GEPHE SUMMARY

Gephebase Gene

SCN4A (Nav1.4) (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^SCN4A (Nav1.4)^#gephebase-summary-title)

Entry Status

Published

GepheID

GP00001588

Main curator

Prigent

PHENOTYPIC CHANGE

Trait Category

Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Physiology^#gephebase-summary-title)

Trait

Xenobiotic resistance (poison frog alkaloids) (https://www.gephebase.org/search-criteria?/and+Trait=^Xenobiotic resistance (poison frog alkaloids)^#gephebase-summary-title)

Trait State in Taxon A

Frogs susceptible to alkaloids

Trait State in Taxon B

Poison frog Phyllobates terribilis (Dendrobatidae) resistant to toxin

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

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

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) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 41666)

NCBI Taxonomy ID

8342 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8342)

is Taxon A an Infraspecies?

No

Taxon B

Latin Name

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

Common Name

-

Synonyms

-

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; Dendrobatinae; Phyllobates

Parent

Phyllobates () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 51961)

NCBI Taxonomy ID

111132 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 111132)

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 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier= 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 (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)

UniProtKB Homo sapiens

P35499 (http://www.uniprot.org/uniprot/P35499)

GenebankID or UniProtKB

()

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)

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

C>A p.N1584T in DIV-S6 domain

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	-	-	-

Main Reference

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

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) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^8342^/and+Trait=Xenobiotic resistance/or+Taxon ID=^111132^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

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=^111132^#gephebase-summary-title)

EXTERNAL LINKS

COMMENTS