

GEPHE SUMMARY

BMP15 (https://www.gephebase.org/search-criteria?/and+GeneGephebase=BMP15^#gephebase-summary-title) Published	Gephebase Gene	GP00002329	GepheID
	Entry Status	Martin	Main curator

PHENOTYPIC CHANGE

Physiology (https://www.gephebase.org/search-criteria?/and+TraitCategory=Physiology^#gephebase-summary-title) Fertility (increased ovulation rate) (https://www.gephebase.org/search-criteria?/and+Trait=Fertility (increased ovulation rate)^#gephebase-summary-title) Ovis aries Ovis aries - Noire du Velay and Blanche du Massif Central populations (France) Taxon A Domesticated (https://www.gephebase.org/search-criteria?/and+TaxonomicStatus=Domesticated^#gephebase-summary-title)		Trait Category Trait Trait State in Taxon A Trait State in Taxon B Ancestral State Taxonomic Status	
Taxon A		Taxon B	
Ovis aries (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=Ovis aries^#gephebase-summary-title)		Ovis aries (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=Ovis aries^#gephebase-summary-title)	
sheep		sheep	
Ovis ammon aries; Ovis orientalis aries; Ovis ovis; sheep; domestic sheep; lambs; wild sheep; Ovis aries Linnaeus, 1758		Ovis ammon aries; Ovis orientalis aries; Ovis ovis; sheep; domestic sheep; lambs; wild sheep; Ovis aries Linnaeus, 1758	
species		species	
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		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	
Ovis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9935)		Ovis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9935)	
9940 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9940)		9940 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=9940)	
No		Yes	
		Taxon B Description	
		-	

GENOTYPIC CHANGE

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

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
Cis-regulatory (https://www.gephebase.org/search-criteria?/and+Molecular Type=~Cis-regulatory~#gephebase-summary-title)	Molecular Type
SNP (https://www.gephebase.org/search-criteria?/and+Aberration Type=~SNP~#gephebase-summary-title)	Aberration Type
T>A SPN upstream of the BMP15 gene associated with the prolificacy variability (P = 1.93E-11). Effect of +0.20 lamb per lambing at the heterozygous state.	Molecular Details of the Mutation
Association Mapping (https://www.gephebase.org/search-criteria?/and+Experimental Evidence=~Association Mapping~#gephebase-summary-title)	Experimental Evidence
Genome-wide association studies identify two novel BMP15 mutations responsible for an atypical hyperprolificacy phenotype in sheep. (2013) (https://pubmed.ncbi.nlm.nih.gov/23637641)	Main Reference
Demars J; Fabre S; Sarry J; Rossetti R; Gilbert H; Persani L; Tosser-Klopp G; Mulsant P; Nowak Z; Drobik W; Martyniuk E; Bodin L	Authors
Some sheep breeds are naturally prolific, and they are very informative for the studies of reproductive genetics and physiology. Major genes increasing litter size (LS) and ovulation rate (OR) were suspected in the French Grivette and the Polish Olkuska sheep populations, respectively. To identify genetic variants responsible for the highly prolific phenotype in these two breeds, genome-wide association studies (GWAS) followed by complementary genetic and functional analyses were performed. Highly prolific ewes (cases) and normal prolific ewes (controls) from each breed were genotyped using the Illumina OvineSNP50 Genotyping Beadchip. In both populations, an X chromosome region, close to the BMP15 gene, harbored clusters of markers with suggestive evidence of association at significance levels between 1E(-05) and 1E(-07). The BMP15 candidate gene was then sequenced, and two novel non-conservative mutations called FecX(Gr) and FecX(O) were identified in the Grivette and Olkuska breeds, respectively. The two mutations were associated with the highly prolific phenotype (p FecX (Gr) = 5.98E(-06) and p FecX(O) = 2.55E(-08)). Homozygous ewes for the mutated allele showed a significantly increased prolificacy (FecX(Gr)/FecX(Gr), LS = 2.50 Å± 0.65 versus FecX(+)/FecX(Gr), LS = 1.93 Å± 0.42, p<1E(-03) and FecX(O)/FecX(O), OR = 3.28 Å± 0.85 versus FecX(+)/FecX(O), OR = 2.02 Å± 0.47, p<1E(-03)). Both mutations are located in very well conserved motifs of the protein and altered the BMP15 signaling activity in vitro using a BMP-responsive luciferase test in COV434 granulosa cells. Thus, we have identified two novel mutations in the BMP15 gene associated with increased LS and OR. Notably, homozygous FecX(Gr)/FecX(Gr) Grivette and homozygous FecX(O)/FecX(O) Olkuska ewes are hyperprolific in striking contrast with the sterility exhibited by all other known homozygous BMP15 mutations. Our results bring new insights into the key role played by the BMP15 protein in ovarian function and could contribute to a better understanding of the pathogenesis of women’s fertility disorders.	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

@SexualTrait @AllelicSeries ; Homozygous FecXN carrier ewes were fertile with increased prolificacy in contrast to numerous mutations affecting BMP15 coding sequence (ovarian failure)

