GEPHE SUMMARY

Gephebase Gene
Cyp12d1 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^Cyp12d1^#gephebase-summary-title)

GepheID
GP00000198

Entry Status
Published

Main curator
Martin

PHENOTYPIC CHANGE

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

Trait
Xenobiotic resistance (caffeine tolerance) (https://www.gephebase.org/search-criteria?/and+Trait=^Xenobiotic resistance (caffeine tolerance)^#gephebase-summary-title)

Trait State in Taxon A
Drosophila melanogaster ; non-tolerant DSRP lines

Trait State in Taxon B
Drosophila melanogaster - caffeine-tolerant DSRP lines

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
Cyp12d1-d

Synonyms
12d1; 12D1; CG18239; CG18240; CG33503; CT26082; Cyp 12d1; Cyp12d1; CYP12D1; CYP12d1-d; Cyp12d2; Dmel\CG33503

String
7227.FBpp0088436 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier= 7227.FBpp0088436)

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)
GO:0004497 : monooxygenase activity

UniProtKB Drosophila melanogaster
Q7KR10 (http://www.uniprot.org/uniprot/Q7KR10)

GenebankID or UniProtKB
()

(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:0030342 : 1-alpha,25-dihydroxyvitamin D3 24-hydroxylase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0030342)

GO - Biological Process

GO:0055114 : oxidation-reduction process (https://www.ebi.ac.uk/QuickGO/term/GO:0055114)
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 - Cellular Component

GO:0031966 : mitochondrial membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0031966)
GO:0005739 : mitochondrion (https://www.ebi.ac.uk/QuickGO/term/GO:0005739)

Presumptive Null

No (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^No^#gephebase-summary-title)

Molecular Type

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

Aberration Type

Insertion (https://www.gephebase.org/search-criteria?/and+Aberration Type=^Insertion^#gephebase-summary-title)

Insertion Size

1-10 kb

Molecular Details of the Mutation

Copy number Variant

Experimental Evidence

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

Main Reference

Identifying Loci Contributing to Natural Variation in Xenobiotic Resistance in Drosophila. (2015) (https://pubmed.ncbi.nlm.nih.gov/26619284)

Authors

Najarro MA; Hackett JL; Smith BR; Highfill CA; King EG; Long AD; Macdonald SJ

Abstract

Natural populations exhibit a great deal of interindividual genetic variation in the response to toxins, exemplified by the variable clinical efficacy of pharmaceutical drugs in humans, and the evolution of pesticide resistant insects. Such variation can result from several phenomena, including variable metabolic detoxification of the xenobiotic, and differential sensitivity of the molecular target of the toxin. Our goal is to genetically dissect variation in the response to xenobiotics, and characterize naturally-segregating polymorphisms that modulate toxicity. Here, we use the Drosophila Synthetic Population Resource (DSPR), a multiparent advanced intercross panel of recombinant inbred lines, to identify QTL (Quantitative Trait Loci) underlying xenobiotic resistance, and employ caffeine as a model toxic compound. Phenotyping over 1,700 genotypes led to the identification of ten QTL, each explaining 4.5-14.4% of the broad-sense heritability for caffeine resistance. Four QTL harbor members of the cytochrome P450 family of detoxification enzymes, which represent strong a priori candidate genes. The case is especially strong for Cyp12d1, with multiple lines of evidence indicating the gene causally impacts caffeine resistance. Cyp12d1 is implicated by QTL mapped in both panels of DSPR RILs, is significantly upregulated in the presence of caffeine, and RNAi knockdown robustly decreases caffeine tolerance. Furthermore, copy number variation at Cyp12d1 is strongly associated with phenotype in the DSPR, with a trend in the same direction observed in the DGRP (Drosophila Genetic Reference Panel). No additional plausible causative polymorphisms were observed in a full genomewide association study in the DGRP, or in analyses restricted to QTL regions mapped in the DSPR. Just as in human populations, replicating modest-effect, naturally-segregating causative variants in an association study framework in flies will likely require very large sample sizes.

Additional References

RELATED GEPHE

Related Genes

19 (Acetylcholinesterase (Ace-2), alcohol dehydrogenase (Adh), Aldehyde dehydrogenase (Aldh), CG11699, Cyp28d1, Cyp28d1-Cyp28d2, cyp6d2, 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

No matches found.

EXTERNAL LINKS

COMMENTS