GEPHE SUMMARY

Gephebase Gene
Dishevelled

GephelD
GP00002110

Entry Status
Published

Main curator
Courtier

PHENOTYPIC CHANGE

Trait Category
Morphology

Trait
Organ size (tail)

Trait State in Taxon A
Canis familiaris

Trait State in Taxon B
Canis familiaris - 3 breeds with a screw tail

Ancestral State
Taxon A

Taxonomic Status
Domesticated

Taxon A

Latin Name
Canis lupus familiaris

Common Name
dog

Synonyms
Canis canis; Canis domesticus; Canis familiaris; dog; dogs

Rank
subspecies

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; Caniformia; Canidae; Canis; Canis lupus

Parent
Canis lupus (gray wolf) - (Rank: species)

NCBI Taxonomy ID
9615

is Taxon A an Infraspecies?
No

Taxon B

Latin Name
Canis lupus familiaris

Common Name
dog

Synonyms
Canis canis; Canis domesticus; Canis familiaris; dog; dogs

Rank
subspecies

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; Caniformia; Canidae; Canis; Canis lupus

Parent
Canis lupus (gray wolf) - (Rank: species)

NCBI Taxonomy ID
9615

is Taxon B an Infraspecies?
Yes

Taxon B Description
Bulldog; French Bulldog and Boston Terrier

GENOTYPIC CHANGE

Generic Gene Name
Dvl2

Synonyms
-

String
10090.ENSMUSP00000019362

Sequence Similarities
Belongs to the DSH family.

GO - Molecular Function
GO:0042802 : identical protein binding
GO:0019901 : protein kinase binding
GO:0030674 : protein binding, bridging
GO:0019904 : protein domain specific binding
GO:0005109 : frizzled binding
GO:0048365 : Rac GTPase binding
GO:0043621 : protein self-association

GO - Biological Process

UniProtKB Mus musculus
Q60838

GenebankID or UniProtKB

GO:0007507 : heart development
GO:0001843 : neural tube closure
GO:0045893 : positive regulation of transcription, DNA-templated
GO:0043547 : positive regulation of GTPase activity
GO:0001934 : positive regulation of protein phosphorylation
GO:0006366 : transcription by RNA polymerase II
GO:0035556 : intracellular signal transduction
GO:0051091 : positive regulation of DNA-binding transcription factor activity
GO:0060070 : canonical Wnt signaling pathway
GO:0003007 : heart morphogenesis
GO:0035567 : non-canonical Wnt signaling pathway
GO:0043507 : positive regulation of JUN kinase activity
GO:0003151 : outflow tract morphogenesis
GO:0007379 : segment specification
GO:0044340 : canonical Wnt signaling pathway involved in regulation of cell proliferation
GO:0034613 : cellular protein localization
GO:0090103 : cochlea morphogenesis
GO:0022007 : convergent extension involved in neural plate elongation
GO:0060029 : convergent extension involved in organogenesis
GO:0090179 : planar cell polarity pathway involved in neural tube closure
GO:0150012 : positive regulation of neuron projection arborization
GO:0061098 : positive regulation of protein tyrosine kinase activity
GO:0035282 : segmentation
GO:0060071 : Wnt signaling pathway, planar cell polarity pathway

GO - Cellular Component
GO:0005886 : plasma membrane
GO:0030136 : clathrin-coated vesicle
GO:0005737 : cytoplasm
GO:0005829 : cytosol
GO:0005654 : nucleoplasm
GO:0005634 : nucleus
GO:0016604 : nuclear body
GO:0005856 : cytoskeleton
GO:0031410 : cytoplasmic vesicle
GO:0045177 : apical part of cell
GO:0005938 : cell cortex
GO:0016235 : aggresome
GO:0016328 : lateral plasma membrane

Presumptive Null
Yes

Molecular Type
Coding

Aberration Type
Deletion

Deletion Size
1-9 bp

Molecular Details of the Mutation
single base deletion found on CFA 5(g.32195043_32195044del) that is homozygous in the three screw tail breeds - predicted to lead to a frameshift mutation and cause a premature stop codon that truncates the translated protein by 23 amino acids (p.Pro684LeufsX26) - 26 altered amino acids are predicted to be present in the highly conserved C-terminus of the mutant protein.

Experimental Evidence
Association Mapping

Main Reference
Whole genome variant association across 100 dogs identifies a frame shift mutation in DISHEVELLED 2 which contributes to Robinow-like syndrome in Bulldogs and related screw tail dog breeds. (2018)

Authors
Mansour TA; Lucot K; Konopelski SE; Dickinson PJ; Sturges BK; Vernau KL; Choi S; Stern JA; Thomasy SM; DÃ¶ring S; Verstraete FJM; Johnson EG; York D; Rebhun RB; Ho HH; Brown CT; Bannasch DL

Abstract
Domestic dog breeds exhibit remarkable morphological variations that result from centuries of artificial selection and breeding. Identifying the genetic changes that contribute to these variations could provide critical insights into the molecular basis of tissue and organismal morphogenesis. Bulldogs, French Bulldogs and Boston Terriers share many morphological and disease-predisposition traits, including brachycephalic skull morphology, widely set eyes and short stature. Unlike other brachycephalic dogs, these breeds also exhibit vertebral malformations that result in a truncated, kinked tail (screw tail). Whole genome sequencing of 100 dogs from 21 breeds identified 12.4 million bi-allelic variants that met inclusion criteria. Whole Genome Association of these variants with the breed defining phenotype of screw tail was performed using 10 cases and 84 controls and identified a frameshift mutation in the WNT pathway gene DISHEVELLED 2 (DVL2) (Chr5: 32195043_32195044del, p = 4.37 X 10-37) as the most strongly associated variant in the canine genome. This DVL2 variant was fixed in Bulldogs and French Bulldogs and had a high allele frequency (0.94) in Boston Terriers. The DVL2 variant segregated with thoracic and caudal vertebral column malformations in a recessive manner with incomplete and variable penetrance for thoracic vertebral malformations between different breeds. Importantly, analogous frameshift mutations in the human DVL1 and DVL3 genes cause Robinow syndrome, a congenital disorder characterized by similar craniofacial, limb and vertebral malformations. Analysis of the canine DVL2 variant protein showed that its ability to undergo WNT-induced phosphorylation is reduced, suggesting that altered WNT signaling may contribute to the Robinow-like syndrome in the screwtail breeds.

Additional References

RELATED GEPHE

Related Genes

No matches found.

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS

the screw tail phenotype corresponds to malformed and fused vertebrae and lack of approximately 8 to 15 caudal vertebrae; which normally form the canine tail. Analogous frameshift mutations in the human DVL1 and DVL3 genes cause Robinow syndrome (a congenital disorder characterized by similar craniofacial; limb and vertebral malformations).