GEPHE SUMMARY

Gephebase Gene

Ptch1 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^Ptch1^#gephebase-summary-title)

Entry Status

Published

GepheID

GP00001389

Main curator

Courtier

PHENOTYPIC CHANGE

Trait Category

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

Trait

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

Trait State in Taxon A

Mouse

Trait State in Taxon B

Cattle

Ancestral State

Taxon A

Taxonomic Status

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

Taxon A

Latin Name

Mus musculus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Mus musculus^#gephebase-summary-title)

Common Name

house mouse

Synonyms

house mouse; mouse; Mus musculus Linnaeus, 1758; mice C57BL/6xCBA/CaJ hybrid

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; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus

Parent

Mus () - (Rank: subgenus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 862507)

NCBI Taxonomy ID

10090 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 10090)

is Taxon A an Infraspecies?

No

Taxon B

Latin Name

Bos taurus (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Bos taurus^#gephebase-summary-title)

Common Name

cattle

Synonyms

Bos bovis; Bos primigenius taurus; cattle; bovine; cow; dairy cow; domestic cattle; domestic cow; Bos taurus Linnaeus, 1758; Bos Tauurus

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; Artiodactyla; Ruminantia; Pecora; Bovidae; Bovinae; Bos

Parent

Bos (oxen, cattle) - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9903)

NCBI Taxonomy ID

9913 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9913)

is Taxon B an Infraspecies?

No

GENOTYPIC CHANGE

Generic Gene Name

Ptch1

Synonyms

Ptc; mes; wig; Ptc1; Ptch; A230106A15Rik

String

10090.ENSMUSP00000021921 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier= 10090.ENSMUSP00000021921)

Sequence Similarities

Belongs to the patched family.

GO - Molecular Function

GO:0008270 : zinc ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0008270)
GO:0015485 : cholesterol binding (https://www.ebi.ac.uk/QuickGO/term/GO:0015485)
GO:0008201 : heparin binding (https://www.ebi.ac.uk/QuickGO/term/GO:0008201)
GO:0044877 : protein-containing complex binding (https://www.ebi.ac.uk/QuickGO/term/GO:0044877)
GO:0097108 : hedgehog family protein binding

UniProtKB Mus musculus

Q61115 (http://www.uniprot.org/uniprot/Q61115)

GenebankID or UniProtKB

()

(https://www.ebi.ac.uk/QuickGO/term/GO:0097108)
GO:0008158 : hedgehog receptor activity (https://www.ebi.ac.uk/QuickGO/term/GO:0008158)
GO:0005119 : smoothened binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005119)
GO:0030332 : cyclin binding (https://www.ebi.ac.uk/QuickGO/term/GO:0030332)
GO:0005113 : patched binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005113)

