**Interpretive summary:** The genetic basis of morphological traits has not been investigated in depth in goats despite its great impact on productive performance. Herewith, we have genotyped 825 Murciano-Granadina goats with records for 17 morphological traits with a chip containing 54,241 markers. Statistical analyses have made possible to identify two genomic regions displaying highly significant associations with medial suspensory ligament (chromosomes 16 and 28). This is a first step towards identifying the genetic factors that influence morphological traits with the goal of incorporating such information to breeding plans.

**RUNNING HEAD: GWAS FOR MORPHOLOGY TRAITS IN GOATS**

# A genome-wide association analysis for body, udder and leg conformation traits recorded in Murciano-Granadina goats

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**ABSTRACT**

Morphological traits are of great importance to dairy goat production given their incidence on phenotypes of economic interest. However, their genomic architecture has not yet been extensively characterized. Herewith we aimed to identify genomic regions associated with 17 body, udder and leg conformation traits recorded in 825 Murciano-Granadina goats. We have gernotyped this resource population with the Illumina GoatSNP50 Beadchip (Illumina inc, San Diego, CA) and we have performed genome-wide association analyses with the GEMMA software. By doing so, we have found two genome-wide significant associations between markers rs268273468 (CHI 16:69617700) and rs268249346 (CHI 28:18321523) and medial suspensory ligament. In contrast, we have not detected any genome-wide significant associations for body and leg traits. Moreover, we have found 12, 19 and 7 chromosome-wide significant associations for udder, body, and leg traits, respectively. Comparison of our data with previous studies revealed a low level of positional concordance between regions associated with morphological traits. Besides technical factors, this observation could be due to the existence of a substantial level of genetic heterogeneity amongst breeds and/or to the strong polygenic background of morphological traits, a circumstance that makes it difficult to detect genetic factors with small phenotypic effects.

***Key Words.*** GWAS, goat, Murciano-Granadina, morphological traits.

# INTRODUCTION

Since its establishment in 1975 (Delgado et al., 2018), Murciano-Granadina has become the most important dairy goat breed in Spain, reaching a census of 112,417 heads in 2019 (https://www.mapa.gob.es/es/ganaderia/temas/zootecnia/razas-ganaderas/razas). Murciano-granadina shows a great capacity to adapt to harsh environments, yielding 530 kg of milk per lactation (250 days) with fat and protein contents of 5.6% and 3.6%, respectively (https://www.mapa.gob.es/es/ganaderia/temas/zootecnia/razas-ganaderas/razas). The genetic improvement program of the Murciano-Granadina breed is mostly focused on augmenting milk yield and quality as well as on optimizing body and dairy conformation traits. The association of Murciano-Granadina breeders (Caprigran) records systematically information about milk yield and composition and they also perform the linear scoring of 17 morphological traits (Delgado et al., 2018). The inclusion of morphological traits as selection criteria is motivated by their relationship with mammary health and longevity (Shelton, 1978; Manfredi et al., 2001; Montaldo and Manfredi, 2002). Studies performed in cattle (Seykora and McDaniel, 1985; Rogers et al., 1991; Boettcher et al., 1998; Rupp and Boichard, 1999; Miglior et al., 2017) support a relationship between udder morphology and health. Indeed, higher, non-pendulous and more tightly attached udders are less susceptible to mastitis (Seykora and McDaniel, 1985; Rupp and Boichard, 2003). Moreover, flat, disk, or inverted teat ends are associated with an increased risk of suffering mastitis, while funnel shaped teats seem to be less prone to this disease (Seykora and McDaniel, 1985). There are also numerous reports that associate body traits with fertility and longevity (Bastin and Gengler 2013; Miglior et al., 2017). For instance, feet and leg conformation traits could be considered as indicators of claw health which, after reproduction and

mastitis, is one of the main determinants for culling animals (Egger-Danner et al., 2014).

Far less studies about the genetics of morphological traits have been performed in goats. According to Rupp et al. (2011), udder floor position showed negative genetic correlations with somatic cell score both in Alpine ($r_g$ = -0.24) and Saanen goats ($r_g$ = -0.19). The same authors demonstrated that in the Saanen breed, somatic cell score was genetically correlated with teat length ($r_g$ = 0.29), teat width (rg = 0.34), and teat form ($r_g$ = -0.27). These results suggest that a reduction in somatic cell count can be achieved by selection, while still improving milk production and udder type and teat traits. In Tinerfeña goats, moderate to high and mostly positive phenotypic correlations have been detected between udder traits and milk yield (Capote et al., 2006).

Manfredi et al. (2001) found a high heritability ($h^2$ > 0.4) for thorax perimeter in Alpine and Saanen goats, while other body traits such as rump angle, feet angle and hock distance showed low heritabilities ($h^2$ = 0.03-0.16). In contrast, heritabilities for udder and teat scores reached values around 0.3 for most traits, with teat angle displaying the lowest value ($h^2$ = 0.15 in Saanen). Genetic correlations among teat dimension traits and between udder floor and rear udder attachment ($r_g$ > 0.7 in Alpine and Saanen) were generally high, while the majority of genetic correlations between body and udder scores reached values below 0.3 (Manfredi et al., 2001).

In a more recent study, McLaren et al. (2016) described low to moderate heritabilities (from 0.02 to 0.38) for conformation traits recorded in mixed-breed dairy goats: while udder and teat traits displayed the highest heritabilities ($h^2$ ~ 0.28, from 0.15 to 0.38), feet and leg traits showed lower values ($h^2$ ~ 0.13, from 0.02 to 0.25). Although the majority of the correlations estimated between milk yield and udder and teat traits were

negative, their magnitude and sign fluctuated across the first lactation. For instance, the estimates of the genetic correlation between udder furrow and milk yield went from −0.42 to 0.18 depending on the time point of the 1st lactation at which they were calculated (McLaren et al., 2016). Castañeda-Bustos et al. (2017) described a high genetic correlation between the productive life of dairy goats (*i.e.* total days in production until 72 months of age) and final score (appraisal of the general conformation of the animal), fore udder attachment and rump width. These findings demonstrate that taking into account conformation and udder traits in selection schemes could be expected to increase productivity without compromising the fitness of the animals (Castañeda-Bustos et al., 2017).

Few investigations have been carried out to identify genomic regions associated with body conformation and udder traits in goats. Mucha et al. (2018) performed a genome-wide association study (GWAS) for morphology traits in mixed-breed dairy goats and found a significant association between a region on chromosome 19 and udder attachment, udder depth and front legs morphology. Moreover, Martin et al. (2018) detected 37 genome-wide significant QTL for type and somatic cell count phenotypes with linkage analyses, while a much larger number of QTL were identified by association mapping. These authors concluded that the inheritance of body and udder conformation traits is markedly polygenic and that genetic determinants are often breed-specific. In the current work, we aimed to identify genomic regions associated with the phenotypic variation of 17 morphological traits in Murciano-Granadina goats.

## MATERIALS AND METHODS

***Phenotypic Recording***

A total of 825 female goats distributed in 13 farms, with an average herd size of 500 individuals, were scored for 17 morphological traits included in the breeding program of the Murciano-Granadina goat breed. The scoring is performed only once in the lifetime of the animal. The majority of the goats comprised in our study were scored during their first lactation, although there is a group of 89 animals that were scored between the 2$^{nd}$ and 6$^{th}$ lactation. All traits were scored by the same specialist, using a personal digital device with specific software (Kalifadroid app) for carrying out scoring tasks. The following phenotypes were evaluated, with linear scores ranging from 1 to 9 according to the measures established in Sánchez-Rodríguez (2012):

***(1) Udder Traits***

***Fore Udder Attachment (FUA).*** Corresponds to the angle formed by the line of the udder insertion and the abdominal wall. Scores 1 and 9 correspond to angles of 45º and 120º, respectively.

***Rear Udder Height (RUH).*** This variable is scored by measuring the distance between the bottom of the vulva and the top of the secretory tissue of the mammary gland. Scores 1 and 9 correspond to distances of 11 cm and 3 cm, respectively.

***Udder Depth (UD).*** It is the distance from the lowest part of the udder floor to the hock joint (tibiotarsal joint). A linear score of 1 corresponds to an udder with its deepest part 10 cm over the hock, while a score of 9 would define an udder with its deepest part 10 cm down the hock joint

***Medial Suspensory Ligament (MSL).*** Is the depth of the udder cleft measured at the base of the rear udder. Scores 1 and 9 correspond to 1 cm and 9 cm (or more) deep udder clefts, respectively.

***Udder Width (UW).*** Is measured at the crease where the udder meets the leg. Scores of 1 and 9 correspond to measurements of 3 cm and 11 cm (or more), respectively.

***Teat Diameter (TD).*** It is the diameter of the teat at its base, when it meets the udder. Score 1 = diameter of 0.5 cm and score 9 = diameter of 4.5 cm or more.

***Teat Placement (TP).*** It defines the position of the teats on the udder half. Teats located on the outside third of the udder half are scored with 1, whilst teats located very close to the medial suspensory ligament, that almost touch each other, are scored with 9. Teats on the center of the udder half, with an intermediate placement, are considered as desirable and they are scored with 5.

***(2) Body conformation traits***

***Height (HT).*** It measures the distance from the level ground to the top of the withers. Goats with 62 cm or less receive a score of 1, while those over 78 cm are scored with 9.

***Chest Width (CW).*** Measured from the inside surface of the chest between the top of the front legs. Score 1 = 15 cm or less. Score 9 = 23 cm or more.

***Body Depth (BD).*** Is the distance between the top of the spine and bottom of the body at the beginning of the last rib. Score 1 = low depth, if the beginning of the last rib

is located above the elbow joint, and score 9 = high depth, if the beginning of the last rib is located below the elbow joint.

***Rump Width (RW).*** Distance between the most posterior points of the pin bones (ischial tuberosities). Score 1 = 13 cm (or less) and score 9 = 21 cm (or more).

