Gephebase Gene GephelD alcohol dehydrogenase (Adh) (https://www.gephebase.org/search-criteria?/and+Gene GP00001963 Gephebase=^alcohol dehydrogenase (Adh)^#gephebase-summary-title) Main curator Entry Status Courtier **Published** PHENOTYPIC CHANGE Trait Category Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Physiology^#gephebase-summary-title) Trait Xenobiotic resistance (alcohol) (https://www.gephebase.org/searchcriteria?/and+Trait=^Xenobiotic resistance (alcohol)^#gephebase-summary-title) Trait State in Taxon A Drosophila santomea - lower enzyme activity Trait State in Taxon B Drosophila yakuba - higher enzyme activity Ancestral State Unknown Taxonomic Status Interspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Interspecific^#gephebase-summary-title) Taxon A Taxon B Latin Name Latin Name Drosophila santomea Drosophila yakuba (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Drosophila (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Drosophila santomea^#gephebase-summary-title) yakuba^#gephebase-summary-title) Common Name Common Name Synonyms Synonyms Drosophila yakuba Burla, 1954 Rank Rank species species Lineage cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda; Insecta; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda; Insecta; Dicondylia; Pterygota; Neoptera; Holometabola; Diptera; Brachycera; Muscomorpha; Dicondylia; Pterygota; Neoptera; Holometabola; Diptera; Brachycera; Muscomorpha; Eremoneura; Cyclorrhapha; Schizophora; Acalyptratae; Ephydroidea; Drosophilidae;Eremoneura; Cyclorrhapha; Schizophora; Acalyptratae; Ephydroidea; Drosophilidae;Drosophilinae; Drosophilini; Drosophila; Sophophora; melanogaster group; melanogaster Drosophilinae; Drosophilini; Drosophila; Sophophora; melanogaster group; melanogaster subgroup Parent Parent melanogaster subgroup () - (Rank: species subgroup) melanogaster subgroup () - (Rank: species subgroup) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 32351) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 32351) NCBI Taxonomy ID NCBI Taxonomy ID (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 129105) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 7245) is Taxon A an Infraspecies? is Taxon B an Infraspecies? Nο Nο **GENOTYPIC CHANGE** Generic Gene Name UniProtKB Drosophila melanogaster Adh P00334 (http://www.uniprot.org/uniprot/P00334) GenebankID or UniProtKB Synonyms adh; ADH; Adh3; BG:DS01486.8; CG32954; CG3481; dADH; DM-ADH; DmADH; 0 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

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)

Belongs to the short-chain dehydrogenases/reductases (SDR) family

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= N o^#gephebase-summary-title)

 $Coding \ (https://www.gephebase.org/search-criteria?/and+Molecular \ Type=^Coding^* \\ gephebase-summary-title)$

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

Nonsynonymous

In vitro assay by replacement of the entire coding region. Three possible amino acid changes. Exact causal amino acid change(s) not identified.

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

Presumptive Null

Molecular Type

Aberration Type

SNP Coding Change

Molecular Details of the Mutation

Experimental Evidence

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	-	-	-

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

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.

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Additional References

Presumptive Null

Molecular Type

Aberration Type

Mutation #2

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

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

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

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

Molecular Details of the Mutation

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)

 $Candidate\ Gene\ (https://www.gephebase.org/search-criteria?/and+Experimental\ Evidence=`Candidate\ Gene`\#gephebase-summary-title)$

Authors

Abstract

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.

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Additional References

Mutation #3

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

 $Cis-regulatory \ (https://www.gephebase.org/search-criteria?/and+Molecular\ Type=^Cis-regulatory^\#gephebase-summary-title)$

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

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

 $Candidate \ Gene \ (https://www.gephebase.org/search-criteria?/and+Experimental \ Evidence=`Candidate \ Gene ``#gephebase-summary-title)$

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

Presumptive Null

Molecular Type

Aberration Type

Molecular Details of the Mutation

Experimental Evidence

Main Reference

Authors

Abstract

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

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Additional References

Mutation #4

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

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

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

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

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

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

Loehlin DW; Ames JR; Vaccaro K; Carroll SB

Presumptive Null

Molecular Type

Aberration Type

Molecular Details of the Mutation

Experimental Evidence

Main Reference

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.

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Related Genes
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Related Haplotypes
No matches found.

EXTERNAL LINKS

COMMENTS

©SeveralMutationsWithEffect - There is a consensus phenotype of moderate ADH activity in the broader taxonomic group (Mercot et al. 1994). With the transformed alleles David Loehlin also observed "moderate" activity in mel-slow; D. erecta and D. yakuba. This suggests that D. santomea and D. orena have derived low phenotypes but the phylogenetic signal is weak. - Entry validated by David Loehlin