

SCN4A (Nav1.4) (https://www.gephebase.org/search-criteria?/and+GeneGephebase=^SCN4A (Nav1.4)^#gephebase-summary-title)	Gephebase Gene	GP00000724	GepheID
Published	Entry Status	Martin	Main curator

Trait Category		Trait	
Physiology (#https://www.gephebase.org/search-criteria?/and+Trait+Category=~Physiology)			
Xenobiotic resistance (TTX) (#https://www.gephebase.org/search-criteria?/and+Trait=~Xenobiotic+resistance+(TTX)#gephebase-summary-title)			
Erythrolamprus (=Liophis) poecilogyrus		Trait State in Taxon A	
Liophis (= Erythrolamprus) epinephelus		Trait State in Taxon B	
Taxon A		Ancestral State	
Interspecific (#https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=~Interspecific)		Taxonomic Status	
Taxon A		Taxon B	
Latin Name		Latin Name	
Erythrolamprus poecilogyrus (#https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Erythrolamprus+poecilogyrus)		Erythrolamprus epinephelus (#https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Erythrolamprus+epinephelus)	
Common Name		Common Name	
-		-	
Synonyms		Synonyms	
Coluber poecilogyrus; Liophis poecilogyrus; Coluber poecilogyrus Wied-Neuwied, 1825; Liophis poecilogyrus (Wied-Neuwied, 1825); AMNH 3594; AMNH:3594		Erythrolamprus epinephalus; Leimadophis epinephelus; Liophis epinephelus; Liophis epinephelus Cope, 1862; ANSP 3688; ANSP:3688	
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; Episuamata; Toxicofera; Serpentes; Colubroidea; Dipsadidae; Erythrolamprus		cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Sauropsida; Sauria; Lepidosauria; Squamata; Bifurcata; Unidentata; Episuamata; Toxicofera; Serpentes; Colubroidea; Dipsadidae; Erythrolamprus	
Parent		Parent	
Erythrolamprus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=121327)		Erythrolamprus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=121327)	
NCBI Taxonomy ID		NCBI Taxonomy ID	
338838 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=338838)		758879 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=758879)	
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.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

G1569D in DIV domain and D1568S in DIV domain with D1568S supposed to increase the resistance - exact causing mutation(s) unknown

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

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

Authors

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

Abstract

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 ~4170 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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Additional References

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

RELATED GEPHE

Related Genes

1 (SCN8A (Nav1.6)) (<https://www.gephebase.org/search-criteria?/or+Taxon ID=~338838^/and+Trait=Xenobiotic resistance/or+Taxon ID=~758879^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title>)

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