## GEPHE SUMMARY

Gephebase Gene
TRPV4 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^TRPV4^#gephebase-summary-title)

GepheID
GP00002279

Entry Status
Published

Main curator
Martin

## PHENOTYPIC CHANGE

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

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

Trait State in Taxon A
WT ears

Trait State in Taxon B
Scottish fold cat - breed selected for heterozygotes of a dominant mutation resulting in dropped ears ; homozygotes have more severe osteochondrodysplasia than heterozygotes and breeders are recommend to always outcross

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?
No

## GENOTYPIC CHANGE

Generic Gene Name
TRPV4

Synonyms
SMAL; VRL2; BCYM3; CMT2C; SPSMA; TRP12; VROAC; HMSN2C; OTRPC4; SSQTL1

String
9606.ENSP00000406191 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000406191 )

Sequence Similarities
Belongs to the transient receptor (TC 1.A.4) family. TrpV subfamily. TRPV4 sub-subfamily.

GO - Molecular Function
GO:0005524 : ATP binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005524)
GO:0042802 : identical protein binding (https://www.ebi.ac.uk/QuickGO/term/GO:0042802)

UniProtKB Homo sapiens
Q9HBA0 (http://www.uniprot.org/uniprot/Q9HBA0)

GenebankID or UniProtKB
()

GO:0046872 : metal ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0046872)
GO:0008289 : lipid binding (https://www.ebi.ac.uk/QuickGO/term/GO:0008289)
GO:0005516 : calmodulin binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005516)
GO:0019901 : protein kinase binding (https://www.ebi.ac.uk/QuickGO/term/GO:0019901)
GO:0005216 : ion channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005216)
GO:0003779 : actin binding (https://www.ebi.ac.uk/QuickGO/term/GO:0003779)
GO:0042169 : SH2 domain binding (https://www.ebi.ac.uk/QuickGO/term/GO:0042169)
GO:0051015 : actin filament binding (https://www.ebi.ac.uk/QuickGO/term/GO:0051015)
GO:0048487 : beta-tubulin binding (https://www.ebi.ac.uk/QuickGO/term/GO:0048487)
GO:0005262 : calcium channel activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0005262)
GO:0008017 : microtubule binding (https://www.ebi.ac.uk/QuickGO/term/GO:0008017)
GO:0005080 : protein kinase C binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0005080)
GO:0043014 : alpha-tubulin binding (https://www.ebi.ac.uk/QuickGO/term/GO:0043014)
GO:0005261 : cation channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005261)
GO:0005034 : osmosensor activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005034)
GO:0015275 : stretch-activated, cation-selective, calcium channel activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0015275)

