GEPHE SUMMARY

Gephebase Gene
Dvl2 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^Dvl2^#gephebase-summary-title)

GepheID
GP00002110

Entry Status
Published

Main curator
Courtier

PHENOTYPIC CHANGE

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

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

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

Taxon A

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

Common Name
dog

Synonyms
Canis canis; Canis domesticus; Canis familiaris; dog; dogs; Canis familiaris Linnaeus, 1758; Canis lupus familiaris Linnaeus, 1758

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) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9612)

NCBI Taxonomy ID
9615 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9615)

is Taxon A an Infraspecies?
No

Taxon B

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

Common Name
dog

Synonyms
Canis canis; Canis domesticus; Canis familiaris; dog; dogs; Canis familiaris Linnaeus, 1758; Canis lupus familiaris Linnaeus, 1758

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) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9612)

NCBI Taxonomy ID
9615 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?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
9606.ENSP00000005340 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000005340)

Sequence Similarities
Belongs to the DSH family.

GO - Molecular Function
GO:0042802 : identical protein binding (https://www.ebi.ac.uk/QuickGO/term/GO:0042802)
GO:0019901 : protein kinase binding (https://www.ebi.ac.uk/QuickGO/term/GO:0019901)
GO:0030674 : protein binding, bridging

UniProtKB Homo sapiens
O14641 (http://www.uniprot.org/uniprot/O14641)

GenebankID or UniProtKB
()

(https://www.ebi.ac.uk/QuickGO/term/GO:0030674)
GO:0019904 : protein domain specific binding
(https://www.ebi.ac.uk/QuickGO/term/GO:0019904)
GO:0005109 : frizzled binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005109)
GO:0048365 : Rac GTPase binding (https://www.ebi.ac.uk/QuickGO/term/GO:0048365)
GO:0043621 : protein self-association (https://www.ebi.ac.uk/QuickGO/term/GO:0043621)

GO - Biological Process

GO:0007507 : heart development (https://www.ebi.ac.uk/QuickGO/term/GO:0007507)
GO:0001843 : neural tube closure (https://www.ebi.ac.uk/QuickGO/term/GO:0001843)
GO:0045893 : positive regulation of transcription, DNA-templated
(https://www.ebi.ac.uk/QuickGO/term/GO:0045893)
GO:0090090 : negative regulation of canonical Wnt signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0090090)
GO:0043547 : positive regulation of GTPase activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0043547)
GO:0001934 : positive regulation of protein phosphorylation
(https://www.ebi.ac.uk/QuickGO/term/GO:0001934)
GO:0006366 : transcription by RNA polymerase II
(https://www.ebi.ac.uk/QuickGO/term/GO:0006366)
GO:0061024 : membrane organization
(https://www.ebi.ac.uk/QuickGO/term/GO:0061024)
GO:0051091 : positive regulation of DNA-binding transcription factor activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0051091)
GO:0060070 : canonical Wnt signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0060070)
GO:0035567 : non-canonical Wnt signaling pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0035567)
GO:0043507 : positive regulation of JUN kinase activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0043507)
GO:0003151 : outflow tract morphogenesis
(https://www.ebi.ac.uk/QuickGO/term/GO:0003151)
GO:0007379 : segment specification (https://www.ebi.ac.uk/QuickGO/term/GO:0007379)
GO:0044340 : canonical Wnt signaling pathway involved in regulation of cell proliferation
(https://www.ebi.ac.uk/QuickGO/term/GO:0044340)
GO:0034613 : cellular protein localization
(https://www.ebi.ac.uk/QuickGO/term/GO:0034613)
GO:0090103 : cochlea morphogenesis
(https://www.ebi.ac.uk/QuickGO/term/GO:0090103)
GO:0022007 : convergent extension involved in neural plate elongation
(https://www.ebi.ac.uk/QuickGO/term/GO:0022007)
GO:0090179 : planar cell polarity pathway involved in neural tube closure
(https://www.ebi.ac.uk/QuickGO/term/GO:0090179)
GO:0150012 : positive regulation of neuron projection arborization
(https://www.ebi.ac.uk/QuickGO/term/GO:0150012)
GO:0061098 : positive regulation of protein tyrosine kinase activity
(https://www.ebi.ac.uk/QuickGO/term/GO:0061098)
GO:0060071 : Wnt signaling pathway, planar cell polarity pathway
(https://www.ebi.ac.uk/QuickGO/term/GO:0060071)
GO:1904886 : beta-catenin destruction complex disassembly
(https://www.ebi.ac.uk/QuickGO/term/GO:1904886)
GO:0035329 : hippo signaling (https://www.ebi.ac.uk/QuickGO/term/GO:0035329)

GO - Cellular Component

GO:0005737 : cytoplasm (https://www.ebi.ac.uk/QuickGO/term/GO:0005737)
GO:0005829 : cytosol (https://www.ebi.ac.uk/QuickGO/term/GO:0005829)
GO:0005654 : nucleoplasm (https://www.ebi.ac.uk/QuickGO/term/GO:0005654)
GO:0005634 : nucleus (https://www.ebi.ac.uk/QuickGO/term/GO:0005634)
GO:0016604 : nuclear body (https://www.ebi.ac.uk/QuickGO/term/GO:0016604)
GO:0031410 : cytoplasmic vesicle (https://www.ebi.ac.uk/QuickGO/term/GO:0031410)
GO:0045177 : apical part of cell (https://www.ebi.ac.uk/QuickGO/term/GO:0045177)
GO:0016235 : aggresome (https://www.ebi.ac.uk/QuickGO/term/GO:0016235)
GO:0016328 : lateral plasma membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0016328)
GO:0045334 : clathrin-coated endocytic vesicle
(https://www.ebi.ac.uk/QuickGO/term/GO:0045334)

Presumptive Null

Yes (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^Yes^#gephebase-summary-title)

Molecular Type

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

Aberration Type

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

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

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) (https://pubmed.ncbi.nlm.nih.gov/30521570)

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

1 (TBXT) (https://www.gephebase.org/search-criteria?/or+Taxon ID=^9615^/and+Trait=Organ size/and+groupHaplotypes=true#gephebase-summary-title)

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS

@Pleiotropy 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). https://omia.org/OMIA002186/9615/