

GEPHE SUMMARY

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

PHENOTYPIC CHANGE

Trait Category			
Physiology (https://www.gephebase.org/search-criteria?/and+TraitCategory=~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+TaxonomicStatus=~Intraspecific^#gephebase-summary-title)			
Taxon A		Taxon B	
Latin Name		Latin Name	
Mus musculus (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Mus+musculus^#gephebase-summary-title)		Mus spretus (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Mus+spretus^#gephebase-summary-title)	
Common Name		Common Name	
house mouse		western wild mouse	
Synonyms		Synonyms	
house mouse; mouse; Mus musculus Linnaeus, 1758; mice C57BL/6xCBA/CaJ hybrid		Mus musculus spretus; western wild mouse; Algerian mouse	
Rank		Rank	
species		species	
Lineage		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		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	
Parent		Parent	
Mus () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 862507)		Mus () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 862507)	
NCBI Taxonomy ID		NCBI Taxonomy ID	
10090 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10090)		10096 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10096)	
is Taxon A an Intraspecies?		is Taxon B an Intraspecies?	
No		No	

GENOTYPIC CHANGE

Generic Gene Name		UniProtKB Homo sapiens
VKORC1	Q9BQB6 (http://www.uniprot.org/uniprot/Q9BQB6)	
Synonyms		GenebankID or UniProtKB
VKOR; MST134; MST576; VKCFD2; EDTP308; MSTP134; MSTP576; UNQ308/PRO351		ADN94694 (https://www.ncbi.nlm.nih.gov/nuccore/ADN94694)
String		
9606.ENSPP00000378426 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPP00000378426)		
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 (<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

Several candidate coding changes

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

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; Klemann 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* ($K_a/K_s = 1.54\text{-}1.93$) 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 GEPHE

Related Genes

2 (AHR, Na/K-ATPase alpha-subunit) (<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#gephebase-summary-title>)

Related Haplotypes

2 (<https://www.gephebase.org/search-criteria?/or+Gene Gephebase=~Vkorc1~/and+Taxon ID=~10090~/or+Gene Gephebase=~Vkorc1~/and+Taxon ID=~10096~#gephebase-summary-title>)

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 Shaw'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.