

GEPHE SUMMARY

aggrecan (https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=^aggrecan^#gephebase-summary-title)	Gephebase Gene	GP00002140	GepheID
Published	Entry Status	Martin	Main curator

PHENOTYPIC CHANGE

Morphology (https://www.gephebase.org/search-criteria?/and+Trait+Category=^Morphology^#gephebase-summary-title)	Trait Category		
Body size (dwarfism) (https://www.gephebase.org/search-criteria?/and+Trait=^Body size (dwarfism)^#gephebase-summary-title)	Trait		
European cattle breeds with normal size	Trait State in Taxon A		
Dexter cattle (dwarf = dominant trait ; recessive lethal)	Trait State in Taxon B		
Taxon A	Ancestral State		
Domesticated (https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=^Domesticated^#gephebase-summary-title)	Taxonomic Status		
	Taxon A	Taxon B	
Bos taurus (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Bos+taurus^#gephebase-summary-title)	Latin Name	Bos taurus (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Bos+taurus^#gephebase-summary-title)	Latin Name
cattle	Common Name	cattle	Common Name
Bos bovis; Bos primigenius taurus; cattle; bovine; cow; dairy cow; domestic cattle; domestic cow; Bos taurus Linnaeus, 1758; Bos Taurus	Synonyms	Bos bovis; Bos primigenius taurus; cattle; bovine; cow; dairy cow; domestic cattle; domestic cow; Bos taurus Linnaeus, 1758; Bos Taurus	Synonyms
species	Rank	species	Rank
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Laurasiatheria; Artiodactyla; Ruminantia; Pecora; Bovidae; Bovinae; Bos	Lineage	cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Laurasiatheria; Artiodactyla; Ruminantia; Pecora; Bovidae; Bovinae; Bos	Lineage
Bos (oxen, cattle) - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9903)	Parent	Bos (oxen, cattle) - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9903)	Parent
9913 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9913)	NCBI Taxonomy ID	9913 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9913)	NCBI Taxonomy ID
No	is Taxon A an Intraspecies?	No	is Taxon B an Intraspecies?

GENOTYPIC CHANGE

ACAN	Generic Gene Name	P16112 (http://www.uniprot.org/uniprot/P16112)	UniProtKB Homo sapiens
AGC1; SEDK; AGCAN; CSPG1; MSK16; CSPGCP; SSOAOD	Synonyms	()	GenebankID or UniProtKB
9606.ENSP00000387356 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000387356)	String		
Belongs to the aggrecan/versican proteoglycan family.	Sequence Similarities		
GO:0046872 : metal ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0046872)	GO - Molecular Function		
GO:0030246 : carbohydrate binding (https://www.ebi.ac.uk/QuickGO/term/GO:0030246)			
GO:0005201 : extracellular matrix structural constituent (https://www.ebi.ac.uk/QuickGO/term/GO:0005201)			
GO:0030021 : extracellular matrix structural constituent conferring compression resistance (https://www.ebi.ac.uk/QuickGO/term/GO:0030021)			

GO:0005540 : hyaluronic acid binding
(<https://www.ebi.ac.uk/QuickGO/term/GO:0005540>)

GO - Biological Process

GO:0007155 : cell adhesion (<https://www.ebi.ac.uk/QuickGO/term/GO:0007155>)
GO:0007417 : central nervous system development
(<https://www.ebi.ac.uk/QuickGO/term/GO:0007417>)
GO:0001502 : cartilage condensation
(<https://www.ebi.ac.uk/QuickGO/term/GO:0001502>)
GO:0002063 : chondrocyte development
(<https://www.ebi.ac.uk/QuickGO/term/GO:0002063>)
GO:0030199 : collagen fibril organization
(<https://www.ebi.ac.uk/QuickGO/term/GO:0030199>)
GO:0030198 : extracellular matrix organization
(<https://www.ebi.ac.uk/QuickGO/term/GO:0030198>)
GO:0007507 : heart development (<https://www.ebi.ac.uk/QuickGO/term/GO:0007507>)
GO:0018146 : keratan sulfate biosynthetic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0018146>)
GO:0042340 : keratan sulfate catabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0042340>)
GO:0030166 : proteoglycan biosynthetic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0030166>)
GO:0006508 : proteolysis (<https://www.ebi.ac.uk/QuickGO/term/GO:0006508>)
GO:0001501 : skeletal system development
(<https://www.ebi.ac.uk/QuickGO/term/GO:0001501>)

