

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

	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)	

GENOTYPIC CHANGE

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>)

No (https://www.gephebase.org/search-criteria?/and+Presumptive Null=~No~#gephebase-summary-title)	Presumptive Null
Coding (https://www.gephebase.org/search-criteria?/and+Molecular Type=~Coding~#gephebase-summary-title)	Molecular Type
SNP (https://www.gephebase.org/search-criteria?/and+Aberration Type=~SNP~#gephebase-summary-title)	Aberration Type
Nonsynonymous	SNP Coding Change
M1240T	Molecular Details of the Mutation
Candidate Gene (https://www.gephebase.org/search-criteria?/and+Experimental Evidence=~Candidate Gene~#gephebase-summary-title)	Experimental Evidence

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

Toxin-resistant sodium channels: parallel adaptive evolution across a complete gene family. (2008) (https://pubmed.ncbi.nlm.nih.gov/18258611)	Main Reference
Jost MC; Hillis DM; Lu Y; Kyle JW; Fozzard HA; Zakon HH	Authors

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.	Abstract
	Additional References

RELATED GEPHE

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=~31033~/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title)	Related Genes
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=~31033~#gephebase-summary-title)	Related Haplotypes

EXTERNAL LINKS

COMMENTS

