## GEPHE SUMMARY

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

GepheID
GP00001175

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 -Denmark; UK; Germany

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 -Denmark; UK; Germany

## 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
BAM22603 (https://www.ncbi.nlm.nih.gov/nuccore/BAM22603)

(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

Y139C

Experimental Evidence

Linkage Mapping (https://www.gephebase.org/search-criteria?/and+Experimental Evidence=^Linkage Mapping^#gephebase-summary-title)

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

Main Reference

Mutations in VKORC1 cause warfarin resistance and multiple coagulation factor deficiency type 2. (2004) (https://pubmed.ncbi.nlm.nih.gov/14765194)

Authors

Rost S; Fregin A; Ivaskevicius V; Conzelmann E; HÃ¶rtnagel K; Pelz HJ; Lappegard K; Seifried E; Scharrer I; Tuddenham EG; MÃ¼ller CR; Strom TM; Oldenburg J

Abstract

Coumarin derivatives such as warfarin represent the therapy of choice for the long-term treatment and prevention of thromboembolic events. Coumarins target blood coagulation by inhibiting the vitamin K epoxide reductase multiprotein complex (VKOR). This complex recycles vitamin K 2,3-epoxide to vitamin K hydroquinone, a cofactor that is essential for the post-translational gamma-carboxylation of several blood coagulation factors. Despite extensive efforts, the components of the VKOR complex have not been identified. The complex has been proposed to be involved in two heritable human diseases: combined deficiency of vitamin-K-dependent clotting factors type 2 (VKCFD2; Online Mendelian Inheritance in Man (OMIM) 607473), and resistance to coumarin-type anticoagulant drugs (warfarin resistance, WR; OMIM 122700). Here we identify, by using linkage information from three species, the gene vitamin K epoxide reductase complex subunit 1 (VKORC1), which encodes a small transmembrane protein of the endoplasmic reticulum. VKORC1 contains missense mutations in both human disorders and in a warfarin-resistant rat strain. Overexpression of wild-type VKORC1, but not VKORC1 carrying the VKCFD2 mutation, leads to a marked increase in VKOR activity, which is sensitive to warfarin inhibition.

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