

## GEPHE SUMMARY

**Gephebase Gene**  
Na/K-ATPase alpha-subunit

**Entry Status**  
Published

**GepheID**  
GP00000702

**Main curator**  
Courtier

## PHENOTYPIC CHANGE

**Trait Category**  
Physiology

**Trait**  
Xenobiotic resistance (cardiac glycosides)

**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

### Taxon A

**Latin Name**  
*Hyloidea*

**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)

**NCBI Taxonomy ID**  
8417

**is Taxon A an Intraspecies?**  
No

### Taxon B #1

**Latin Name**  
*Atelopus spumarius*

**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)

**NCBI Taxonomy ID**  
330828

**is Taxon B an Intraspecies?**  
No

### Taxon B #2

**Latin Name**  
*Rhinella marina*

**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)

**NCBI Taxonomy ID**  
8386

**is Taxon B an Intraspecies?**  
No

### Taxon B #3

**Latin Name**

*Rhinella granulosa*

**Common Name**

granular toad

**Synonyms**

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

**Rank**

species

**Lineage**

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

**Parent**

*Rhinella* (beaked toads) - (Rank: genus)

**NCBI Taxonomy ID**

30332

**is Taxon B an Intraspecies?**

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  
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

**UniProtKB Mus musculus**

Q8VDN2

**GenebankID or UniProtKB**

FJ976618

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**

Q111R

**Experimental Evidence**

Candidate Gene

	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)

**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)

**Mutation #2**

**Presumptive Null**

No

**Molecular Type**

Coding

**Aberration Type**

SNP

**SNP Coding Change**

Nonsynonymous

**Molecular Details of the Mutation**

N119/122D

**Experimental Evidence**

Candidate Gene

	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)

#### 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. \(2015\)](#)

## RELATED GEPHE

#### Related Genes

1 (SCN4A (Nav1.4))

#### Related Haplotypes

1

## 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*