GO - Biological Process

GO:0007165 : signal transduction (https://www.ebi.ac.uk/QuickGO/term/GO:0007165)
GO:0007346 : regulation of mitotic cell cycle (https://www.ebi.ac.uk/QuickGO/term/GO:0007346)
GO:0030326 : embryonic limb morphogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:0030326)
GO:0000122 : negative regulation of transcription by RNA polymerase II (https://www.ebi.ac.uk/QuickGO/term/GO:0000122)
GO:0045892 : negative regulation of transcription, DNA-templated (https://www.ebi.ac.uk/QuickGO/term/GO:0045892)
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:0010875 : positive regulation of cholesterol efflux (https://www.ebi.ac.uk/QuickGO/term/GO:0010875)
GO:0001701 : in utero embryonic development (https://www.ebi.ac.uk/QuickGO/term/GO:0001701)
GO:0008285 : negative regulation of cell proliferation (https://www.ebi.ac.uk/QuickGO/term/GO:0008285)
GO:0050680 : negative regulation of epithelial cell proliferation (https://www.ebi.ac.uk/QuickGO/term/GO:0050680)
GO:0030850 : prostate gland development (https://www.ebi.ac.uk/QuickGO/term/GO:0030850)
GO:0009887 : animal organ morphogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:0009887)
GO:0009953 : dorsal/ventral pattern formation (https://www.ebi.ac.uk/QuickGO/term/GO:0009953)
GO:0032526 : response to retinoic acid (https://www.ebi.ac.uk/QuickGO/term/GO:0032526)
GO:0042493 : response to drug (https://www.ebi.ac.uk/QuickGO/term/GO:0042493)
GO:0032355 : response to estradiol (https://www.ebi.ac.uk/QuickGO/term/GO:0032355)
GO:0008544 : epidermis development (https://www.ebi.ac.uk/QuickGO/term/GO:0008544)
GO:0040015 : negative regulation of multicellular organism growth (https://www.ebi.ac.uk/QuickGO/term/GO:0040015)
GO:0043433 : negative regulation of DNA-binding transcription factor activity (https://www.ebi.ac.uk/QuickGO/term/GO:0043433)
GO:0007420 : brain development (https://www.ebi.ac.uk/QuickGO/term/GO:0007420)
GO:0048568 : embryonic organ development (https://www.ebi.ac.uk/QuickGO/term/GO:0048568)
GO:0008589 : regulation of smoothened signaling pathway (https://www.ebi.ac.uk/QuickGO/term/GO:0008589)
GO:0035137 : hindlimb morphogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:0035137)
GO:0009612 : response to mechanical stimulus (https://www.ebi.ac.uk/QuickGO/term/GO:0009612)
GO:0009957 : epidermal cell fate specification (https://www.ebi.ac.uk/QuickGO/term/GO:0009957)
GO:0032880 : regulation of protein localization (https://www.ebi.ac.uk/QuickGO/term/GO:0032880)
GO:0001658 : branching involved in ureteric bud morphogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:0001658)
GO:0072203 : cell proliferation involved in metanephros development (https://www.ebi.ac.uk/QuickGO/term/GO:0072203)
GO:0045879 : negative regulation of smoothened signaling pathway (https://www.ebi.ac.uk/QuickGO/term/GO:0045879)
GO:0040008 : regulation of growth (https://www.ebi.ac.uk/QuickGO/term/GO:0040008)
GO:0042593 : glucose homeostasis (https://www.ebi.ac.uk/QuickGO/term/GO:0042593)
GO:0042127 : regulation of cell proliferation (https://www.ebi.ac.uk/QuickGO/term/GO:0042127)
GO:0030879 : mammary gland development (https://www.ebi.ac.uk/QuickGO/term/GO:0030879)
GO:0007224 : smoothened signaling pathway (https://www.ebi.ac.uk/QuickGO/term/GO:0007224)
GO:0021904 : dorsal/ventral neural tube patterning (https://www.ebi.ac.uk/QuickGO/term/GO:0021904)
GO:0043616 : keratinocyte proliferation (https://www.ebi.ac.uk/QuickGO/term/GO:0043616)
GO:0007389 : pattern specification process (https://www.ebi.ac.uk/QuickGO/term/GO:0007389)
GO:0001709 : cell fate determination (https://www.ebi.ac.uk/QuickGO/term/GO:0001709)

GO:0060644 : mammary gland epithelial cell differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0060644)
GO:0061005 : cell differentiation involved in kidney development
(https://www.ebi.ac.uk/QuickGO/term/GO:0061005)
GO:0071397 : cellular response to cholesterol
(https://www.ebi.ac.uk/QuickGO/term/GO:0071397)
GO:0071679 : commissural neuron axon guidance
(https://www.ebi.ac.uk/QuickGO/term/GO:0071679)
GO:0003007 : heart morphogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:0003007)
GO:0035108 : limb morphogenesis (https://www.ebi.ac.uk/QuickGO/term/GO:0035108)
GO:0097421 : liver regeneration (https://www.ebi.ac.uk/QuickGO/term/GO:0097421)
GO:0060603 : mammary gland duct morphogenesis
(https://www.ebi.ac.uk/QuickGO/term/GO:0060603)
GO:0051782 : negative regulation of cell division
(https://www.ebi.ac.uk/QuickGO/term/GO:0051782)
GO:0045668 : negative regulation of osteoblast differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0045668)
GO:0021997 : neural plate axis specification
(https://www.ebi.ac.uk/QuickGO/term/GO:0021997)
GO:0001841 : neural tube formation (https://www.ebi.ac.uk/QuickGO/term/GO:0001841)
GO:0021532 : neural tube patterning (https://www.ebi.ac.uk/QuickGO/term/GO:0021532)
GO:0060037 : pharyngeal system development
(https://www.ebi.ac.uk/QuickGO/term/GO:0060037)
GO:0045606 : positive regulation of epidermal cell differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0045606)
GO:0072659 : protein localization to plasma membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0072659)
GO:0016485 : protein processing (https://www.ebi.ac.uk/QuickGO/term/GO:0016485)
GO:0010157 : response to chlorate (https://www.ebi.ac.uk/QuickGO/term/GO:0010157)
GO:0060831 : smoothened signaling pathway involved in dorsal/ventral neural tube patterning (https://www.ebi.ac.uk/QuickGO/term/GO:0060831)
GO:0061053 : somite development (https://www.ebi.ac.uk/QuickGO/term/GO:0061053)
GO:0021522 : spinal cord motor neuron differentiation
(https://www.ebi.ac.uk/QuickGO/term/GO:0021522)

