

GEPHE SUMMARY

Vkorc1 (https://www.gephebase.org/search-criteria?/and+GeneGephebase=~Vkorc1^#gephebase-summary-title)	Gephebase Gene	GP00001176	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	
Rattus norvegicus		Trait State in Taxon A	
Rattus norvegicus - Germany		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)		Rattus norvegicus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=~Rattus norvegicus^#gephebase-summary-title)	
Norway rat		Norway rat	
rat; rats; Norway rat; brown rat; Rattus norvegicus8; Rattus norvegicus		rat; rats; Norway rat; brown rat; Rattus norvegicus8; Rattus norvegicus	
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; Rattus		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	
Rattus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10114)		Rattus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10114)	
10116 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10116)		10116 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10116)	
No		Yes	
		Taxon B Description	
		Rattus norvegicus - Germany	

GENOTYPIC CHANGE

VKORC1		Generic Gene Name		UniProtKB Homo sapiens
VKOR; MST134; MST576; VKCFD2; EDTP308; MSTP134; MSTP576; UNQ308/PRO351		Synonyms		GenebankID or UniProtKB
9606.ENSPO0000378426 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSPO0000378426)		String		AAR82917 (https://www.ncbi.nlm.nih.gov/nuccore/AAR82917)
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](https://www.gephebase.org/search-criteria?/and+Presumptive Null=))

Molecular Type

Coding ([https://www.gephebase.org/search-criteria?/and+Molecular Type="+Coding^#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Molecular Type=))

Aberration Type

SNP ([https://www.gephebase.org/search-criteria?/and+Aberration Type="+SNP^#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Aberration Type=))

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

S56P

Experimental Evidence

Candidate Gene ([https://www.gephebase.org/search-criteria?/and+Experimental Evidence="+Candidate Gene^#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Experimental Evidence=))

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

Main Reference

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

Authors

Pelz HJ; Rost S; HÄ34nerberg M; Fregin A; Heiberg AC; Baert K; MacNicol AD; Prescott CV; Walker AS; Oldenburg J; MÄ34ller CR

Abstract

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.

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](https://www.gephebase.org/search-criteria?/or+Taxon ID=))

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](https://www.gephebase.org/search-criteria?/or+Gene Gephebase=))

EXTERNAL LINKS

