

## GEPHE SUMMARY

		Gephebase Gene	GepheID
alcohol dehydrogenase (Adh) ( <a href="https://www.gephebase.org/search-criteria?/and+Gene">https://www.gephebase.org/search-criteria?/and+Gene</a> )		GP00001965	
Gephebase="alcohol dehydrogenase (Adh)"#gephebase-summary-title)			Main curator
	Entry Status	Courtier	
Published			

## PHENOTYPIC CHANGE

		Trait Category
Physiology ( <a href="https://www.gephebase.org/search-criteria?/and+Trait">https://www.gephebase.org/search-criteria?/and+Trait</a> )		
Category="Physiology"#gephebase-summary-title)		
	Trait	
Xenobiotic resistance (alcohol) ( <a #gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Trait=Xenobiotic+resistance+(alcohol)">https://www.gephebase.org/search-criteria?/and+Trait=Xenobiotic+resistance+(alcohol)"#gephebase-summary-title</a> )		
	Trait State in Taxon A	
Drosophila americana - lower enzyme activity		
	Trait State in Taxon B	
Drosophila virilis - higher enzyme activity		
	Ancestral State	
Taxon A		
	Taxonomic Status	
Interspecific ( <a href="https://www.gephebase.org/search-criteria?/and+Taxonomic">https://www.gephebase.org/search-criteria?/and+Taxonomic</a> )		
Status="Interspecific"#gephebase-summary-title)		

Taxon A	Latin Name	Taxon B	Latin Name
Drosophila americana ( <a #gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=Drosophila+americana">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=Drosophila+americana"#gephebase-summary-title</a> )		Drosophila virilis ( <a #gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=Drosophila+virilis">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=Drosophila+virilis"#gephebase-summary-title</a> )	
-	Common Name	-	Common Name
-	Synonyms		Synonyms
species	Rank	Drosophila virilis Sturtevant, 1916; Drosophila irilis	Rank
	Lineage	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; Acalyptera; Ephydroidea; Drosophilidae; Drosophilinae; Drosophilini; Drosophila; Drosophila; virilis group		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; Drosophila; virilis group	
virilis group () - (Rank: species group)	Parent	virilis group () - (Rank: species group)	Parent
( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=32335">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=32335</a> )	NCBI Taxonomy ID	( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=32335">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=32335</a> )	NCBI Taxonomy ID
40366		7244	
( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=40366">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=40366</a> )		( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=7244">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=7244</a> )	
	is Taxon A an Intraspecies?		is Taxon B an Intraspecies?
No		No	

## GENOTYPIC CHANGE

		Generic Gene Name	UniProtKB Drosophila melanogaster
Adh		P00334 ( <a href="http://www.uniprot.org/uniprot/P00334">http://www.uniprot.org/uniprot/P00334</a> )	
	Synonyms		GenebankID or UniProtKB
adh; ADH; Adh3; BG:DS01486.8; CG32954; CG3481; dADH; DM-ADH; DmADH; Dmel\CG3481; Dreg-1; Reg-1; T16		()	
	String		
7227.FBpp0100048 ( <a href="http://string-db.org/newstring.cgi/show_network_section.pl?identifier=7227.FBpp0100048">http://string-db.org/newstring.cgi/show_network_section.pl?identifier=7227.FBpp0100048</a> )			
	Sequence Similarities		
Belongs to the short-chain dehydrogenases/reductases (SDR) family.			
	GO - Molecular Function		
GO:0042803 : protein homodimerization activity ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0042803">https://www.ebi.ac.uk/QuickGO/term/GO:0042803</a> )			
GO:0008774 : acetaldehyde dehydrogenase (acetylating) activity ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0008774">https://www.ebi.ac.uk/QuickGO/term/GO:0008774</a> )			
GO:0004022 : alcohol dehydrogenase (NAD) activity			

(<https://www.ebi.ac.uk/QuickGO/term/GO:0004022>)  
GO:0016491 : oxidoreductase activity (<https://www.ebi.ac.uk/QuickGO/term/GO:0016491>)  
GO - Biological Process

GO:0006117 : acetaldehyde metabolic process  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006117>)  
GO:0046164 : alcohol catabolic process  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0046164>)  
GO:0006066 : alcohol metabolic process  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006066>)  
GO:0048149 : behavioral response to ethanol  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0048149>)  
GO:0006067 : ethanol metabolic process  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006067>)  
GO:0006069 : ethanol oxidation (<https://www.ebi.ac.uk/QuickGO/term/GO:0006069>)  
GO:0055114 : oxidation-reduction process  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0055114>)

GO - Cellular Component

GO:0005829 : cytosol (<https://www.ebi.ac.uk/QuickGO/term/GO:0005829>)  
GO:0032991 : protein-containing complex  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0032991>)

#### Mutation #1

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

Presumptive Null

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

Molecular Type

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

Aberration Type

1-10 kb

Insertion Size

Duplication of the Adh gene.

