GEPHE SUMMARY

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

GepheID
GP00001182

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
BAM22603 (https://www.ncbi.nlm.nih.gov/nuccore/BAM22603)

(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

R33P

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

A novel mutation in VKORC1 and its effect on enzymatic activity in Japanese warfarin-resistant rats. (2013) (https://pubmed.ncbi.nlm.nih.gov/23018795)

Authors

Tanaka KD; Kawai YK; Ikenaka Y; Harunari T; Tanikawa T; Fujita S; Ishizuka M

Abstract

Warfarin is a rodenticide commonly used worldwide. It inhibits coagulation of blood by inhibiting vitamin K 2,3-epoxide reductase (VKOR) activity. An inadequate supply of vitamin K blocks the production of prothrombin and causes hemorrhage. Recently, warfarin-resistant brown rats (Rattus norvegicus) were found around the Aomori area of Japan. There is no significant difference in the metabolic activity of warfarin in sensitive and resistant brown rats. To clarify the mechanism underlying warfarin resistance, we cloned the VKORC1 gene from rats and identified a novel substitution of arginine to proline at position 33 of the VKORC1 amino acid sequence. Then, we determined the differences in kinetics of VKOR activity between warfarin-resistant and sensitive rats. Hepatic microsomal VKOR-dependent activity was measured over a range of vitamin K epoxide concentrations from 6.25 to 150 ÂµM. The Vmax values of resistant rats (0.0029 Â± 0.020 nmol/min/mg) were about one tenth of those of sensitive rats (0.29 Â± 0.12 nmol/min/mg). The Km values of resistant rats (47 Â± 32 ÂµM) were similar to those of sensitive rats (59 Â± 18 ÂµM). Warfarin-sensitive rats exhibited enzyme efficiencies (Vmax/Km) which were ten-fold greater than those observed in resistant rats. It may mean that VKOR activity of warfarin-resistant Aomori rats is almost lost, because their enzymatic efficiencies are very low even without warfarin. Further studies are needed to clarify how these rats can survive with a markedly reduced VKOR activity and how they simultaneously exhibit warfarin resistance.

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