

## GEPHE SUMMARY

**Gephebase Gene**  
SCN4A (Nav1.4)

**Entry Status**  
Published

**GepheID**  
GP00000731

**Main curator**  
Martin

## PHENOTYPIC CHANGE

**Trait Category**  
Physiology

**Trait**  
Xenobiotic resistance (TTX)

**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

### Taxon A

**Latin Name**  
*Thamnophis sirtalis*

**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)

**NCBI Taxonomy ID**  
35019

**is Taxon A an Intraspecies?**  
No

### Taxon B

**Latin Name**  
*Thamnophis sirtalis*

**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)

**NCBI Taxonomy ID**  
35019

**is Taxon B an Intraspecies?**  
No

## GENOTYPIC CHANGE

**Generic Gene Name**  
SCN4A

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

**String**  
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  
GO:0005248 : voltage-gated sodium channel activity

**GO - Biological Process**  
GO:0006814 : sodium ion transport  
GO:0019228 : neuronal action potential  
GO:0034765 : regulation of ion transmembrane transport  
GO:0086010 : membrane depolarization during action potential  
GO:0006936 : muscle contraction  
GO:0035725 : sodium ion transmembrane transport

**UniProtKB Homo sapiens**  
P35499

**GenebankID or UniProtKB**  
DAA64623

#### GO - Cellular Component

GO:0005886 : plasma membrane

GO:0005887 : integral component of plasma membrane

GO:0030424 : axon

GO:0001518 : voltage-gated sodium channel complex

#### Presumptive Null

No

#### Molecular Type

Coding

#### Aberration Type

SNP

#### SNP Coding Change

Nonsynonymous

#### Molecular Details of the Mutation

I1561V in DIV domain

#### Experimental Evidence

Candidate Gene

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

#### Main Reference

Evolutionary diversification of TTX-resistant sodium channels in a predator-prey interaction. (2005)

#### 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)

## RELATED GEPHE

#### Related Genes

2 (Nav1.6 sodium channel, Nav1.7 sodium channel)

#### Related Haplotypes

2

## 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