

GEPHE SUMMARY

	Gephebase Gene	GephelD
TMEM154 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^TMEM154^#gephebase-summary-title)	GP00002242	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
Pathogen resistance (lentivirus) (https://www.gephebase.org/search-criteria?/and+Trait =^Pathogen resistance (lentivirus)^#gephebase-summary-title)		Trait State in Taxon A
Susceptible to ovine progressive pneumonia virus (OPPV)		Trait State in Taxon B
Resistant to ovine progressive pneumonia virus (OPPV)		Ancestral State
Taxon A		Taxonomic Status
Ovis aries (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=^Ovis+aries^#gephebase-summary-title)	Latin Name	
sheep	Common Name	
Ovis ammon aries; Ovis orientalis aries; Ovis ovis; sheep; domestic sheep; lambs; wild sheep; Ovis aries Linnaeus, 1758	Synonyms	
species	Rank	
Ovis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9935)	Lineage	
9940 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9940)	NCBI Taxonomy ID	
No	is Taxon A an Infraspecies?	
Ovis aries	Latin Name	
sheep	Common Name	
Ovis ammon aries; Ovis orientalis aries; Ovis ovis; sheep; domestic sheep; lambs; wild sheep; Ovis aries Linnaeus, 1758	Synonyms	
species	Rank	
Ovis () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9935)	Lineage	
9940 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9940)	NCBI Taxonomy ID	
No	is Taxon B an Infraspecies?	

GENOTYPIC CHANGE

	Generic Gene Name	UniProtKB Homo sapiens
TMEM154		
-	Synonyms	GenebankID or UniProtKB
-	0	
-	String	
9606.ENSP00000302144 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000302144)	Sequence Similarities	
-	GO - Molecular Function	
-	GO - Biological Process	
-	GO - Cellular Component	
GO:0016021 : integral component of membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0016021)		

No (#gephebase-summary-title)	Presumptive Null
Coding (#gephebase-summary-title)	Molecular Type
SNP (#gephebase-summary-title)	Aberration Type
Nonsynonymous	SNP Coding Change
Mutation at conserved position associated to resistance in homozygous state	Molecular Details of the Mutation
Association Mapping (#gephebase-summary-title)	Experimental Evidence

Taxon A	Taxon B	Position
Codon	-	-
Amino-acid	Glu	Lys

Main Reference

Reduced lentivirus susceptibility in sheep with TMEM154 mutations. (2012) (<https://pubmed.ncbi.nlm.nih.gov/22291605/>)

Authors

Heaton MP; Clawson ML; Chitko-Mckown CG; Leymaster KA; Smith TP; Harhay GP; White SN; Herrmann-Hoesing LM; Mousel MR; Lewis GS; Kalbfleisch TS; Keen JE; Laegreid WW

Abstract

Visna/Maedi, or ovine progressive pneumonia (OPP) as it is known in the United States, is an incurable slow-acting disease of sheep caused by persistent lentivirus infection. This disease affects multiple tissues, including those of the respiratory and central nervous systems. Our aim was to identify ovine genetic risk factors for lentivirus infection. Sixty-nine matched pairs of infected cases and uninfected controls were identified among 736 naturally exposed sheep older than five years of age. These pairs were used in a genome-wide association study with 50,614 markers. A single SNP was identified in the ovine transmembrane protein (TMEM154) that exceeded genome-wide significance (unadjusted p-value 3Å–10(-9)). Sanger sequencing of the ovine TMEM154 coding region identified six missense and two frameshift deletion mutations in the predicted signal peptide and extracellular domain. Two TMEM154 haplotypes encoding glutamate (E) at position 35 were associated with infection while a third haplotype with lysine (K) at position 35 was not. Haplotypes encoding full-length E35 isoforms were analyzed together as genetic risk factors in a multi-breed, matched case-control design, with 61 pairs of 4-year-old ewes. The odds of infection for ewes with one copy of a full-length TMEM154 E35 allele were 28 times greater than the odds for those without (p-value<0.0001, 95% CI 5-1,100). In a combined analysis of nine cohorts with 2,705 sheep from Nebraska, Idaho, and Iowa, the relative risk of infection was 2.85 times greater for sheep with a full-length TMEM154 E35 allele (p-value<0.0001, 95% CI 2.36-3.43). Although rare, some sheep were homozygous for TMEM154 deletion mutations and remained uninfected despite a lifetime of significant exposure. Together, these findings indicate that TMEM154 may play a central role in ovine lentivirus infection and removing sheep with the most susceptible genotypes may help eradicate OPP and protect flocks from reinfection.

Additional References

RELATED GEPHE

No matches found.	Related Genes
No matches found.	Related Haplotypes

EXTERNAL LINKS

COMMENTS

@AllelicSeries : two deletion - frameshift haplotypes exist in populations but were not tested for association with resistance. <https://omia.org/OMIA001694/9940/>