***Rump Angle (RA).*** Angle between the hook (coxal tuberosity) and pin (ischial tuberosity) bones. Scores 1 and 9 correspond to angles of 55º and 31º (approximately), respectively.

***Angularity or Dairyness (ANG).*** Is the angle and openness of the ribs. Score 1 defines an animal extremely coarse for this trait and score 9 is assigned to goats that are very angular.

***Bone Quality (BQ).*** It is an appraisal of the thickness and width of the bone structure, assessed by examining the rear leg from the rear and from the side. Score 1 corresponds to goats with thick and round bones, while 9 is assigned to goats with flat and sharp bones.

***(3) Feet structure***

***Rear Legs Rear View (RLR).*** Direction of rear feet when viewed from the rear. Score 1: extreme toe-out feet and score 9: parallel feet.

***Rear Legs Side View (RLS).*** Curvature of the hock viewed laterally. Score 1: straight legs and score 9: very curved legs.

***Mobility (MOB).*** Evaluates the locomotion patterns, including the length and direction of the step. Score 1: bad locomotion, with severe abduction and short steps, and score 9: harmonic, long and uniform locomotion.

**Isolation of Genomic DNA from Blood and Genotyping with the Goat SNP50 Beadchip**

Blood samples from the 825 Murciano-Granadina goats with morphology records were collected in vacuum tubes coated with EDTA K3 anticoagulant and stored at -20 ºC until processing. The purification of genomic DNA was achieved with a modified salting-out procedure (Miller et al., 1988). To do so, we combined 3 mL of whole blood plus 4 volumes of Red Cell Lysis Solution (Tris-HCl 10mM, pH = 6.5; EDTA 2 mM; Tween 20 1%) and then this mixture was centrifuged at a speed of 2000 g. The resulting cell pellet was resuspended in 3 mL of lysis buffer (Tris-HCl 200mM, pH = 8, EDTA 30 mM, SDS 1%; NACl 250 mM) and 100 µl proteinase K (20 mg/mL) and incubated during 3 hours at 55° C. The lysate was chilled, and 1 mL of ammonium acetate 10 M was added. Next, a centrifugation step at 2000 g during 10 minutes was carried out, and the supernatant (~4 mL) was transferred to a new tube with 3 mL of isopropanol 96%. Subsequently, samples were centrifuged at 2000 g for 3 minutes. The resulting DNA pellet was washed with 3 mL of ethanol 70% and an additional centrifugation step at 2000 g for 1 minute was performed. The DNA pellet was left at room temperature until it dried, and it was subsequently resuspended in 1 mL of TE buffer (Tris-HCl 10 mM, EDTA 1 mM, pH = 8). All 825 goats were genotyped with the Illumina Goat SNP50 BeadChip (Illumina Inc., San Diego, CA), which contains 54,241 SNPs, following the instructions of the manufacturer. The genomic location of the SNPs was obtained by using the goat ARS1 genome (Bickhart et al., 2017) as reference, and the position and the name of each SNP was updated using the software PLINK v 1.9 (Chang et al., 2015). The genotypic information was filtered using PLINK v 1.9 (Chang et al., 2015). Only individuals with less than 5% of missing genotypes were taken into consideration. With regard to SNPs, only those meeting the following requirements were used in the

GWAS: (1) Mapping to autosomes, (2) Displaying a minor allele frequency of 0.05 or higher, (3) Not deviating significantly ($P < 0.001$) from the Hardy-Weinberg expectation, and (4) With a genotype call rate over 90%. After applying these filtering criteria, 47,880 SNPs and 811 animals were selected to perform subsequent analyses. Population structure was assessed with a principal component analysis (PCA) approach implemented in PLINK v1.9 (Chang et al., 2015). The visualization of the PCA results was based on the first two components of the PCA.

**Statistical Analyses**

We calculated summary statistics for each one of the morphological traits using R (R core Team, 2017) as well as Pearson correlations ($r_p$) between conformation traits and milk composition and yield records, i.e. Total milk yield (RMY), milk yield at 210 days (MY210), milk yield at 240 days (MY240), milk yield at 305 days (MY305), somatic cell count (SCC), fat percentage (FP), protein percentage (PP) and lactose percentage (LP). The correlations were estimated using R software (R Core Team, 2017). Heatmap plots were constructed with R software (R Core Team, 2017) to visualize the correlation matrix and the *P-values* of each correlation.

The software GEMMA (Zhou and Stephens, 2012) was used to carry out the GWAS. This method corrects population structure by considering the relatedness matrix, which is built by taking into account all genome-wide SNPs as a random effect. Morphological phenotypes were rank-based transformed by using the package GenAbel from R (Aulchenko et al., 2007) because we assessed, with our data, that this transformation yields residuals that are normally distributed. A univariate linear mixed model was fit for each trait as follows,

$$y = W\alpha + x\beta + u + \epsilon$$

where y is a vector of corrected scores for morphological traits recorded in 811 individuals; W = (w1, · · · , wc) is an n×c matrix of three fixed effects (farm, with 13 levels; year of birth, with 10 levels; number of lactations, with 6 levels) and one covariate (days producing milk); α is a c-vector of the corresponding fixed effects including the intercept; x is a n-vector of marker genotypes; β is the effect size of the marker (allele substitution effect); u is a n-vector of random individual genetic effects with a normal distribution $\mathbf{u} \sim \mathrm{N}(\mathbf{0}, \lambda\, \tau^{-1}\, \mathbf{K})$, being $\tau^{-1}$ the variance of the residual error, **λ** the ratio between the two variance components and **K** the relatedness matrix derived from SNP genotypes. Finally, ϵ is a n-vector of errors.

A false discovery rate (FDR) approach was applied to correct for multiple testing, setting the significance level to a *q*-value of 0.05 (Benjamini and Hochberg, 1995). Graphical visualization of the results of the GWAS was achieved by using the R software (R core Team, 2017).

The proportion of the phenotypic variance explained by the significant SNPs (PVE) was estimated using the formula reported by Shim et al. (2015),

$$PVE = \frac{2\hat{\beta}^2\ \mathrm{MAF}\ (1 - \mathrm{MAF})}{2\hat{\beta}^2\ \mathrm{MAF}\ (1 - \mathrm{MAF}) + (se(\hat{\beta}))^2 2\mathrm{N}\ \mathrm{MAF}\ (1 - \mathrm{MAF})}$$

Where **β** is the effect size of the SNP variant estimated from the association analysis; **MAF** is the minor allele frequency of the SNP; *se* is the standard error and **N** is the sample size. Lambda inflation factors were calculated with the median method (1 d.f.) implemented in GenABEL (Aulchenko et al. 2007), while Q-Q plots were built with the gg_qqplot() function (https://www.rdocumentation.org/packages/lindia/versions/0.9 /topics/gg_qqplot).

In order to retrieve candidate genes mapping close to significant SNPs we considered an interval of ± 1 Mb based on data previously reported by Guan et al., (2020) for the same population. Genes mapping within these defined boundaries were listed by using the Biomart tool from Ensemble (Kinsella et al., 2011), and subsequently analyzed with Uniprot (Bateman, 2019) and David Bioinformatic Resources (Huang et al., 2009) to annotate their function.

## RESULTS AND DISCUSSION

### Population Structure and Analysis of Morphological Traits

The first two components C1 and C2 of the principal component analysis accounted for 42.64% and 21.76 % of the genetic variance, respectively (**Supplementary Figure 1**). A number of samples grouped according to their farm of origin, but in general we did not find an obvious within-population substructure in this sample of Murciano-Granadina goats. Descriptive statistics of the raw conformation scores are reported in **Supplementary Table 1 and Supplementary Figures 2 and 3**. The estimated phenotypic correlations and their significances are depicted 1n **Supplementary Table 2** and **Figure 2**. We have classified phenotypic correlations as low ($r_P < 0.2$), moderate ($r_P = 0.2$-$0.4$) or high ($r_P > 0.4$). Phenotypic correlations between udder traits were in general low and positive, with the exception of the correlation between *medial suspensory ligament* and *udder depth* that was moderate ($r_P = 0.369$, *P*-value < 0.001). In the study of McLaren et al. (2016) genetic correlations between udder traits ranged from 0.12 to 0.77, while those between teat traits were in the range of -0.10 to 0.69.

Udder and teat traits were positively correlated, a result coincident with our findings, and also with those reported by Manfredi et al. (2001). We found low and positive correlations between somatic cell score and *medial suspensory ligament* ($r_p$ = 0.14, *P-value* < 0.001), UD ($r_p$ = 0.189, *P*-value < 0.001) and TD ($r_p$ = 0.131, *P*-value < 0.001). Udder depth ($r_G$ = 0.10) and teat size ($r_G$ = 0.29) also showed positive genetic correlations with somatic cell score in Latxa sheep (Legarra and Ugarte, 2005). It is well known that pendulous udders are closer to the floor, exposing the mammary gland to direct contact with fecal and other environmental contaminants (Pugh and Baird, 2012). Moreover, teat diameter is highly correlated with the diameter of the internal cistern (Guarín et al., 2017), and it is expected that sphincters in animals with wider cisterns do not close completely, leaving a channel open for pathogens, thus increasing the risk of suffering mastitis (Seykora and McDaniel, 1985). In contrast, *udder width* ($r_P$ = -0.109, *P*-value < 0.001) and *teat placement* ($r_P$ = -0.126, *P*-value < 0.001) were negatively correlated with somatic cell score, but these two values were low and in other studies these two parameters do not show strong genetic correlations with somatic cell score (Legarra and Ugarte, 2005; Pérez-Cabal et al., 2013). Notably, *udder width* ($r_P$ = 0.20-0.21, *P*-values < 0.001) and *udder depth* ($r_P$ = 0.29-0.32, *P*-values < 0.001) showed moderate positive correlations with milk yield. Pérez-Cabal et al. (2013) found moderate to high and positive phenotypic correlations between milk yield and *udder width* ($r_P$ = 0.29) and *udder depth* ($r_P$ = 0.47) in Spanish Assaf sheep, and Legarra and Ugarte (2005) reported a strong positive genetic correlation between milk yield and *udder depth* (rG = 0.43). In the end, it is reasonable to infer that goats with wider and deeper udders produce more milk.

