

MC1R (https://www.gephebase.org/search-criteria?/and+GeneGephebase=^MC1R^#gephebase-summary-title)	Gephebase Gene	GP00000573	GepheID
Published	Entry Status	Martin	Main curator

	Trait Category
Morphology (https://www.gephebase.org/search-criteria?/and+TraitCategory=^Morphology^#gephebase-summary-title)	Trait
Coloration (coat) (https://www.gephebase.org/search-criteria?/and+Trait=^Coloration(coat)^#gephebase-summary-title)	Trait
WT coat	Trait State in Taxon A
red/yellow coat in Irish Setter and Labrador Retriever	Trait State in Taxon B
Taxon A	Ancestral State
Domesticated (https://www.gephebase.org/search-criteria?/and+TaxonomicStatus=^Domesticated^#gephebase-summary-title)	Taxonomic Status

GENOTYPIC CHANGE

MC1R	Generic Gene Name	UniProtKB Homo sapiens
	Synonyms	GenebankID or UniProtKB
CMM5; MSH-R; SHEP2; MSHR	String	
9606.ENSPP00000451605 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPP00000451605)	Sequence Similarities	
Belongs to the G-protein coupled receptor 1 family.	GO - Molecular Function	
GO:0008528 : G protein-coupled peptide receptor activity (https://www.ebi.ac.uk/QuickGO/term/GO:0008528)		
GO:0004977 : melanocortin receptor activity (https://www.ebi.ac.uk/QuickGO/term/GO:0004977)		
GO:0004980 : melanocyte-stimulating hormone receptor activity (https://www.ebi.ac.uk/QuickGO/term/GO:0004980)		

GO:0031625 : ubiquitin protein ligase binding
(<https://www.ebi.ac.uk/QuickGO/term/GO:0031625>)

GO - Biological Process

GO:0007275 : multicellular organism development
(<https://www.ebi.ac.uk/QuickGO/term/GO:0007275>)
GO:0045944 : positive regulation of transcription by RNA polymerase II
(<https://www.ebi.ac.uk/QuickGO/term/GO:0045944>)
GO:0042438 : melanin biosynthetic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0042438>)
GO:0043473 : pigmentation (<https://www.ebi.ac.uk/QuickGO/term/GO:0043473>)
GO:0007186 : G protein-coupled receptor signaling pathway
(<https://www.ebi.ac.uk/QuickGO/term/GO:0007186>)
GO:0051897 : positive regulation of protein kinase B signaling
(<https://www.ebi.ac.uk/QuickGO/term/GO:0051897>)
GO:0019233 : sensory perception of pain
(<https://www.ebi.ac.uk/QuickGO/term/GO:0019233>)
GO:0007189 : adenylate cyclase-activating G protein-coupled receptor signaling pathway
(<https://www.ebi.ac.uk/QuickGO/term/GO:0007189>)
GO:0035556 : intracellular signal transduction
(<https://www.ebi.ac.uk/QuickGO/term/GO:0035556>)
GO:0007187 : G protein-coupled receptor signaling pathway, coupled to cyclic nucleotide second messenger (<https://www.ebi.ac.uk/QuickGO/term/GO:0007187>)
GO:0032720 : negative regulation of tumor necrosis factor production
(<https://www.ebi.ac.uk/QuickGO/term/GO:0032720>)
GO:0010739 : positive regulation of protein kinase A signaling
(<https://www.ebi.ac.uk/QuickGO/term/GO:0010739>)
GO:0090037 : positive regulation of protein kinase C signaling
(<https://www.ebi.ac.uk/QuickGO/term/GO:0090037>)
GO:0009650 : UV protection (<https://www.ebi.ac.uk/QuickGO/term/GO:0009650>)
GO:0070914 : UV-damage excision repair
(<https://www.ebi.ac.uk/QuickGO/term/GO:0070914>)

