

GEPHE SUMMARY

Vkorc1 (https://www.gephebase.org/search-criteria?/and+GeneGephebase=~Vkorc1^#gephebase-summary-title) Published	Gephebase Gene	GP00001168	GepheID
	Entry Status	Martin	Main curator

PHENOTYPIC CHANGE

Physiology (https://www.gephebase.org/search-criteria?/and+TraitCategory=~Physiology^#gephebase-summary-title)		Trait Category	
Xenobiotic resistance (anti-coagulant drug response; warfarin) (https://www.gephebase.org/search-criteria?/and+Trait=~Xenobiotic resistance (anti-coagulant drug response; warfarin)^#gephebase-summary-title)		Trait	
Homo sapiens - Caucasians and Japanase		Trait State in Taxon A	
Homo sapiens - Caucasians and Japanase		Trait State in Taxon B	
Taxon A		Ancestral State	
Intraspecific (https://www.gephebase.org/search-criteria?/and+TaxonomicStatus=~Intraspecific^#gephebase-summary-title)		Taxonomic Status	
Taxon A		Taxon B	
Homo sapiens (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=~Homo sapiens^#gephebase-summary-title)		Homo sapiens (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=~Homo sapiens^#gephebase-summary-title)	
human		human	
human; man; Homo sapiens Linnaeus, 1758; Home sapiens; Homo sampiens; Homo sapeins; Homo sapian; Homo sapians; Homo sapien; Homo sapience; Homo sapiense; Homo sapients; Homo sapines; Homo spaiens; Homo spiens; Humo sapiens		human; man; Homo sapiens Linnaeus, 1758; Home sapiens; Homo sampiens; Homo sapeins; Homo sapian; Homo sapians; Homo sapien; Homo sapience; Homo sapiense; Homo sapients; Homo sapines; Homo spaiens; Homo spiens; Humo sapiens	
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; Primates; Haplorrhini; Simiiformes; Catarrhini; Hominoidea; Hominidae; Homininae; Homo		cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Euarchontoglires; Primates; Haplorrhini; Simiiformes; Catarrhini; Hominoidea; Hominidae; Homininae; Homo	
Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9605)		Homo () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9605)	
9606 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9606)		9606 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9606)	
No		No	

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	BC002911 (https://www.ncbi.nlm.nih.gov/nucore/BC002911)	GenebankID or UniProtKB
9606.ENSPO0000378426 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPO0000378426)	String		
	Sequence Similarities		
Belongs to the VKOR family.			
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>)

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

R98W

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; Härtl nagel 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

A genome-wide association study confirms VKORC1, CYP2C9, and CYP4F2 as principal genetic determinants of warfarin dose. (2009) (<https://pubmed.ncbi.nlm.nih.gov/19300499>)
Genome-wide association study identifies genetic determinants of warfarin responsiveness for Japanese. (2010) (<https://pubmed.ncbi.nlm.nih.gov/20833655>)

RELATED GEPHE

Related Genes

4 (alcohol dehydrogenase (ADH1B), CYP2C9, CYP4F2, MDR1) (<https://www.gephebase.org/search-criteria?/or+Taxon ID=^9606^/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title>)

Related Haplotypes

3 (<https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^Vkorc1^/and+Taxon ID=^9606^/or+Gene Gephebase=^Vkorc1^/and+Taxon ID=^9606^#gephebase-summary-title>)

EXTERNAL LINKS

