GEPHE SUMMARY

Gephebase Gene
SCN4A (Nav1.4)

GephelD
GP00001581

Entry Status
Published

Main curator
Prigent

PHENOTYPIC CHANGE

Trait Category
Physiology

Trait
Xenobiotic resistance (poison frog alkaloids)

Trait State in Taxon A
Frogs susceptible to alkaloids

Trait State in Taxon B
Poison frog Ameerega parvula (Dendrobatidae) resistant to toxin

Ancestral State
Taxon A

Taxonomic Status
Intergeneric or Higher

Taxon A

Latin Name
Anura

Common Name
frogs and toads

Synonyms
Salientia; frogs and toads; anurans; frogs

Rank
order

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

Parent
Batrachia () - (Rank: superorder)

NCBI Taxonomy ID
8342

is Taxon A an Infraspecies?
No

Taxon B

Latin Name
Ameerega parvula

Common Name
ruby poison frog

Synonyms
Dendrobates parvulus; Epipedobates parvulus; Phyllobates parvulus; ruby poison frog; ruby poison-arrow frog; Ameerega parvula (Boulenger, 1882); Dendrobates parvulus Boulenger, 1882

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; Dendrobatidae; Colostethinae; Ameerega

Parent
Ameerega () - (Rank: genus)

NCBI Taxonomy ID
111128

is Taxon B an Infraspecies?
No

GENOTYPIC CHANGE

Generic Gene Name
SCN4A

Synonyms
HYPP; SkM1; CMS16; HYKPP; NAC1A; HOKPP2; Nav1.4; Na(V)1.4

String
9606.ENSP00000396320

Sequence Similarities
Belongs to the sodium channel (TC 1.A.1.10) family. Nav1.4/SCN4A subfamily.

GO - Molecular Function
GO:0005244 : voltage-gated ion channel activity
GO:0005248 : voltage-gated sodium channel activity

GO - Biological Process
GO:0006814 : sodium ion transport
GO:0019228 : neuronal action potential
GO:0034765 : regulation of ion transmembrane transport
GO:0086010 : membrane depolarization during action potential
GO:0006936 : muscle contraction
GO:0035725 : sodium ion transmembrane transport

UniProtKB Homo sapiens
P35499

GenebankID or UniProtKB

GO - Cellular Component
GO:0005886 : plasma membrane
GO:0005887 : integral component of plasma membrane
GO:0030424 : axon
GO:0001518 : voltage-gated sodium channel complex

Presumptive Null
No

Molecular Type
Coding

Aberration Type
SNP

SNP Coding Change
Nonsynonymous

Molecular Details of the Mutation
C>A p.A446D in DI-S6 domain

Experimental Evidence
Candidate Gene

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	-	-	-

Main Reference
Convergent Substitutions in a Sodium Channel Suggest Multiple Origins of Toxin Resistance in Poison Frogs. (2016)

Authors
Tarvin RD; Santos JC; O'Connell LA; Zakon HH; Cannatella DC

Abstract
Complex phenotypes typically have a correspondingly multifaceted genetic component. However, the genotype-phenotype association between chemical defense and resistance is often simple: genetic changes in the binding site of a toxin alter how it affects its target. Some toxic organisms, such as poison frogs (Anura: Dendrobatidae), have defensive alkaloids that disrupt the function of ion channels, proteins that are crucial for nerve and muscle activity. Using protein-docking models, we predict that three major classes of poison frog alkaloids (histrionicotoxins, pumiliotoxins, and batrachotoxins) bind to similar sites in the highly conserved inner pore of the muscle voltage-gated sodium channel, Nav1.4. We predict that poison frogs are somewhat resistant to these compounds because they have six types of amino acid replacements in the Nav1.4 inner pore that are absent in all other frogs except for a distantly related alkaloid-defended frog from Madagascar, Mantella aurantiaca. Protein-docking models and comparative phylogenetics support the role of these replacements in alkaloid resistance. Taking into account the four independent origins of chemical defense in Dendrobatidae, phylogenetic patterns of the amino acid replacements suggest that 1) alkaloid resistance in Nav1.4 evolved independently at least seven times in these frogs, 2) variation in resistance-conferring replacements is likely a result of differences in alkaloid exposure across species, and 3) functional constraint shapes the evolution of the Nav1.4 inner pore. Our study is the first to demonstrate the genetic basis of autoresistance in frogs with alkaloid defenses.

Additional References

RELATED GEPHE

Related Genes
1 (Na/K-ATPase alpha-subunit)
Related Haplotypes
15

COMMENTS

Non-null mutation