

GEPHE SUMMARY

	Gephebase Gene	GephelD
SCN4A (Nav1.4a gene copy) (https://www.gephebase.org/search-criteria/?and+Gene Gephebase=^SCN4A (Nav1.4a gene copy)^#gephebase-summary-title)	GP00000722	
Published	Entry Status	Main curator

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	
Other fishes	Trait State in Taxon B	
Takifugu rubripes	Ancestral State	
Data not curated	Taxonomic Status	
Interspecific (https://www.gephebase.org/search-criteria/?and+Taxonomic Status=^Interspecific^#gephebase-summary-title)		
Taxon A		Taxon B
Teleostei (https://www.gephebase.org/search-criteria/?and+Taxon+and+Synonyms=^Teleostei^#gephebase-summary-title)	Latin Name	Latin Name
teleost fishes	Common Name	Common Name
teleost fishes	Synonyms	Synonyms
infraclass	Rank	Rank
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Actinopterygii; Actinopteri; Neopterygii	Lineage	Lineage
Neopterygii () - (Rank: subclass) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 41665)	Parent	Parent
32443 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 32443)	NCBI Taxonomy ID	NCBI Taxonomy ID
No	is Taxon A an Infraspecies?	is Taxon B an Infraspecies?

GENOTYPIC CHANGE

	Generic Gene Name	UniProtKB Homo sapiens
SCN4A	P35499 (http://www.uniprot.org/uniprot/P35499)	
HYPP; SkM1; CMS16; HYKPP; NAC1A; HOKPP2; Nav1.4; Na(V)1.4	String	GenebankID or UniProtKB
9606.ENSP00000396320 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000396320)	Sequence Similarities	ABB29442 (https://www.ncbi.nlm.nih.gov/nuccore/ABB29442)
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 ([#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Presumptive+Null=^No))

Molecular Type

Coding ([#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Molecular+Type=^Coding))

Aberration Type

SNP ([#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Aberration+Type=^SNP))

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

Y401N

Experimental Evidence

Candidate Gene ([#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Experimental+Evidence=^Candidate+Gene))

	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

RELATED GEPHE

Related Genes

5 (AHR2, AIP, ARNT-1c, ARNT-L2a, SCN4A (Nav1.4b gene copy)) ([#gephebase-summary-title](https://www.gephebase.org/search-criteria?/or+Taxon+ID=^32443^/and+Trait=Xenobiotic+resistance/or+Taxon+ID=^31033^/and+Trait=Xenobiotic+resistance/and+groupHaplotypes=true))

Related Haplotypes

1 ([#gephebase-summary-title](https://www.gephebase.org/search-criteria?/or+Gene+Gephebase=^SCN4A+(Nav1.4a+gene+copy)^/and+Taxon+ID=^32443^/or+Gene+Gephebase=^SCN4A+(Nav1.4a+gene+copy)^/and+Taxon+ID=^31033^))

EXTERNAL LINKS

COMMENTS

