

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

Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category=~Physiology~#gephebase-summary-title)		Trait Category	Xenobiotic resistance (alcohol) (https://www.gephebase.org/search-criteria?/and+Trait=~Xenobiotic resistance (alcohol)~#gephebase-summary-title)		Trait
Drosophila americana - lower enzyme activity		Trait State in Taxon A	Drosophila virilis - higher enzyme activity		Trait State in Taxon B
Taxon A		Ancestral State	Taxon B		Ancestral State
Interspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=~Interspecific~#gephebase-summary-title)		Taxonomic Status	Interspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=~Interspecific~#gephebase-summary-title)		Taxonomic Status
Taxon A			Taxon B		
Drosophila americana		Latin Name	Drosophila virilis		Latin Name
(https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=~Drosophila americana~#gephebase-summary-title)			(https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=~Drosophila virilis~#gephebase-summary-title)		
-		Common Name	-		Common Name
-		Synonyms	-		Synonyms
species		Rank	Drosophila virilis Sturtevant, 1916; Drosophila irilis		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; Ephydroidea; Drosophilidae; Drosophilinae; Drosophilini; Drosophila; Drosophila; virilis group		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; Drosophila; virilis group		Lineage
virilis group () - (Rank: species group)		Parent	virilis group () - (Rank: species group)		Parent
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 32335)		NCBI Taxonomy ID	(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 32335)		NCBI Taxonomy ID
40366			7244		
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 40366)			(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 7244)		
is Taxon A an Intraspecies?			is Taxon B an Intraspecies?		
No			No		

Adh	Generic Gene Name	UniProtKB Drosophila melanogaster
		P00334 (http://www.uniprot.org/uniprot/P00334)
	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 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier= 7227.FBpp0100048)		
	Sequence Similarities	
Belongs to the short-chain dehydrogenases/reductases (SDR) family.		
	GO - Molecular Function	
GO:0042803 : protein homodimerization activity (https://www.ebi.ac.uk/QuickGO/term/GO:0042803)		
GO:0008774 : acetaldehyde dehydrogenase (acetylating) activity (https://www.ebi.ac.uk/QuickGO/term/GO:0008774)		
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)	Presumptive Null
Gene Amplification (https://www.gephebase.org/search-criteria?/and+Molecular Type=^Gene Amplification^#gephebase-summary-title)	Molecular Type
Insertion (https://www.gephebase.org/search-criteria?/and+Aberration Type=^Insertion^#gephebase-summary-title)	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)	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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Mutation #2	
No (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^No^#gephebase-summary-title)	Presumptive Null
Cis-regulatory (https://www.gephebase.org/search-criteria?/and+Molecular Type=^Cis-regulatory^#gephebase-summary-title)	Molecular Type
Unknown (https://www.gephebase.org/search-criteria?/and+Aberration Type=^Unknown^#gephebase-summary-title)	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
Candidate Gene (https://www.gephebase.org/search-criteria?/and+Experimental Evidence=^Candidate Gene^#gephebase-summary-title)	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
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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

Presumptive Null

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

Molecular Type

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=))

Aberration Type

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

Molecular Details of the Mutation

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.

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

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

Authors

Loehlin DW; Ames JR; Vaccaro K; Carroll SB

Abstract

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Additional References

Mutation #4

Presumptive Null

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

Molecular Type

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=))

Aberration Type

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

Molecular Details of the Mutation

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

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

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

Authors

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Additional References

Mutation #5

Presumptive Null

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

Molecular Type

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=))

Unknown (https://www.gephebase.org/search-criteria?/and+Aberration+Type=~Unknown~#gephebase-summary-title)	Aberration Type
	Molecular Details of the Mutation
3' UTR region. Exact mutation(s) not identified.	
Candidate Gene (https://www.gephebase.org/search-criteria?/and+Experimental+Evidence=~Candidate+Gene~#gephebase-summary-title)	Experimental Evidence
	Main Reference
A major role for noncoding regulatory mutations in the evolution of enzyme activity. (2019) (https://pubmed.ncbi.nlm.nih.gov/31152141)	
Loehlin DW; Ames JR; Vaccaro K; Carroll SB	Authors
	Abstract
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Additional References	

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EXTERNAL LINKS

COMMENTS

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