GEPHE SUMMARY

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

GepheID
GP00000729

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
Amphiesma vibakari

Trait State in Taxon B
Amphiesma pryeri

Ancestral State
Taxon A

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

Taxon A

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

Common Name
Japanese keelback

Synonyms
Amphiesma vibakari; Tropidonotus vibakari; Japanese keelback; Amphiesma vibakari (Boie, 1826)

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; Hebius

Parent
Hebius () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 1591003)

NCBI Taxonomy ID
1159329 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 1159329)

is Taxon A an Infraspecies?
No

Taxon B

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

Common Name
Pryer's keelback

Synonyms
Amphiesma pryeri; Tropidonotus pryeri; Pryer's keelback; Amphiesma pryeri (Boulenger, 1887)

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; Hebius

Parent
Hebius () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 1591003)

NCBI Taxonomy ID
1159330 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 1159330)

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

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

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

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

D1227E = D945E 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

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

Authors

Feldman CR; Brodie ED; Brodie ED; Pfrender ME

Abstract

Natural selection often produces convergent changes in unrelated lineages, but the degree to which such adaptations occur via predictable genetic paths is unknown. If only a limited subset of possible mutations is fixed in independent lineages, then it is clear that constraint in the production or function of molecular variants is an important determinant of adaptation. We demonstrate remarkably constrained convergence during the evolution of resistance to the lethal poison, tetrodotoxin, in six snake species representing three distinct lineages from around the globe. Resistance-conferring amino acid substitutions in a voltage-gated sodium channel, Na(v)1.4, are clustered in only two regions of the protein, and a majority of the replacements are confined to the same three positions. The observed changes represent only a small fraction of the experimentally validated mutations known to increase Na(v)1.4 resistance to tetrodotoxin. These results suggest that constraints resulting from functional tradeoffs between ion channel function and toxin resistance led to predictable patterns of evolutionary convergence at the molecular level. Our data are consistent with theoretical predictions and recent microcosm work that suggest a predictable path is followed during an adaptive walk along a mutational landscape, and that natural selection may be frequently constrained to produce similar genetic outcomes even when operating on independent lineages.

Additional References

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

RELATED GEPHE

Related Genes

No matches found.

Related Haplotypes

No matches found.

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