GEPHE SUMMARY

Gephebase Gene
Kit (type III receptor protein-tyrosine kinase) (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^Kit (type III receptor protein-tyrosine kinase)^#gephebase-summary-title)

Entry Status
Published

GepheID
GP00000519

Main curator
Martin

PHENOTYPIC CHANGE

Trait Category
Morphology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Morphology^#gephebase-summary-title)

Trait
Coloration (coat) (https://www.gephebase.org/search-criteria?/and+Trait=^Coloration (coat)^#gephebase-summary-title)

Trait State in Taxon A
Felis catus - white-spotted

Trait State in Taxon B
Felis catus - Dominant White/blue iris

Ancestral State
Taxon A

Taxonomic Status
Domesticated (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Domesticated^#gephebase-summary-title)

Taxon A

Latin Name
Felis catus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Felis catus^#gephebase-summary-title)

Common Name
domestic cat

Synonyms
Felis domesticus; Felis silvestris catus; domestic cat; cat; cats; Felis catus Linnaeus, 1758; Korat cats L.

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; Laurasiatheria; Carnivora; Feliformia; Felidae; Felinae; Felis

Parent
Felis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9682)

NCBI Taxonomy ID
9685 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9685)

is Taxon A an Infraspecies?
No

Taxon B

Latin Name
Felis catus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Felis catus^#gephebase-summary-title)

Common Name
domestic cat

Synonyms
Felis domesticus; Felis silvestris catus; domestic cat; cat; cats; Felis catus Linnaeus, 1758; Korat cats L.

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; Laurasiatheria; Carnivora; Feliformia; Felidae; Felinae; Felis

Parent
Felis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9682)

NCBI Taxonomy ID
9685 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9685)

is Taxon B an Infraspecies?
Yes

Taxon B Description
Felis catus - Dominant White/blue iris

GENOTYPIC CHANGE

Generic Gene Name
Kit

Synonyms
W; Bs; Fdc; Ssm; SCO1; SCO5; SOW3; CD117; c-KIT; Tr-kit; Gsfsco1; Gsfsco5; Gsfsow3; Sl

String
10090.ENSMUSP00000005815 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier= 10090.ENSMUSP00000005815)

Sequence Similarities
Belongs to the protein kinase superfamily. Tyr protein kinase family. CSF-1/PDGF receptor subfamily.

GO - Molecular Function
GO:0004888 : transmembrane signaling receptor activity (https://www.ebi.ac.uk/QuickGO/term/GO:0004888)

UniProtKB Mus musculus
P05532 (http://www.uniprot.org/uniprot/P05532)

GenebankID or UniProtKB
()

GO:0005524 : ATP binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005524)
GO:0042803 : protein homodimerization activity (https://www.ebi.ac.uk/QuickGO/term/GO:0042803)
GO:0046872 : metal ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0046872)
GO:0002020 : protease binding (https://www.ebi.ac.uk/QuickGO/term/GO:0002020)
GO:0004714 : transmembrane receptor protein tyrosine kinase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0004714)
GO:0004713 : protein tyrosine kinase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0004713)
GO:0019955 : cytokine binding (https://www.ebi.ac.uk/QuickGO/term/GO:0019955)
GO:0005020 : stem cell factor receptor activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005020)

