GEPHE SUMMARY

Gephebase Gene
BMP15

Entry Status
Published

GepheID
GP00002156

Main curator
Martin

PHENOTYPIC CHANGE

Trait Category
Physiology

Trait
Fertility (increased ovulation rate)

Trait State in Taxon A
Ovis aries

Trait State in Taxon B
Ovis aries - Lacaune - High fertility in heterozygotes

Ancestral State
Taxon A

Taxonomic Status
Domesticated

Taxon A

Latin Name
Ovis aries

Common Name
sheep

Synonyms
Ovis ammon aries; Ovis orientalis aries; Ovis ovis; sheep; domestic sheep; lambs; wild sheep; Ovis aries Linnaeus, 1758

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; Caprinae; Ovis

Parent
Ovis () - (Rank: genus)

NCBI Taxonomy ID
9940

is Taxon A an Infraspecies?
No

Taxon B

Latin Name
Ovis aries

Common Name
sheep

Synonyms
Ovis ammon aries; Ovis orientalis aries; Ovis ovis; sheep; domestic sheep; lambs; wild sheep; Ovis aries Linnaeus, 1758

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; Caprinae; Ovis

Parent
Ovis () - (Rank: genus)

NCBI Taxonomy ID
9940

is Taxon B an Infraspecies?
Yes

Taxon B Description
Ovis aries - Lacaune

GENOTYPIC CHANGE

Generic Gene Name
Bmp15

Synonyms
Bmp-15; C86824; C87336; GDF-9B; AU015375; AU018861; AU021453; Gdf9b

String
10090.ENSMUSP00000024049

Sequence Similarities
Belongs to the TGF-beta family.

GO - Molecular Function
GO:0005125 : cytokine activity
GO:0008083 : growth factor activity
GO:0005160 : transforming growth factor beta receptor binding

GO - Biological Process
GO:0045893 : positive regulation of transcription, DNA-templated
GO:0001541 : ovarian follicle development
GO:0030509 : BMP signaling pathway

UniProtKB Mus musculus
Q9Z0L4

GenebankID or UniProtKB
AHB23439

GO:0048468 : cell development
GO:0060016 : granulosa cell development
GO:0010862 : positive regulation of pathway-restricted SMAD protein phosphorylation
GO:0042981 : regulation of apoptotic process
GO:0043408 : regulation of MAPK cascade
GO:0060395 : SMAD protein signal transduction

GO - Cellular Component
GO:0005737 : cytoplasm
GO:0005615 : extracellular space

Presumptive Null
No

Molecular Type
Coding

Aberration Type
SNP

SNP Coding Change
Nonsynonymous

Molecular Details of the Mutation
c.G>A p.C321Y missense nonconservative substitution ; in vitro studies showed that the C53Y mutation was responsible for the impairment of the maturation process of the BMP15 protein resulting in a defective secretion of both the precursor and mature peptide

Experimental Evidence
Linkage Mapping

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Cys	Tyr	321

Main Reference
Mutations in an oocyte-derived growth factor gene (BMP15) cause increased ovulation rate and infertility in a dosage-sensitive manner. (2000)

Authors
Galloway SM; McNatty KP; Cambridge LM; Laitinen MP; Juengel JL; Jokiranta TS; McLaren RJ; Luiro K; Dodds KG; Montgomery GW; Beattie AE; Davis GH; Ritvos O

Abstract
Multiple ovulations are uncommon in humans, cattle and many breeds of sheep. Pituitary gonadotrophins and as yet unidentified ovarian factors precisely regulate follicular development so that, normally, only one follicle is selected to ovulate. The Inverdale (FecXI) sheep, however, carries a naturally occurring X-linked mutation that causes increased ovulation rate and twin and triplet births in heterozygotes (FecXI/FecX+; ref. 1), but primary ovarian failure in homozygotes (FecXI/FecXI; ref. 2). Germ-cell development, formation of the follicle and the earliest stages of follicular growth are normal in FecXI/FecXI sheep, but follicular development beyond the primary stage is impaired. A second family unrelated to the Inverdale sheep also has the same X-linked phenotype (Hanna, FecXH). Crossing FecXI with FecXH animals produces FecXI/FecXH infertile females phenotypically indistinguishable from FecXI/FecXI females. We report here that the FecXI locus maps to an orthologous chromosomal region syntenic to human Xp11.2-11.4, which contains BMP15, encoding bone morphogenetic protein 15 (also known as growth differentiation factor 9B (GDF9B)). Whereas BMP15 is a member of the transforming growth factor beta (TGFbeta) superfamily and is specifically expressed in oocytes, its function is unknown. We show that independent germline point mutations exist in FecXI and FecXH carriers. These findings establish that BMP15 is essential for female fertility and that natural mutations in an ovary-derived factor can cause both increased ovulation rate and infertility phenotypes in a dosage-sensitive manner.

Additional References

RELATED GEPHE

Related Genes
3 (B4GALNT2, BMP receptor IB (BMPRIB), GDF9)
Related Haplotypes
9

EXTERNAL LINKS

COMMENTS

Heterozygote shows phenotype; homozygote results in ovarian failure ; @HeterozygoteAdvantage @SexualTrait https://omia.org/OMIA001357/9940/