GEPHE SUMMARY

Gephebase Gene
SCN4A (Nav1.4) (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^SCN4A (Nav1.4)^#gephebase-summary-title)

GepheID
GP00000726

Entry Status
Published

Main curator
Martin

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
Thamnophis couchii

Trait State in Taxon B
Thamnophis atratus

Ancestral State
Taxon A

Taxonomic Status
Interspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Interspecific^#gephebase-summary-title)

Taxon A

Latin Name
Thamnophis couchii (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Thamnophis couchii^#gephebase-summary-title)

Common Name
-

Synonyms
USNM 866; USNM:866

Rank
species

Lineage
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

Parent
Thamnophis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 34999)

NCBI Taxonomy ID
35003 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 35003)

is Taxon A an Infraspecies?
No

Taxon B

Latin Name
Thamnophis atratus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Thamnophis atratus^#gephebase-summary-title)

Common Name
-

Synonyms
Thamnophis couchii atratus; USNM 970A; USNM:970A

Rank
species

Lineage
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

Parent
Thamnophis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 34999)

NCBI Taxonomy ID
35000 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 35000)

is Taxon B an Infraspecies?
No

GENOTYPIC CHANGE

Generic Gene Name
SCN4A

Synonyms
HYPP; SkM1; CMS16; HYKPP; NAC1A; HOKPP2; Nav1.4; Na(V)1.4

String
9606.ENSP00000396320 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000396320)

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)

UniProtKB Homo sapiens
P35499 (http://www.uniprot.org/uniprot/P35499)

GenebankID or UniProtKB
AFD23228 (https://www.ncbi.nlm.nih.gov/nuccore/AFD23228)

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

D1277E in DIII domain

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

Historical Contingency in a Multigene Family Facilitates Adaptive Evolution of Toxin Resistance. (2016) (https://pubmed.ncbi.nlm.nih.gov/27291053)

Authors

McGlothlin JW; Kobiela ME; Feldman CR; Castoe TA; Geffeney SL; Hanifin CT; Toledo G; Vonk FJ; Richardson MK; Brodie ED; Pfrender ME; Brodie ED

Abstract

Novel adaptations must originate and function within an already established genome [1]. As a result, the ability of a species to adapt to new environmental challenges is predicted to be highly contingent on the evolutionary history of its lineage [2-6]. Despite a growing appreciation of the importance of historical contingency in the adaptive evolution of single proteins [7-11], we know surprisingly little about its role in shaping complex adaptations that require evolutionary change in multiple genes. One such adaptation, extreme resistance to tetrodotoxin (TTX), has arisen in several species of snakes through coevolutionary arms races with toxic amphibian prey, which select for TTX-resistant voltage-gated sodium channels (Nav) [12-16]. Here, we show that the relatively recent origins of extreme toxin resistance, which involve the skeletal muscle channel Nav1.4, were facilitated by ancient evolutionary changes in two other members of the same gene family. A substitution conferring TTX resistance to Nav1.7, a channel found in small peripheral neurons, arose in lizards â^¼170 million years ago (mya) and was present in the common ancestor of all snakes. A second channel found in larger myelinated neurons, Nav1.6, subsequently evolved resistance in four different snake lineages beginning â^¼438 mya. Extreme TTX resistance has evolved at least five times within the past 12 million years via changes in Nav1.4, but only within lineages that previously evolved resistant Nav1.6 and Nav1.7. Our results show that adaptive protein evolution may be contingent upon enabling substitutions elsewhere in the genome, in this case, in paralogs of the same gene family.

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Additional References

Constraint shapes convergence in tetrodotoxin-resistant sodium channels of snakes. (2012) (https://pubmed.ncbi.nlm.nih.gov/22392995)

RELATED GEPHE

Related Genes

No matches found.

Related Haplotypes

2 (https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^SCN4A (Nav1.4)^/and+Taxon ID=^35003^/or+Gene Gephebase=^SCN4A (Nav1.4)^/and+Taxon ID=^35000^#gephebase-summary-title)

EXTERNAL LINKS

COMMENTS

Non-null mutation. Extreme TTX resistance evolved 5 times in Nav1.4 channel but only in lineages that had previously evolved resistance in paralogous NaV channels