

GEPHE SUMMARY

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

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 - France and Belgium	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 (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Rattus+norvegicus^#gephebase-summary-title)	Latin Name	Latin Name
Norway rat	Common Name	Common Name
rat; rats; Norway rat; brown rat; Rattus norvegicus8; Rattus norvegicus	Synonyms	Synonyms
species	Rank	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	Lineage
Rattus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10114)	Parent	Parent
10116 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10116)	NCBI Taxonomy ID	NCBI Taxonomy ID
No	is Taxon A an Infraspecies?	is Taxon B an Infraspecies?
	Yes	Taxon B Description
		Rattus norvegicus - France and Belgium

GENOTYPIC CHANGE

VKORC1	Generic Gene Name	UniProtKB Homo sapiens
	Synonyms	GenebankID or UniProtKB
VKOR; MST134; MST576; VKCFD2; EDTP308; MSTP134; MSTP576; UNQ308/PRO351		BAM22603 (https://www.ncbi.nlm.nih.gov/nuccore/BAM22603)
9606.ENSP00000378426 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000378426)	String	
Belongs to the VKOR family.	Sequence Similarities	
	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

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	-	-	-

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

Main Reference

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

Authors

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

COMMENTS