

## GEPHE SUMMARY

**Gephebase Gene**  
BMP15

**Entry Status**  
Published

**GepheID**  
GP00000148

**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 - Inverdale

**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 Intraspecies?**  
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 Intraspecies?**  
Yes

**Taxon B Description**  
Ovis aries - Inverdale

## 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**

A distinct single T>A transition occurs in FecXI carriers at nucleotide position 92 of the mature peptide . . . The mutation substitutes valine (V) with aspartic acid (D) at residue 31 (residue 299 of unprocessed protein) . . . The FecXI mutation is a non-conservative change in a highly conserved region of the protein

**Experimental Evidence**

[Linkage Mapping](#)

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Val	Asp	31

**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 (BMPRI3), GDF9)

**Related Haplotypes**

9

**EXTERNAL LINKS**

**COMMENTS**

Heterozygote shows phenotype; homozygote results in ovarian failure ; @HeterozygoteAdvantage @SexualTrait <https://omia.org/OMIA000386/9940/>

