

GEPHE SUMMARY

Vkorc1 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase="Vkorc1">#gephebase-summary-title)	Gephebase Gene	GP00001182	GephelD
Published	Entry Status	Martin	Main curator

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)			
Rattus norvegicus	Trait State in Taxon A		
Rattus norvegicus - Japan	Trait State in Taxon B		
Data not curated	Ancestral State		
Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status="Intraspecific">#gephebase-summary-title)	Taxonomic Status		
Taxon A		Taxon B	
Rattus norvegicus (#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Rattus+norvegicus">#gephebase-summary-title)	Latin Name	Rattus norvegicus (#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Rattus+norvegicus">#gephebase-summary-title)	Latin Name
Norway rat	Common Name	Norway rat	Common Name
rat; rats; Norway rat; brown rat; Rattus norvegicus8; Rattus norvegicus	Synonyms	rat; rats; Norway rat; brown rat; Rattus norvegicus8; Rattus norvegicus	Synonyms
species	Rank	species	Rank
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	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	Lineage
Rattus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10114)	Parent	Rattus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10114)	Parent
10116 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10116)	NCBI Taxonomy ID	10116 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10116)	NCBI Taxonomy ID
No	is Taxon A an Infraspecies?	Yes	is Taxon B an Infraspecies?
		Rattus norvegicus - Japan	Taxon B Description

GENOTYPIC CHANGE

VKORC1	Generic Gene Name	UniProtKB Homo sapiens
	Synonyms	GenebankID or UniProtKB
VKOR; MST134; MST576; VKCFD2; EDTP308; MSTP134; MSTP576; UNQ308/PRO351	String	BAM22603 (https://www.ncbi.nlm.nih.gov/nuccore/BAM22603)
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		

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: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 μ M. The Vmax values of resistant rats (0.0029 ± 0.020 nmol/min/mg) were about one tenth of those of sensitive rats (0.29 ± 0.12 nmol/min/mg). The Km values of resistant rats ($47 \pm 32 \mu$ M) were similar to those of sensitive rats ($59 \pm 18 \mu$ M). 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