

GEPHE SUMMARY

	Gephebase Gene	GepheID
Na/K-ATPase alpha-subunit (https://www.gephebase.org/search-criteria?/and+Gene)	GP00000699	
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
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	
<p>Varanus tristis (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="Varanus tristis"#gephebase-summary-title)</p> <p style="text-align: right;">Latin Name</p> <p>-</p> <p style="text-align: right;">Common Name</p> <p>Varanus tristis (Schlegel, 1839); RMNH 3858; RMNH:3858</p> <p style="text-align: right;">Synonyms</p> <p>species</p> <p style="text-align: right;">Rank</p> <p>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</p> <p style="text-align: right;">Lineage</p> <p>Varanus () - (Rank: genus)</p> <p>(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8556)</p> <p style="text-align: right;">Parent</p> <p>62052</p> <p>(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 62052)</p> <p style="text-align: right;">NCBI Taxonomy ID</p> <p>is Taxon A an Infrapopulation?</p> <p>No</p>	<p>Varanus salvator (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="Varanus salvator"#gephebase-summary-title)</p> <p style="text-align: right;">Latin Name</p> <p>water monitor</p> <p style="text-align: right;">Common Name</p> <p>Hydrosaurus salvator; Stello salvator; water monitor; Varanus salvator (Laurenti, 1768); ZFMK 22092; ZFMK:22092</p> <p style="text-align: right;">Synonyms</p> <p>species</p> <p style="text-align: right;">Rank</p> <p>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</p> <p style="text-align: right;">Lineage</p> <p>Varanus () - (Rank: genus)</p> <p>(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8556)</p> <p style="text-align: right;">Parent</p> <p>62051</p> <p>(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 62051)</p> <p style="text-align: right;">NCBI Taxonomy ID</p> <p>is Taxon B an Infrapopulation?</p> <p>No</p>

Taxon A #2	
<p>Varanus mitchelli (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="Varanus mitchelli"#gephebase-summary-title)</p> <p style="text-align: right;">Latin Name</p> <p>-</p> <p style="text-align: right;">Common Name</p> <p>SAMA R3230</p> <p style="text-align: right;">Synonyms</p> <p>species</p> <p style="text-align: right;">Rank</p> <p>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</p> <p style="text-align: right;">Lineage</p> <p>Varanus () - (Rank: genus)</p> <p>(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8556)</p> <p style="text-align: right;">Parent</p> <p>NCBI Taxonomy ID</p>	<p>Varanus niloticus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="Varanus niloticus"#gephebase-summary-title)</p> <p style="text-align: right;">Latin Name</p> <p>-</p> <p style="text-align: right;">Common Name</p> <p>Nile monitor; Nile monitor lizard; Varanus niloticus (Linnaeus, 1766); NRM 9185; NRM:9185</p> <p style="text-align: right;">Synonyms</p> <p>species</p> <p style="text-align: right;">Rank</p> <p>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</p> <p style="text-align: right;">Lineage</p> <p>Varanus () - (Rank: genus)</p> <p style="text-align: right;">Parent</p> <p>NCBI Taxonomy ID</p>

Taxon B #1	
<p>Varanus salvator (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="Varanus salvator"#gephebase-summary-title)</p> <p style="text-align: right;">Latin Name</p> <p>water monitor</p> <p style="text-align: right;">Common Name</p> <p>Hydrosaurus salvator; Stello salvator; water monitor; Varanus salvator (Laurenti, 1768); ZFMK 22092; ZFMK:22092</p> <p style="text-align: right;">Synonyms</p> <p>species</p> <p style="text-align: right;">Rank</p> <p>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</p> <p style="text-align: right;">Lineage</p> <p>Varanus () - (Rank: genus)</p> <p>(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8556)</p> <p style="text-align: right;">Parent</p> <p>62051</p> <p>(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 62051)</p> <p style="text-align: right;">NCBI Taxonomy ID</p> <p>is Taxon B an Infrapopulation?</p> <p>No</p>	<p>Varanus niloticus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="Varanus niloticus"#gephebase-summary-title)</p> <p style="text-align: right;">Latin Name</p> <p>-</p> <p style="text-align: right;">Common Name</p> <p>Nile monitor; Nile monitor lizard; Varanus niloticus (Linnaeus, 1766); NRM 9185; NRM:9185</p> <p style="text-align: right;">Synonyms</p> <p>species</p> <p style="text-align: right;">Rank</p> <p>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</p> <p style="text-align: right;">Lineage</p> <p>Varanus () - (Rank: genus)</p> <p style="text-align: right;">Parent</p> <p>NCBI Taxonomy ID</p>

