

## GEPHE SUMMARY

BMP15 ( <a href="https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=BMP15^#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=BMP15^#gephebase-summary-title</a> )	Gephebase Gene	GP00002156	GepheID
Published	Entry Status	Martin	Main curator

## PHENOTYPIC CHANGE

Physiology ( <a href="https://www.gephebase.org/search-criteria?/and+Trait+Category=Physiology^#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Trait+Category=Physiology^#gephebase-summary-title</a> )	Trait Category		
Fertility (increased ovulation rate) ( <a href="https://www.gephebase.org/search-criteria?/and+Trait=Fertility+(increased+ovulation+rate)^#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Trait=Fertility+(increased+ovulation+rate)^#gephebase-summary-title</a> )	Trait		
Ovis aries	Trait State in Taxon A		
Ovis aries - Lacaune - High fertility in heterozygotes	Trait State in Taxon B		
Taxon A	Ancestral State		
Domesticated ( <a href="https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=Domesticated^#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=Domesticated^#gephebase-summary-title</a> )	Taxonomic Status		
	Taxon A		Taxon B
Ovis aries ( <a href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=Ovis+aries^#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=Ovis+aries^#gephebase-summary-title</a> )	Latin Name	Ovis aries ( <a href="https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=Ovis+aries^#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=Ovis+aries^#gephebase-summary-title</a> )	Latin Name
sheep	Common Name	sheep	Common Name
Ovis ammon aries; Ovis orientalis aries; Ovis ovis; sheep; domestic sheep; lambs; wild sheep; Ovis aries Linnaeus, 1758	Synonyms	Ovis ammon aries; Ovis orientalis aries; Ovis ovis; sheep; domestic sheep; lambs; wild sheep; Ovis aries Linnaeus, 1758	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; Caprinae; Ovis	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	Lineage
Ovis () - (Rank: genus) ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9935">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9935</a> )	Parent	Ovis () - (Rank: genus) ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9935">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9935</a> )	Parent
9940 ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9940">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9940</a> )	NCBI Taxonomy ID	9940 ( <a href="https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9940">https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9940</a> )	NCBI Taxonomy ID
No	is Taxon A an Intraspecies?	Yes	is Taxon B an Intraspecies?
		Ovis aries - Lacaune	Taxon B Description

## GENOTYPIC CHANGE

Bmp15	Generic Gene Name	Q9Z0L4 ( <a href="http://www.uniprot.org/uniprot/Q9Z0L4">http://www.uniprot.org/uniprot/Q9Z0L4</a> )	UniProtKB Mus musculus
Bmp-15; C86824; C87336; GDF-9B; AU015375; AU018861; AU021453; Gdf9b	Synonyms	AHB23439 ( <a href="https://www.ncbi.nlm.nih.gov/nucore/AHB23439">https://www.ncbi.nlm.nih.gov/nucore/AHB23439</a> )	GenebankID or UniProtKB
10090.ENSMUSP00000024049 ( <a href="http://string-db.org/newstring.cgi/show_network_section.pl?identifier=10090.ENSMUSP00000024049">http://string-db.org/newstring.cgi/show_network_section.pl?identifier=10090.ENSMUSP00000024049</a> )	String		
Belongs to the TGF-beta family.	Sequence Similarities		
GO:0005125 : cytokine activity ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0005125">https://www.ebi.ac.uk/QuickGO/term/GO:0005125</a> )	GO - Molecular Function		
GO:0008083 : growth factor activity ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0008083">https://www.ebi.ac.uk/QuickGO/term/GO:0008083</a> )			
GO:0005160 : transforming growth factor beta receptor binding ( <a href="https://www.ebi.ac.uk/QuickGO/term/GO:0005160">https://www.ebi.ac.uk/QuickGO/term/GO:0005160</a> )			

GO - Biological Process

- GO:0045893 : positive regulation of transcription, DNA-templated  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0045893>)
- GO:0001541 : ovarian follicle development  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0001541>)
- GO:0030509 : BMP signaling pathway  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0030509>)
- GO:0048468 : cell development (<https://www.ebi.ac.uk/QuickGO/term/GO:0048468>)
- GO:0060016 : granulosa cell development  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0060016>)
- GO:0010862 : positive regulation of pathway-restricted SMAD protein phosphorylation  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0010862>)
- GO:0042981 : regulation of apoptotic process  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0042981>)
- GO:0043408 : regulation of MAPK cascade  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0043408>)
- GO:0060395 : SMAD protein signal transduction  
(<https://www.ebi.ac.uk/QuickGO/term/GO:0060395>)

GO - Cellular Component

- GO:0005737 : cytoplasm (<https://www.ebi.ac.uk/QuickGO/term/GO:0005737>)
- GO:0005615 : extracellular space (<https://www.ebi.ac.uk/QuickGO/term/GO:0005615>)

- No (<https://www.gephebase.org/search-criteria?/and+Presumptive Null=~No^#gephebase-summary-title>) Presumptive Null
- Coding (<https://www.gephebase.org/search-criteria?/and+Molecular Type=~Coding^#gephebase-summary-title>) Molecular Type
- SNP (<https://www.gephebase.org/search-criteria?/and+Aberration Type=~SNP^#gephebase-summary-title>) Aberration Type
- Nonsynonymous SNP Coding Change
- 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 Molecular Details of the Mutation
- Linkage Mapping (<https://www.gephebase.org/search-criteria?/and+Experimental Evidence=~Linkage Mapping^#gephebase-summary-title>) Experimental Evidence

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

- Mutations in an oocyte-derived growth factor gene (BMP15) cause increased ovulation rate and infertility in a dosage-sensitive manner. (2000) (<https://pubmed.ncbi.nlm.nih.gov/10888873/>) Main Reference
- 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 Authors
- 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. Abstract
- Additional References

RELATED GEPHE

- 3 (B4GALNT2, BMP receptor IB (BMPRII), GDF9) (<https://www.gephebase.org/search-criteria?/or+Taxon ID=~9940^/and+Trait=Fertility/and+groupHaplotypes=true#gephebase-summary-title>) Related Genes
- 9 (<https://www.gephebase.org/search-criteria?/or+Gene Gephebase=~BMP15^/and+Taxon ID=~9940^/or+Gene Gephebase=~BMP15^/and+Taxon ID=~9940^#gephebase-summary-title>) Related Haplotypes

EXTERNAL LINKS

## COMMENTS

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