

## GEPHE SUMMARY

	Gephebase Gene	GephelD
SCN4A (Nav1.4b gene copy) ( <a href="https://www.gephebase.org/search-criteria/?and+Gene">https://www.gephebase.org/search-criteria/?and+Gene</a> Gephebase=^SCN4A (Nav1.4b gene copy)^#gephebase-summary-title)	GP00000734	
Published	Entry Status	Main curator

## PHENOTYPIC CHANGE

	Trait Category	
Physiology ( <a href="https://www.gephebase.org/search-criteria/?and+Trait">https://www.gephebase.org/search-criteria/?and+Trait</a> Category="Physiology">#gephebase-summary-title)	Trait	
Xenobiotic resistance (TTX) ( <a href="https://www.gephebase.org/search-criteria/?and+Trait=^Xenobiotic+resistance+(TTX)^#gephebase-summary-title">https://www.gephebase.org/search-criteria/?and+Trait=^Xenobiotic+resistance+(TTX)^#gephebase-summary-title</a> )	Trait State in Taxon A	
Other fishes	Trait State in Taxon B	
Takifugu rubripes	Ancestral State	
Data not curated	Taxonomic Status	
Interspecific ( <a href="https://www.gephebase.org/search-criteria/?and+Taxonomic">https://www.gephebase.org/search-criteria/?and+Taxonomic</a> Status="Interspecific">#gephebase-summary-title)		
Taxon A		Taxon B
Teleostei ( <a href="https://www.gephebase.org/search-criteria/?and+Taxon+and+Synonyms=^Teleostei^#gephebase-summary-title">https://www.gephebase.org/search-criteria/?and+Taxon+and+Synonyms=^Teleostei^#gephebase-summary-title</a> )	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) ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 41665">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 41665</a> )	Parent	Parent
32443 ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 32443">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 32443</a> )	NCBI Taxonomy ID	NCBI Taxonomy ID
No	is Taxon A an Infraspecies?	is Taxon B an Infraspecies?

## GENOTYPIC CHANGE

	Generic Gene Name		
SCN4A			UniProtKB Homo sapiens
HYPP; SkM1; CMS16; HYKPP; NAC1A; HOKPP2; Nav1.4; Na(V)1.4	Synonyms		GenebankID or UniProtKB
9606.ENSP00000396320 ( <a href="http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000396320">http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000396320</a> )	String		ABB29442 ( <a href="https://www.ncbi.nlm.nih.gov/nuccore/ABB29442">https://www.ncbi.nlm.nih.gov/nuccore/ABB29442</a> )
Belongs to the sodium channel (TC 1.A.1.10) family. Nav1.4/SCN4A subfamily.	Sequence Similarities		
	GO - Molecular Function		
GO:0005244 : voltage-gated ion channel activity ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0005244">https://www.ebi.ac.uk/QuickGO/term/GO:0005244</a> )			
GO:0005248 : voltage-gated sodium channel activity ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0005248">https://www.ebi.ac.uk/QuickGO/term/GO:0005248</a> )			

## 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

M1240T

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

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

Authors

Jost MC; Hillis DM; Lu Y; Kyle JW; Fozard HA; Zakon HH

Abstract

Approximately 75% of vertebrate proteins belong to protein families encoded by multiple evolutionarily related genes, a pattern that emerged as a result of gene and genome duplications over the course of vertebrate evolution. In families of genes with similar or related functions, adaptation to a strong selective agent should involve multiple adaptive changes across the entire gene family. However, we know of no evolutionary studies that have explicitly addressed this point. Here, we show how 4 taxonomically diverse species of pufferfishes (Tetraodontidae) each evolved resistance to the guanidinium toxins tetrodotoxin (TTX) and saxitoxin (STX) via parallel amino acid replacements across all 8 sodium channels present in teleost fish genomes. This resulted in diverse suites of coexisting sodium channel types that all confer varying degrees of toxin resistance, yet show remarkable convergence among genes and phylogenetically diverse species. Using site-directed mutagenesis and expression of a vertebrate sodium channel, we also demonstrate that resistance to TTX/STX is enhanced up to 15-fold by single, frequently observed replacements at 2 sites that have not previously been implicated in toxin binding but show similar or identical replacements in pufferfishes and in distantly related vertebrate and nonvertebrate animals. This study presents an example of natural selection acting upon a complete gene family, repeatedly arriving at a diverse but limited number of adaptive changes within the same genome. To be maximally informative, we suggest that future studies of molecular adaptation should consider all functionally similar paralogs of the affected gene family.

Additional References

## RELATED GEPHE

## Related Genes

5 (AHR2, AIP, ARNT-1c, ARNT-L2a, SCN4A (Nav1.4a 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+(Nav1.4b+gene+copy)^/and+Taxon+ID=^32443^/or+Gene+Gephebase=^SCN4A+(Nav1.4b+gene+copy)^/and+Taxon+ID=^31033^))

## EXTERNAL LINKS

## COMMENTS

