GEPHE SUMMARY

Gephebase Gene
Na/K-ATPase alpha-subunit (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^Na/K-ATPase alpha-subunit^#gephebase-summary-title)

GepheID
GP00000710

Entry Status
Published

Main curator
Courtier

PHENOTYPIC CHANGE

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

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

Trait State in Taxon A
Other insects

Trait State in Taxon B
Labidomera clivicollis

Ancestral State
Taxon A

Taxonomic Status
Intergeneric or Higher (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Intergeneric or Higher^#gephebase-summary-title)

Taxon A

Latin Name
Insecta (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Insecta^#gephebase-summary-title)

Common Name
true insects

Synonyms
true insects

Rank
class

Lineage
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda

Parent
Hexapoda (insects) - (Rank: subphylum) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 6960)

NCBI Taxonomy ID
50557 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 50557)

is Taxon A an Infraspecies?
No

Taxon B

Latin Name
Labidomera clivicollis (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Labidomera clivicollis^#gephebase-summary-title)

Common Name
-

Synonyms
-

Rank
species

Lineage
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda; Insecta; Dicondylia; Pterygota; Neoptera; Holometabola; Coleoptera; Polyphaga; Cucujiformia; Chrysomeloidea; Chrysomelidae; Chrysomelinae; Doryphorini; Labidomera

Parent
Labidomera () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 131651)

NCBI Taxonomy ID
131652 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 131652)

is Taxon B an Infraspecies?
No

GENOTYPIC CHANGE

Generic Gene Name
Atp1a1

Synonyms
Atpa-1; BC010319

String
10090.ENSMUSP00000039657 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier= 10090.ENSMUSP00000039657)

Sequence Similarities
Belongs to the cation transport ATPase (P-type) (TC 3.A.3) family. Type IIC subfamily.

GO - Molecular Function
GO:0005524 : ATP binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005524)
GO:0043531 : ADP binding (https://www.ebi.ac.uk/QuickGO/term/GO:0043531)
GO:0019901 : protein kinase binding (https://www.ebi.ac.uk/QuickGO/term/GO:0019901)
GO:0043548 : phosphatidylinositol 3-kinase binding (https://www.ebi.ac.uk/QuickGO/term/GO:0043548)
GO:0005391 : sodium:potassium-exchanging ATPase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005391)

UniProtKB Mus musculus
Q8VDN2 (http://www.uniprot.org/uniprot/Q8VDN2)

GenebankID or UniProtKB
()

GO:0051087 : chaperone binding (https://www.ebi.ac.uk/QuickGO/term/GO:0051087)
GO:0019904 : protein domain specific binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0019904)
GO:0030506 : ankyrin binding (https://www.ebi.ac.uk/QuickGO/term/GO:0030506)
GO:0016791 : phosphatase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0016791)
GO:0030955 : potassium ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0030955)
GO:0031402 : sodium ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0031402)
GO:1990239 : steroid hormone binding
(https://www.ebi.ac.uk/QuickGO/term/GO:1990239)

GO - Biological Process

GO:0071383 : cellular response to steroid hormone stimulus
(https://www.ebi.ac.uk/QuickGO/term/GO:0071383)
GO:0006813 : potassium ion transport
(https://www.ebi.ac.uk/QuickGO/term/GO:0006813)
GO:0006814 : sodium ion transport (https://www.ebi.ac.uk/QuickGO/term/GO:0006814)
GO:0071260 : cellular response to mechanical stimulus
(https://www.ebi.ac.uk/QuickGO/term/GO:0071260)
GO:0042493 : response to drug (https://www.ebi.ac.uk/QuickGO/term/GO:0042493)
GO:0008217 : regulation of blood pressure
(https://www.ebi.ac.uk/QuickGO/term/GO:0008217)
GO:0015991 : ATP hydrolysis coupled proton transport
(https://www.ebi.ac.uk/QuickGO/term/GO:0015991)
GO:0030007 : cellular potassium ion homeostasis
(https://www.ebi.ac.uk/QuickGO/term/GO:0030007)
GO:0006883 : cellular sodium ion homeostasis
(https://www.ebi.ac.uk/QuickGO/term/GO:0006883)
GO:1990573 : potassium ion import across plasma membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:1990573)
GO:0036376 : sodium ion export across plasma membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0036376)
GO:0090662 : ATP hydrolysis coupled transmembrane transport
(https://www.ebi.ac.uk/QuickGO/term/GO:0090662)
GO:0060081 : membrane hyperpolarization
(https://www.ebi.ac.uk/QuickGO/term/GO:0060081)
GO:0086009 : membrane repolarization
(https://www.ebi.ac.uk/QuickGO/term/GO:0086009)
GO:0031947 : negative regulation of glucocorticoid biosynthetic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0031947)
GO:0045822 : negative regulation of heart contraction
(https://www.ebi.ac.uk/QuickGO/term/GO:0045822)
GO:0045823 : positive regulation of heart contraction
(https://www.ebi.ac.uk/QuickGO/term/GO:0045823)
GO:0045989 : positive regulation of striated muscle contraction
(https://www.ebi.ac.uk/QuickGO/term/GO:0045989)
GO:0086004 : regulation of cardiac muscle cell contraction
(https://www.ebi.ac.uk/QuickGO/term/GO:0086004)
GO:0002028 : regulation of sodium ion transport
(https://www.ebi.ac.uk/QuickGO/term/GO:0002028)
GO:0002026 : regulation of the force of heart contraction
(https://www.ebi.ac.uk/QuickGO/term/GO:0002026)

