GEPHE SUMMARY

Gephebase Gene
AMPD1 (=CG32626) (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^AMPD1 (=CG32626)^#gephebase-summary-title)

Entry Status
Published

GepheID
GP00000083

Main curator
Martin

PHENOTYPIC CHANGE

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

Trait
Drug resistance (https://www.gephebase.org/search-criteria?/and+Trait=^Drug resistance^#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

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
AMPD1

Synonyms
MAD; MADA; MMDD

String
9606.ENSP00000430075 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000430075)

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)

UniProtKB Homo sapiens
P23109 (http://www.uniprot.org/uniprot/P23109)

GenebankID or UniProtKB
AHN59704 (https://www.ncbi.nlm.nih.gov/nuccore/AHN59704)

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

Related Genes

No matches found.

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS

Distant orthology between Drosophila melanogaster CG32626 and Homo sapiens AMPD1