

GEPHE SUMMARY

	Gephebase Gene		GepheID
SCN4A (Nav1.4) (https://www.gephebase.org/search-criteria?/and+GeneGephebase=~SCN4A (Nav1.4)^#gephebase-summary-title)		GP00000728	
	Entry Status	Martin	Main curator
Published			

PHENOTYPIC CHANGE

	Trait Category		
Physiology (https://www.gephebase.org/search-criteria?/and+TraitCategory=~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		
Thamnophis atratus			
	Trait State in Taxon B		
Thamnophis couchii			
	Ancestral State		
Taxon A			
	Taxonomic Status		
Interspecific (https://www.gephebase.org/search-criteria?/and+TaxonomicStatus=~Interspecific^#gephebase-summary-title)			
	Taxon A		Taxon B
	Latin Name		Latin Name
Thamnophis atratus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=~Thamnophis atratus^#gephebase-summary-title)		Thamnophis couchii (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=~Thamnophis couchii^#gephebase-summary-title)	
	Common Name		Common Name
-		-	
	Synonyms		Synonyms
Thamnophis couchii atratus; USNM 970A; USNM:970A		USNM 866; USNM:866	
	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; 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	
	Parent		Parent
Thamnophis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 34999)		Thamnophis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 34999)	
	NCBI Taxonomy ID		NCBI Taxonomy ID
35000 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 35000)		35003 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 35003)	
	is Taxon A an Intraspecies?		is Taxon B an Intraspecies?
No		No	

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		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>)

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

M1276T in DIII 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=~35000~/or+Gene Gephebase=~SCN4A \(Nav1.4\)~/and+Taxon ID=~35003~#gephebase-summary-title](https://www.gephebase.org/search-criteria?/or+Gene Gephebase=~SCN4A (Nav1.4)~/and+Taxon ID=~35000~/or+Gene Gephebase=~SCN4A (Nav1.4)~/and+Taxon ID=~35003~#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

