

GEPHE SUMMARY

SCN4A (Nav1.4) (https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=^SCN4A (Nav1.4)^#gephebase-summary-title)	Gephebase Gene	GP00000730	GepheID
Published	Entry Status	Martin	Main curator

PHENOTYPIC CHANGE

Physiology (https://www.gephebase.org/search-criteria?/and+Trait+Category=^Physiology^#gephebase-summary-title)	Trait Category
Xenobiotic resistance (TTX) (https://www.gephebase.org/search-criteria?/and+Trait=^Xenobiotic resistance (TTX)^#gephebase-summary-title)	Trait
Thamnophis sirtalis - sensitive	Trait State in Taxon A
Thamnophis sirtalis - resistant - Benton	Trait State in Taxon B
Data not curated	Ancestral State
Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=^Intraspecific^#gephebase-summary-title)	Taxonomic Status

Taxon A	Latin Name	Taxon B	Latin Name
Thamnophis sirtalis (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Thamnophis+sirtalis^#gephebase-summary-title)	Thamnophis sirtalis (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Thamnophis+sirtalis^#gephebase-summary-title)	Thamnophis sirtalis (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Thamnophis+sirtalis^#gephebase-summary-title)	Thamnophis sirtalis (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Thamnophis+sirtalis^#gephebase-summary-title)
-	Common Name	-	Common Name
FMNH 73660; FMNH:73660	Synonyms	FMNH 73660; FMNH:73660	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; Colubridae; Natricinae; Thamnophis	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	Lineage
Thamnophis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=34999)	Parent	Thamnophis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=34999)	Parent
35019 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=35019)	NCBI Taxonomy ID	35019 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=35019)	NCBI Taxonomy ID
No	is Taxon A an Intraspecies?	No	is Taxon B an Intraspecies?

GENOTYPIC CHANGE

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	DAA64623 (https://www.ncbi.nlm.nih.gov/nuccore/DAA64623)	GenebankID or UniProtKB
9606.ENSPO0000396320 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPO0000396320)	String		
Belongs to the sodium channel (TC 1.A.1.10) family. Nav1.4/SCN4A subfamily.	Sequence Similarities		
GO:0005244 : voltage-gated ion channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005244)	GO - Molecular Function		
GO:0005248 : voltage-gated sodium channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005248)			
GO:0006814 : sodium ion transport (https://www.ebi.ac.uk/QuickGO/term/GO:0006814)	GO - Biological Process		

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

G1566A in DIV domain

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

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=^35019^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

2 (https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^SCN4A (Nav1.4)^/and+Taxon ID=^35019^/or+Gene Gephebase=^SCN4A (Nav1.4)^/and+Taxon ID=^35019^#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

