

GEPHE SUMMARY

GDF9 (https://www.gephebase.org/search-criteria?/and+GeneGephebase=GDF9#gephebase-summary-title)	Gephebase Gene	GP00002186	GepheID
	Entry Status	Martin	Main curator
	Published		

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 - Norwegian White Sheep ; Finnsheep - Increased ovulation rate; Heterozygote shows phenotype; homozygote results in ovarian failure		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 - Norwegian White Sheep ; Finnsheep	

GENOTYPIC CHANGE

GDF9	Generic Gene Name	UniProtKB Homo sapiens
	Synonyms	O60383 (http://www.uniprot.org/uniprot/O60383)
	String	CCl87994 (https://www.ncbi.nlm.nih.gov/nuccore/CCl87994)
9606.ENSPO0000296875 (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPO0000296875)		
Sequence Similarities		
Belongs to the TGF-beta family.		
GO - Molecular Function		
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 - Biological Process

GO:0008284 : positive regulation of cell proliferation
(<https://www.ebi.ac.uk/QuickGO/term/GO:0008284>)
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: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:0030308 : negative regulation of cell growth
(<https://www.ebi.ac.uk/QuickGO/term/GO:0030308>)
GO:0007179 : transforming growth factor beta receptor signaling pathway
(<https://www.ebi.ac.uk/QuickGO/term/GO:0007179>)
GO:0007292 : female gamete generation
(<https://www.ebi.ac.uk/QuickGO/term/GO:0007292>)
GO:0001555 : oocyte growth (<https://www.ebi.ac.uk/QuickGO/term/GO:0001555>)
GO:2000870 : regulation of progesterone secretion
(<https://www.ebi.ac.uk/QuickGO/term/GO:2000870>)

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
g.41841285G>A c.1111G>A p.V371M	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	Val	Met	371

A missense mutation in growth differentiation factor 9 (GDF9) is strongly associated with litter size in sheep. (2013) (https://pubmed.ncbi.nlm.nih.gov/23280002)	Main Reference
VÃ¥ge DI; Husdal M; Kent MP; Klemetsdal G; Boman IA	Authors
A genome wide association study for litter size in Norwegian White Sheep (NWS) was conducted using the recently developed ovine 50K SNP chip from Illumina. After genotyping 378 progeny tested artificial insemination (AI) rams, a GWAS analysis was performed on estimated breeding values (EBVs) for litter size.	Abstract
A QTL-region was identified on sheep chromosome 5, close to the growth differentiation factor 9 (GDF9), which is known to be a strong candidate gene for increased ovulation rate/litter size. Sequencing of the GDF9 coding region in the most extreme sires (high and low BLUP values) revealed a single nucleotide polymorphism (c.1111G>A), responsible for a Valâ†Met substitution at position 371 (V371M). This polymorphism has previously been identified in Belclare and Cambridge sheep, but was not found to be associated with fertility. In our NWS-population the c.1111G>A SNP showed stronger association with litter size than any other single SNP on the Illumina 50K ovine SNP chip. Based on the estimated breeding values, daughters of AI rams homozygous for c.1111A will produce minimum 0.46 - 0.57 additional lambs compared to daughters of wild-type rams.	
We have identified a missense mutation in the bioactive part of the GDF9 protein that shows strong association with litter size in NWS. Based on the NWS breeding history and the marked increase in the c.1111A allele frequency in the AI ram population since 1983, we hypothesize that c.1111A allele originate from Finnish landrace imported to Norway around 1970. Because of the widespread use of Finnish landrace and the fact that the ewes homozygous for the c.1111A allele are reported to be fertile, we expect the commercial impact of this mutation to be high.	
Direct evidence on the contribution of a missense mutation in GDF9 to variation in ovulation rate of Finnsheep. (2014) (https://pubmed.ncbi.nlm.nih.gov/24751660)	Additional References

RELATED GEPHE

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

EXTERNAL LINKS

COMMENTS

@HeterozygoteAdvantage ; <https://omia.org/OMIA001763/9940/>