GO - Biological Process

GO:0043066 : negative regulation of apoptotic process (https://www.ebi.ac.uk/QuickGO/term/GO:0043066)
GO:0030154 : cell differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0030154)
GO:0043473 : pigmentation (https://www.ebi.ac.uk/QuickGO/term/GO:0043473)
GO:0070374 : positive regulation of ERK1 and ERK2 cascade (https://www.ebi.ac.uk/QuickGO/term/GO:0070374)
GO:0035234 : ectopic germ cell programmed cell death (https://www.ebi.ac.uk/QuickGO/term/GO:0035234)
GO:0035162 : embryonic hemopoiesis (https://www.ebi.ac.uk/QuickGO/term/GO:0035162)
GO:0008584 : male gonad development (https://www.ebi.ac.uk/QuickGO/term/GO:0008584)
GO:0001541 : ovarian follicle development (https://www.ebi.ac.uk/QuickGO/term/GO:0001541)
GO:0008284 : positive regulation of cell proliferation (https://www.ebi.ac.uk/QuickGO/term/GO:0008284)
GO:0043406 : positive regulation of MAP kinase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0043406)
GO:0010628 : positive regulation of gene expression (https://www.ebi.ac.uk/QuickGO/term/GO:0010628)
GO:0043410 : positive regulation of MAPK cascade (https://www.ebi.ac.uk/QuickGO/term/GO:0043410)
GO:0007283 : spermatogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:0007283)
GO:0008360 : regulation of cell shape (https://www.ebi.ac.uk/QuickGO/term/GO:0008360)
GO:0048070 : regulation of developmental pigmentation (https://www.ebi.ac.uk/QuickGO/term/GO:0048070)
GO:0006468 : protein phosphorylation (https://www.ebi.ac.uk/QuickGO/term/GO:0006468)
GO:0060326 : cell chemotaxis (https://www.ebi.ac.uk/QuickGO/term/GO:0060326)
GO:0006935 : chemotaxis (https://www.ebi.ac.uk/QuickGO/term/GO:0006935)
GO:0048565 : digestive tract development (https://www.ebi.ac.uk/QuickGO/term/GO:0048565)
GO:0006954 : inflammatory response (https://www.ebi.ac.uk/QuickGO/term/GO:0006954)
GO:0019221 : cytokine-mediated signaling pathway (https://www.ebi.ac.uk/QuickGO/term/GO:0019221)
GO:0048863 : stem cell differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0048863)
GO:0048066 : developmental pigmentation (https://www.ebi.ac.uk/QuickGO/term/GO:0048066)
GO:0030318 : melanocyte differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0030318)
GO:0009968 : negative regulation of signal transduction (https://www.ebi.ac.uk/QuickGO/term/GO:0009968)
GO:0046777 : protein autophosphorylation (https://www.ebi.ac.uk/QuickGO/term/GO:0046777)
GO:0030218 : erythrocyte differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0030218)
GO:0018108 : peptidyl-tyrosine phosphorylation (https://www.ebi.ac.uk/QuickGO/term/GO:0018108)
GO:0097067 : cellular response to thyroid hormone stimulus (https://www.ebi.ac.uk/QuickGO/term/GO:0097067)
GO:1904349 : positive regulation of small intestine smooth muscle contraction (https://www.ebi.ac.uk/QuickGO/term/GO:1904349)
GO:0000187 : activation of MAPK activity (https://www.ebi.ac.uk/QuickGO/term/GO:0000187)
GO:0046427 : positive regulation of JAK-STAT cascade (https://www.ebi.ac.uk/QuickGO/term/GO:0046427)
GO:0042531 : positive regulation of tyrosine phosphorylation of STAT protein (https://www.ebi.ac.uk/QuickGO/term/GO:0042531)
GO:0030335 : positive regulation of cell migration (https://www.ebi.ac.uk/QuickGO/term/GO:0030335)
GO:0046686 : response to cadmium ion (https://www.ebi.ac.uk/QuickGO/term/GO:0046686)

