

GEPHE SUMMARY

Gephebase Gene		GepheID
Na/K-ATPase alpha-subunit (https://www.gepibase.org/search-criteria?/and+Gene	GP00000715	Main curator
Gepibase="Na/K-ATPase alpha-subunit"#gepibase-summary-title)		
Published	Entry Status 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
several <i>Varanus</i> spp. (resistant; non-Australian species)	Trait State in Taxon B
several <i>Varanus</i> spp. (Australian species) - non-resistant	Ancestral State
Taxon A	Taxonomic Status
Interspecific (#https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=~Interspecific #gephebase-summary-title)	

Taxon A #1	Latin Name
Varanus salvator (<a +varanus+salvator+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms="+Varanus+salvator+"#gephebase-summary-title)	
water monitor	Common Name
	Synonyms
Hydrosaurus salvator; Stellio salvator; water monitor; Varanus salvator (Laurenti, 1768); ZFMK 22092; ZFMK:22092	
species	Rank
	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; Episuamata; Toxicofera; Anguimorpha; Paleanguimorpha; Varanoidea; Varanidae; Varanus	
Varanus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8556)	Parent
	NCBI Taxonomy ID
62051 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 62051)	
is Taxon A an Infrasppecies?	
No	

Taxon B #1	
Varanus varius	Latin Name
(<a +varanus="" href="https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=" varius+"#gephebase-summary-title"="">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="+Varanus varius+"#gephebase-summary-title)	
	Common Name
lace monitor	
	Synonyms
lace monitor	
	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; Anguimorpha; Paleoanguimorpha; Varanoidea; Varanidae; Varanus	
	Parent
Varanus () - (Rank: genus)	
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8556)	
	NCBI Taxonomy ID
8559	
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8559)	
	is Taxon B an Infrappecies?
No	

Taxon A #2	
	Latin Name
Varanus rudicollis (<a +varanus="" href="https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=" rudicollis*#gephebase-summary-title"="">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="+Varanus rudicollis*#gephebase-summary-title)	
	Common Name
roughneck monitor	
	Synonyms
roughneck monitor; Varanus rudicollis (Gray, 1845); Varanus rudicolis	
	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; Anguimorpha; Paleoanguimorpha; Varanoidea; Varanidae; Varanus	
	Parent
Varanus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8556)	

Taxon B #2	
Varanus tristis (<a +varanus+tristis+"#gephebase-summary-title"="" href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="+Varanus tristis+"#gephebase-summary-title)	Latin Name
-	Common Name
Varanus tristis (Schlegel, 1839); RMNH 3858; RMNH:3858	Synonyms
species	Rank
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; Anguimorpha; Paleoanguimorpha; Varanoidea; Varanidae; Varanus	Lineage
Varanus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=8556)	Parent
NCBI Taxonomy ID	

NCBI Taxonomy ID		62052	
169851		(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 62052)	
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 169851)		is Taxon B an Intraspecies?	
No		No	

Taxon A #3		Taxon B #3	
Varanus dumerilii		Varanus scalaris	
(https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=~Varanus dumerilii~#gephebase-summary-title)		(https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=~Varanus scalaris~#gephebase-summary-title)	
Dumeril monitor		-	
Varanus dumerili; Varanus dumerilli; Dumeril monitor; Varanus dumerilii Schlegel, 1839; RMNH 3168; RMNH:3168		SMF 32806; SMF:32806	
species		species	
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; Anguimorpha; Paleoanguimorpha; Varanoidea; Varanidae; Varanus		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; Anguimorpha; Paleoanguimorpha; Varanoidea; Varanidae; Varanus	
Varanus () - (Rank: genus)		Varanus () - (Rank: genus)	
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 169837)		(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8556)	
169837		169852	
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 169837)		(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 169852)	
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

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=~No~#gephebase-summary-title))

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=~Coding~#gephebase-summary-title))

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~#gephebase-summary-title))

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

L111Q+ R120Q

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=~Candidate+Gene~#gephebase-summary-title))

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Leu	Gln	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>)

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

L111Q+ R120Q

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	Arg	Gln	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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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

No matches found.

Related Haplotypes

1 (<https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^62051^/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^169851^/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^169837^/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^8559^/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^62052^/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^169852^#gephebase-summary-title>)

EXTERNAL LINKS

COMMENTS

Reverse Evolution (Loss of Resistance)