GO - Cellular Component

GO:0005886 : plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005886)
GO:0005887 : integral component of plasma membrane
(https://www.ebi.ac.uk/QuickGO/term/GO:0005887)
GO:0005634 : nucleus (https://www.ebi.ac.uk/QuickGO/term/GO:0005634)
GO:0005576 : extracellular region (https://www.ebi.ac.uk/QuickGO/term/GO:0005576)
GO:0005794 : Golgi apparatus (https://www.ebi.ac.uk/QuickGO/term/GO:0005794)
GO:0005901 : caveola (https://www.ebi.ac.uk/QuickGO/term/GO:0005901)
GO:0043231 : intracellular membrane-bounded organelle
(https://www.ebi.ac.uk/QuickGO/term/GO:0043231)
GO:0014069 : postsynaptic density (https://www.ebi.ac.uk/QuickGO/term/GO:0014069)
GO:0048471 : perinuclear region of cytoplasm
(https://www.ebi.ac.uk/QuickGO/term/GO:0048471)
GO:0005929 : cilium (https://www.ebi.ac.uk/QuickGO/term/GO:0005929)
GO:0044295 : axonal growth cone (https://www.ebi.ac.uk/QuickGO/term/GO:0044295)
GO:0044294 : dendritic growth cone (https://www.ebi.ac.uk/QuickGO/term/GO:0044294)
GO:0030496 : midbody (https://www.ebi.ac.uk/QuickGO/term/GO:0030496)

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

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

Molecular Details of the Mutation

LRM enhancer located between coding exons 15 and 19 at 37 kb of the transcription start site - exact causing mutation(s) unknown - Loss of activity of the LRM enhancer that normally upregulates Ptch1 expression in the limb-bud mesenchyme in response to SHH signalling

Experimental Evidence

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

Main Reference

Attenuated sensing of SHH by Ptch1 underlies evolution of bovine limbs. (2014) (https://pubmed.ncbi.nlm.nih.gov/24990743)

Authors

Lopez-Rios J; Duchesne A; Speziale D; Andrey G; Peterson KA; Germann P; Unal E; Liu J; Floriot S; Barbey S; Gallard Y; MÃ¼ller-Gerbl M; Courtney AD; Klopp C; Rodriguez S; Ivanek R; Beisel C; Wicking C; Iber D; Robert B; McMahon AP; Duboule D; Zeller R

Abstract

The large spectrum of limb morphologies reflects the wide evolutionary diversification of the basic pentadactyl pattern in tetrapods. In even-toed ungulates (artiodactyls, including cattle), limbs are adapted for running as a consequence of progressive reduction of their distal skeleton to symmetrical and elongated middle digits with hoofed phalanges. Here we analyse bovine embryos to establish that polarized gene expression is progressively lost during limb development in comparison to the mouse. Notably, the transcriptional upregulation of the Ptch1 gene, which encodes a Sonic hedgehog (SHH) receptor, is disrupted specifically in the bovine limb bud mesenchyme. This is due to evolutionary alteration of a Ptch1 cis-regulatory module, which no longer responds to graded SHH signalling during bovine handplate development. Our study provides a molecular explanation for the loss of digit asymmetry in bovine limb buds and suggests that modifications affecting the Ptch1 cis-regulatory landscape have contributed to evolutionary diversification of artiodactyl limbs.

Additional References

RELATED GEPHE

Related Genes

No matches found.

Related Haplotypes

No matches found.

EXTERNAL LINKS

COMMENTS