

GEPHE SUMMARY

	Gephebase Gene		GepheID
Na/K-ATPase alpha-subunit (https://www.gephebase.org/search-criteria?/and+Gene Gephebase="Na/K-ATPase alpha-subunit"#gephebase-summary-title)		GP00001742	
Published	Entry Status	Courtier	Main curator

PHENOTYPIC CHANGE

	Trait Category		
Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category="Physiology"#gephebase-summary-title)			
	Trait		
Xenobiotic resistance (cardiac glycosides) (<a (cardiac="" glycosides)"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Trait=" resistance="" xenobiotic="">https://www.gephebase.org/search-criteria?/and+Trait="Xenobiotic resistance (cardiac glycosides)"#gephebase-summary-title)			
	Trait State in Taxon A		
sensitive			
	Trait State in Taxon B		
resistant			
	Ancestral State		
Taxon A			
	Taxonomic Status		
Intergenic or Higher (https://www.gephebase.org/search-criteria?/and+Taxonomic Status="Intergenic or Higher"#gephebase-summary-title)			
Taxon A		Taxon B	
	Latin Name		Latin Name
Holometabola (<a holometabola"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="Holometabola"#gephebase-summary-title)		Saucrobotys futilalis (<a futilalis"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=" saucrobotys="">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="Saucrobotys futilalis"#gephebase-summary-title)	
	Common Name		Common Name
-		dogbane pyralid moth	
	Synonyms		Synonyms
Endopterygota		dogbane pyralid moth; dogbane pyralid	
	Rank		Rank
cohort		species	
	Lineage		Lineage
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda; Insecta; Dicondylia; Pterygota; Neoptera		cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Protostomia; Ecdysozoa; Panarthropoda; Arthropoda; Mandibulata; Pancrustacea; Hexapoda; Insecta; Dicondylia; Pterygota; Neoptera; Holometabola; Amphimesnoptera; Lepidoptera; Glossata; Neolepidoptera; Heteroneura; Ditrysia; Obtectomera; Pyraloidea; Crambidae; Pyraustinae; Saucrobotys	
	Parent		Parent
Neoptera () - (Rank: infraclass) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 33340)		Saucrobotys () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 263371)	
	NCBI Taxonomy ID		NCBI Taxonomy ID
33392 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 33392)		263372 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 263372)	
	is Taxon A an Intraspecies?		is Taxon B an Intraspecies?
No		No	

GENOTYPIC CHANGE

	Generic Gene Name		UniProtKB Mus musculus
Atp1a1		Q8VDN2 (http://www.uniprot.org/uniprot/Q8VDN2)	
	Synonyms		GenebankID or UniProtKB
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:000524 : ATP binding (https://www.ebi.ac.uk/QuickGO/term/GO:000524)			
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>)
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>)

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

Q111L

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	Leu	111

Main Reference

Widespread convergence in toxin resistance by predictable molecular evolution. (2015) (<https://pubmed.ncbi.nlm.nih.gov/26372961>)

Authors

Ujvari B; Casewell NR; Sunagar K; Arbuckle K; WÅ¼aster W; Lo N; O'Meally D; Beckmann C; King GF; Deplazes E; Madsen T

Abstract

The question about whether evolution is unpredictable and stochastic or intermittently constrained along predictable pathways is the subject of a fundamental debate in biology, in which understanding convergent evolution plays a central role. At the molecular level, documented examples of convergence are rare and limited to occurring within specific taxonomic groups. Here we provide evidence of constrained convergent molecular evolution across the metazoan tree of life. We show that resistance to toxic cardiac glycosides produced by plants and bufonid toads is mediated by similar molecular changes to the sodium-potassium-pump (Na⁽⁺⁾/K⁽⁺⁾-ATPase) in insects, amphibians, reptiles, and mammals. In toad-feeding reptiles, resistance is conferred by two point mutations that have evolved convergently on four occasions, whereas evidence of a molecular reversal back to the susceptible state in varanid lizards migrating to toad-free areas suggests that toxin resistance is maladaptive in the absence of selection. Importantly, resistance in all taxa is mediated by replacements of 2 of the 12 amino acids comprising the Na⁽⁺⁾/K⁽⁺⁾-ATPase H1-H2 extracellular domain that constitutes a core part of the cardiac glycoside binding site. We provide mechanistic insight into the basis of resistance by showing that these alterations perturb the interaction between the cardiac glycoside bufalin and the Na⁽⁺⁾/K⁽⁺⁾-ATPase. Thus, similar selection pressures have resulted in convergent evolution of the same molecular solution across the breadth of the animal kingdom, demonstrating how a scarcity of possible solutions to a selective challenge can lead to highly predictable evolutionary responses.

Additional References

RELATED GEPHE

Related Genes

61 (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, SAP-2, Cpm1, esterase A8 and B8, esterase B4, esterase B5, Acetylcholinesterase (Ace-2), esterase B1, 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, Nav1 sodium channel, CHKov1, CYP6B1, CYP6B4, FMO1) (<https://www.gephebase.org/search-criteria?/or+Taxon+ID=~33392^/and+Trait=Xenobiotic+resistance/or+Taxon+ID=~263372^/and+Trait=Xenobiotic+resistance/and+groupHaplotypes=true#gephebase-summary-title>)

Related Haplotypes

8 (<https://www.gephebase.org/search-criteria?/or+Gene+Gephebase=~Na/K-ATPase+alpha-subunit^/and+Taxon+ID=~33392^/or+Gene+Gephebase=~Na/K-ATPase+alpha-subunit^/and+Taxon+ID=~263372^#gephebase-summary-title>)

EXTERNAL LINKS

COMMENTS