

GEPHE SUMMARY

	Gephebase Gene		GepheID
Na/K-ATPase alpha-subunit (https://www.gephebase.org/search-criteria?/and+Gene)		GP00000716	
Gephebase="Na/K-ATPase alpha-subunit"#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 (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
Vipera berus - sensitive	
	Trait State in Taxon B
Bitis spp. - resistant	
	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
Vipera berus	
(<a berus"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=" vipera="">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="Vipera berus"#gephebase-summary-title)	
	Common Name
adder	
	Synonyms
Coluber berus; adder; Kreuzotter; Vipera berus (Linnaeus, 1758); NMR:5995; NMR:5995	
	Rank
species	
	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; Viperidae; Viperinae; Vipera	
	Parent
Vipera () - (Rank: genus)	
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=8703)	
	NCBI Taxonomy ID
31155	
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=31155)	
	is Taxon A an Intraspecies?
No	

Taxon B #1	Latin Name
Bitis arietans	
(<a arietans"#gephebase-summary-title"="" bitis="" href="https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="Bitis arietans"#gephebase-summary-title)	
	Common Name
puff adder	
	Synonyms
puff adder; African puff adder	
	Rank
species	
	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; Viperidae; Viperinae; Bitis	
	Parent
Bitis () - (Rank: genus)	
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=8691)	
	NCBI Taxonomy ID
8692	
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=8692)	
	is Taxon B an Intraspecies?
No	

Taxon B #2	Latin Name
Bitis nasicornis	
(https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="Bitis nasicornis"#gephebase-summary-title)	
	Common Name
rhinoceros viper	
	Synonyms
Coluber nasicornis; rhinoceros viper; rhinoceros adder	
	Rank
species	
	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; Viperidae; Viperinae; Bitis	
	Parent
Bitis () - (Rank: genus)	
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=8691)	
	NCBI Taxonomy ID

GENOTYPIC CHANGE

	Generic Gene Name	UniProtKB Mus musculus
Atp1a1	Q8VDN2 (http://www.uniprot.org/uniprot/Q8VDN2)	
Atpa-1; BC010319	Synonyms	GenebankID or UniProtKB
	String	0
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

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

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; WÅ¼ster 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>)

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

G120R

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	Gly	Arg	120

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

RELATED GEPHE

No matches found.

Related Genes

No matches found.

Related Haplotypes

EXTERNAL LINKS

COMMENTS

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