

GEPHE SUMMARY

Vkorc1 (https://www.gephebase.org/search-criteria?/and+GeneGephebase=~Vkorc1^#gephebase-summary-title)	Gephebase Gene	GP00001181	GepheID
Published	Entry Status	Martin	Main curator

PHENOTYPIC CHANGE

Physiology (https://www.gephebase.org/search-criteria?/and+TraitCategory=~Physiology^#gephebase-summary-title)	Trait Category		
Xenobiotic resistance (rodenticide; warfarin) (https://www.gephebase.org/search-criteria?/and+Trait=~Xenobiotic resistance (rodenticide; warfarin)^#gephebase-summary-title)	Trait		
Rattus norvegicus	Trait State in Taxon A		
Rattus norvegicus - France and Belgium	Trait State in Taxon B		
Data not curated	Ancestral State		
Intraspecific (https://www.gephebase.org/search-criteria?/and+TaxonomicStatus=~Intraspecific^#gephebase-summary-title)	Taxonomic Status		
Taxon A		Taxon B	
Rattus norvegicus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=~Rattus norvegicus^#gephebase-summary-title)	Latin Name	Rattus norvegicus (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 Intraspecies?	Yes	is Taxon B an Intraspecies?
			Taxon B Description
		Rattus norvegicus - France and Belgium	

GENOTYPIC CHANGE

VKORC1	Generic Gene Name	Q9BQB6 (http://www.uniprot.org/uniprot/Q9BQB6)	UniProtKB Homo sapiens
VKOR; MST134; MST576; VKCFD2; EDTP308; MSTP134; MSTP576; UNQ308/PRO351	Synonyms	BAM22603 (https://www.ncbi.nlm.nih.gov/nuccore/BAM22603)	GenebankID or UniProtKB
9606.ENSPO0000378426 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPO0000378426)	String		
Belongs to the VKOR family.	Sequence Similarities		
GO:0048038 : quinone binding (https://www.ebi.ac.uk/QuickGO/term/GO:0048038)	GO - Molecular Function		
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			

(<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

Y139F

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

Warfarin resistance in a French strain of rats. (2005) (<https://pubmed.ncbi.nlm.nih.gov/16421894>)

Authors

Lasseur R; Longin-Sauvageon C; Videmann B; Billeret M; Berny P; Benoit E

Abstract

A warfarin-resistant strain and a warfarin-susceptible strain of wild rats (*Rattus norvegicus*) maintained in enclosures of the National Veterinary School of Lyon (France) were studied to determine the mechanism of the resistance to anticoagulant rodenticides. A low vitamin K epoxide reductase (VKOR) activity has been reported for many resistant rat strains. As recently suggested, mutations in the vitamin K epoxide reductase subunit 1 (VKORC1) gene are the genetic basis of anticoagulant resistance in wild populations of rats from various locations in Europe. Here we report, for our strain, one of the seven described mutations (Tyr139Phe) for VKORC1 in rats. In addition, a low expression of mRNA encoding VKORC1 gene is observed in resistant rats, which could explain their low VKOR activity. We calculated kinetic parameters of VKOR in the warfarin-resistant and warfarin-susceptible rats. The V(max) and the K(m) of the VKOR obtained in resistant rats were lowered by 57 and 77%, respectively, compared to those obtained in susceptible rats. As a consequence, the enzymatic efficiency (V(m)/K(m)) of the VKOR was similar between resistant and susceptible rats. This result could be a good explanation to the observation that no clinical signs of vitamin K deficiency was observed in the warfarin-resistant strain, while a low VKOR activity was found. VKOR activity in warfarin-resistant rats was poorly inhibited by warfarin (K(i) for warfarin is 29 microM and 0.72 microM for resistant and susceptible rats, respectively).

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Additional References

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

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

