meigen, 1830; Sophophora melanogaster (Meigen, 1830); Drosophila melangaster	
species		species	
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		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	
melanogaster subgroup () - (Rank: species subgroup) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=32351)		melanogaster subgroup () - (Rank: species subgroup) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=32351)	
7227 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=7227)		7227 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=7227)	
No		No	
is Taxon A an Intraspecies?		is Taxon B an Intraspecies?	

GENOTYPIC CHANGE

Generic Gene Name		UniProtKB Homo sapiens
AMPD1	P23109 (http://www.uniprot.org/uniprot/P23109)	GenebankID or UniProtKB
MAD; MADA; MMDD	AHN59704 (https://www.ncbi.nlm.nih.gov/nuccore/AHN59704)	
9606.ENSPP00000430075 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPP00000430075)	String	
Sequence Similarities		
Belongs to the metallo-dependent hydrolases superfamily. Adenosine and AMP deaminases family.		
GO - Molecular Function		
GO:0046872 : metal ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0046872)		
GO:0003876 : AMP deaminase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0003876)		

GO:0032036 : myosin heavy chain binding
(<https://www.ebi.ac.uk/QuickGO/term/GO:0032036>)

GO - Biological Process

GO:0032264 : IMP salvage (<https://www.ebi.ac.uk/QuickGO/term/GO:0032264>)

GO:0043101 : purine-containing compound salvage
(<https://www.ebi.ac.uk/QuickGO/term/GO:0043101>)

GO:0010033 : response to organic substance
(<https://www.ebi.ac.uk/QuickGO/term/GO:0010033>)

GO - Cellular Component

GO:0005829 : cytosol (<https://www.ebi.ac.uk/QuickGO/term/GO:0005829>)

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

No matches found.

Related Genes

No matches found.

Related Haplotypes

EXTERNAL LINKS

COMMENTS

Distant orthology between *Drosophila melanogaster* CG32626 and *Homo sapiens* AMPD1