## GEPHE SUMMARY

Gephebase Gene
Vkorc1 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^Vkorc1^#gephebase-summary-title)

GepheID
GP00001179

Entry Status
Published

Main curator
Martin

## 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)

Trait State in Taxon A
Rattus norvegicus

Trait State in Taxon B
Rattus norvegicus - UK

Ancestral State
Data not curated

Taxonomic Status
Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Intraspecific^#gephebase-summary-title)

### Taxon A

Latin Name
Rattus norvegicus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Rattus norvegicus^#gephebase-summary-title)

Common Name
Norway rat

Synonyms
rat; rats; Norway rat; brown rat; Rattus norvegicus8; Rattus norwegicus

Rank
species

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

Parent
Rattus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10114 )

NCBI Taxonomy ID
10116 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10116 )

is Taxon A an Infraspecies?
No

### Taxon B

Latin Name
Rattus norvegicus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Rattus norvegicus^#gephebase-summary-title)

Common Name
Norway rat

Synonyms
rat; rats; Norway rat; brown rat; Rattus norvegicus8; Rattus norwegicus

Rank
species

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

Parent
Rattus () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10114 )

NCBI Taxonomy ID
10116 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10116 )

is Taxon B an Infraspecies?
Yes

Taxon B Description
Rattus norvegicus - UK

## GENOTYPIC CHANGE

Generic Gene Name
VKORC1

Synonyms
VKOR; MST134; MST576; VKCFD2; EDTP308; MSTP134; MSTP576; UNQ308/PRO351

String
9606.ENSP00000378426 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000378426 )

Sequence Similarities
Belongs to the VKOR family.

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

UniProtKB Homo sapiens
Q9BQB6 (http://www.uniprot.org/uniprot/Q9BQB6)

GenebankID or UniProtKB
AAR82917 (https://www.ncbi.nlm.nih.gov/nuccore/AAR82917)

(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

L120Q

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

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

Authors

Pelz HJ; Rost S; HÃ¼nerberg M; Fregin A; Heiberg AC; Baert K; MacNicoll AD; Prescott CV; Walker AS; Oldenburg J; MÃ¼ller 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)

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