

GEPHE SUMMARY

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

PHENOTYPIC CHANGE

	Trait Category
Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Physiology^#gephebase-summary-title)	Trait
Fertility (increased ovulation rate) (https://www.gephebase.org/search-criteria?/and+Trait=^Fertility+(increased+ovulation+rate)^#gephebase-summary-title)	Trait State in Taxon A
Ovis aries	Trait State in Taxon B
Ovis aries - Norwegian White Sheep ; Finnsheep - Increased ovulation rate; Heterozygote shows phenotype; homozygote results in ovarian failure	Ancestral State
Taxon A	Taxonomic Status
Domesticated (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Domesticated^#gephebase-summary-title)	

Taxon A		Taxon B	
Latin Name		Latin Name	
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	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) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9935)	Parent	Ovis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9935)	Parent
9940 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9940)	NCBI Taxonomy ID	9940 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9940)	NCBI Taxonomy ID
is Taxon A an Infraspecies?		is Taxon B an Infraspecies?	
No	Yes		
		Ovis aries - Norwegian White Sheep ; Finnsheep	Taxon B Description

GENOTYPIC CHANGE

GDF9	Generic Gene Name	UniProtKB Homo sapiens
POF14	Synonyms	GenebankID or UniProtKB
9606.ENSP00000296875 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000296875)	String	CCl87994 (https://www.ncbi.nlm.nih.gov/nuccore/CCl87994)
Belongs to the TGF-beta family.	Sequence Similarities	
	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>)

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.41841285G>A c.1111G>A p.V371M

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Val	Met	371

Main Reference

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>)

Authors

Vägne Dl; Husdal M; Kent MP; Klemetsdal G; Boman IA

Abstract

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.

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 Val→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.

Additional References

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>)

RELATED GEPHE

Related Genes

3 (B4GALNT2, BMP receptor 1B (BMPR1B), BMP15) (<https://www.gephebase.org/search-criteria?/or+Taxon+ID=^9940^/and+Trait=Fertility/and+groupHaplotypes=true#gephebase-summary-title>)

Related Haplotypes

4 (<https://www.gephebase.org/search-criteria?/or+Gene+Gephebase=^GDF9^/and+Taxon+ID=^9940^/or+Gene+Gephebase=^GDF9^/and+Taxon+ID=^9940^#gephebase-summary-title>)

EXTERNAL LINKS

COMMENTS

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