GEPHE SUMMARY

Gephebase Gene
SCN4A (Nav1.4) (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^SCN4A (Nav1.4)^#gephebase-summary-title)

GepheID
GP00000731

Entry Status
Published

Main curator
Martin

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 - Warrenton; Benton; 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

Latin Name
Thamnophis sirtalis (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Thamnophis sirtalis^#gephebase-summary-title)

Common Name
-

Synonyms
FMNH 73660; FMNH:73660

Rank
species

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

Parent
Thamnophis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 34999)

NCBI Taxonomy ID
35019 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 35019)

is Taxon A an Infraspecies?
No

Taxon B

Latin Name
Thamnophis sirtalis (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Thamnophis sirtalis^#gephebase-summary-title)

Common Name
-

Synonyms
FMNH 73660; FMNH:73660

Rank
species

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

Parent
Thamnophis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 34999)

NCBI Taxonomy ID
35019 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 35019)

is Taxon B an Infraspecies?
No

GENOTYPIC CHANGE

Generic Gene Name
SCN4A

Synonyms
HYPP; SkM1; CMS16; HYKPP; NAC1A; HOKPP2; Nav1.4; Na(V)1.4

String
9606.ENSP00000396320 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000396320)

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)

UniProtKB Homo sapiens
P35499 (http://www.uniprot.org/uniprot/P35499)

GenebankID or UniProtKB
DAA64623 (https://www.ncbi.nlm.nih.gov/nuccore/DAA64623)

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

I1561V 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