Molecular Details of the Mutation

Candidate Gene ([https://www.gephebase.org/search-criteria?/and+Experimental Evidence="Candidate Gene"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Experimental+Evidence=))

Experimental Evidence

A major role for noncoding regulatory mutations in the evolution of enzyme activity. (2019) (<https://pubmed.ncbi.nlm.nih.gov/31152141>)

Main Reference

Loehlin DW; Ames JR; Vaccaro K; Carroll SB

Authors

The quantitative evolution of protein activity is a common phenomenon, yet we know little about any general mechanistic tendencies that underlie it. For example, an increase (or decrease) in enzyme activity may evolve from changes in protein sequence that alter specific activity, or from changes in gene expression that alter the amount of protein produced. The latter in turn could arise via mutations that affect gene transcription, posttranscriptional processes, or copy number. Here, to determine the types of genetic changes underlying the quantitative evolution of protein activity, we dissected the basis of ecologically relevant differences in Alcohol dehydrogenase (Adh) enzyme activity between and within several *Drosophila* species. By using recombinant Adh transgenes to map the functional divergence of ADH enzyme activity *in vivo*, we find that amino acid substitutions explain only a minority (0 to 25%) of between- and within-species differences in enzyme activity. Instead, noncoding substitutions that occur across many parts of the gene (enhancer, promoter, and 5' and 3' untranslated regions) account for the majority of activity differences. Surprisingly, one substitution in a transcriptional Initiator element has occurred in parallel in two species, indicating that core promoters can be an important natural source of the tuning of gene activity. Furthermore, we show that both regulatory and coding substitutions contribute to fitness (resistance to ethanol toxicity). Although qualitative changes in protein specificity necessarily derive from coding mutations, these results suggest that regulatory mutations may be the primary source of quantitative changes in protein activity, a possibility overlooked in most analyses of protein evolution.

Abstract

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Additional References

#### Mutation #2

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

Presumptive Null

Cis-regulatory ([https://www.gephebase.org/search-criteria?/and+Molecular Type="Cis-regulatory"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Molecular+Type=))

Molecular Type

Unknown ([https://www.gephebase.org/search-criteria?/and+Aberration Type="Unknown"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Aberration+Type=))

Aberration Type

segment 1 of the 5' flanking region (upstream of 5'UTR). The two segments of the 5' flanking region have significant but opposite effects on activity. Exact mutation(s) not identified.

Molecular Details of the Mutation

Experimental Evidence

Candidate Gene ([https://www.gephebase.org/search-criteria?/and+Experimental Evidence="Candidate Gene"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Experimental+Evidence=))

Main Reference

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Abstract

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indicating that core promoters can be an important natural source of the tuning of gene activity. Furthermore, we show that both regulatory and coding substitutions contribute to fitness (resistance to ethanol toxicity). Although qualitative changes in protein specificity necessarily derive from coding mutations, these results suggest that regulatory mutations may be the primary source of quantitative changes in protein activity, a possibility overlooked in most analyses of protein evolution.

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Additional References

#### Mutation #3

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Presumptive Null

Cis-regulatory ([https://www.gephebase.org/search-criteria?/and+Molecular Type="Cis-regulatory"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Molecular Type=))

Molecular Type

Unknown ([https://www.gephebase.org/search-criteria?/and+Aberration Type="Unknown"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Aberration Type=))

Aberration Type

segment 2 of the 5' flanking region (upstream of 5'UTR). The two segments of the 5' flanking region have significant but opposite effects on activity. Exact mutation(s) not identified.

Molecular Details of the Mutation

Candidate Gene ([https://www.gephebase.org/search-criteria?/and+Experimental Evidence="Candidate Gene"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Experimental Evidence=))

Experimental Evidence

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Additional References

#### Mutation #4

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

Presumptive Null

Cis-regulatory ([https://www.gephebase.org/search-criteria?/and+Molecular Type="Cis-regulatory"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Molecular Type=))

Molecular Type

Unknown ([https://www.gephebase.org/search-criteria?/and+Aberration Type="Unknown"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Aberration Type=))

Aberration Type

5' UTR region. Exact mutation(s) not identified.

Molecular Details of the Mutation

Candidate Gene ([https://www.gephebase.org/search-criteria?/and+Experimental Evidence="Candidate Gene"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Experimental Evidence=))

Experimental Evidence

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Additional References

#### Mutation #5

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

Presumptive Null

Cis-regulatory ([https://www.gephebase.org/search-criteria?/and+Molecular Type="Cis-regulatory"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Molecular Type=))

Molecular Type

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

Aberration Type

3' UTR region. Exact mutation(s) not identified.

Molecular Details of the Mutation

Candidate Gene ([https://www.gephebase.org/search-criteria?/and+Experimental Evidence=~Candidate Gene^#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Experimental+Evidence=~Candidate+Gene^#gephebase-summary-title))

Experimental Evidence

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Main Reference

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Additional References

## RELATED GEPHE

No matches found.

Related Genes

No matches found.

Related Haplotypes

## EXTERNAL LINKS

## COMMENTS

@SeveralMutationsWithEffect - Entry validated by David Loehlin