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)

GepheID
GP00000699

Entry Status
Published

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
Eleven Varanus species - sensitive

Trait State in Taxon B
other Varanus species - 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 tristis (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Varanus tristis^#gephebase-summary-title)

Common Name
-

Synonyms
Varanus tristis (Schlegel, 1839); RMNH 3858; RMNH:3858

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
62052 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 62052)

is Taxon A an Infraspecies?
No

Taxon B #1

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

Common Name
water monitor

Synonyms
Hydrosaurus salvator; Stellio salvator; water monitor; Varanus salvator (Laurenti, 1768); ZFMK 22092; ZFMK:22092

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
62051 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 62051)

is Taxon B an Infraspecies?
No

Taxon A #2

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

Common Name
-

Synonyms
SAMA R3230

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

Taxon B #2

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

Common Name
-

Synonyms
Nile monitor; Nile monitor lizard; Varanus niloticus (Linnaeus, 1766); NRM 9185; NRM:9185

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)

62045
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 62045)
is Taxon A an Infraspecies?
No

Taxon A #3

Latin Name
Varanus scalaris
(https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Varanus scalaris^#gephebase-summary-title)
Common Name
-
Synonyms
SMF 32806; SMF:32806
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
169852
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 169852)
is Taxon A an Infraspecies?
No

(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8556)
NCBI Taxonomy ID
62046
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 62046)
is Taxon B an Infraspecies?
No

Taxon B #3

Latin Name
Varanus albigularis
(https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Varanus albigularis^#gephebase-summary-title)
Common Name
cape monitor
Synonyms
Varanus exanthematicus albigularis; cape monitor; Varanus albigularis (Daudin, 1802); Varanus exanthematicus albigularis Schmidt, 1919; MNHN 6513; MNHN:6513
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
8558
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8558)
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)
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

UniProtKB Mus musculus
Q8VDN2 (http://www.uniprot.org/uniprot/Q8VDN2)
GenebankID or UniProtKB
()

(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

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=^62052^/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^62045^/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^169852^/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^62051^/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^62046^/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^8558^#gephebase-summary-title)

EXTERNAL LINKS

COMMENTS

@SeveralMutationsWithEffect