Phenotypic correlations between body conformation traits were generally high and positive. For instance, *height* was correlated with *chest width* ($r_P$ = 0.646, *P*-value <

0.001), *rump width* ($r_P$ = 0.673, *P*-value < 0.001) and *angularity* ($r_P$ = 0.424, *P*-value < 0.001), and *chest width* also showed positive correlations with *body depth* ($r_P$ = 0.415, *P*-value < 0.001), *rump width* ($r_P$ = 0.744, *P*-value < 0.001) and *angularity* ($r_P$ = 0.682, *P*-value < 0.001). Zujovic et al. (2011) also observed high phenotypic correlations between body traits measured in Balkan goats, and a similar trend was observed by Chacón et al. (2011) in Cuban goats. In general, taller goats are also bigger and have a wider chest and rump. We also observed moderate positive correlations between *chest width* and *body depth* and milk yield ($r_P$ = 0.2-0.3, *P*-values < 0.001) and between *rump width* and milk yield ($r_P$ =0.15-0.2, *P*-values < 0.001). In cows it has been reported that animals with a wider rump and increased space across their hooks and pins can accommodate a higher and wider udder Campbell and Marshall (2016). These results suggest that the increment of the udder capacity leads to a higher milk yield while at the same time it decreases the percentages of solid milk components (% lactose, % fat and % protein). There are also indications that cows with a short and round body often lack dairy character and udder capacity (Campbell and Marshall, 2016), supporting the observed positive correlation between angularity and milk yield in our Murciano-Granadina population.

With regard to leg traits, *mobility* displayed a positive phenotypic correlation with *rear legs rear view* ($r_P$ = 0.425, *P*-value < 0.001) and RLS ($r_P$ = 0.231, *P*-value < 0.001). Interestingly *rear legs rear view* and *rear legs side view* showed low positive and low negative correlations with milk yield, respectively. McLaren et al. (2016) observed a correlation of 0.33 between back legs and milk yield at 305 days, while de la Fuente et al. (2011) estimated a small genetic correlation of −0.09 between the back legs and milk yield of Churra ewes. Our interpretation is that leg morphology could be associated with

the predisposition of goats to suffer lameness, a pathology that results in a decreased milk production and often in the culling of the affected animal (Archer et al., 2010).

**Identification of Genetic Determinants for Udder Traits**

After performing the GWAS analysis we detected two genome-wide significant associations for the trait *medial suspensory ligament* (**Table 1**). We also found chromosome-wide associations for the traits *medial suspensory ligament* (2 SNPs), *udder width* (1 SNPs), *udder depth* (3 SNPs), *teat placement* (4 SNPs) and *teat diameter* (2 SNPs), as shown in **Table 1** and **Supplementary Figures 4 (Manhattan plots) and 7 (Q-Q plots)**. No significant SNPs were found for *fore udder attachment* and *rear udder height.*

The rs268273468 (CHI 16: 69617700) marker, which was significantly associated to *medial suspensory ligament* at the genome-wide level of significance (**Table 1 and Figure 1),** is located less than 1 Mb away from the lysophosphatidylglycerol acyltransferase 1 (*LPGAT1*) gene (**Supplementary Table 3**). This gene encodes an enzyme involved in the conversion of lysophosphatidylglycerol into phosphatidylglycerol, a membrane phospholipid that is a key precursor in the biosynthesis of cardiolipin (Yang et al., 2004). Interestingly, cardiolipin is located in the inner mitochondrial membrane and plays a fundamental role in maintaining mitochondrial membrane stability and dynamics, as well as regulating apoptosis (Paradies et al., 2014). Proper mitochondrial function, in turn, is essential to ensure the integrity of tendons and other connective tissues (Lowes et al., 2009; Thankam et al., 2018). With regard to rs268249346 (CHI 28: 18321523), the other genome-wide significant SNP for *medial suspensory ligament*, we found that it maps close to the ADAM metallopeptidase with thrombospondin type 1 motif 14 (*ADAMTS14*) locus

(**Supplementary Table 3**). This gene has been reported to encode a procollagen N-proteinase that cleaves the amino-propeptide of procollagen to allow the assembly of elongated and cylindrical collagen fibrils (Bekhouche and Colige, 2015), although one recent study indicates that the main role of this molecule would be the regulation of the immune response (Dupont et al., 2018).

We also identified twelve SNPs showing significant associations with udder traits at the chromosome-wide level (**Table 1, Supplementary Figures 4** and **7**). The activating transcription factor 3 (*ATF3*) gene is located close to the SNP rs268273468 (CHI 16: 69617700) associated with *medial suspensory ligament* (**Supplementary Table 3**). Interestingly, this gene modulates the synthesis of collagen I and III (Zhou et al., 2011), and regulates matrix metalloproteinases which are fundamental for the development, renewal and remodeling of tendons (Guenzle et al., 2017). Another interesting association is that between the rs268288193 marker (CHI 19: 38362152) and teat *placement.* The region containing this SNP was associated with somatic cell count in Saanen goats (Martin et al., 2018). Interestingly, Lund et al., (1994) reported that cows with bad teat placement tend to be more susceptible to mastitis. Less than 1 Mb apart from this SNP, we identified the suppressor of cytokine signaling 7 (*SOCS7*) gene (**Supplementary Table 3)**, which inhibits prolactin, growth hormone, and leptin signaling (Martens et al., 2005). Members of this gene family are regulators of mammary gland physiology. For instance, in mice *SOCS1* and *SOCS2* attenuate prolactin signaling, thus preventing premature lactation (Sutherland et al., 2007). Besides, *SOCS3* is a key regulator of mammary gland involution (Sutherland et al., 2007). In dairy cattle, the polymorphism of the *SOCS7* gene has been associated to different milk traits like protein yield and percentage, and milk yield (Arun et al., 2015).

The collagen type XIV $\alpha_1$ chain (*COL14A1*) gene is located just 0.1 Mb away from the rs268281312 SNP (CHI 14:868624) which is significantly associated to *udder depth* (**Supplementary Table 3)**. This gene encodes a fibril-associated collagen that regulates fibrillogenesis ( Lindholm, 2019). In the human mammary gland, large amounts of type XIV collagen have been found in interlobular stroma, which, compared with intralobular stroma, contains densely packed collagen (Atherton et al., 1998). This differential distribution of type XIV collagen might have an important effect on the architecture of the mammary connective tissue.

**Identification of Genetic Determinants for Body Conformation Traits**

Although we did not detect any genome-wide significant association for body conformation traits, at the chromosome-wide level we found 19 SNPs significantly associated with *angularity* (4 SNPs), *rump width* (2 SNPs), *rump angle* (1 SNPs), *chest width* (5 SNPs), *height* (3 SNPs), *body depth* (3 SNPs) and *bone quality* (1 SNPs). These results are displayed in **Table 2** as well as in **Supplementary Figures 5 (Manhattan plots) and 8 (Q-Q plots**).

Several of the aforementioned SNPs map close to genes involved in bone homeostasis and skeletal development (**Supplementary Table 3**). For instance, the rs268245664 SNP which is associated with *angularity* maps to the parathyroid hormone 1 receptor (*PTH1R*) locus (**Figure 5**, **Table 2,** and **Supplementary Table 3**). This gene encodes a protein that acts as a receptor for parathyroid hormone (PHT) and parathyroid related peptide (PTHrP), two factors regulating mineral ion homeostasis (Mannstadt et al., 1999). The dysfunction of the *PTH1R* gene is associated with diseases that affect skeletal development and calcium homeostasis (Mannstadt et al., 1999). With regard to the association between *angularity* and the rs268265191 SNP (CHI 1: 35829812), it is

worth to mention that this marker maps near to the ephrin receptor A3 gene (*EPHA3*) (**Supplementary Table 3)**. Ephrin receptors and their associated ligands are essential modulators of bone remodeling and they ensure an adequate coupling between bone resorption and formation (Edwards and Mundy, 2008). Interestingly, the inactivation of the ephrin-B1gene causes perinatal lethality, abdominal wall closure defects, and skeletal abnormalities, especially of the thoracic cage (Compagni et al., 2003). Another interesting gene is the one encoding the CGG triplet repeat binding protein 1 (*CGGBP1*), which is located 1 Mb away from rs268265191 (CHI 1: 35829812) (**Supplementary Table 3)**. The polymorphism of this gene has been associated to several carcass traits in cattle (Calonge M., 2004), having a considerable effect on growth (Sevane et al., 2014). Moreover, Sevane et al. (2014) described a non-synonymous mutation, rs477676137 (c.206A>G, 1: 36060631), in the *CGGBP1* gene associated with an increase in pelvis width and wither height measured at 9 months. On the other hand, the rs268255133 marker (CHI 18: 34112104), which is associated with *rump width*, maps close to the cadherin 11 gene (*CDH11*) (**Supplementary Table 3**),which modulates postnatal bone growth and osteoblast differentiation (Di Benedetto et al., 2010). Furthermore, the rs268262472 marker (CHI 27: 38084358), which is associated with *rump angle*, lies near to the spermatogenesis associated 4 gene (*SPATA4*), also involved in promoting osteoblast differentiation (Wang et al., 2011).