GO - Cellular Component

GO:0016021 : integral component of membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0016021)
GO:0005886 : plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005886)
GO:0016324 : apical plasma membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0016324)
GO:0016020 : membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0016020)
GO:0045121 : membrane raft (https://www.ebi.ac.uk/QuickGO/term/GO:0045121)
GO:0005794 : Golgi apparatus (https://www.ebi.ac.uk/QuickGO/term/GO:0005794)
GO:0032991 : protein-containing complex
(https://www.ebi.ac.uk/QuickGO/term/GO:0032991)
GO:0005783 : endoplasmic reticulum
(https://www.ebi.ac.uk/QuickGO/term/GO:0005783)
GO:0005768 : endosome (https://www.ebi.ac.uk/QuickGO/term/GO:0005768)
GO:0016323 : basolateral plasma membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0016323)
GO:0005901 : caveola (https://www.ebi.ac.uk/QuickGO/term/GO:0005901)
GO:0030315 : T-tubule (https://www.ebi.ac.uk/QuickGO/term/GO:0030315)
GO:0014069 : postsynaptic density (https://www.ebi.ac.uk/QuickGO/term/GO:0014069)
GO:0014704 : intercalated disc (https://www.ebi.ac.uk/QuickGO/term/GO:0014704)
GO:0043209 : myelin sheath (https://www.ebi.ac.uk/QuickGO/term/GO:0043209)
GO:0042383 : sarcolemma (https://www.ebi.ac.uk/QuickGO/term/GO:0042383)
GO:0005890 : sodium:potassium-exchanging ATPase complex
(https://www.ebi.ac.uk/QuickGO/term/GO:0005890)

Mutation #1

Presumptive Null

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

Molecular Type

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

Aberration Type

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

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

Q111V + N122H

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Gln	Val	111

Main Reference

Community-wide convergent evolution in insect adaptation to toxic cardenolides by substitutions in the Na,K-ATPase. (2012) (https://pubmed.ncbi.nlm.nih.gov/22826239)

Authors

Dobler S; Dalla S; Wagschal V; Agrawal AA

Abstract

The extent of convergent molecular evolution is largely unknown, yet is critical to understanding the genetics of adaptation. Target site insensitivity to cardenolides is a prime candidate for studying molecular convergence because herbivores in six orders of insects have specialized on these plant poisons, which gain their toxicity by blocking an essential transmembrane carrier, the sodium pump (Na,K-ATPase). We investigated gene sequences of the Na,K-ATPase Î±-subunit in 18 insects feeding on cardenolide-containing plants (spanning 15 genera and four orders) to screen for amino acid substitutions that might lower sensitivity to cardenolides. The replacement N122H that was previously shown to confer resistance in the monarch butterfly (Danaus plexippus) and Chrysochus leaf beetles was found in four additional species, Oncopeltus fasciatus and Lygaeus kalmii (Heteroptera, Lygaeidae), Labidomera clivicollis (Coleoptera, Chrysomelidae), and Liriomyza asclepiadis (Diptera, Agromyzidae). Thus, across 300 Myr of insect divergence, specialization on cardenolide-containing plants resulted in molecular convergence for an adaptation likely involved in coevolution. Our screen revealed a number of other substitutions connected to cardenolide binding in mammals. We confirmed that some of the particular substitutions provide resistance to cardenolides by introducing five distinct constructs of the Drosophila melanogaster gene into susceptible eucaryotic cells under an ouabain selection regime. These functional assays demonstrate that combined substitutions of Q(111) and N(122) are synergistic, with greater than twofold higher resistance than either substitution alone and >12-fold resistance over the wild type. Thus, even across deep phylogenetic branches, evolutionary degrees of freedom seem to be limited by physiological constraints, such that the same molecular substitutions confer adaptation.