GO - Cellular Component

GO:0005886 : plasma membrane (<https://www.ebi.ac.uk/QuickGO/term/GO:0005886>)
GO:0005887 : integral component of plasma membrane
(<https://www.ebi.ac.uk/QuickGO/term/GO:0005887>)

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

Nonsense

Molecular Details of the Mutation

R306ter; deletes 12 of 17 a.a. from C-terminus

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	CGA	TGA	-
Amino-acid	Arg	STP	306

Main Reference

Melanocortin 1 receptor variation in the domestic dog. (2000) (<https://pubmed.ncbi.nlm.nih.gov/10602988>)

Authors

Newton JM; Wilkie AL; He L; Jordan SA; Metallinos DL; Holmes NG; Jackson IJ; Barsh GS

Abstract

The melanocortin 1 receptor (Mc1r) is encoded by the Extension locus in many different mammals, where a loss-of-function causes exclusive production of red/yellow pheomelanin, and a constitutively activating mutation causes exclusive production of black/brown eumelanin. In the domestic dog, breeds with a wild-type E allele, e. g., the Doberman, can produce either pigment type, whereas breeds with the e allele, e.g., the Golden Retriever, produce exclusively yellow pigment. However, a black coat color in the Newfoundland and similar breeds is thought to be caused by an unusual allele of Agouti, which encodes the physiologic ligand for the Mc1r. Here we report that the predicted dog Mc1r is 317 residues in length and 96% identical to the fox Mc1r. Comparison of the Doberman, Newfoundland, Black Labrador, Yellow Labrador, Flat-coated Retriever, Irish Setter, and Golden Retriever revealed six sequence variants, of which two, S90G and R306ter, partially correlated with a black/brown coat and red/yellow coat, respectively. R306ter was found in the Yellow Labrador, Golden Retriever, and Irish Setter; the latter two had identical haplotypes but differed from the Yellow Labrador at three positions other than R306ter. In a larger survey of 194 dogs and 19 breeds, R306ter and a red/yellow coat were completely concordant except for the Red Chow. These results indicate that the e allele is caused by a common Mc1r loss-of-function mutation that either reoccurred or was subject to gene conversion during recent evolutionary history, and suggest that the allelic and locus relationships for dog coat color genes may be more analogous to those found in other mammals than previously thought.

Additional References

Identification of a premature stop codon in the melanocyte-stimulating hormone receptor gene (MC1R) in Labrador and Golden retrievers with yellow coat colour. (2000) (<https://pubmed.ncbi.nlm.nih.gov/10895310>)

Related Genes

13 (Agouti (ASIP), GPR22, MFSD12, PMEL17, SLC45A2=MATP, FGF3; FGF4; FGF19; ORAOV1, Kit, Melanophilin (MLPH), Microphthalmia-associated transcription factor, PSMB7, tyrosinase-related protein 1 (TYRP1), beta-defensin 103 (CBD103), RALY (hnRNP associated with lethal yellow)) ([https://www.gephebase.org/search-criteria?/or+Taxon ID=^9612^/and+Trait=Coloration/or+Taxon ID=^9615^/and+Trait=Coloration/and+groupHaplotypes=true#gephebase-summary-title](https://www.gephebase.org/search-criteria?/or+Taxon+ID=^9612^/and+Trait=Coloration/or+Taxon+ID=^9615^/and+Trait=Coloration/and+groupHaplotypes=true#gephebase-summary-title))

Related Haplotypes

4 ([https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^MC1R^/and+Taxon ID=^9612^/or+Gene Gephebase=^MC1R^/and+Taxon ID=^9615^#gephebase-summary-title](https://www.gephebase.org/search-criteria?/or+Gene+Gephebase=^MC1R^/and+Taxon+ID=^9612^/or+Gene+Gephebase=^MC1R^/and+Taxon+ID=^9615^#gephebase-summary-title))

EXTERNAL LINKS

COMMENTS

<https://omia.org/OMIA001199/9615/>