

## GEPHE SUMMARY

SCN9A (Nav1.7) ( <a href="https://www.gephebase.org/search-criteria?/and+Gene+Gephebase+SCN9A+Nav1.7">#https://www.gephebase.org/search-criteria?/and+Gene+Gephebase+SCN9A+Nav1.7</a> ) Gephebase=^SCN9A (Nav1.7)^#gephebase-summary-title	Gephebase Gene	GP00001648	GepheID
Published	Entry Status	Prigent	Main curator

## PHENOTYPIC CHANGE

Physiology ( <a href="https://www.gephebase.org/search-criteria?/and+Trait+Category+Physiology">#https://www.gephebase.org/search-criteria?/and+Trait+Category+Physiology</a> ) Category=^Physiology^#gephebase-summary-title	Trait Category		
Xenobiotic resistance (TTX) ( <a href="https://www.gephebase.org/search-criteria?/and+Trait+Xenobiotic+resistance+TTX">#https://www.gephebase.org/search-criteria?/and+Trait+Xenobiotic+resistance+TTX</a> ) criteria?/and+Trait=Xenobiotic resistance (TTX)^#gephebase-summary-title	Trait		
TTX-Sensitive Ramphotyphlops bituberculatus	Trait State in Taxon A		
TTX-Resistant Leptotyphlops	Trait State in Taxon B		
Taxon A	Ancestral State		
Intergenic or Higher ( <a href="https://www.gephebase.org/search-criteria?/and+Taxonomic+Status+Intergenic+or+Higher">#https://www.gephebase.org/search-criteria?/and+Taxonomic+Status+Intergenic+or+Higher</a> ) Status=^Intergenic or Higher^#gephebase-summary-title	Taxonomic Status		
	Taxon A	Taxon B	
Anilius bituberculatus ( <a href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms+Anilius+bituberculatus">#https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms+Anilius+bituberculatus</a> ) bituberculatus^#gephebase-summary-title	Latin Name	Leptotyphlops ( <a href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms+Leptotyphlops">#https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms+Leptotyphlops</a> ) Synonyms=^Leptotyphlops^#gephebase-summary-title	Latin Name
prong-snouted blind snake	Common Name	-	Common Name
Ramphotyphlops bituberculatus; Typhlops bituberculatus; prong-snouted blind snake; Typhlops bituberculatus Peters 1863; ZMB 4723; ZMB:4723	Synonyms	-	Synonyms
species	Rank	genus	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; Typhlopoidea; Typhlopidae; Anilius	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; Typhlopoidea; Leptotyphlopidae	Lineage
Anilius () - (Rank: genus) ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=1539840">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=1539840</a> )	Parent	Leptotyphlopidae (slender blind snakes) - (Rank: family) ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=34977">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=34977</a> )	Parent
261707 ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=261707">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=261707</a> )	NCBI Taxonomy ID	39070 ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=39070">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=39070</a> )	NCBI Taxonomy ID
No	is Taxon A an Intraspecies?	No	is Taxon B an Intraspecies?

## GENOTYPIC CHANGE

SCN9A	Generic Gene Name	Q15858 ( <a href="http://www.uniprot.org/uniprot/Q15858">http://www.uniprot.org/uniprot/Q15858</a> )	UniProtKB Homo sapiens
PN1; ETHA; NENA; SFNP; FEB3B; NE-NA; GEFSP7; HSN2D; Nav1.7	Synonyms	()	GenebankID or UniProtKB
9606.ENSP00000386306 ( <a href="http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSP00000386306">http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSP00000386306</a> )	String		
Belongs to the sodium channel (TC 1.A.1.10) family. Nav1.7/SCN9A subfamily.	Sequence Similarities		
GO:0031402 : sodium ion binding ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0031402">https://www.ebi.ac.uk/QuickGO/term/GO:0031402</a> )	GO - Molecular Function		
GO:0005244 : voltage-gated ion channel activity ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0005244">https://www.ebi.ac.uk/QuickGO/term/GO:0005244</a> )			
GO:0005248 : voltage-gated sodium channel activity ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0005248">https://www.ebi.ac.uk/QuickGO/term/GO:0005248</a> )			

GO - Biological Process

- GO:0006814 : sodium ion transport (<https://www.ebi.ac.uk/QuickGO/term/GO:0006814>)
- GO:0006954 : inflammatory response (<https://www.ebi.ac.uk/QuickGO/term/GO:0006954>)
- GO:0019228 : neuronal action potential (<https://www.ebi.ac.uk/QuickGO/term/GO:0019228>)
- GO:0009791 : post-embryonic development (<https://www.ebi.ac.uk/QuickGO/term/GO:0009791>)
- GO:0019233 : sensory perception of pain (<https://www.ebi.ac.uk/QuickGO/term/GO:0019233>)
- 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:0035725 : sodium ion transmembrane transport (<https://www.ebi.ac.uk/QuickGO/term/GO:0035725>)
- GO:0048266 : behavioral response to pain (<https://www.ebi.ac.uk/QuickGO/term/GO:0048266>)
- GO:0009636 : response to toxic substance (<https://www.ebi.ac.uk/QuickGO/term/GO:0009636>)

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>)

Presumptive Null

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

Molecular Type

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

Aberration Type

Nonsynonymous

SNP Coding Change

A1681G (1.5x resistance) in DIV

Molecular Details of the Mutation

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

Experimental Evidence

	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>)

Main Reference

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

Authors

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  $\hat{\sim}$ 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  $\hat{\sim}$ 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.

Abstract

Copyright © 2016 Elsevier Ltd. All rights reserved.

Additional References

RELATED GEPHE

No matches found.

Related Genes

2 ([https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^SCN9A \(Nav1.7\)^/and+Taxon ID=^261707^/or+Gene Gephebase=^SCN9A \(Nav1.7\)^/and+Taxon ID=^39070^#gephebase-summary-title](https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^SCN9A (Nav1.7)^/and+Taxon ID=^261707^/or+Gene Gephebase=^SCN9A (Nav1.7)^/and+Taxon ID=^39070^#gephebase-summary-title))

Related Haplotypes

## EXTERNAL LINKS

## COMMENTS

Non-null mutation