

## GEPHE SUMMARY

### Gephebase Gene

Vkorc1

### Entry Status

Published

### GepheID

GP00001175

### Main curator

Martin

## PHENOTYPIC CHANGE

### Trait Category

Physiology

### Trait

Xenobiotic resistance (rodenticide; warfarin)

### 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

### Taxon A

#### Latin Name

*Rattus norvegicus*

#### Common Name

Norway rat

#### Synonyms

rat; rats; Norway rat; brown rat; Rattus norvegicus8; Rattus norvegicus

#### 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)

#### NCBI Taxonomy ID

10116

#### is Taxon A an Intraspecies?

No

### Taxon B

#### Latin Name

*Rattus norvegicus*

#### Common Name

Norway rat

#### Synonyms

rat; rats; Norway rat; brown rat; Rattus norvegicus8; Rattus norvegicus

#### Rank

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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)

#### NCBI Taxonomy ID

10116

#### is Taxon B an Intraspecies?

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

### Sequence Similarities

Belongs to the VKOR family.

### GO - Molecular Function

GO:0048038 : quinone binding

GO:0047058 : vitamin-K-epoxide reductase (warfarin-insensitive) activity

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### GO - Biological Process

GO:0014070 : response to organic cyclic compound

GO:0017144 : drug metabolic process

GO:0007596 : blood coagulation

GO:0060348 : bone development

### UniProtKB Homo sapiens

Q9BQB6

### GenebankID or UniProtKB

BAM22603

GO:0017187 : peptidyl-glutamic acid carboxylation  
GO:0030193 : regulation of blood coagulation  
GO:0046677 : response to antibiotic  
GO:0010243 : response to organonitrogen compound  
GO:0042373 : vitamin K metabolic process

**GO - Cellular Component**

GO:0016021 : integral component of membrane  
GO:0005783 : endoplasmic reticulum  
GO:0005789 : endoplasmic reticulum membrane

**Presumptive Null**

No

**Molecular Type**

Coding

**Aberration Type**

SNP

**SNP Coding Change**

Nonsynonymous

**Molecular Details of the Mutation**

Y139C

**Experimental Evidence**

Linkage Mapping

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

**Main Reference**

Mutations in VKORC1 cause warfarin resistance and multiple coagulation factor deficiency type 2. (2004)

**Authors**

Rost S; Fregin A; Ivaskevicius V; Conzelmann E; Härtel 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)

**Related Haplotypes**

7

**EXTERNAL LINKS**

**COMMENTS**