Another marker of interest is rs268285858 (CHI 22: 45075519). This SNP was associated with *body depth* and it is located close to the Wnt family member 5A (*WNT5A* ) gene, (**Supplementary Table 3)**, that regulates planar cell polarity signaling during embryonic development (Qian et al., 2007). The loss of the gene results in a shortened and widened cochlea in knockout mice embryos and severe shortening of the anterior-posterior axis and limb truncations due to abnormal convergent extension

(Yamaguchi et al., 1999; Qian et al., 2007; Andre et al., 2015). Finally, we would like to highlight that the rs268249930 (CHI 16: 26773653) marker associated with *height* co-localizes with the *DNAH14* gene (**Supplementary Table 3)**, which encodes an axonemal dynein heavy chain. Mutations in dynein genes can cause skeletal ciliopathies characterized by thoracic narrowing, short long bones and pelvis dysplasia (Yildiz, 2018).

**Identification of Genetic Determinants for Leg Structure Traits**

No genome-wide significant SNPs were found for leg structure traits, but 7 SNPs showed significant associations at the chromosome-wide level. These findings are reported in **Table 3** as well as in **Supplementary Figures 6 (Manhattan plot) and 9 (Q-Q plot)**. For the *mobility* trait, an association was found with the rs268236663 SNP (CHI 2:16211260), located 600 Kb away from the endothelin converting enzyme like 1 (*ECEL1*) gene (**Supplementary Table 3**), which encodes an endopeptidase member of the M13 family involved in the regulation of neuropeptide and peptide hormone activity. This molecule has an important function in the development of the neuromuscular junctions of the limbs in mice (Nagata et al., 2016). Mice lacking this gene display a poor arborization of the neuromotor nerves and a significant reduction of the number of neuromuscular junctions (Nagata et al., 2016). In humans, digital arthrogryposis is caused by mutations in *ECEL1* and affected individuals show limited flexion of the knee and flexion of the fingers as well as muscular atrophy (Dieterich et al., 2013).

Another interesting association was that between *rear leg rear view* and the genotype of the rs268286224 marker (CHI 24:42536581), which is positioned nearby the piezo type mechanosensitive ion channel component 2 (*PIEZO2*) gene, (**Supplementary Table 3)**,

which is also involved in the etiology of digital arthrogryposis (Delle Vedove et al., 2016). Homozygous individuals for mutations inactivating *PIEZO2* suffer from arthrogryposis and scoliosis (Haliloglu et al., 2017), while carriers of gain-of-function mutations can present multiple congenital contractures of limbs and variable absence of cruciate knee ligaments, amongst other symptoms (Coste et al., 2013).

**About the Genomic Architecture of Morphological Traits**

Comparing our results with those obtained by Martin et al., (2018) and by Mucha et al., (2018), we can state that there is a general lack of positional coincidence between the genomic regions associated with conformation traits in the aforementioned studies. Furthermore, in the study of Martin et al. (2018) different regions were identified in the Alpine and Saanen breeds as associated with body phenotypes, suggesting that this lack of concordance is not produced by technical factors. Indeed, we have found only 2 SNPs displaying genome-wide significant associations with morphological traits (2 SNPs). Such limited results are probably due to the fact that the inheritance of morphological traits in goats is highly polygenic, with many genetic variants with small effects determining phenotypic variation. In other words, the success of GWAS largely depends on the genomic architecture of the trait rather than on the magnitude of its heritability. Stature is a good example of this because it is a highly heritable and, at the same time, a highly polygenic trait. In cattle 163 genomic regions associated with stature have been detected, but they only explain 13.8% of the phenotypic variance (Bouwman et al., 2018). Similarly, in humans at least 180 genetic markers mostly segregating in populations of European descent explain ∼10% of the variance in height, a phenotype that has a large heritability close to ∼0.8 (Yang et al., 2010). This remarkable gap between genealogical heritability and the percentage of the phenotypic

variance explained by the SNPs is caused, at least in part, by the existence of hundreds or thousands of genetic determinants with small phenotypic effects on stature. A similar reasonment can be probably made for the majority of body, leg and udder morphological traits, because with the population sizes often employed in bovine, ovine or caprine GWAS generally the number of significant hits is very low (Schmid and Bennewitz, 2017).

Currently, we do not know whether the lack of positional concordance between GWAS for morphology traits recorded in goats are due to the existence of a substantial genetic heterogeneity across populations or to the modest size of the populations employed in GWAS, a circumstance that limits the ability to detect variants with small effects that explain the majority of the phenotypic variance of morphological traits. Indeed, large GWAS analyses performed in humans have demonstrated that many of the genetic variants that are associated with height are shared between individuals of European and African descent (N'Diaye et al., 2011), thus reinforcing the notion that the magnitude of genetic heterogeneity between populations is greatly reduced when large sample sizes are used in GWAS.

## CONCLUSIONS

The number of hits detected in our GWAS for body conformation, udder and leg traits was quite limited, a result that agrees well with those reported in previous studies (Martin et al., 2018; Mucha et al., 2018). Very probably, this outcome reflects the highly polygenic nature of morphological traits in ruminants. By comparing our results with previous reports, we have also detected a low positional concordance. This could be the consequence of genetic heterogeneity in the genetic determinism of

morphological traits or to the fact that GWAS carried out so far are too low powered to detect reliably the genetic determinants of such phenotypes. Despite these limitations, we have been able to identify several genes related with collagen synthesis (*ATF3*, *ADAMTS14* and *COL14A1*), growth (*CGGBP1*), development (*WNT5A* and *DNAH14*), bone homeostasis and remodeling (*PTH1R*, *CDH11*, *SPATA4*, and *EPHA3*), limb development (*ECEL1* and *PIEZO2*) and mammary physiology (*SOCS7*) mapping close to GWAS hits. Such information, combined with candidate gene sets generated in other GWAS, if possible, with much larger reference populations, could provide very valuable hints about the identity of the loci shaping the body, udder and leg morphology of goats.

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**Table 1.** Genome-wide and chromosome-wide significant associations between SNPs and udder traits (MSL, medial suspensory ligament; TD, teat diameter; TP, teat placement; UD, udder depth; UW, udder width) recorded in 811 Murciano-Granadina goats.

| | Trait | Chr[1] | rs[2] | Pos[3] | A1[4] | MAF[5] | β ± SE[6] | *P-value*[7] | *q-value*[8] | *PVE*[9] |
|---|---|---|---|---|---|---|---|---|---|---|
| **Genome Wide** | MSL | 16 | rs268273468 | 69617700 | C | 0.469 | -0.220 ± 0.045 | 1.45E-06 | 0.034 | 0.010 |
| | | 28 | rs268249346 | 18321523 | A | 0.485 | -0.241 ± 0.049 | 1.28E-06 | 0.034 | 0.008 |
| **Chromosome Wide** | MSL | 16 | rs268273468 | 69617700 | C | 0.469 | -0.220 ± 0.045 | 1.45E-06 | 0.002 | 0.010 |
| | | 28 | rs268249346 | 18321523 | A | 0.485 | -0.241 ± 0.049 | 1.28E-06 | 0.001 | 0.008 |
| | TD | 28 | rs268248647 | 9579785 | G | 0.460 | -0.214 ± 0.054 | 6.93E-05 | 0.042 | 0.007 |
| | | 28 | rs268243765 | 10586645 | G | 0.404 | -0.215 ± 0.055 | 9.45E-05 | 0.042 | 0.007 |
| | TP | 9 | rs268282545 | 20855427 | G | 0.498 | -0.208 ± 0.047 | 1.09E-05 | 0.020 | 0.009 |
| | | 19 | rs268288193 | 38362152 | G | 0.181 | 0.243 ± 0.059 | 4.05E-05 | 0.047 | 0.006 |
| | | 25 | rs268246864 | 40499453 | G | 0.391 | -0.205 ± 0.047 | 1.32E-05 | 0.011 | 0.009 |
| | | 26 | rs268291440 | 37970238 | A | 0.316 | -0.238 ± 0.052 | 5.33E-06 | 0.005 | 0.008 |
| | UD | 14 | rs268281312 | 868624 | A | 0.263 | 0.216 ± 0.051 | 2.83E-05 | 0.041 | 0.008 |
| | | 14 | rs268276674 | 90209603 | A | 0.480 | 0.193 ± 0.047 | 4.48E-05 | 0.041 | 0.009 |
| | | 15 | rs268268821 | 47457448 | A | 0.430 | -0.207 ± 0.050 | 3.14E-05 | 0.049 | 0.008 |
| | UW | 27 | rs268251218 | 10045474 | G | 0.444 | 0.277 ± 0.062 | 1.00E-05 | 0.009 | 0.005 |

[1]**Chr**, chromosome; [2]**rs**, identifier code of the SNP according to the RefSNP database; [3]**Pos**, position in base pairs; [4]**A1,** minority allele; [5]**MAF**, allele frequency; [6]**β ± SE**, allelic substitution effect ± standard error; [7]***P-value***, raw *P*-values; [8]***q-value***, *P*-values corrected for multiple testing using a false discovery rate approach; [9]***PVE,*** percentage of proportion of variance in phenotype explained by a given SNP.

