

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)		GP00000700	
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 href="https://www.gephebase.org/search-criteria?/and+Trait=<sup>^</sup>Xenobiotic resistance (cardiac glycosides)<sup>^</sup>#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Trait=[^]Xenobiotic resistance (cardiac glycosides)[^]#gephebase-summary-title)			
	Trait State in Taxon A		
colubrid snakes			
	Trait State in Taxon B		
natricine snakes			
	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		Taxon B	
	Latin Name		Latin Name
Colubridae (https://www.gephebase.org/search-criteria?/and+Taxon Synonyms= [^] Colubridae [^] #gephebase-summary-title)		Natricinae (https://www.gephebase.org/search-criteria?/and+Taxon Synonyms= [^] Natricinae [^] #gephebase-summary-title)	
	Common Name		Common Name
colubrid snakes		-	
	Synonyms		Synonyms
colubrid snakes			
	Rank		Rank
family		Natricidae	
	Lineage		Lineage
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Sauropsida; Sauria; Lepidosauria; Squamata; Bifurcata; Unidentata; Episquamata; Toxicofera; Serpentes; Colubroidea		cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Sauropsida; Sauria; Lepidosauria; Squamata; Bifurcata; Unidentata; Episquamata; Toxicofera; Serpentes; Colubroidea; Colubridae	
	Parent		Parent
Colubroidea () - (Rank: superfamily) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 34989)		Colubridae (colubrid snakes) - (Rank: family) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8578)	
	NCBI Taxonomy ID		NCBI Taxonomy ID
8578 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8578)		169862 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 169862)	
	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		XP_007437634 (https://www.ncbi.nlm.nih.gov/nucore/XP_007437634)	
	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)			

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

No (<https://www.gephebase.org/search-criteria?/and+Presumptive+Null+No+Gephebase-summary-title>)

Presumptive Null

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

Molecular Type

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

Aberration Type

Nonsynonymous

SNP Coding Change

Q111L

Molecular Details of the Mutation

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

Experimental Evidence

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

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

Main Reference

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

Authors

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

Mutation #2

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

Presumptive Null

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

Molecular Type

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

Aberration Type

Nonsynonymous

SNP Coding Change

G120R

Molecular Details of the Mutation

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

Experimental Evidence

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Gly	Arg	120

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

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Additional References

RELATED GEPHE

Related Genes

4 (Nav1.6 sodium channel, Nav1.7 sodium channel, SCN4A (Nav1.4), SCN8A (Nav1.6)) (<https://www.gephebase.org/search-criteria?/or+Taxon+ID=~8578~/and+Trait=Xenobiotic+resistance/or+Taxon+ID=~169862~/and+Trait=Xenobiotic+resistance/and+groupHaplotypes=true#gephebase-summary-title>)

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS

@SeveralMutationsWithEffect