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
GP00000702

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
non-bufonid hyloid frogs - sensitive

Trait State in Taxon B
resistant

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

Common Name
-

Synonyms
Bufonoidea

Rank
superfamily

Lineage
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amphibia; Batrachia; Anura; Neobatrachia

Parent
Neobatrachia () - (Rank: suborder) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8416)

NCBI Taxonomy ID
8417 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8417)

is Taxon A an Infraspecies?
No

Taxon B #1

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

Common Name
Pebas stubfoot toad

Synonyms
Pebas stubfoot toad; Atelopus spumarius Cope, 1871

Rank
species

Lineage
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amphibia; Batrachia; Anura; Neobatrachia; Hyloidea; Bufonidae; Atelopus

Parent
Atelopus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 47578)

NCBI Taxonomy ID
330828 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 330828)

is Taxon B an Infraspecies?
No

Taxon B #2

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

Common Name
marine toad

Synonyms
Bufo marinus; Chaunus marinus; Rana marina; marine toad; cane toad; giant toad; Bufo marinus (Linnaeus, 1758); Rhinella marina (Linnaeus, 1758)

Rank
species

Lineage
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amphibia; Batrachia; Anura; Neobatrachia; Hyloidea; Bufonidae; Rhinella

Parent
Rhinella (beaked toads) - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 651667)

NCBI Taxonomy ID
8386

(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8386)

is Taxon B an Infraspecies?

No

Taxon B #3

Latin Name

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

Common Name

granular toad

Synonyms

Bufo granulosus; Chaunus granulosus; granular toad; common lesser toad; Bufo granulosus Spix, 1824; Rhinella granulosa (Spix, 1824); Rhinella granulosus

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amphibia; Batrachia; Anura; Neobatrachia; Hyloidea; Bufonidae; Rhinella

Parent

Rhinella (beaked toads) - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 651667)

NCBI Taxonomy ID

30332 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 30332)

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 (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

UniProtKB Mus musculus

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

GenebankID or UniProtKB

FJ976618 (https://www.ncbi.nlm.nih.gov/nuccore/FJ976618)

(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

Q111R

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	Arg	111

Main Reference

Positive Darwinian selection results in resistance to cardioactive toxins in true toads (Anura: Bufonidae). (2009) (https://pubmed.ncbi.nlm.nih.gov/19465576)

Authors

Moore DJ; Halliday DC; Rowell DM; Robinson AJ; Keogh JS

Abstract

Members of the Family Bufonidae, true toads, are famous for their endogenously synthesized cardioactive steroids that serve as defensive toxins. Evolution of resistance to these toxins is not understood. We sequenced a key region of the toxin's binding site in the Na(+)/K(+) ATPase for relevant taxa representing Hyloidea (including bufonids), Ranoidea and Archaeobatrachia and tested for positive selection in a phylogenetic context. Bufonidae were distinct from other Hyloidea at 4-6 of 12 sites and, with one exception, had a homologous amino acid sequence. Melanophryniscus stelzneri had a distinct sequence, consistent with other independent evidence for a differentiated toxin. Tests within Bufonidae detected positive selection within the binding region, providing, to our knowledge, the first evidence of this type for positive selection within Amphibia. There was no evidence for positive selection on

Bufonidae or M. stelzneri lineages. Sequence change in Leptodactylus ocellatus, a leptodactylid predator of Bufonidae, provides a molecular basis for predator resistance possibly associated with gene duplication.

Additional References

Widespread convergence in toxin resistance by predictable molecular evolution. (2015) (https://pubmed.ncbi.nlm.nih.gov/26372961)

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

N119/122D

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	Asn	Asp	119

Main Reference

Positive Darwinian selection results in resistance to cardioactive toxins in true toads (Anura: Bufonidae). (2009) (https://pubmed.ncbi.nlm.nih.gov/19465576)

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Additional References

Widespread convergence in toxin resistance by predictable molecular evolution. (2015) (https://pubmed.ncbi.nlm.nih.gov/26372961)

RELATED GEPHE

Related Genes

1 (SCN4A (Nav1.4)) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^8417^/and+Trait=Xenobiotic resistance/or+Taxon ID=^330828^/and+Trait=Xenobiotic resistance/or+Taxon ID=^8386^/and+Trait=Xenobiotic resistance/or+Taxon ID=^30332^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

1 (https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^8417^/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^330828^/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^8386^/or+Gene Gephebase=^Na/K-ATPase alpha-subunit^/and+Taxon ID=^30332^#gephebase-summary-title)

EXTERNAL LINKS

COMMENTS

@SeveralMutationsWithEffect - The two amino acid changes occurred in the ancestor of the three frog species (see Figure S5 of Ujvari et al. 2015) NB: Rhinella marina = Bufo marinus