GO - Cellular Component

GO:0005576 : extracellular region (<https://www.ebi.ac.uk/QuickGO/term/GO:0005576>)
GO:0062023 : collagen-containing extracellular matrix
(<https://www.ebi.ac.uk/QuickGO/term/GO:0062023>)
GO:0005604 : basement membrane (<https://www.ebi.ac.uk/QuickGO/term/GO:0005604>)
GO:0031012 : extracellular matrix (<https://www.ebi.ac.uk/QuickGO/term/GO:0031012>)
GO:0098982 : GABA-ergic synapse (<https://www.ebi.ac.uk/QuickGO/term/GO:0098982>)
GO:0098978 : glutamatergic synapse
(<https://www.ebi.ac.uk/QuickGO/term/GO:0098978>)
GO:0005796 : Golgi lumen (<https://www.ebi.ac.uk/QuickGO/term/GO:0005796>)
GO:0043202 : lysosomal lumen (<https://www.ebi.ac.uk/QuickGO/term/GO:0043202>)
GO:0098966 : perisynaptic extracellular matrix
(<https://www.ebi.ac.uk/QuickGO/term/GO:0098966>)

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

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

Insertion Size

1-9 bp

Molecular Details of the Mutation

2266_2267insGGCA mutation introduces a frameshift and a premature termination codon into exon 11; the frameshift occurs at amino acid position 756 ; the termination codon occurs at position 914 compared to the normal aggrecan product of 2327 amino acids

Experimental Evidence

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

Main Reference

Bulldog dwarfism in Dexter cattle is caused by mutations in ACAN. (2007) (<https://pubmed.ncbi.nlm.nih.gov/17952705>)

Authors

Cavanagh JA; Tammen I; Windsor PA; Bateman JF; Savarirayan R; Nicholas FW; Raadsma HW

Abstract

Bulldog dwarfism in Dexter cattle is one of the earliest single-locus disorders described in animals. Affected fetuses display extreme disproportionate dwarfism, reflecting abnormal cartilage development (chondrodysplasia). Typically, they die around the seventh month of gestation, precipitating a natural abortion. Heterozygotes show a milder form of dwarfism, most noticeably having shorter legs. Homozygosity mapping in candidate regions in a small Dexter pedigree suggested aggrecan (ACAN) as the most likely candidate gene. Mutation screening revealed a 4-bp insertion in exon 11 (2266_2267insGGCA) (called BD1 for diagnostic testing) and a second, rarer transition in exon 1 (-198C>T) (called BD2) that cosegregate with the disorder. In chondrocytes from cattle heterozygous for the insertion, mutant mRNA is subject to nonsense-mediated decay, showing only 8% of normal expression. Genotyping in Dexter families throughout the world shows a one-to-one correspondence between genotype and phenotype at this locus. The heterozygous and homozygous-affected Dexter cattle could prove invaluable as a model for human disorders caused by mutations in ACAN.

Additional References

RELATED GEPHE

Related Genes

5 (GH, LCORL, PLAG1, PRKG2, RNF11) (<https://www.gephebase.org/search-criteria?/or+Taxon ID=~9913^/and+Trait=Body size/and+groupHaplotypes=true#gephebase-summary-title>)

Related Haplotypes

1 (<https://www.gephebase.org/search-criteria?/or+Gene Gephabase=~aggrecan^/and+Taxon ID=~9913^/or+Gene Gephabase=~aggrecan^/and+Taxon ID=~9913^#gephebase-summary-title>)

EXTERNAL LINKS

COMMENTS

<https://omia.org/OMIA001271/9913/> @AllelicSeries @HeterozygoteAdvantage