

GEPHE SUMMARY

BMP15 (https://www.gephebase.org/search-criteria?/and+GeneGephebase=BMP15^#gephebase-summary-title) Published	Gephebase Gene	GP00000150	GepheID
	Entry Status	Martin	Main curator

PHENOTYPIC CHANGE

Physiology (https://www.gephebase.org/search-criteria?/and+TraitCategory=Physiology^#gephebase-summary-title)		Trait Category	
Fertility (increased ovulation rate) (https://www.gephebase.org/search-criteria?/and+Trait=Fertility (increased ovulation rate)^#gephebase-summary-title)		Trait	
Ovis aries		Trait State in Taxon A	
Ovis aries - Polish Olkusa		Trait State in Taxon B	
Taxon A		Ancestral State	
Domesticated (https://www.gephebase.org/search-criteria?/and+TaxonomicStatus=Domesticated^#gephebase-summary-title)		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	
		Ovis aries - Polish Olkusa	

GENOTYPIC CHANGE

Bmp15		Q9Z0L4 (http://www.uniprot.org/uniprot/Q9Z0L4)	
Bmp-15; C86824; C87336; GDF-9B; AU015375; AU018861; AU021453; Gdf9b		AHB23439 (https://www.ncbi.nlm.nih.gov/nuccore/AHB23439)	
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)			

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>)

Presumptive Null

No (<https://www.gephebase.org/search-criteria?/and+Presumptive Null=~No~#gephebase-summary-title>)

Molecular Type

Coding (<https://www.gephebase.org/search-criteria?/and+Molecular Type=~Coding~#gephebase-summary-title>)

Aberration Type

SNP (<https://www.gephebase.org/search-criteria?/and+Aberration Type=~SNP~#gephebase-summary-title>)

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

c.1009A>C p.N337H

Experimental Evidence

Association Mapping (<https://www.gephebase.org/search-criteria?/and+Experimental Evidence=~Association Mapping~#gephebase-summary-title>)

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Asn	His	337

Main Reference

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>)

Authors

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

Abstract

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.

Additional References

RELATED GEPHE

Related Genes

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 Haplotypes

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>)

EXTERNAL LINKS

COMMENTS

Heterozygote shows phenotype; homozygote results in ovarian failure ; <https://omia.org/OMIA001799/9940/> ; @SexualTrait @HeterozygoteAdvantage