GEPHE SUMMARY

Gephebase Gene

Vkorc1 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^Vkorc1^#gephebase-summary-title)

GepheID

GP00001177

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 (rodenticide; warfarin) (https://www.gephebase.org/search-criteria?/and+Trait=^Xenobiotic resistance (rodenticide; warfarin)^#gephebase-summary-title)

Trait State in Taxon A

Rattus norvegicus

Trait State in Taxon B

Rattus norvegicus - Japan

Ancestral State

Data not curated

Taxonomic Status

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

Taxon A

Latin Name

Rattus norvegicus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Rattus norvegicus^#gephebase-summary-title)

Common Name

Norway rat

Synonyms

rat; rats; Norway rat; brown rat; Rattus norvegicus8; Rattus norwegicus

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Rattus

Parent

Rattus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10114)

NCBI Taxonomy ID

10116 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10116)

is Taxon A an Infraspecies?

No

Taxon B

Latin Name

Rattus norvegicus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Rattus norvegicus^#gephebase-summary-title)

Common Name

Norway rat

Synonyms

rat; rats; Norway rat; brown rat; Rattus norvegicus8; Rattus norwegicus

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Rattus

Parent

Rattus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10114)

NCBI Taxonomy ID

10116 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10116)

is Taxon B an Infraspecies?

Yes

Taxon B Description

Rattus norvegicus - Japan

GENOTYPIC CHANGE

Generic Gene Name

VKORC1

Synonyms

VKOR; MST134; MST576; VKCFD2; EDTP308; MSTP134; MSTP576; UNQ308/PRO351

String

9606.ENSP00000378426 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000378426)

Sequence Similarities

Belongs to the VKOR family.

GO - Molecular Function

GO:0048038 : quinone binding (https://www.ebi.ac.uk/QuickGO/term/GO:0048038)
GO:0047058 : vitamin-K-epoxide reductase (warfarin-insensitive) activity (https://www.ebi.ac.uk/QuickGO/term/GO:0047058)
GO:0047057 : vitamin-K-epoxide reductase (warfarin-sensitive) activity

UniProtKB Homo sapiens

Q9BQB6 (http://www.uniprot.org/uniprot/Q9BQB6)

GenebankID or UniProtKB

AAR82917 (https://www.ncbi.nlm.nih.gov/nuccore/AAR82917)

(https://www.ebi.ac.uk/QuickGO/term/GO:0047057)

GO - Biological Process

GO:0014070 : response to organic cyclic compound
(https://www.ebi.ac.uk/QuickGO/term/GO:0014070)
GO:0017144 : drug metabolic process (https://www.ebi.ac.uk/QuickGO/term/GO:0017144)
GO:0007596 : blood coagulation (https://www.ebi.ac.uk/QuickGO/term/GO:0007596)
GO:0060348 : bone development (https://www.ebi.ac.uk/QuickGO/term/GO:0060348)
GO:0017187 : peptidyl-glutamic acid carboxylation
(https://www.ebi.ac.uk/QuickGO/term/GO:0017187)
GO:0030193 : regulation of blood coagulation
(https://www.ebi.ac.uk/QuickGO/term/GO:0030193)
GO:0046677 : response to antibiotic (https://www.ebi.ac.uk/QuickGO/term/GO:0046677)
GO:0010243 : response to organonitrogen compound
(https://www.ebi.ac.uk/QuickGO/term/GO:0010243)
GO:0042373 : vitamin K metabolic process
(https://www.ebi.ac.uk/QuickGO/term/GO:0042373)

GO - Cellular Component

GO:0016021 : integral component of membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0016021)
GO:0005783 : endoplasmic reticulum
(https://www.ebi.ac.uk/QuickGO/term/GO:0005783)
GO:0005789 : endoplasmic reticulum membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0005789)

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

L128S

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

The genetic basis of resistance to anticoagulants in rodents. (2005) (https://pubmed.ncbi.nlm.nih.gov/15879509)

Authors

Pelz HJ; Rost S; HÃ¼nerberg M; Fregin A; Heiberg AC; Baert K; MacNicoll AD; Prescott CV; Walker AS; Oldenburg J; MÃ¼ller CR

Abstract

Anticoagulant compounds, i.e., derivatives of either 4-hydroxycoumarin (e.g., warfarin, bromadiolone) or indane-1,3-dione (e.g., diphacinone, chlorophacinone), have been in worldwide use as rodenticides for >50 years. These compounds inhibit blood coagulation by repression of the vitamin K reductase reaction (VKOR). Anticoagulant-resistant rodent populations have been reported from many countries and pose a considerable problem for pest control. Resistance is transmitted as an autosomal dominant trait although, until recently, the basic genetic mutation was unknown. Here, we report on the identification of eight different mutations in the VKORC1 gene in resistant laboratory strains of brown rats and house mice and in wild-caught brown rats from various locations in Europe with five of these mutations affecting only two amino acids (Tyr139Cys, Tyr139Ser, Tyr139Phe and Leu128Gln, Leu128Ser). By recombinant expression of VKORC1 constructs in HEK293 cells we demonstrate that mutations at Tyr139 confer resistance to warfarin at variable degrees while the other mutations, in addition, dramatically reduce VKOR activity. Our data strongly argue for at least seven independent mutation events in brown rats and two in mice. They suggest that mutations in VKORC1 are the genetic basis of anticoagulant resistance in wild populations of rodents, although the mutations alone do not explain all aspects of resistance that have been reported. We hypothesize that these mutations, apart from generating structural changes in the VKORC1 protein, may induce compensatory mechanisms to maintain blood clotting. Our findings provide the basis for a DNA-based field monitoring of anticoagulant resistance in rodents.

Additional References

RELATED GEPHE

Related Genes

2 (AHR, Na/K-ATPase alpha-subunit) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^10116^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

7 (https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^Vkorc1^/and+Taxon ID=^10116^/or+Gene Gephebase=^Vkorc1^/and+Taxon ID=^10116^#gephebase-summary-title)

EXTERNAL LINKS

COMMENTS