

Gephebase Gene		GepheID
SCN4A (Nav1.4b gene copy) (https://www.gephebase.org/search-criteria?/and+Gene+Gephebase+SCN4A (Nav1.4b gene copy)*#gephebase-summary-title)	GP00000733	Main curator
Entry Status	Martin	
Published		

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		
Other fishes	Trait State in Taxon A		
Tetraodon nigroviridis	Trait State in Taxon B		
Data not curated	Ancestral State		
Interspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=~Interspecific~#gephebase-summary-title)	Taxonomic Status		
Taxon A		Taxon B	
Teleostei (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Teleostei~#gephebase-summary-title)	Latin Name	Tetraodon nigroviridis (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Tetraodon+nigroviridis~#gephebase-summary-title)	Latin Name
teleost fishes	Common Name	spotted green pufferfish	Common Name
teleost fishes	Synonyms	spotted green pufferfish; Tetraodon nigroviridis Marion de Proce, 1822	Synonyms
infraclass	Rank	species	Rank
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Actinopterygii; Actinopteri; Neopterygii	Lineage	cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Actinopterygii; Actinopteri; Neopterygii; Teleostei; Osteoglossocephalai; Clupeocephala; Euteleosteiomorphia; Neoteleostei; Eurypterygia; Ctenosquamata; Acanthomorphata; Euacanthomorphacea; Percomorphaceae; Eupercaria; Tetraodontiformes; Tetraodontidae; Tetraodon	Lineage
Neopterygii () - (Rank: subclass) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=41665)	Parent	Tetraodon () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=47144)	Parent
32443 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=32443)	NCBI Taxonomy ID	99883 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=99883)	NCBI Taxonomy ID
No	is Taxon A an Intraspecies?	No	is Taxon B an Intraspecies?

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	ABB29442 (https://www.ncbi.nlm.nih.gov/nuccore/ABB29442)	GenebankID or UniProtKB
9606.ENSPO0000396320 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPO0000396320)	String		
	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=~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

E945D

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

Genetic basis of tetrodotoxin resistance in pufferfishes. (2005) (<https://pubmed.ncbi.nlm.nih.gov/16303569>)

Authors

Venkatesh B; Lu SQ; Dandona N; See SL; Brenner S; Soong TW

Abstract

Tetrodotoxin (TTX) is a highly potent neurotoxin that selectively binds to the outer vestibule of voltage-gated sodium channels. Pufferfishes accumulate extremely high concentrations of TTX without any adverse effect. A nonaromatic amino acid (Asn) residue present in domain I of the pufferfish, *Takifugu pardalis*, Na v1.4 channel has been implicated in the TTX resistance of pufferfishes . However, the effect of this residue on TTX sensitivity has not been investigated, and it is not known if this residue is conserved in all pufferfishes. We have investigated the genetic basis of TTX resistance in pufferfishes by comparing the sodium channels from two pufferfishes (*Takifugu rubripes* [fugu] and *Tetraodon nigroviridis*) and the TTX-sensitive zebrafish. Although all three fishes contain duplicate copies of Na v1.4 channels (Na v1.4a and Na v1.4b), several substitutions were found in the TTX binding outer vestibule of the two pufferfish channels. Electrophysiological studies showed that the nonaromatic residue (Asn in fugu and Cys in *Tetraodon*) in domain I of Na v1.4a channels confers TTX resistance. The Glu-to-Asp mutation in domain II of *Tetraodon* channel Na v1.4b is similar to that in the saxitoxin- and TTX-resistant Na⁺ channels of softshell clams . Besides helping to deter predators, TTX resistance enables pufferfishes to selectively feed on TTX-bearing organisms.

Additional References

Toxin-resistant sodium channels: parallel adaptive evolution across a complete gene family. (2008) (<https://pubmed.ncbi.nlm.nih.gov/18258611>)

RELATED GEPHE

Related Genes

5 (AHR2, AIP, ARNT-1c, ARNT-L2a, SCN4A (Nav1.4a gene copy)) (<https://www.gephebase.org/search-criteria?/or+Taxon ID=~32443^/and+Trait=Xenobiotic resistance/or+Taxon ID=~99883^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title>)

Related Haplotypes

1 ([https://www.gephebase.org/search-criteria?/or+Gene Gephebase=~SCN4A \(Nav1.4b gene copy\)^/and+Taxon ID=~32443^/or+Gene Gephebase=~SCN4A \(Nav1.4b gene copy\)^/and+Taxon ID=~99883^#gephebase-summary-title](https://www.gephebase.org/search-criteria?/or+Gene Gephebase=~SCN4A (Nav1.4b gene copy)^/and+Taxon ID=~32443^/or+Gene Gephebase=~SCN4A (Nav1.4b gene copy)^/and+Taxon ID=~99883^#gephebase-summary-title))

EXTERNAL LINKS

COMMENTS

