

Gephebase Gene		GepheID
Na/K-ATPase alpha-subunit (https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=~Na/K-ATPase alpha-subunit*#gepbase-summary-title)	GP00000708	Main curator
Published	Entry Status: Courtier	

Taxon A	Taxon B	Trait Category
Physiology (https://www.gephebase.org/search-criteria?/and+TraitCategory=~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 Insectivora ; <i>Condylura cristata</i>		Trait State in Taxon B
<i>Erinaceus europaeus</i>		Ancestral State
Intergeneric or Higher (https://www.gephebase.org/search-criteria?/and+TaxonomicStatus=~Intergeneric or Higher~#gephebase-summary-title)		Taxonomic Status

Taxon A		Taxon B	
	Latin Name		Latin Name
Condylura cristata (<a `condylura="" cristata`#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="`Condylura cristata`#gephebase-summary-title)		Erinaceus europaeus (<a `erinaceus="" europaeus`#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="`Erinaceus europaeus`#gephebase-summary-title)	
star-nosed mole	Common Name	western European hedgehog	Common Name
star-nosed mole; Condylura cristata (Linnaeus, 1758)	Synonyms	western European hedgehog; European hedgehog; common hedgehog; Erinaceus europaeus Linnaeus, 1758; Erinaceus europaeus; Erinaceus europeus	Synonyms
species	Rank		Rank
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Laurasiatheria; Insectivora; Talpidae; Condylura	Lineage	cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Laurasiatheria; Insectivora; Erinaceidae; Erinaceinae; Erinaceus	Lineage
Condylura () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=143301)	Parent	Erinaceus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9364)	Parent
143302 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=143302)	NCBI Taxonomy ID	9365 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9365)	NCBI Taxonomy ID
No	is Taxon A an Intraspecies?	No	is Taxon B an Intraspecies?

Generic Gene Name		UniProtKB Mus musculus
Atp1a1		Q8VDN2 (http://www.uniprot.org/uniprot/Q8VDN2)
Atpa-1; BC010319	Synonyms	GenebankID or UniProtKB
	String	NP_659149 (https://www.ncbi.nlm.nih.gov/nuccore/NP_659149)
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	Presumptive Null
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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

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

Aberration Type

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

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

Q111R+ Q119D

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=))

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Gln	Arg	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; WÄ¼ster 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

Mutation #2

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

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

Aberration Type

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

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

Q111R+ Q119D

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=))

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Gln	Asp	119

Main Reference

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

Authors

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Additional References

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