GO:0035556 : intracellular signal transduction (https://www.ebi.ac.uk/QuickGO/term/GO:0035556)
GO:0031532 : actin cytoskeleton reorganization (https://www.ebi.ac.uk/QuickGO/term/GO:0031532)
GO:0002371 : dendritic cell cytokine production (https://www.ebi.ac.uk/QuickGO/term/GO:0002371)
GO:0050910 : detection of mechanical stimulus involved in sensory perception of sound (https://www.ebi.ac.uk/QuickGO/term/GO:0050910)
GO:0050673 : epithelial cell proliferation (https://www.ebi.ac.uk/QuickGO/term/GO:0050673)
GO:0038162 : erythropoietin-mediated signaling pathway (https://www.ebi.ac.uk/QuickGO/term/GO:0038162)
GO:0038093 : Fc receptor signaling pathway (https://www.ebi.ac.uk/QuickGO/term/GO:0038093)
GO:0007281 : germ cell development (https://www.ebi.ac.uk/QuickGO/term/GO:0007281)
GO:0008354 : germ cell migration (https://www.ebi.ac.uk/QuickGO/term/GO:0008354)
GO:0006687 : glycosphingolipid metabolic process (https://www.ebi.ac.uk/QuickGO/term/GO:0006687)
GO:0035701 : hematopoietic stem cell migration (https://www.ebi.ac.uk/QuickGO/term/GO:0035701)
GO:0030097 : hemopoiesis (https://www.ebi.ac.uk/QuickGO/term/GO:0030097)
GO:0002327 : immature B cell differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0002327)
GO:0038109 : Kit signaling pathway (https://www.ebi.ac.uk/QuickGO/term/GO:0038109)
GO:0030032 : lamellipodium assembly (https://www.ebi.ac.uk/QuickGO/term/GO:0030032)
GO:0002320 : lymphoid progenitor cell differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0002320)
GO:0002551 : mast cell chemotaxis (https://www.ebi.ac.uk/QuickGO/term/GO:0002551)
GO:0032762 : mast cell cytokine production (https://www.ebi.ac.uk/QuickGO/term/GO:0032762)
GO:0043303 : mast cell degranulation (https://www.ebi.ac.uk/QuickGO/term/GO:0043303)
GO:0060374 : mast cell differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0060374)
GO:0035855 : megakaryocyte development (https://www.ebi.ac.uk/QuickGO/term/GO:0035855)
GO:0097326 : melanocyte adhesion (https://www.ebi.ac.uk/QuickGO/term/GO:0097326)
GO:0097324 : melanocyte migration (https://www.ebi.ac.uk/QuickGO/term/GO:0097324)
GO:0002573 : myeloid leukocyte differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0002573)
GO:0002318 : myeloid progenitor cell differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0002318)
GO:0043069 : negative regulation of programmed cell death (https://www.ebi.ac.uk/QuickGO/term/GO:0043069)
GO:1904343 : positive regulation of colon smooth muscle contraction (https://www.ebi.ac.uk/QuickGO/term/GO:1904343)
GO:0051091 : positive regulation of DNA-binding transcription factor activity (https://www.ebi.ac.uk/QuickGO/term/GO:0051091)
GO:0048170 : positive regulation of long-term neuronal synaptic plasticity (https://www.ebi.ac.uk/QuickGO/term/GO:0048170)
GO:0045747 : positive regulation of Notch signaling pathway (https://www.ebi.ac.uk/QuickGO/term/GO:0045747)
GO:0031274 : positive regulation of pseudopodium assembly (https://www.ebi.ac.uk/QuickGO/term/GO:0031274)
GO:0120072 : positive regulation of pyloric antrum smooth muscle contraction (https://www.ebi.ac.uk/QuickGO/term/GO:0120072)
GO:1905065 : positive regulation of vascular smooth muscle cell differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:1905065)
GO:1904251 : regulation of bile acid metabolic process (https://www.ebi.ac.uk/QuickGO/term/GO:1904251)
GO:0009314 : response to radiation (https://www.ebi.ac.uk/QuickGO/term/GO:0009314)
GO:0048103 : somatic stem cell division (https://www.ebi.ac.uk/QuickGO/term/GO:0048103)
GO:0035019 : somatic stem cell population maintenance (https://www.ebi.ac.uk/QuickGO/term/GO:0035019)
GO:0007286 : spermatid development (https://www.ebi.ac.uk/QuickGO/term/GO:0007286)
GO:0030217 : T cell differentiation (https://www.ebi.ac.uk/QuickGO/term/GO:0030217)
GO:0043586 : tongue development (https://www.ebi.ac.uk/QuickGO/term/GO:0043586)
GO:0008542 : visual learning (https://www.ebi.ac.uk/QuickGO/term/GO:0008542)

