

GEPHE SUMMARY

	Gephebase Gene	GephelD
SCN4A (Nav1.4) (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^SCN4A (Nav1.4)^#gephebase-summary-title)	GP00000732	
Published	Entry Status	Main curator

PHENOTYPIC CHANGE

	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	
Thamnophis sirtalis - sensitive	Trait State in Taxon B	
Thamnophis sirtalis - resistant - Willow creek	Ancestral State	
Data not curated	Taxonomic Status	
Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Intraspecific^#gephebase-summary-title)		
Taxon A		Taxon B
Thamnophis sirtalis (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Thamnophis+sirtalis^#gephebase-summary-title)	Latin Name	Latin Name
-	Common Name	Common Name
FMNH 73660; FMNH:73660	Synonyms	Synonyms
species	Rank	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; Colubridae; Natricinae; Thamnophis	Lineage	Lineage
Thamnophis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 34999)	Parent	Parent
35019 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 35019)	NCBI Taxonomy ID	NCBI Taxonomy ID
No	is Taxon A an Infraspecies?	is Taxon B an Infraspecies?

GENOTYPIC CHANGE

	Generic Gene Name	UniProtKB Homo sapiens
SCN4A		
HYPP; SkM1; CMS16; HYKPP; NAC1A; HOKPP2; Nav1.4; Na(V)1.4 9606.ENSP00000396320 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000396320)	Synonyms	GenebankID or UniProtKB
	String	DAA64623 (https://www.ncbi.nlm.nih.gov/nuccore/DAA64623)
	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=%27No%27#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Presumptive%20Null=%27No%27#gephebase-summary-title))

Molecular Type

Coding ([https://www.gephebase.org/search-criteria?/and+Molecular Type=%27Coding%27#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Molecular%20Type=%27Coding%27#gephebase-summary-title))

Aberration Type

SNP ([https://www.gephebase.org/search-criteria?/and+Aberration Type=%27SNP%27#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Aberration%20Type=%27SNP%27#gephebase-summary-title))

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

I1556L and/or D1568N and/or G1569V

Experimental Evidence

Candidate Gene ([https://www.gephebase.org/search-criteria?/and+Experimental Evidence=%27Candidate Gene%27#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Experimental%20Evidence=%27Candidate%20Gene%27#gephebase-summary-title))

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

Main Reference

Evolutionary diversification of TTX-resistant sodium channels in a predator-prey interaction. (2005) (<https://pubmed.ncbi.nlm.nih.gov/15815629>)

Authors

Geffeney SL; Fujimoto E; Brodie ED; Brodie ED; Ruben PC

Abstract

Understanding the molecular genetic basis of adaptations provides incomparable insight into the genetic mechanisms by which evolutionary diversification takes place. Whether the evolution of common traits in different lineages proceeds by similar or unique mutations, and the degree to which phenotypic evolution is controlled by changes in gene regulation as opposed to gene function, are fundamental questions in evolutionary biology that require such an understanding of genetic mechanisms. Here we identify novel changes in the molecular structure of a sodium channel expressed in snake skeletal muscle, tsNa(V)1.4, that are responsible for differences in tetrodotoxin (TTX) resistance among garter snake populations coevolving with toxic newts. By the functional expression of tsNa(V)1.4, we show how differences in the amino-acid sequence of the channel affect TTX binding and impart different levels of resistance in four snake populations. These results indicate that the evolution of a physiological trait has occurred through a series of unique functional changes in a gene that is otherwise highly conserved among vertebrates.

Additional References

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

RELATED GEPHE

	Related Genes
2 (Nav1.6 sodium channel, Nav1.7 sodium channel) (https://www.gephebase.org/search-criteria?/or+Taxon ID=%2735019%27/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title)	Related Genes
2 (https://www.gephebase.org/search-criteria?/or+Gene Gephebase=%27SCN4A (Nav1.4)%27/and+Taxon ID=%2735019%27/or+Gene Gephebase=%27SCN4A (Nav1.4)%27/and+Taxon ID=%2735019%27#gephebase-summary-title)	Related Haplotypes

EXTERNAL LINKS

COMMENTS

Extreme TTX resistance evolved 5 times in Nav1.4 channel; but only in lineages that had previously evolved resistance in paralogous NaV channels

