

GEPHE SUMMARY

Vkorc1 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^Vkorc1^#gephebase-summary-title)	Gephebase Gene GP00001174	GephelD Main curator
Published	Entry Status Courtier	

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		
Mus musculus	Trait State in Taxon B		
Mus spretus (North Africa) and Mus musculus (Spain)	Ancestral State		
Data not curated	Taxonomic Status		
Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Intraspecific^#gephebase-summary-title)			
Taxon A		Taxon B	
Mus musculus (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Mus+musculus^#gephebase-summary-title)	Latin Name	Mus spretus (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Mus+spretus^#gephebase-summary-title)	Latin Name
house mouse	Common Name	western wild mouse	Common Name
house mouse; mouse; Mus musculus Linnaeus, 1758; mice C57BL/6xCBA/CaJ hybrid	Synonyms	Mus musculus spretus; western wild mouse; Algerian mouse	Synonyms
species	Rank	species	Rank
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; Mus; Mus	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; Mus; Mus	Lineage
Mus () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 862507)	Parent	Mus () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 862507)	Parent
10090 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10090)	NCBI Taxonomy ID	10096 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10096)	NCBI Taxonomy ID
is Taxon A an Infraspecies?		is Taxon B an Infraspecies?	
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 String	GenebankID or UniProtKB ADN94694 (https://www.ncbi.nlm.nih.gov/nuccore/ADN94694)
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 (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 ([#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Presumptive+Null=^No))

Molecular Type

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

Aberration Type

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

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

Several candidate coding changes

Experimental Evidence

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

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

Main Reference

Adaptive introgression of anticoagulant rodent poison resistance by hybridization between old world mice. (2011) (<https://pubmed.ncbi.nlm.nih.gov/21782438>)

Authors

Song Y; Endepols S; Kleemann N; Richter D; Matuschka FR; Shih CH; Nachman MW; Kohn MH

Abstract

Polymorphisms in the vitamin K 2,3-epoxide reductase subcomponent 1 (vkorc1) of house mice (*Mus musculus domesticus*) can cause resistance to anticoagulant rodenticides such as warfarin [1-3]. Here we show that resistant house mice can also originate from selection on vkorc1 polymorphisms acquired from the Algerian mouse (*M. spretus*) through introgressive hybridization. We report on a polymorphic introgressed genomic region in European *M. m. domesticus* that stems from *M. spretus*, spans >10 Mb on chromosome 7, and includes the molecular target of anticoagulants vkorc1 [1-4]. We show that in the laboratory, the homozygous complete vkorc1 allele of *M. spretus* confers resistance when introgressed into *M. m. domesticus*. Consistent with selection on the introgressed allele after the introduction of rodenticides in the 1950s, we found signatures of selection in patterns of variation in *M. m. domesticus*. Furthermore, we detected adaptive protein evolution of vkorc1 in *M. spretus* ($K_a/K_s = 1.54-1.93$) resulting in radical amino acid substitutions that apparently cause anticoagulant tolerance in *M. spretus* as a pleiotropic effect. Thus, positive selection produced an adaptive, divergent, and pleiotropic vkorc1 allele in the donor species, *M. spretus*, which crossed a species barrier and produced an adaptive polymorphic trait in the recipient species, *M. m. domesticus*.

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Additional References

Related Genes

2 (AHR, Na/K-ATPase alpha-subunit) ([#gephebase-summary-title\)](https://www.gephebase.org/search-criteria?/or+Taxon+ID=^10090#/and+Trait=Xenobiotic+resistance/or+Taxon+ID=^10096#/and+Trait=Xenobiotic+resistance/and+groupHaplotypes=true)

Related Haplotypes

2 ([#gephebase-summary-title\)](https://www.gephebase.org/search-criteria?/or+Gene+Gephebase=^Vkcrc1#/and+Taxon+ID=^10090#/or+Gene+Gephebase=^Vkcrc1#/and+Taxon+ID=^10096)

EXTERNAL LINKS

COMMENTS

@Introgression @Pleiotropy - One hypothesis to explain the adaptive evolution of *vkorc1* in *M. spretus* implicates adaptation to a granivorous vitamin K-deficient diet. The tolerance of *M. spretus* to rodenticides could thus be a pleiotropic effect of a physiological adaptation unrelated to rodenticide selection. Other granivorous rodents, including Shawâ€™s gerbil (*Meriones shawi*), the Egyptian spiny mouse (*Acomys cahirinus*), and the golden hamster (*Mesocricetus auratus*), display similar high levels of tolerance to rodenticides despite being naive to the poisons.