

GEPHE SUMMARY

Vkorc1 (https://www.gephebase.org/search-criteria?/and+GeneGephebase=~Vkorc1^#gephebase-summary-title)	Gephebase Gene	GP00001172	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		
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)	Latin Name	Mus musculus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=~Mus musculus^#gephebase-summary-title)	Latin Name
house mouse	Common Name	house mouse	Common Name
house mouse; mouse; Mus musculus Linnaeus, 1758; mice C57BL/6xCBA/CaJ hybrid	Synonyms	house mouse; mouse; Mus musculus Linnaeus, 1758; mice C57BL/6xCBA/CaJ hybrid	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; Mus; Mus	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; Mus; Mus	Lineage
Mus () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 862507)	Parent	Mus () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 862507)	Parent
10090 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10090)	NCBI Taxonomy ID	10090 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10090)	NCBI Taxonomy ID
No	is Taxon A an Intraspecies?	No	is Taxon B an Intraspecies?

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	NP_848715 (https://www.ncbi.nlm.nih.gov/nuccore/NP_848715)	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>)

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
L128S	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

