

GEPHE SUMMARY

Vkorc1 (https://www.gephebase.org/search-criteria?/and+GeneGephebase=~Vkorc1^#gephebase-summary-title)	Gephebase Gene	GP00001173	GepheID
	Entry Status	Martin	Main curator
	Published		

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	
Mus musculus		Trait State in Taxon A	
Mus musculus - UK		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	
Mus musculus (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Mus+musculus^#gephebase-summary-title)		Mus musculus (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Mus+musculus^#gephebase-summary-title)	
house mouse		house mouse	
house mouse; mouse; Mus musculus Linnaeus, 1758; mice C57BL/6xCBA/CaJ hybrid		house mouse; mouse; Mus musculus Linnaeus, 1758; mice C57BL/6xCBA/CaJ hybrid	
species		species	
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; Mus; Mus		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; Mus; Mus	
Mus () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=862507)		Mus () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=862507)	
10090 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10090)		10090 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=10090)	
No		No	

GENOTYPIC CHANGE

VKORC1		Q9BQB6 (http://www.uniprot.org/uniprot/Q9BQB6)	
VKOR; MST134; MST576; VKCFD2; EDTP308; MSTP134; MSTP576; UNQ308/PRO351		NP_848715 (https://www.ncbi.nlm.nih.gov/nuccore/NP_848715)	
9606.ENSPO0000378426 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPO0000378426)			
Belongs to the VKOR family.			
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 (https://www.ebi.ac.uk/QuickGO/term/GO:0047057)			

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>)

No (https://www.gephebase.org/search-criteria?/and+Presumptive Null=~No~#gephebase-summary-title)	Presumptive Null
Coding (https://www.gephebase.org/search-criteria?/and+Molecular Type=~Coding~#gephebase-summary-title)	Molecular Type
SNP (https://www.gephebase.org/search-criteria?/and+Aberration Type=~SNP~#gephebase-summary-title)	Aberration Type
Nonsynonymous	SNP Coding Change
Y139C	Molecular Details of the Mutation
Candidate Gene (https://www.gephebase.org/search-criteria?/and+Experimental Evidence=~Candidate Gene~#gephebase-summary-title)	Experimental Evidence

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	-	-	-

The genetic basis of resistance to anticoagulants in rodents. (2005) (https://pubmed.ncbi.nlm.nih.gov/15879509)	Main Reference
Pelz HJ; Rost S; HÄnerberg M; Fregin A; Heiberg AC; Baert K; MacNicol AD; Prescott CV; Walker AS; Oldenburg J; MÄller CR	Authors
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.	Abstract
	Additional References

RELATED GEPHE

2 (AHR, Na/K-ATPase alpha-subunit) (https://www.gephebase.org/search-criteria?/or+Taxon ID=~10090~/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title)	Related Genes
2 (https://www.gephebase.org/search-criteria?/or+Gene Gephebase=~Vkorc1~/and+Taxon ID=~10090~/or+Gene Gephebase=~Vkorc1~/and+Taxon ID=~10090~#gephebase-summary-title)	Related Haplotypes

EXTERNAL LINKS