**Table 2.** Chromosome-wide significant associations between SNPs and body traits (ANG, angularity; BD, body depth; BQ, bone quality; CW, chest width; HT, height; RA, rump angle; RW, rump width) recorded in 811 Murciano-Granadina goats.

| | Trait | Chr[1] | rs[2] | Pos[3] | A1[4] | MAF[5] | β ± SE[6] | *P-value*[7] | *q-value*[8] | *PVE*[9] |
|---|---|---|---|---|---|---|---|---|---|---|
| **Chromosome Wide** | ANG | 1 | rs268265191 | 35829812 | G | 0.496 | -0.199 ± 0.045 | 0.032 | 4.980 | 0.010 |
| | | 1 | rs268280713 | 135255901 | A | 0.352 | -0.200 ± 0.048 | 0.049 | 4.504 | 0.009 |
| | | 22 | rs268245662 | 52518237 | A | 0.074 | -0.358 ± 0.083 | 0.010 | 4.759 | 0.003 |
| | | 22 | rs268245664 | 52649718 | G | 0.043 | -0.512 ± 0.105 | 0.001 | 5.900 | 0.002 |
| | BD | 9 | rs268236956 | 24849991 | G | 0.281 | 0.224 ± 0.050 | 0.012 | 5.161 | 0.008 |
| | | 13 | rs268290607 | 55121535 | A | 0.394 | -0.190 ± 0.045 | 0.044 | 4.553 | 0.010 |
| | | 22 | rs268285858 | 45075519 | G | 0.48 | -0.180 ± 0.044 | 0.045 | 4.393 | 0.011 |
| | BQ | 15 | rs268289470 | 13689629 | A | 0.394 | 0.217 ± 0.052 | 0.012 | 5.109 | 0.008 |
| | CW | 3 | rs268243320 | 53360997 | C | 0.139 | -0.265 ± 0.062 | 0.044 | 4.715 | 0.005 |
| | | 7 | rs268240258 | 51615185 | A | 0.311 | -0.214 ± 0.045 | 0.006 | 5.548 | 0.010 |
| | | 17 | rs268248977 | 26865599 | A | 0.454 | 0.174 ± 0.040 | 0.021 | 4.824 | 0.013 |
| | | 17 | rs268248975 | 26942955 | G | 0.252 | 0.193 ± 0.049 | 0.044 | 4.022 | 0.008 |
| | | 17 | rs268264934 | 58534119 | G | 0.494 | 0.171 ± 0.041 | 0.027 | 4.411 | 0.012 |
| | HT | 16 | rs268249920 | 26376843 | A | 0.419 | 0.172 ± 0.043 | 0.031 | 4.213 | 0.011 |
| | | 16 | rs268249930 | 26773653 | G | 0.348 | -0.207 ± 0.044 | 0.005 | 5.477 | 0.011 |
| | | 16 | rs268236696 | 59779757 | A | 0.126 | -0.238 ± 0.059 | 0.031 | 4.262 | 0.006 |
| | RA | 27 | rs268262472 | 38084358 | G | 0.207 | -0.255 ± 0.063 | 0.044 | 4.299 | 0.005 |
| | RW | 17 | rs268264930 | 58698058 | G | 0.359 | 0.182 ± 0.040 | 0.009 | 5.190 | 0.013 |
| | | 18 | rs268255133 | 34112104 | G | 0.134 | -0.259 ± 0.055 | 0.003 | 5.553 | 0.007 |

[1]**Chr**, chromosome; [2]**rs**, identifier code of the SNP according to the RefSNP database; [3]**Pos**, position in base pairs; [4]**A1,** minority allele; [5]**MAF**, allele frequency; [6]**β ± SE**, allelic substitution effect ± standard error; [7]***P-value***, raw *P*-values; [8]***q-value***, *P*-values corrected for multiple testing using a false discovery rate approach; [9]***PVE,*** percentage of proportion of variance in phenotype explained by a given SNP.

**Table 3.** Chromosome-wide significant associations between SNPs and leg traits (MOB, mobility; RLR, rear legs rear view; RLS, rear legs side view) recorded in 811 Murciano-Granadina goats.

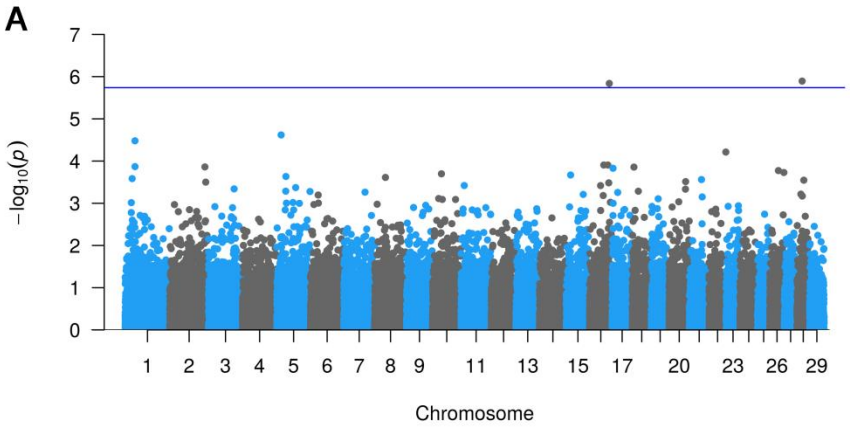
| | Trait | Chr[1] | rs[2] | Pos[3] | A1[4] | MAF[5] | β ± SE[6] | *P-value*[7] | *q-value*[8] | *PVE*[9] |
|---|---|---|---|---|---|---|---|---|---|---|
| **Chromosome Wide** | MOB | 2 | rs268236663 | 16211260 | G | 0.237 | 0.325 ± 0.072 | 8.13E-06 | 0.022 | 0.004 |
| | RLR | 17 | rs268258221 | 21284278 | G | 0.367 | -0.255 ± 0.061 | 2.98E-05 | 0.041 | 0.006 |
| | | 19 | rs268288174 | 39252784 | G | 0.188 | 0.340 ± 0.074 | 4.69E-06 | 0.005 | 0.004 |
| | | 24 | rs268259571 | 38761188 | A | 0.422 | -0.278 ± 0.065 | 1.78E-05 | 0.023 | 0.005 |
| | | 24 | rs268286224 | 42536581 | A | 0.117 | -0.376 ± 0.092 | 4.26E-05 | 0.027 | 0.002 |
| | RLS | 3 | rs268254620 | 8818355 | G | 0.356 | -0.188 ± 0.046 | 4.41E-05 | 0.050 | 0.010 |
| | | 3 | rs268285963 | 43496497 | A | 0.3 | 0.211 ± 0.048 | 1.20E-05 | 0.027 | 0.009 |

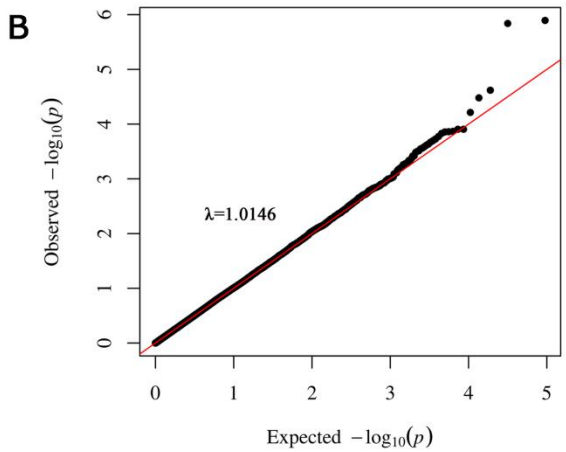
[1]**Chr**, chromosome; [2]**rs**, identifier code of the SNP according to the RefSNP database; [3]**Pos**, position in base pairs; [4]**A1,** minority allele; [5]**MAF**, allele frequency; [6]**β ± SE**, allelic substitution effect ± standard error; [7]***P-value***, raw *P*-values; [8]***q-value***, *P*-values corrected for multiple testing using a false discovery rate approach; [9]***PVE,*** proportion of variance in phenotype explained by a given SNP.

## LEGENDS TO FIGURES

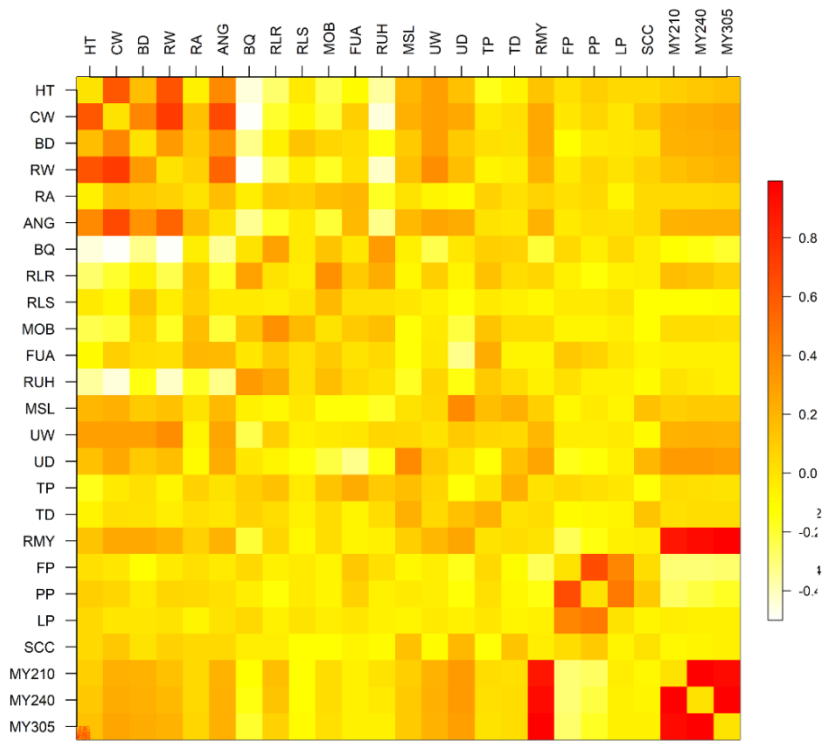
**Figure 1A**. Negative $\log_{10}$ *P-values* (*y*-axis) of the associations between SNPs and the m*edial suspensory ligament* phenotype are plotted against the genomic location of each SNP marker (*x*-axis). Markers on different chromosomes are denoted by different colors. The blue line indicates the significance of the association after false discovery rate correction for multiple testing (*q-value*= 0.05). **1B.** Quantile-Quantile plots corresponding to the genome-wide corrected *P*-values of the GWAS for the trait *medial suspensory ligament* and its lambda (λ) inflation factor.