GO - Biological Process

GO:0000122 : negative regulation of transcription by RNA polymerase II
(https://www.ebi.ac.uk/QuickGO/term/GO:0000122)
GO:0006874 : cellular calcium ion homeostasis
(https://www.ebi.ac.uk/QuickGO/term/GO:0006874)
GO:0010977 : negative regulation of neuron projection development
(https://www.ebi.ac.uk/QuickGO/term/GO:0010977)
GO:0070374 : positive regulation of ERK1 and ERK2 cascade
(https://www.ebi.ac.uk/QuickGO/term/GO:0070374)
GO:0010628 : positive regulation of gene expression
(https://www.ebi.ac.uk/QuickGO/term/GO:0010628)
GO:0070588 : calcium ion transmembrane transport
(https://www.ebi.ac.uk/QuickGO/term/GO:0070588)
GO:0007204 : positive regulation of cytosolic calcium ion concentration
(https://www.ebi.ac.uk/QuickGO/term/GO:0007204)
GO:0050729 : positive regulation of inflammatory response
(https://www.ebi.ac.uk/QuickGO/term/GO:0050729)
GO:0007015 : actin filament organization
(https://www.ebi.ac.uk/QuickGO/term/GO:0007015)
GO:0042538 : hyperosmotic salinity response
(https://www.ebi.ac.uk/QuickGO/term/GO:0042538)
GO:0046330 : positive regulation of JNK cascade
(https://www.ebi.ac.uk/QuickGO/term/GO:0046330)
GO:0034605 : cellular response to heat
(https://www.ebi.ac.uk/QuickGO/term/GO:0034605)
GO:0009612 : response to mechanical stimulus
(https://www.ebi.ac.uk/QuickGO/term/GO:0009612)
GO:0042593 : glucose homeostasis (https://www.ebi.ac.uk/QuickGO/term/GO:0042593)
GO:0031532 : actin cytoskeleton reorganization
(https://www.ebi.ac.uk/QuickGO/term/GO:0031532)
GO:0097009 : energy homeostasis (https://www.ebi.ac.uk/QuickGO/term/GO:0097009)
GO:0010759 : positive regulation of macrophage chemotaxis
(https://www.ebi.ac.uk/QuickGO/term/GO:0010759)
GO:0006816 : calcium ion transport (https://www.ebi.ac.uk/QuickGO/term/GO:0006816)
GO:0032868 : response to insulin (https://www.ebi.ac.uk/QuickGO/term/GO:0032868)
GO:0002024 : diet induced thermogenesis
(https://www.ebi.ac.uk/QuickGO/term/GO:0002024)
GO:0006884 : cell volume homeostasis
(https://www.ebi.ac.uk/QuickGO/term/GO:0006884)
GO:0050891 : multicellular organismal water homeostasis
(https://www.ebi.ac.uk/QuickGO/term/GO:0050891)
GO:0007043 : cell-cell junction assembly
(https://www.ebi.ac.uk/QuickGO/term/GO:0007043)
GO:0071651 : positive regulation of chemokine (C-C motif) ligand 5 production
(https://www.ebi.ac.uk/QuickGO/term/GO:0071651)
GO:2000778 : positive regulation of interleukin-6 secretion
(https://www.ebi.ac.uk/QuickGO/term/GO:2000778)
GO:0047484 : regulation of response to osmotic stress
(https://www.ebi.ac.uk/QuickGO/term/GO:0047484)
GO:0071639 : positive regulation of monocyte chemotactic protein-1 production
(https://www.ebi.ac.uk/QuickGO/term/GO:0071639)
GO:0097497 : blood vessel endothelial cell delamination
(https://www.ebi.ac.uk/QuickGO/term/GO:0097497)
GO:0070509 : calcium ion import (https://www.ebi.ac.uk/QuickGO/term/GO:0070509)
GO:1902656 : calcium ion import into cytosol
(https://www.ebi.ac.uk/QuickGO/term/GO:1902656)
GO:0060351 : cartilage development involved in endochondral bone morphogenesis
(https://www.ebi.ac.uk/QuickGO/term/GO:0060351)
GO:0071476 : cellular hypotonic response

(https://www.ebi.ac.uk/QuickGO/term/GO:0071476)
GO:0071477 : cellular hypotonic salinity response
(https://www.ebi.ac.uk/QuickGO/term/GO:0071477)
GO:0071470 : cellular response to osmotic stress
(https://www.ebi.ac.uk/QuickGO/term/GO:0071470)
GO:0043622 : cortical microtubule organization
(https://www.ebi.ac.uk/QuickGO/term/GO:0043622)
GO:0046785 : microtubule polymerization
(https://www.ebi.ac.uk/QuickGO/term/GO:0046785)
GO:1903444 : negative regulation of brown fat cell differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:1903444)
GO:0007231 : osmosensory signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0007231)
GO:2000340 : positive regulation of chemokine (C-X-C motif) ligand 1 production
(https://www.ebi.ac.uk/QuickGO/term/GO:2000340)
GO:0071642 : positive regulation of macrophage inflammatory protein 1 alpha production
(https://www.ebi.ac.uk/QuickGO/term/GO:0071642)
GO:0031117 : positive regulation of microtubule depolymerization
(https://www.ebi.ac.uk/QuickGO/term/GO:0031117)
GO:0043117 : positive regulation of vascular permeability
(https://www.ebi.ac.uk/QuickGO/term/GO:0043117)
GO:1903759 : signal transduction involved in regulation of aerobic respiration
(https://www.ebi.ac.uk/QuickGO/term/GO:1903759)
GO:0030103 : vasopressin secretion (https://www.ebi.ac.uk/QuickGO/term/GO:0030103)

