

## GEPHE SUMMARY

SCN8A (Nav1.6) ( <a href="https://www.gephebase.org/search-criteria?/and+Gene">https://www.gephebase.org/search-criteria?/and+Gene</a> ) Gephebase= <sup>^</sup> SCN8A (Nav1.6) <sup>^</sup> #gephebase-summary-title	Gephebase Gene	GP00001654	GepheID
Published	Entry Status	Prigent	Main curator

## PHENOTYPIC CHANGE

Physiology ( <a href="https://www.gephebase.org/search-criteria?/and+Trait">https://www.gephebase.org/search-criteria?/and+Trait</a> ) Category= <sup>^</sup> Physiology <sup>^</sup> #gephebase-summary-title	Trait Category		
Xenobiotic resistance (TTX) ( <a href="https://www.gephebase.org/search-criteria?/and+Trait=&lt;sup&gt;^&lt;/sup&gt;Xenobiotic resistance (TTX)&lt;sup&gt;^&lt;/sup&gt;#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Trait=<sup>^</sup>Xenobiotic resistance (TTX)<sup>^</sup>#gephebase-summary-title</a> )	Trait		
TTX-Sensitive <i>Naja kaouthia</i>	Trait State in Taxon A		
TTX-Resistant <i>Elapsoidea nigra</i> (Elapidae)	Trait State in Taxon B		
Taxon A	Ancestral State		
Interspecific ( <a href="https://www.gephebase.org/search-criteria?/and+Taxonomic">https://www.gephebase.org/search-criteria?/and+Taxonomic</a> ) Status= <sup>^</sup> Interspecific <sup>^</sup> #gephebase-summary-title	Taxonomic Status		
	Taxon A	Taxon B	
<i>Naja kaouthia</i> ( <a href="https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=&lt;sup&gt;^&lt;/sup&gt;Naja kaouthia&lt;sup&gt;^&lt;/sup&gt;#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=<sup>^</sup>Naja kaouthia<sup>^</sup>#gephebase-summary-title</a> )	Latin Name	<i>Elapsoidea nigra</i> ( <a href="https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=&lt;sup&gt;^&lt;/sup&gt;Elapsoidea nigra&lt;sup&gt;^&lt;/sup&gt;#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=<sup>^</sup>Elapsoidea nigra<sup>^</sup>#gephebase-summary-title</a> )	Latin Name
monocled cobra	Common Name	-	Common Name
<i>Naja naja kaouthia</i> ; monocled cobra; <i>Naja kaouthia</i> Lesson, 1831	Synonyms	BMNH 1946.1.18.95; BMNH:1946.1.18.95	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; Elapidae; Elapinae; <i>Naja</i>	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; Elapidae; Elapinae; <i>Elapsoidea</i>	Lineage
<i>Naja</i> () - (Rank: genus) ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8638">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8638</a> )	Parent	<i>Elapsoidea</i> () - (Rank: genus) ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 55265">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 55265</a> )	Parent
8649 ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8649">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 8649</a> )	NCBI Taxonomy ID	66178 ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 66178">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 66178</a> )	NCBI Taxonomy ID
No	is Taxon A an Intraspecies?	No	is Taxon B an Intraspecies?

## GENOTYPIC CHANGE

SCN8A	Generic Gene Name	A0A1B0Z7G3 ( <a href="http://www.uniprot.org/uniprot/A0A1B0Z7G3">http://www.uniprot.org/uniprot/A0A1B0Z7G3</a> )	UniProtKB <i>Elapsoidea nigra</i>
-	Synonyms	()	GenebankID or UniProtKB
-	String		
Belongs to the sodium channel (TC 1.A.1.10) family.	Sequence Similarities		
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 - Molecular Function		
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:0034765 : regulation of ion transmembrane transport ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0034765">https://www.ebi.ac.uk/QuickGO/term/GO:0034765</a> )	GO - Biological Process		
	GO - Cellular Component		

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

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

I1709V in DIV domain (2x resistance)

Experimental Evidence

Candidate Gene ([https://www.gephebase.org/search-criteria?/and+Experimental Evidence=~Candidate Gene^#gephebase-summary-title](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; Geffeney SL; Hanifin CT; Toledo G; Vonk FJ; Richardson MK; Brodie ED; Pfrender 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  $\sim 170$  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  $\sim 438$  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.

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Additional References

## RELATED GEPHE

Related Genes

No matches found.

Related Haplotypes

1 ([https://www.gephebase.org/search-criteria?/or+Gene Gephebase=~SCN8A \(Nav1.6\)^/and+Taxon ID=~8649^/or+Gene Gephebase=~SCN8A \(Nav1.6\)^/and+Taxon ID=~66178^#gephebase-summary-title](https://www.gephebase.org/search-criteria?/or+Gene+Gephebase=~SCN8A+(Nav1.6)^/and+Taxon+ID=~8649^/or+Gene+Gephebase=~SCN8A+(Nav1.6)^/and+Taxon+ID=~66178^#gephebase-summary-title))

## EXTERNAL LINKS

## COMMENTS

Non-null mutation