**Figure 2A**. Heatmap depicting Pearson correlations between morphological and milk yield phenotypes recorded in 811 Murciano-Granadina goats. The intensity of the color indicates the magnitude of the correlation **2B.** Heatmap displaying the significances of the Pearson correlations shown in **2A**. The intensity of the color indicates the significance of the association. The following abbreviations have been used, **HT**, height; **CW**, chest width; **BD**, body depth; **RW**, rump width; **RA**, rump angle; **ANG**, angularity; **BQ**, bone quality; **RLR**, rear legs rear view; **RLS**, rear legs side view; **MOB**, mobility; **FUA**, fore udder attachment; **RUH**, rear udder height; **MSL**, medial suspensory ligament; **UW**, udder width; **UD**, udder depth; **TP**, teat placement; **TD**, teat diameter; **RMY**, total milk yield; **SCC**, somatic cell count; **MY210**, milk yield corrected at 210 days milking; **MY240**, milk yield corrected at 240 days milking; **M305**, milk yield corrected at 305 days milking.

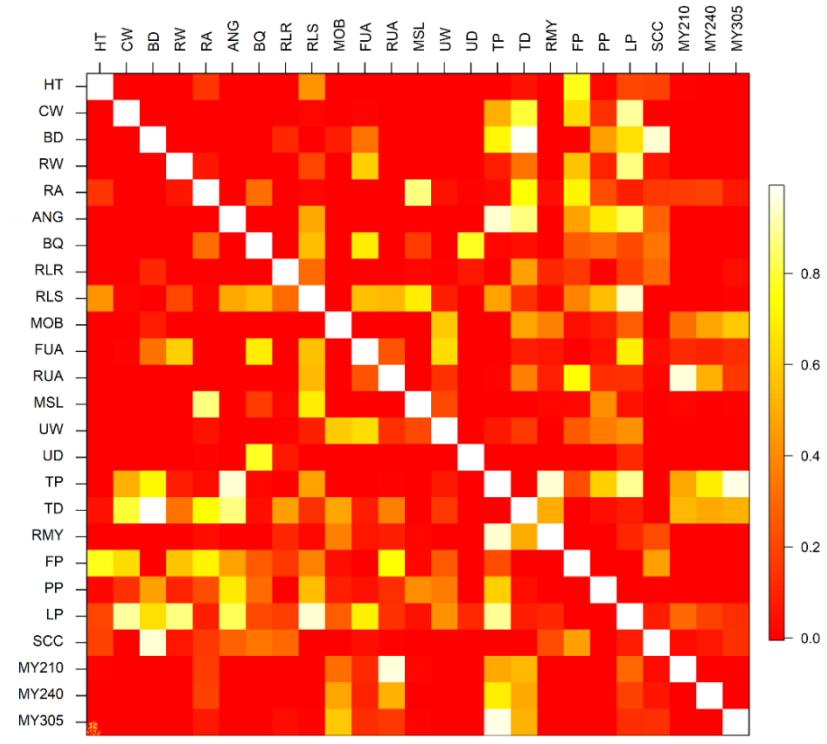

A
7
6
5
4
3
2
1
0
$-\log_{10}(p)$
1 2 3 4 5 6 7 8 9 11 13 15 17 20 23 26 29
Chromosome


B
Observed $-\log_{10}(p)$
λ=1.0146
0 1 2 3 4 5 6
0 1 2 3 4 5
Expected $-\log_{10}(p)$

**A**


HT
CW
BD
RW
RA
ANG
BQ
RLR
RLS
MOB
FUA
RUH
MSL
UW
UD
TP
TD
RMY
FP
PP
LP
SCC
MY210
MY240
MY305
0.8
0.6
0.4
0.2
0.0

**B**


HT
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MSL
UW
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RMY
FP
PP
LP
SCC
MY210
MY240
MY305
0.8
0.6
0.4
0.2
0.0

**Supplementary Table 1.** Descriptive statistics of body, udder and leg phenotypes recorded in 811 Murciano-Granadina goats and expressed as linear scores.

| Phenotype | Mean ± SE[1] | Min[2] | Max[3] |
|---|---|---|---|
| Height | 3.205 ± 0.092 | 1 | 8 |
| Chest width | 4.857 ± 0.087 | 2 | 9 |
| Body depth | 5.821 ± 0.061 | 3 | 9 |
| Rump width | 5.167 ± 0.094 | 3 | 8 |
| Rump angle | 5.655 ± 0.090 | 4 | 7 |
| Angularity | 5.204 ± 0.086 | 2 | 9 |
| Bone quality | 7.421 ± 0.094 | 5 | 9 |
| Fore udder attachment | 5.917 ± 0.089 | 2 | 8 |
| Rear udder height | 6.365 ± 0.084 | 3 | 8 |
| Medial suspensory ligament | 3.212 ± 0.090 | 1 | 8 |
| Udder width | 7.147 ± 0.098 | 3 | 9 |
| Udder depth | 4.406 ± 0.095 | 1 | 8 |
| Teat placement | 6.536 ± 0.085 | 3 | 9 |
| Teat diameter | 5.152 ± 0.094 | 2 | 9 |
| Rear legs side view | 6.673 ± 0.079 | 4 | 8 |
| Rear legs rear view | 3.342 ± 0.083 | 2 | 6 |
| Mobility | 6.926 ± 0.075 | 4 | 8 |

[1]**Mean** ± **SE**, mean ± standard error;[2]**Min**, minimum values measured in the population; [3]**Max**, maximum values measured in the population.

**Supplementary Table 2.** Phenotypic Pearson correlations matrix among morphological and milk yield traits recorded in 811 Murciano-Granadina goats. The lower diagonal shows the correlation between each pair of traits, the upper diagonal indicates the *P-value* of each correlation.

Attached in excel file.

**Supplementary Table 3.** Distance in base pairs between SNPs showing significant associations with morphological traits and the closest functional and positional candidate gene identified in the goat ARS1 reference genome.

| Trait | Gene | Chr[1] | Pos1 [2] | Pos2[3] | rs[4] | Pos[5] | Distance Gene-SNP[6] |
|---|---|---|---|---|---|---|---|
| **MSL**[7] | *LPGAT1* | 16 | 70237593 | 70372062 | rs268273468 | 69617700 | 619893 |
| **MSL**[7] | *ATF3* | 16 | 69579015 | 69584224 | rs268273468 | 69617700 | 38685 |
| **MSL**[7] | *ADAMTS14* | 28 | 18733706 | 18830075 | rs268249346 | 18321523 | 412183 |
| **TP**[8] | *SOCS7* | 19 | 38654621 | 38680473 | rs268288193 | 38362152 | 292469 |
| **UD**[9] | *COL14A1* | 14 | 490458 | 701160 | rs268281312 | 868624 | 167464 |
| **ANG**[10] | *PTH1R* | 22 | 52630037 | 52650450 | rs268245664 | 52649718 | 19681 |
| **RW**[11] | *CDH11* | 18 | 33975536 | 34062591 | rs268255133 | 34112104 | 136568 |
| **RA**[12] | *SPATA4* | 27 | 37814782 | 37824810 | rs268262472 | 38084358 | 269576 |
| **ANG**[10] | *EPHA3* | 1 | 35895723 | 36304923 | rs268265191 | 35829812 | 65911 |
| **ANG**[10] | *CGGBP1* | 1 | 34861253 | 34861756 | rs268265191 | 35829812 | 968559 |
| **BD**[13] | *WNT5A* | 22 | 45489607 | 45511154 | rs268285858 | 45075519 | 414088 |
| **HT**[14] | *DNAH14* | 16 | 26597510 | 26999792 | rs268249930 | 26773653 | - |
| **MOB**[15] | *ECEL1* | 2 | 15610337 | 15619144 | rs268236663 | 16211260 | 592116 |
| **RLR**[16] | *PIEZO2* | 24 | 42556947 | 42810419 | rs268286224 | 42536581 | 20366 |

[1]**Chr**, chromosome; [2]**Pos1**, start position of the gene in base pairs; [3]**Pos2**, end position of the gene in base pairs; [4]**rs**, identifier code of the SNP according to the RefSNP database; [5]**Pos**, position of the SNP; [6]**Distance Gene-SNP,** distance in base pairs between the significant related SNP and the functional putative gene; [7]**MSL**, medial suspensory; [8]**TP**, teat placement; [9]**UD**, udder depth; [10]**ANG**, angularity; [11]**RW**, rump width; [12]**RA**, rump angle; [13]**BD**, body depth; [14]**HT**, height; [15]**MOB**, mobility; [16]**RLR**, rear legs rear view.

