

GEPHE SUMMARY

SCN4A (Nav1.4) (https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=~SCN4A (Nav1.4)~#gephebase-summary-title)	Gephebase Gene	GP00000729	GepheID
Published	Entry Status	Martin	Main curator

PHENOTYPIC CHANGE

Physiology (https://www.gephebase.org/search-criteria?/and+Trait+Category=~Physiology^#gephebase-summary-title)		Trait Category	
Xenobiotic resistance (TTX) (https://www.gephebase.org/search-criteria?/and+Trait=~Xenobiotic+resistance+(TTX)^#gephebase-summary-title)		Trait	
Amphiesma vibakari		Trait State in Taxon A	
Amphiesma pryeri		Trait State in Taxon B	
Taxon A		Ancestral State	
Interspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=~Interspecific^#gephebase-summary-title)		Taxonomic Status	
Taxon A		Taxon B	
Hebius vibakari (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Hebius+vibakari^#gephebase-summary-title)		Hebius pryeri (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Hebius+pryeri^#gephebase-summary-title)	
Common Name		Common Name	
Japanese keelback		Pryer’s keelback	
Synonyms		Synonyms	
Amphiesma vibakari; Tropidonotus vibakari; Japanese keelback; Amphiesma vibakari (Boie, 1826)		Amphiesma pryeri; Tropidonotus pryeri; Pryer’s keelback; Amphiesma pryeri (Boulenger, 1887)	
Rank		Rank	
species		species	
Lineage		Lineage	
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Sauropsida; Sauria; Lepidosauria; Squamata; Bifurcata; Unidentata; Episquamata; Toxicofera; Serpentes; Colubroidea; Colubridae; Natricinae; Hebius		cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Sauropsida; Sauria; Lepidosauria; Squamata; Bifurcata; Unidentata; Episquamata; Toxicofera; Serpentes; Colubroidea; Colubridae; Natricinae; Hebius	
Parent		Parent	
Hebius () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=1591003)		Hebius () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=1591003)	
NCBI Taxonomy ID		NCBI Taxonomy ID	
1159329 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=1159329)		1159330 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=1159330)	
is Taxon A an Intraspecies?		is Taxon B an Intraspecies?	
No		No	

GENOTYPIC CHANGE

SCN4A	Generic Gene Name	P35499 (http://www.uniprot.org/uniprot/P35499)	UniProtKB Homo sapiens
	Synonyms		GenebankID or UniProtKB
HYPP; SkM1; CMS16; HYKPP; NAC1A; HOKPP2; Nav1.4; Na(V)1.4		AFD23228 (https://www.ncbi.nlm.nih.gov/nuccore/AFD23228)	
	String		
9606.ENSPP00000396320 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPP00000396320)			
	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>)
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

D1227E = D945E in DIII 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

Constraint shapes convergence in tetrodotoxin-resistant sodium channels of snakes. (2012) (<https://pubmed.ncbi.nlm.nih.gov/22392995>)

Authors

Feldman CR; Brodie ED; Brodie ED; Pfrender ME

Abstract

Natural selection often produces convergent changes in unrelated lineages, but the degree to which such adaptations occur via predictable genetic paths is unknown. If only a limited subset of possible mutations is fixed in independent lineages, then it is clear that constraint in the production or function of molecular variants is an important determinant of adaptation. We demonstrate remarkably constrained convergence during the evolution of resistance to the lethal poison, tetrodotoxin, in six snake species representing three distinct lineages from around the globe. Resistance-conferring amino acid substitutions in a voltage-gated sodium channel, Na(v)1.4, are clustered in only two regions of the protein, and a majority of the replacements are confined to the same three positions. The observed changes represent only a small fraction of the experimentally validated mutations known to increase Na(v)1.4 resistance to tetrodotoxin. These results suggest that constraints resulting from functional tradeoffs between ion channel function and toxin resistance led to predictable patterns of evolutionary convergence at the molecular level. Our data are consistent with theoretical predictions and recent microcosm work that suggest a predictable path is followed during an adaptive walk along a mutational landscape, and that natural selection may be frequently constrained to produce similar genetic outcomes even when operating on independent lineages.

Additional References

Historical Contingency in a Multigene Family Facilitates Adaptive Evolution of Toxin Resistance. (2016) (<https://pubmed.ncbi.nlm.nih.gov/27291053>)

RELATED GEPHE

Related Genes

No matches found.

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS

Non-null mutation. Extreme TTX resistance evolved 5 times in Nav1.4 channel; but only in lineages that had previously evolved resistance in paralogous NaV channels

