

GEPHE SUMMARY

Nav1.6 sodium channel (<https://www.gephebase.org/search-criteria?/and+Gene>
 Gephebase=[^]Nav1.6 sodium channel[^]#gephebase-summary-title) Gephebase Gene GP00000735 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 - Willow creek Trait State in Taxon B
 Taxon A Ancestral State
 Intraspecific (<https://www.gephebase.org/search-criteria?/and+Taxonomic>
 Status=[^]Intraspecific[^]#gephebase-summary-title) Taxonomic Status

| Taxon A | Taxon B |
|---|---|
| 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) |
| - | - |
| FMNH 73660; FMNH:73660 | FMNH 73660; FMNH:73660 |
| species | species |
| 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 | 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 |
| Thamnophis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=34999) | Thamnophis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=34999) |
| 35019 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=35019) | 35019 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=35019) |
| No | No |
| is Taxon A an Intraspecies? | is Taxon B an Intraspecies? |

GENOTYPIC CHANGE

SCN8A Generic Gene Name Q9UQD0 (<http://www.uniprot.org/uniprot/Q9UQD0>) UniProtKB Homo sapiens
 MED; PN4; CIAT; BFIS5; NaCh6; CERIII; EIEE13; Nav1.6 Synonyms () GenebankID or UniProtKB
 9606.ENSPO0000346534 String
 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPO0000346534)
 Belongs to the sodium channel (TC 1.A.1.10) family. Nav1.6/SCN8A subfamily. Sequence Similarities
 GO:000524 : ATP binding (<https://www.ebi.ac.uk/QuickGO/term/GO:000524>) 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:0007399 : nervous system development
 (https://www.ebi.ac.uk/QuickGO/term/GO:0007399)
 GO:0007422 : peripheral nervous system development
 (https://www.ebi.ac.uk/QuickGO/term/GO:0007422)
 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:0035725 : sodium ion transmembrane transport
 (https://www.ebi.ac.uk/QuickGO/term/GO:0035725)
 GO:0042552 : myelination (https://www.ebi.ac.uk/QuickGO/term/GO:0042552)

GO - Cellular Component

GO:0016021 : integral component of membrane
 (https://www.ebi.ac.uk/QuickGO/term/GO:0016021)
 GO:0005886 : plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005886)
 GO:0030018 : Z disc (https://www.ebi.ac.uk/QuickGO/term/GO:0030018)
 GO:0031410 : cytoplasmic vesicle (https://www.ebi.ac.uk/QuickGO/term/GO:0031410)
 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)
 GO:0043194 : axon initial segment (https://www.ebi.ac.uk/QuickGO/term/GO:0043194)
 GO:0033268 : node of Ranvier (https://www.ebi.ac.uk/QuickGO/term/GO:0033268)

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

Ile1709Val

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

Parallel evolution of tetrodotoxin resistance in three voltage-gated sodium channel genes in the garter snake *Thamnophis sirtalis*. (2014) (https://pubmed.ncbi.nlm.nih.gov/25135948)

Authors

McGlothlin JW; Chuckalovcak JP; Janes DE; Edwards SV; Feldman CR; Brodie ED; Pfrender ME; Brodie ED

Abstract

Members of a gene family expressed in a single species often experience common selection pressures. Consequently, the molecular basis of complex adaptations may be expected to involve parallel evolutionary changes in multiple paralogs. Here, we use bacterial artificial chromosome library scans to investigate the evolution of the voltage-gated sodium channel (Nav) family in the garter snake *Thamnophis sirtalis*, a predator of highly toxic *Taricha* newts. Newts possess tetrodotoxin (TTX), which blocks Nav's, arresting action potentials in nerves and muscle. Some *Thamnophis* populations have evolved resistance to extremely high levels of TTX. Previous work has identified amino acid sites in the skeletal muscle sodium channel Nav1.4 that confer resistance to TTX and vary across populations. We identify parallel evolution of TTX resistance in two additional Nav paralogs, Nav1.6 and 1.7, which are known to be expressed in the peripheral nervous system and should thus be exposed to ingested TTX. Each paralog contains at least one TTX-resistant substitution identical to a substitution previously identified in Nav1.4. These sites are fixed across populations, suggesting that the resistant peripheral nerves antedate resistant muscle. In contrast, three sodium channels expressed solely in the central nervous system (Nav1.1-1.3) showed no evidence of TTX resistance, consistent with protection from toxins by the blood-brain barrier. We also report the exon-intron structure of six Nav paralogs, the first such analysis for snake genes. Our results demonstrate that the molecular basis of adaptation may be both repeatable across members of a gene family and predictable based on functional considerations.

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Additional References

RELATED GEPHE

Related Genes

2 (Nav1.7 sodium channel, SCN4A (Nav1.4)) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^35019^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS