

	Gephebase Gene	GepheID
SCN4A (Nav1.4) (https://www.gephebase.org/search-criteria?/and+GeneGephebase=^SCN4A (Nav1.4)^#gephebase-summary-title)	GP00000725	Main curator
Published	Entry Status	Courtier

Physiology (https://www.gephebase.org/search-criteria?/and+Trait+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	
Thamnophis elegans - sensitive		Trait State in Taxon A	
Rhabdophis tigrinus		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	
Thamnophis elegans (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=~Thamnophis elegans~#gephebase-summary-title)		Rhabdophis tigrinus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=~Rhabdophis tigrinus~#gephebase-summary-title)	
Western terrestrial garter snake		Tiger keelback	
Western terrestrial garter snake		Tropidonotus tigrinus; Tiger keelback; Tropidonotus tigrinus Boie 1826; BMNH 1861.12.27.9; BMNH:1861.12.27.9	
species		species	
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Sauropsida; Sauria; Lepidosauria; Squamata; Bifurcata; Unidentata; Episcamata; Toxicofera; Serpentes; Colubroidea; Colubridae; Natricinae; Thamnophis		cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Sauropsida; Sauria; Lepidosauria; Squamata; Bifurcata; Unidentata; Episcamata; Toxicofera; Serpentes; Colubroidea; Colubridae; Natricinae; Rhabdophis	
Thamnophis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=34999)		Rhabdophis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=46270)	
35005 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=35005)		126484 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=126484)	
No is Taxon A an Intraspecies?		No is Taxon B an Intraspecies?	

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	AFD23228 (https://www.ncbi.nlm.nih.gov/nuccore/AFD23228)	GenebankID or UniProtKB
9606.ENSPP00000396320 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPP00000396320)	String		
	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

I1555M

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

The I1555M aa change indicated in Feldman et al 2012 seems to not be associated with resistance according to McGlothlin et al 2016

