

## Genome-wide association reveals the locus responsible for four-horned ruminant.

[Kijas JW](#)<sup>1</sup>, [Hadfield T](#)<sup>2</sup>, [Naval Sanchez M](#)<sup>1</sup>, [Cockett N](#)<sup>2</sup>.

### Author information

1

CSIRO Agriculture, St Lucia, QLD, 4067, Australia.

2

Department of Animal, Dairy, and Veterinary Sciences, Utah State University, Logan, UT, 84322-4700, USA.

### **Abstract**

Phenotypic variability in horn characteristics, such as their size, number and shape, offers the opportunity to elucidate the molecular basis of horn development. The objective of this study was to map the genetic determinant controlling the production of four horns in two breeds, Jacob sheep and Navajo-Churro, and examine whether an eyelid abnormality occurring in the same populations is related. Genome-wide association mapping was performed using 125 animals from the two breeds that contain two- and four-horned individuals. A case-control design analysis of 570 712 SNPs genotyped with the ovine HD SNP Beadchip revealed a strong association signal on sheep chromosome 2. The 10 most strongly associated SNPs were all located in a region spanning Mb positions 131.9-132.6, indicating the genetic architecture underpinning the production of four horns is likely to involve a single gene. The closest genes to the most strongly associated marker (OAR2\_132568092) were MTX2 and the HOXD cluster, located approximately 93 Kb and 251 Kb upstream respectively. The occurrence of an eyelid malformation across both breeds was restricted to polled animals and those carrying more than two horns. This suggests the eyelid abnormality may be associated with departures from the normal developmental production of two-horned animals and that the two conditions are developmentally linked. This study demonstrated the presence of separate loci responsible for the polled and four-horned phenotypes in sheep and advanced our understanding of the complexity that underpins horn morphology in ruminants.

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### **KEYWORDS:**

GWAS; horn morphology; ruminant

## Mapping the four-horned locus and testing the polled locus in three Chinese sheep breeds.

[He X](#)<sup>1,2</sup>, [Zhou Z](#)<sup>1</sup>, [Pu Y](#)<sup>1,2</sup>, [Chen X](#)<sup>1,2</sup>, [Ma Y](#)<sup>3,4</sup>, [Jiang L](#)<sup>5,6</sup>.

### Author information

1

Key Laboratory for Farm Animal Genetic Resources and Utilization of the Ministry of Agriculture of China, Institute of Animal Science, Chinese Academy of Agricultural Science, Beijing, 100193, China.

2

CAAS-ILRI Joint Laboratory on Livestock and Forage Genetic Resources, Institute of Animal Science, Chinese Academy of Agricultural Science, Beijing, 100193, China.

3

Key Laboratory for Farm Animal Genetic Resources and Utilization of the Ministry of Agriculture of China, Institute of Animal Science, Chinese Academy of Agricultural Science, Beijing, 100193, China. yuehui.ma@263.net.

4

CAAS-ILRI Joint Laboratory on Livestock and Forage Genetic Resources, Institute of Animal Science, Chinese Academy of Agricultural Science, Beijing, 100193, China. yuehui.ma@263.net.

5

Key Laboratory for Farm Animal Genetic Resources and Utilization of the Ministry of Agriculture of China, Institute of Animal Science, Chinese Academy of Agricultural Science, Beijing, 100193, China. jianglin@caas.cn.

6

CAAS-ILRI Joint Laboratory on Livestock and Forage Genetic Resources, Institute of Animal Science, Chinese Academy of Agricultural Science, Beijing, 100193, China. jianglin@caas.cn.

## Abstract

Four-horned sheep are an ideal animal model for illuminating the genetic basis of horn development. The objective of this study was to locate the genetic region responsible for the four-horned phenotype and to verify a previously reported polled locus in three Chinese breeds. A genome-wide association study (GWAS) was performed using 34 two-horned and 32 four-horned sheep from three Chinese indigenous breeds: Altay, Mongolian and Sishui Fur sheep. The top two significant single nucleotide polymorphisms (SNPs) associated with the four-horned phenotype were both located in a region spanning positions 132.6 to 132.7 Mb on sheep chromosome 2. Similar locations for the four-horned trait were previously identified in Jacob, Navajo-Churro, Damara and Sishui Fur sheep, suggesting a common genetic component underlying the four-horned phenotype. The two identified SNPs were both downstream of the metaxin 2 (MTX2) gene and the HOXD gene cluster. For the top SNP-OAR2:g.132619300G>A-the strong associations of the AA and AG genotypes with the four-horned phenotype and the GG genotype with the two-horned phenotype indicated the dominant inheritance of the four-horned trait. No significant SNPs for the polled phenotype were identified in the GWAS analysis, and a PCR analysis for the detection of the 1.8-kb insertion associated with polled sheep in other breeds failed to verify the association with polledness in the three Chinese breeds. This study supports the hypothesis that two different loci are responsible for horn existence and number. This study contributes to the understanding of the molecular regulation of horn development and enriches the knowledge of qualitative traits in domestic animals.

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## KEYWORDS:

Ovis aries; four-horned phenotype; genome-wide association study

## **Polyceraty (multi-horns) in Damara sheep maps to ovine chromosome 2.**

[Greyvenstein OF](#)<sup>1</sup>, [Reich CM](#)<sup>2</sup>, [van Marle-Koster E](#)<sup>3</sup>, [Riley DG](#)<sup>1</sup>, [Hayes BJ](#)<sup>2,4</sup>.

### **Author information**

1

Department of Animal Science, Texas A&M University, College Station, TX, 77843, USA.

2

BioSciences Research Division, Department of Economic Developments, Jobs, Transport and Resources, 5 Ring Road, Bundoora, Vic., 3083, Australia.

3

Department of Animal and Wildlife Science, University of Pretoria, Hatfield, 0028, South Africa.

4

La Trobe University, Bundoora, Vic., 3083, Australia.

### **Abstract**

Polyceraty (presence of multiple horns) is rare in modern day ungulates. Although not found in wild sheep, polyceraty does occur in a small number of domestic sheep breeds covering a wide geographical region. Damara are fat-tailed hair sheep, from the south-western region of Africa, which display polyceraty, with horn number ranging from zero to four. We conducted a genome-wide association study for horn number with 43 Damara genotyped with 606 006 SNP markers. The analysis revealed a region with multiple significant SNPs on ovine chromosome 2, in a location different from the mutation for polled in sheep on chromosome 10. The causal mutation for polyceraty was not identified; however, the region associated with polyceraty spans nine HOXD genes, which are critical in embryonic development of appendages. Mutations in HOXD genes are implicated in polydactyl phenotypes in mice and humans. There was no evidence for epistatic interactions contributing to polyceraty. This is the first report on the genetic mechanisms underlying polyceraty in the under-studied Damara.

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### **KEYWORDS:**

GWAS; Ovine Infinium; horns; multiple horns; polycerate