GO - Cellular Component

GO:0005886 : plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005886)
GO:0005737 : cytoplasm (https://www.ebi.ac.uk/QuickGO/term/GO:0005737)
GO:0005887 : integral component of plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005887)
GO:0043235 : receptor complex (https://www.ebi.ac.uk/QuickGO/term/GO:0043235)

GO:0005615 : extracellular space (https://www.ebi.ac.uk/QuickGO/term/GO:0005615)
GO:0009986 : cell surface (https://www.ebi.ac.uk/QuickGO/term/GO:0009986)
GO:0009898 : cytoplasmic side of plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0009898)
GO:0009897 : external side of plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0009897)
GO:0001669 : acrosomal vesicle (https://www.ebi.ac.uk/QuickGO/term/GO:0001669)
GO:0005911 : cell-cell junction (https://www.ebi.ac.uk/QuickGO/term/GO:0005911)
GO:0042629 : mast cell granule (https://www.ebi.ac.uk/QuickGO/term/GO:0042629)

Presumptive Null

No (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^No^#gephebase-summary-title)

Molecular Type

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

Aberration Type

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

Deletion Size

1-10 kb

Molecular Details of the Mutation

Excision of the full-length FERV1 elevement leaving the two LTR residues

Experimental Evidence

Association Mapping (https://www.gephebase.org/search-criteria?/and+Experimental Evidence=^Association Mapping^#gephebase-summary-title)

Main Reference

Endogenous retrovirus insertion in the KIT oncogene determines white and white spotting in domestic cats. (2014) (https://pubmed.ncbi.nlm.nih.gov/25085922)

Authors

David VA; Menotti-Raymond M; Wallace AC; Roelke M; Kehler J; Leighty R; Eizirik E; Hannah SS; Nelson G; SchÃ¤ffer AA; Connelly CJ; O'Brien SJ; Ryugo DK

Abstract

The Dominant White locus (W) in the domestic cat demonstrates pleiotropic effects exhibiting complete penetrance for absence of coat pigmentation and incomplete penetrance for deafness and iris hypopigmentation. We performed linkage analysis using a pedigree segregating White to identify KIT (Chr. B1) as the feline W locus. Segregation and sequence analysis of the KIT gene in two pedigrees (P1 and P2) revealed the remarkable retrotransposition and evolution of a feline endogenous retrovirus (FERV1) as responsible for two distinct phenotypes of the W locus, Dominant White, and white spotting. A full-length (7125 bp) FERV1 element is associated with white spotting, whereas a FERV1 long terminal repeat (LTR) is associated with all Dominant White individuals. For purposes of statistical analysis, the alternatives of wild-type sequence, FERV1 element, and LTR-only define a triallelic marker. Taking into account pedigree relationships, deafness is genetically linked and associated with this marker; estimated P values for association are in the range of 0.007 to 0.10. The retrotransposition interrupts a DNAase I hypersensitive site in KIT intron 1 that is highly conserved across mammals and was previously demonstrated to regulate temporal and tissue-specific expression of KIT in murine hematopoietic and melanocytic cells. A large-population genetic survey of cats (n = 270), representing 30 cat breeds, supports our findings and demonstrates statistical significance of the FERV1 LTR and full-length element with Dominant White/blue iris ($P < 0.0001$) and white spotting ($P < 0.0001$), respectively.

Additional References

RELATED GEPHE

Related Genes

6 (Agouti, MC1R, Melanophilin (MLPH), Taqpep, tyrosinase (TYR), tyrosinase-related protein 1 (TYRP1)) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^9685^/and+Trait=Coloration/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

2 (https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^Kit (type III receptor protein-tyrosine kinase)^/and+Taxon ID=^9685^/or+Gene Gephebase=^Kit (type III receptor protein-tyrosine kinase)^/and+Taxon ID=^9685^#gephebase-summary-title)

EXTERNAL LINKS

COMMENTS

@Pleiotropy @TE; Affects a conserved melanocyte enhancer