GO - Cellular Component

GO:0016021 : integral component of membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0016021)
GO:0005886 : plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005886)
GO:0016324 : apical plasma membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0016324)
GO:0005925 : focal adhesion (https://www.ebi.ac.uk/QuickGO/term/GO:0005925)
GO:0005887 : integral component of plasma membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0005887)
GO:0005623 : cell (https://www.ebi.ac.uk/QuickGO/term/GO:0005623)
GO:0005783 : endoplasmic reticulum
(https://www.ebi.ac.uk/QuickGO/term/GO:0005783)
GO:0030175 : filopodium (https://www.ebi.ac.uk/QuickGO/term/GO:0030175)
GO:0030027 : lamellipodium (https://www.ebi.ac.uk/QuickGO/term/GO:0030027)
GO:0031410 : cytoplasmic vesicle (https://www.ebi.ac.uk/QuickGO/term/GO:0031410)
GO:0009986 : cell surface (https://www.ebi.ac.uk/QuickGO/term/GO:0009986)
GO:0005912 : adherens junction (https://www.ebi.ac.uk/QuickGO/term/GO:0005912)
GO:0032587 : ruffle membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0032587)
GO:0030864 : cortical actin cytoskeleton
(https://www.ebi.ac.uk/QuickGO/term/GO:0030864)
GO:0005929 : cilium (https://www.ebi.ac.uk/QuickGO/term/GO:0005929)
GO:0005881 : cytoplasmic microtubule
(https://www.ebi.ac.uk/QuickGO/term/GO:0005881)
GO:0030426 : growth cone (https://www.ebi.ac.uk/QuickGO/term/GO:0030426)

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

c.1024G>T p.V342F

Experimental Evidence

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

| | Taxon A | Taxon B | Position |
|---|---|---|---|
| Codon | - | - | - |
| Amino-acid | Val | Phe | 342 |

Main Reference

A dominant TRPV4 variant underlies osteochondrodysplasia in Scottish fold cats. (2016) (https://pubmed.ncbi.nlm.nih.gov/27063440)

Authors

Gandolfi B; Alamri S; Darby WG; Adhikari B; Lattimer JC; Malik R; Wade CM; Lyons LA; Cheng J; Bateman JF; McIntyre P; LamandÃ© SR; Haase B

Abstract

Scottish fold cats, named for their unique ear shape, have a dominantly inherited osteochondrodysplasia involving malformation in the distal forelimbs, distal hindlimbs and tail, and progressive joint destruction. This study aimed to identify the gene and the underlying variant responsible for the osteochondrodysplasia.

DNA samples from 44 Scottish fold and 54 control cats were genotyped using a feline DNA array and a case-control genome-wide association analysis conducted. The gene encoding a calcium permeable ion channel, transient receptor potential cation channel, subfamily V, member 4 (TRPV4) was identified as a candidate within the associated region and sequenced. Stably

transfected HEK293 cells were used to compare wild-type and mutant TRPV4 expression, cell surface localisation and responses to activation with a synthetic agonist GSK1016709A, hypo-osmolarity, and protease-activated receptor 2 stimulation.

The dominantly inherited folded ear and osteochondrodysplasia in Scottish fold cats is associated with a p.V342F substitution (c.1024G>T) in TRPV4. The change was not found in 648 unaffected cats. Functional analysis in HEK293 cells showed V342F mutant TRPV4 was poorly expressed at the cell surface compared to wild-type TRPV4 and as a consequence the maximum response to a synthetic agonist was reduced. Mutant TRPV4 channels had a higher basal activity and an increased response to hypotonic conditions.

Access to a naturally-occurring TRPV4 mutation in the Scottish fold cat will allow further functional studies to identify how and why the mutations affect cartilage and bone development.

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Additional References

Incomplete dominant osteochondrodysplasia in heterozygous Scottish Fold cats. (2008) (https://pubmed.ncbi.nlm.nih.gov/18339089)

## RELATED GEPHE

Related Genes

No matches found.

Related Haplotypes

No matches found.

## EXTERNAL LINKS

## COMMENTS

@HeterozygoteAdvantage https://omia.org/OMIA000319/9685/