

GEPHE SUMMARY

SCN4A (Nav1.4) (https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=^SCN4A+(Nav1.4)^#gephebase-summary-title)	Gephebase Gene	GP00001577	GepheID
Published	Entry Status	Prigent	Main curator

PHENOTYPIC CHANGE

Physiology (https://www.gephebase.org/search-criteria?/and+Trait+Category=^Physiology^#gephebase-summary-title)	Trait Category		
Xenobiotic resistance (poison frog alkaloids) (https://www.gephebase.org/search-criteria?/and+Trait=^Xenobiotic+resistance+(poison+frog+alkaloids)^#gephebase-summary-title)	Trait		
Frogs susceptible to alkaloids	Trait State in Taxon A		
Poison frog <i>Dendrobates captivus</i> (Dendrobatidae) resistant to toxin	Trait State in Taxon B		
Taxon A	Ancestral State		
Intergeneric or Higher (https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=^Intergeneric+or+Higher^#gephebase-summary-title)	Taxonomic Status		
		Taxon A	Taxon B
	Latin Name		Latin Name
Anura (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Anura^#gephebase-summary-title)			<i>Excidobates captivus</i> (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Excidobates+captivus^#gephebase-summary-title)
frogs and toads	Common Name		Rio Santiago poison frog
Salientia; frogs and toads; anurans; frogs	Synonyms		
order	Rank		Adelphobates captivus; <i>Dendrobates captivus</i> ; <i>Ranitomeya captiva</i> ; Rio Santiago poison frog; Santiago poison frog; <i>Adelphobates captivus</i> (Myers, 1982); <i>Dendrobates captivus</i> Myers, 1982
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amphibia; Batrachia	Lineage		species
Batrachia () - (Rank: superorder) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=41666)	Parent		cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amphibia; Batrachia; Anura; Neobatrachia; Hyloidea; Dendrobatidae; Dendrobatinae; <i>Excidobates</i>
8342 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=8342)	NCBI Taxonomy ID		<i>Excidobates</i> () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=1004470)
No	is Taxon A an Intraspecies?		NCBI Taxonomy ID
			467706 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=467706)
			is Taxon B an Intraspecies?
			No

GENOTYPIC CHANGE

SCN4A	Generic Gene Name	P35499 (http://www.uniprot.org/uniprot/P35499)	UniProtKB Homo sapiens
HYPP; SkM1; CMS16; HYKPP; NAC1A; HOKPP2; Nav1.4; Na(V)1.4	Synonyms		GenebankID or UniProtKB
9606.ENSPO0000396320 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSPO0000396320)	String		
Belongs to the sodium channel (TC 1.A.1.10) family. Nav1.4/SCN4A subfamily.	Sequence Similarities		
	GO - Molecular Function		
GO:0005244 : voltage-gated ion channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005244)			
GO:0005248 : voltage-gated sodium channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005248)			

GO - Biological Process

- GO:0006814 : sodium ion transport (<https://www.ebi.ac.uk/QuickGO/term/GO:0006814>)
- GO:0019228 : neuronal action potential (<https://www.ebi.ac.uk/QuickGO/term/GO:0019228>)
- GO:0034765 : regulation of ion transmembrane transport (<https://www.ebi.ac.uk/QuickGO/term/GO:0034765>)
- GO:0086010 : membrane depolarization during action potential (<https://www.ebi.ac.uk/QuickGO/term/GO:0086010>)
- GO:0006936 : muscle contraction (<https://www.ebi.ac.uk/QuickGO/term/GO:0006936>)
- GO:0035725 : sodium ion transmembrane transport (<https://www.ebi.ac.uk/QuickGO/term/GO:0035725>)

GO - Cellular Component

- GO:0005886 : plasma membrane (<https://www.ebi.ac.uk/QuickGO/term/GO:0005886>)
- GO:0005887 : integral component of plasma membrane (<https://www.ebi.ac.uk/QuickGO/term/GO:0005887>)
- GO:0030424 : axon (<https://www.ebi.ac.uk/QuickGO/term/GO:0030424>)
- GO:0001518 : voltage-gated sodium channel complex (<https://www.ebi.ac.uk/QuickGO/term/GO:0001518>)

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

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

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

Nonsynonymous SNP Coding Change

A>G p.L433V in DI-S6 domain Molecular Details of the Mutation

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

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

Convergent Substitutions in a Sodium Channel Suggest Multiple Origins of Toxin Resistance in Poison Frogs. (2016) (<https://pubmed.ncbi.nlm.nih.gov/26782998>) Main Reference

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

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. Abstract

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Additional References

RELATED GEPHE

1 (Na/K-ATPase alpha-subunit) (<https://www.gephebase.org/search-criteria?/or+Taxon ID=~8342~/and+Trait=Xenobiotic resistance/or+Taxon ID=~467706~/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title>) Related Genes

15 ([https://www.gephebase.org/search-criteria?/or+Gene Gephebase=~SCN4A \(Nav1.4\)~/and+Taxon ID=~8342~/or+Gene Gephebase=~SCN4A \(Nav1.4\)~/and+Taxon ID=~467706~#gephebase-summary-title](https://www.gephebase.org/search-criteria?/or+Gene Gephebase=~SCN4A (Nav1.4)~/and+Taxon ID=~8342~/or+Gene Gephebase=~SCN4A (Nav1.4)~/and+Taxon ID=~467706~#gephebase-summary-title)) Related Haplotypes

EXTERNAL LINKS

COMMENTS

Non-null mutation