

GEPHE SUMMARY

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

PHENOTYPIC CHANGE

	Trait Category	Trait	
Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Physiology^#gephebase-summary-title)			
Xenobiotic resistance (TTX) (https://www.gephebase.org/search-criteria?/and+Trait=Xenobiotic+resistance+(TTX)^#gephebase-summary-title)	Trait State in Taxon A		
Thamnophis elegans - sensitive	Trait State in Taxon B		
Rhabdophis tigrinus	Ancestral State		
Taxon A	Taxonomic Status		
Interspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Interspecific^#gephebase-summary-title)			
Taxon A	Latin Name	Taxon B	Latin Name
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	Common Name	Tiger keelback	Common Name
Western terrestrial garter snake	Synonyms	Tropidonotus tigrinus; Tiger keelback; Tropidonotus tigrinus Boie 1826; BMNH 1861.12.27.9; BMNH:1861.12.27.9	Synonyms
species	Rank	species	Rank
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; Thamnophis	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; Rhabdophis	Lineage
Thamnophis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 34999)	Parent	Rhabdophis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 46270)	Parent
35005 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 35005)	NCBI Taxonomy ID	126484 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 126484)	NCBI Taxonomy ID
No	is Taxon A an Infraspecies?	No	is Taxon B an Infraspecies?

GENOTYPIC CHANGE

	Generic Gene Name	UniProtKB Homo sapiens
SCN4A	P35499 (http://www.uniprot.org/uniprot/P35499)	
	Synonyms	GenebankID or UniProtKB
HYPP; SkM1; CMS16; HYKPP; NAC1A; HOKPP2; Nav1.4; Na(V)1.4 9606.ENSP00000396320 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000396320)	AFD23228 (https://www.ncbi.nlm.nih.gov/nuccore/AFD23228)	
	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 ([#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Presumptive+Null=^No))

Molecular Type

Coding ([#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Molecular+Type=^Coding))

Aberration Type

SNP ([#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Aberration+Type=^SNP))

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

I1555M

Experimental Evidence

Candidate Gene ([#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Experimental+Evidence=^Candidate+Gene))

	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(ν)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(ν)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

