GEPHE SUMMARY

Gephebase Gene
Na/K-ATPase alpha-subunit

GephelD
GP00000700

Entry Status
Published

Main curator
Courtier

PHENOTYPIC CHANGE

Trait Category
Physiology

Trait
Xenobiotic resistance (cardiac glycosides)

Trait State in Taxon A
colubrid snakes

Trait State in Taxon B
natricine snakes

Ancestral State
Taxon A

Taxonomic Status
Intergeneric or Higher

Taxon A

Latin Name
Colubridae

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)

NCBI Taxonomy ID
8578

is Taxon A an Infraspecies?
No

Taxon B

Latin Name
Natricinae

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)

NCBI Taxonomy ID
169862

is Taxon B an Infraspecies?
No

GENOTYPIC CHANGE

Generic Gene Name
Atp1a1

Synonyms
Atpa-1; BC010319

String
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
GO:0043531 : ADP binding
GO:0019901 : protein kinase binding
GO:0043548 : phosphatidylinositol 3-kinase binding
GO:0005391 : sodium:potassium-exchanging ATPase activity
GO:0051087 : chaperone binding
GO:0019904 : protein domain specific binding
GO:0030506 : ankyrin binding
GO:0016791 : phosphatase activity
GO:0030955 : potassium ion binding
GO:0031402 : sodium ion binding

UniProtKB Mus musculus
Q8VDN2

GenebankID or UniProtKB
XP_007437634

GO:1990239 : steroid hormone binding

GO - Biological Process
GO:0071383 : cellular response to steroid hormone stimulus
GO:0006813 : potassium ion transport
GO:0006814 : sodium ion transport
GO:0071260 : cellular response to mechanical stimulus
GO:0042493 : response to drug
GO:0008217 : regulation of blood pressure
GO:0015991 : ATP hydrolysis coupled proton transport
GO:0030007 : cellular potassium ion homeostasis
GO:0006883 : cellular sodium ion homeostasis
GO:1990573 : potassium ion import across plasma membrane
GO:0036376 : sodium ion export across plasma membrane
GO:0090662 : ATP hydrolysis coupled transmembrane transport
GO:0060081 : membrane hyperpolarization
GO:0086009 : membrane repolarization
GO:0031947 : negative regulation of glucocorticoid biosynthetic process
GO:0045822 : negative regulation of heart contraction
GO:0045823 : positive regulation of heart contraction
GO:0045989 : positive regulation of striated muscle contraction
GO:0086004 : regulation of cardiac muscle cell contraction
GO:0002028 : regulation of sodium ion transport
GO:0002026 : regulation of the force of heart contraction

GO - Cellular Component
GO:0016021 : integral component of membrane
GO:0005886 : plasma membrane
GO:0016324 : apical plasma membrane
GO:0016020 : membrane
GO:0045121 : membrane raft
GO:0005794 : Golgi apparatus
GO:0032991 : protein-containing complex
GO:0005783 : endoplasmic reticulum
GO:0005768 : endosome
GO:0016323 : basolateral plasma membrane
GO:0005901 : caveola
GO:0030315 : T-tubule
GO:0014069 : postsynaptic density
GO:0014704 : intercalated disc
GO:0043209 : myelin sheath
GO:0042383 : sarcolemma
GO:0005890 : sodium:potassium-exchanging ATPase complex

Mutation #1
Presumptive Null
No

Molecular Type
Coding

Aberration Type
SNP

SNP Coding Change
Nonsynonymous

Molecular Details of the Mutation
Q111L

Experimental Evidence
Candidate Gene

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

Main Reference
Widespread convergence in toxin resistance by predictable molecular evolution. (2015)

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

Molecular Type
Coding

Aberration Type
SNP

SNP Coding Change
Nonsynonymous

Molecular Details of the Mutation
G120R

Experimental Evidence
Candidate Gene

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

Main Reference
Widespread convergence in toxin resistance by predictable molecular evolution. (2015)

Authors
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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))
Related Haplotypes
No matches found.

COMMENTS

@SeveralMutationsWithEffect