GEPHE SUMMARY

Gephebase Gene

Na/K-ATPase alpha-subunit (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^Na/K-ATPase alpha-subunit^#gephebase-summary-title)

Entry Status

Published

GepheID

GP00000700

Main curator

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

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

Latin Name

Colubridae
(https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Colubridae^#gephebase-summary-title)

Common Name

colubrid snakes

Synonyms

colubrid snakes

Rank

family

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

Parent

Colubroidea () - (Rank: superfamily)
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 34989)

NCBI Taxonomy ID

8578
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8578)

is Taxon A an Infraspecies?

No

Taxon B

Latin Name

Natricinae
(https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Natricinae^#gephebase-summary-title)

Common Name

-

Synonyms

Natricidae

Rank

subfamily

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; Colubridae

Parent

Colubridae (colubrid snakes) - (Rank: family)
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8578)

NCBI Taxonomy ID

169862
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 169862)

is Taxon B an Infraspecies?

No

GENOTYPIC CHANGE

Generic Gene Name

Atp1a1

Synonyms

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: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)

UniProtKB Mus musculus

Q8VDN2 (http://www.uniprot.org/uniprot/Q8VDN2)

GenebankID or UniProtKB

XP_007437634 (https://www.ncbi.nlm.nih.gov/nuccore/XP_007437634)

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; WÃ¼ster 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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Abstract

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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