Additional References

Parallel molecular evolution in an herbivore community. (2012) (https://pubmed.ncbi.nlm.nih.gov/23019645)

Mutation #2

Presumptive Null

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

Molecular Type

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

Aberration Type

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

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

Q111V + N122H

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Asp	His	122

Main Reference

Community-wide convergent evolution in insect adaptation to toxic cardenolides by substitutions in the Na,K-ATPase. (2012) (https://pubmed.ncbi.nlm.nih.gov/22826239)

Authors

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The extent of convergent molecular evolution is largely unknown, yet is critical to understanding the genetics of adaptation. Target site insensitivity to cardenolides is a prime candidate for studying molecular convergence because herbivores in six orders of insects have specialized on these plant poisons, which gain their toxicity by blocking an essential transmembrane carrier, the sodium pump (Na,K-ATPase). We investigated gene sequences of the Na,K-ATPase Î±-subunit in 18 insects feeding on cardenolide-containing plants (spanning 15 genera and four orders) to screen for amino acid substitutions that might lower sensitivity to cardenolides. The replacement N122H that was previously shown to confer resistance in the monarch butterfly (Danaus plexippus) and Chrysochus leaf beetles was found in four additional species, Oncopeltus fasciatus and Lygaeus kalmii (Heteroptera, Lygaeidae), Labidomera clivicollis (Coleoptera, Chrysomelidae), and Liriomyza asclepiadis (Diptera, Agromyzidae). Thus, across 300 Myr of insect divergence, specialization on cardenolide-containing plants resulted in molecular convergence for an adaptation likely involved in coevolution. Our screen revealed a number of other substitutions connected to cardenolide binding in mammals. We confirmed that some of the particular substitutions provide resistance to cardenolides by introducing five distinct constructs of the Drosophila melanogaster gene into susceptible eucaryotic cells under an ouabain selection regime. These functional assays demonstrate that combined substitutions of Q(111) and N(122) are synergistic, with greater than twofold higher resistance than either substitution alone and >12-fold resistance over the wild type. Thus, even across deep phylogenetic branches, evolutionary degrees of freedom seem to be limited by physiological constraints, such that the same molecular substitutions confer adaptation.

Additional References

Parallel molecular evolution in an herbivore community. (2012) (https://pubmed.ncbi.nlm.nih.gov/23019645)

RELATED GEPHE

Related Genes

73 (ABCA2, Aminopeptidase N (APN), cadherin, CYP337B3, Ha_BtR, para (kdr), tetraspanin, ABCC2, ABCB1, ABCB4, CYP9J26, CYP9M6, resistance to dieldrin, Acetylcholinesterase (Ace-1), Chitin synthase 1 (CHS1), CYP6BG1, FMO2, glutamate-gated chloride channel (GluCl), MAP4K4, nAChR, RYR, CYP321A8, CYP9A186, GSTe, CYP9A, acetyl-CoA carboxylase (ACC), Acetylcholinesterase (Ace-2), CYP6CM1, CYP6CY3, CYP6CY3-CYP6CY4, esterase E4, esterase FE4, SAP-2, Cpm1, esterase A8 and B8, esterase B4, esterase B5, esterase B1, CYP6AY1, CYP6ER1, esterase NI-EST1, GST, CYP6FU1, Acetylcholinesterase (Ace), CYP6D1, esterase isozyme E7 = E3, alcohol dehydrogenase (Adh), Aldehyde dehydrogenase (Aldh), CG11699, Cyp12d1, Cyp28d1, Cyp28d1-Cyp28d2, cyp6d2, cyp6g1, GSS (glutathione synthetase), GSTE1-E10 cluster, kin of irre (kire), PHGPx, RnrS, SOD1, Ugt86Dd, esterase isozyme E3, esterase B1 + esterase A, esterase B1 = esterase beta1, CYP6AB3, CYP6P9 cluster (CYP6P9a and CYP6P9b), CYP6P9; CYP6P4 cluster, esterase type I, Nav1 sodium channel, CHKov1, CYP6B1, CYP6B4, FMO1) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^50557^/and+Trait=Xenobiotic resistance/or+Taxon ID=^131652^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

11 (https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^50557^/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^131652^#gephebase-summary-title)

EXTERNAL LINKS

COMMENTS

@SeveralMutationsWithEffect