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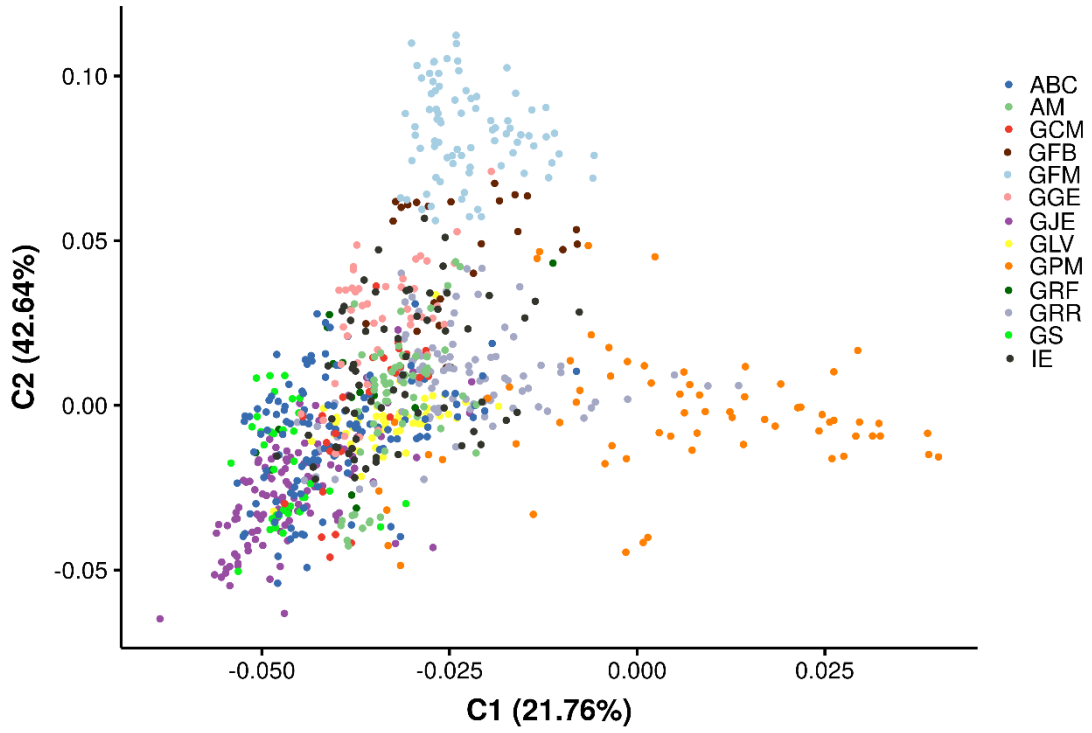
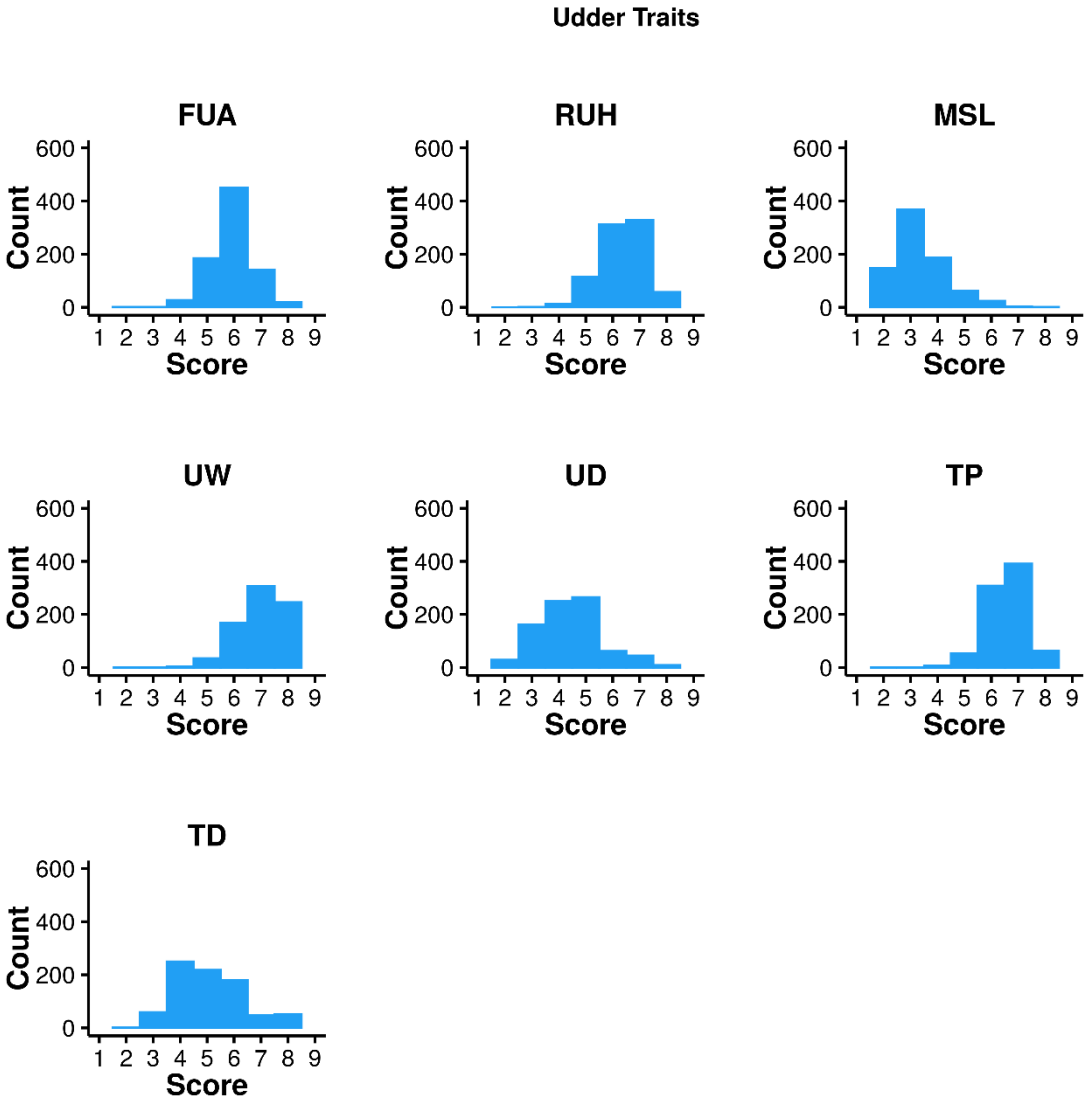
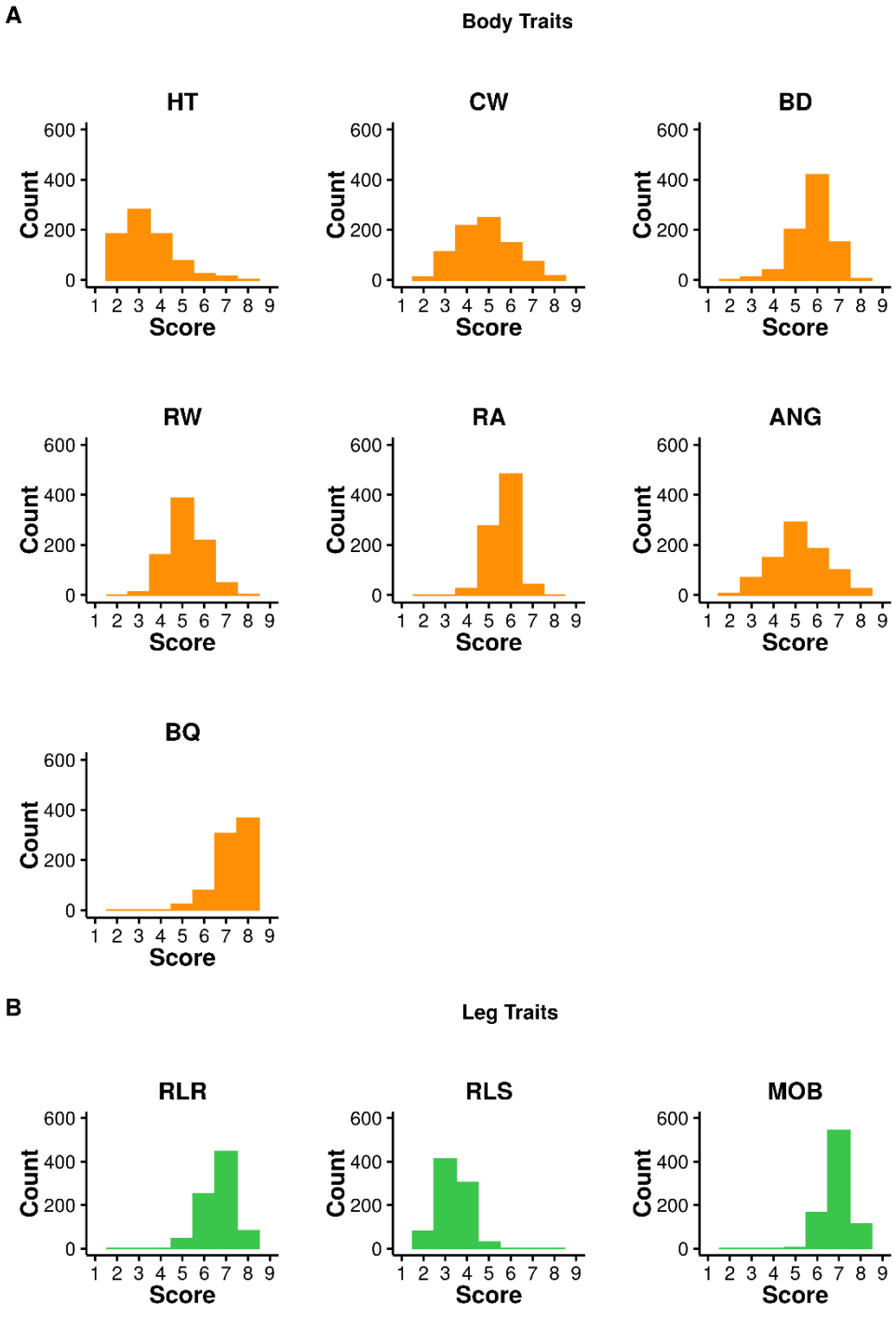
**Supplementary Figure 1**. Principal component analysis based on the Illumina Goat SNP50 BeadChip (Illumina inc, San Diego, CA) genotypes of 811 Murciano-Granadina distributed in 13 farms (each one encoded by a different color) and used in the current GWAS.



