

	Gephebase Gene	GepheID
SCN4A (Nav1.4) (https://www.gepibase.org/search-criteria?/and+GeneGepibase=^SCN4A (Nav1.4)^#gepibase-summary-title)	GP00000727	Main curator
Published	Entry Status: Martin	

	Trait Category
Physiology (https://www.gephebase.org/search-criteria?/and+Trait+Category=~Physiology^#gephebase-summary-title)	Trait
Xenobiotic resistance (TTX) (https://www.gephebase.org/search-criteria?/and+Trait=~Xenobiotic resistance (TTX)^#gephebase-summary-title)	Trait State in Taxon A
<i>Thamnophis couchii</i>	Trait State in Taxon B
<i>Thamnophis atratus</i>	Ancestral State
Taxon A	Taxonomic Status
Interspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=~Interspecific^#gephebase-summary-title)	

Taxon A		Taxon B	
Latin Name	Common Name	Latin Name	Common Name
<i>Thamnophis couchii</i> (#gephebase-summary-title)	-	<i>Thamnophis atratus</i> (#gephebase-summary-title)	-
USNM 866; USNM:866	Thamnophis couchii atratus; USNM 970A; USNM:970A		
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; Episquamata; 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; Episquamata; Toxicofera; Serpentes; Colubroidea; Colubridae; Natricinae; Thamnophis		
Thamnophis () - (Rank: genus)	Thamnophis () - (Rank: genus)		
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 34999)	(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 34999)		
NCBI Taxonomy ID 35003	NCBI Taxonomy ID 35000		
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 35003)	(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 35000)		
is Taxon A an Intraspecies?	is Taxon B an Intraspecies?		
No	No		

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.ENSPO0000396320 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPO0000396320)	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>)

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

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

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

Nonsynonymous

D1568N in DIV domain

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

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

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

McGlothlin JW; Kobiela ME; Feldman CR; Castoe TA; Geffney SL; Hanifin CT; Toledo G; Vonk FJ; Richardson MK; Brodie ED; Pfrender ME; Brodie ED

Novel adaptations must originate and function within an already established genome [1]. As a result, the ability of a species to adapt to new environmental challenges is predicted to be highly contingent on the evolutionary history of its lineage [2-6]. Despite a growing appreciation of the importance of historical contingency in the adaptive evolution of single proteins [7-11], we know surprisingly little about its role in shaping complex adaptations that require evolutionary change in multiple genes. One such adaptation, extreme resistance to tetrodotoxin (TTX), has arisen in several species of snakes through coevolutionary arms races with toxic amphibian prey, which select for TTX-resistant voltage-gated sodium channels (Nav) [12-16]. Here, we show that the relatively recent origins of extreme toxin resistance, which involve the skeletal muscle channel Nav1.4, were facilitated by ancient evolutionary changes in two other members of the same gene family. A substitution conferring TTX resistance to Nav1.7, a channel found in small peripheral neurons, arose in lizards ~170 million years ago (mya) and was present in the common ancestor of all snakes. A second channel found in larger myelinated neurons, Nav1.6, subsequently evolved resistance in four different snake lineages beginning ~438 mya. Extreme TTX resistance has evolved at least five times within the past 12 million years via changes in Nav1.4, but only within lineages that previously evolved resistant Nav1.6 and Nav1.7. Our results show that adaptive protein evolution may be contingent upon enabling substitutions elsewhere in the genome, in this case, in paralogs of the same gene family.

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

RELATED GEPHE

No matches found.

2 ([https://www.gephebase.org/search-criteria?/or+Gene Gephebase=~SCN4A \(Nav1.4\)~/and+Taxon ID=~35003~/or+Gene Gephebase=~SCN4A \(Nav1.4\)~/and+Taxon ID=~35000~#gephebase-summary-title](https://www.gephebase.org/search-criteria?/or+Gene Gephebase=~SCN4A (Nav1.4)~/and+Taxon ID=~35003~/or+Gene Gephebase=~SCN4A (Nav1.4)~/and+Taxon ID=~35000~#gephebase-summary-title))

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