Taxon B #2	
<p>Varanus niloticus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="Varanus niloticus"#gephebase-summary-title)</p> <p style="text-align: right;">Latin Name</p> <p>-</p> <p style="text-align: right;">Common Name</p> <p>Nile monitor; Nile monitor lizard; Varanus niloticus (Linnaeus, 1766); NRM 9185; NRM:9185</p> <p style="text-align: right;">Synonyms</p> <p>species</p> <p style="text-align: right;">Rank</p> <p>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</p> <p style="text-align: right;">Lineage</p> <p>Varanus () - (Rank: genus)</p> <p style="text-align: right;">Parent</p> <p>NCBI Taxonomy ID</p>	<p>Varanus niloticus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms="Varanus niloticus"#gephebase-summary-title)</p> <p style="text-align: right;">Latin Name</p> <p>-</p> <p style="text-align: right;">Common Name</p> <p>Nile monitor; Nile monitor lizard; Varanus niloticus (Linnaeus, 1766); NRM 9185; NRM:9185</p> <p style="text-align: right;">Synonyms</p> <p>species</p> <p style="text-align: right;">Rank</p> <p>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</p> <p style="text-align: right;">Lineage</p> <p>Varanus () - (Rank: genus)</p> <p style="text-align: right;">Parent</p> <p>NCBI Taxonomy ID</p>

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

Taxon A #3

Latin Name
<i>Varanus scalaris</i> (<a +varanus+scalaris"="" href="https://www.gephebase.org/search-criteria/?and+Taxon+and+Synonyms=">#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 Infrappecies? No

Taxon B #3

Latin Name
<i>Varanus albigularis</i> (<a +varanus+albigularis"="" href="https://www.gephebase.org/search-criteria/?and+Taxon+and+Synonyms=">#gephebase-summary-title)
Common Name
cape monitor
Synonyms
<i>Varanus exanthematicus albigularis</i> ; cape monitor; <i>Varanus albigularis</i> (Daudin, 1802); <i>Varanus exanthematicus albigularis</i> 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 Infrappecies? 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
0

(<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

No (<https://www.gephebase.org/search-criteria?/and+Presumptive Null=~No~#gephebase-summary-title>)

Coding (<https://www.gephebase.org/search-criteria?/and+Molecular Type=~Coding~#gephebase-summary-title>)

SNP (<https://www.gephebase.org/search-criteria?/and+Aberration Type=~SNP~#gephebase-summary-title>)

Nonsynonymous

Q111L

Candidate Gene (<https://www.gephebase.org/search-criteria?/and+Experimental Evidence=~Candidate Gene~#gephebase-summary-title>)

Presumptive Null

Molecular Type

Aberration Type

SNP Coding Change

Molecular Details of the Mutation

Experimental Evidence

	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

No ([#https://www.gephebase.org/search-criteria?/and+Presumptive Null=^No^#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Presumptive+Null+No))

Presumptive Null

Coding ([#https://www.gephebase.org/search-criteria?/and+Molecular Type="Coding"#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Molecular+Type+Coding))

Molecular 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))

Aberration Type

Nonsynonymous

SNP Coding Change

G120R

Molecular Details of the Mutation

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))

Experimental Evidence

	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

Ujvari B; Casewell NR; Sunagar K; Arbuckle K; WÅyster 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

RELATED GEPHE

Related Genes

No matches found.

Related Haplotypes

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COMMENTS

@SeveralMutationsWithEffect