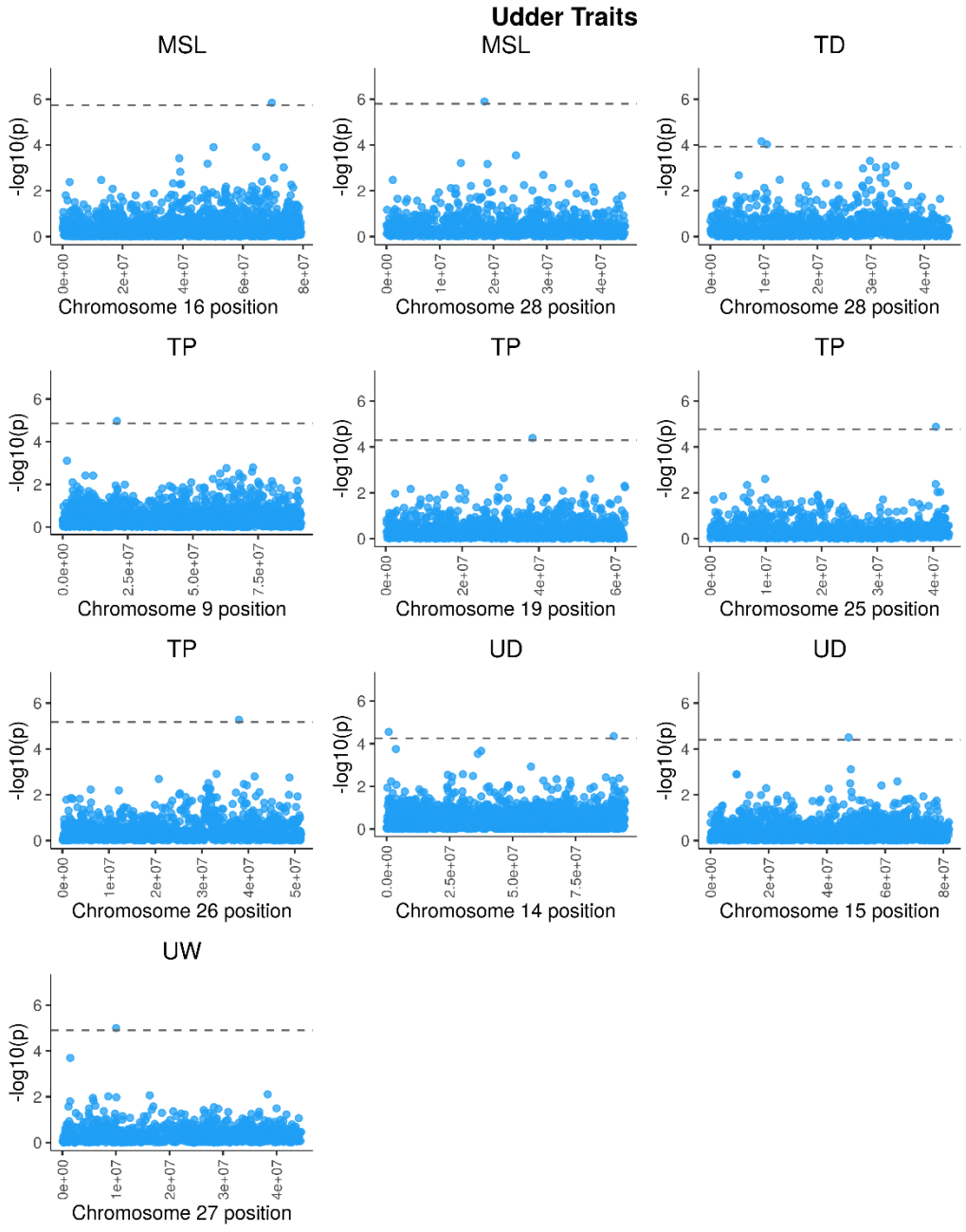
**Supplementary Figure 2.** Histograms depicting the number of Murciano-Granadina goats corresponding to each one of the linear score categories defining udder traits. The following abbreviations have been used, **FUA**, fore udder attachment; **RUH**, rear udder height; **MSL**, medial suspensory ligament; **UW**, udder width; **UD**, udder depth; **TP**, teat placement; **TD**, teat diameter.



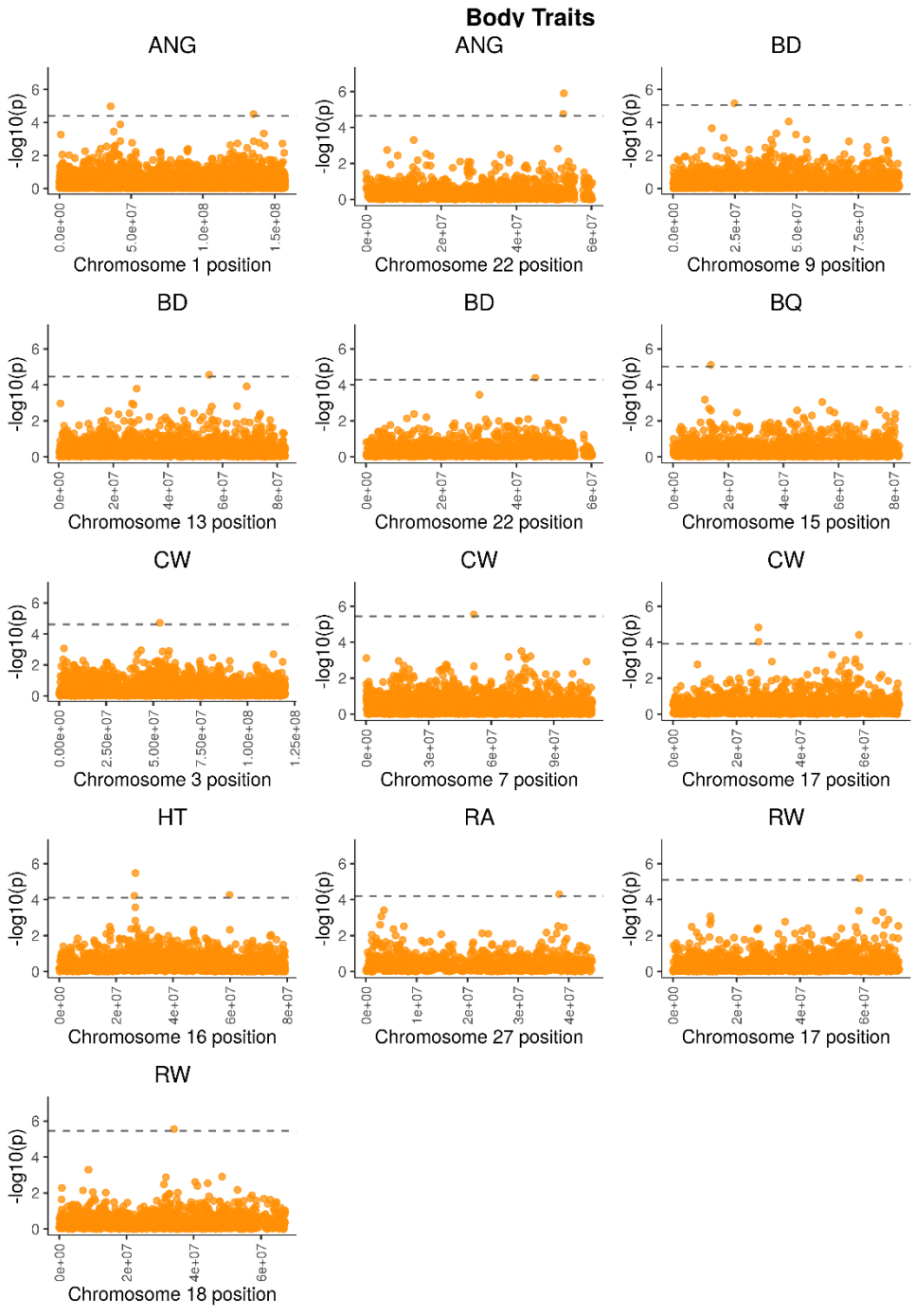
**Supplementary Figure 3.** Histograms depicting the number of Murciano-Granadina goats corresponding to each one of the linear score categories defining body (A) and leg (B) traits. The following abbreviations have been used, **HT**, height; **CW**, chest width; **BD**, body depth; **RW**, rump width; **RA**, rump angle; **ANG**, angularity; **BQ**, bone quality; **RLR**, rear legs rear view; **RLS**, rear legs side view; **MOB**, mobility.



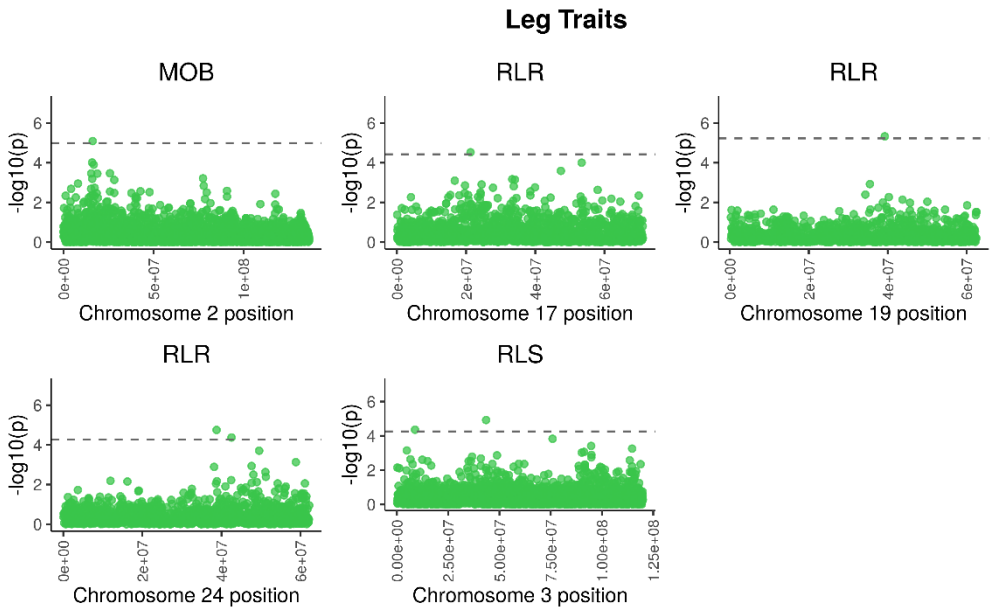
**Supplementary Figure 4**. Manhattan plots depicting negative $\log_{10}$ *P*-values (*y*-axis) of the associations at the chromosome-wide level between SNPs and udder morphology traits plotted against the genomic location of each SNP marker (*x*-axis). Only chromosomes hosting significant associations are shown (*q*-value < 0.05). The following abbreviations have been used, **MSL**, medial suspensory ligament; **TD**, teat diameter; **TP**, teat placement; **UD**, udder depth; **UW**, udder width.



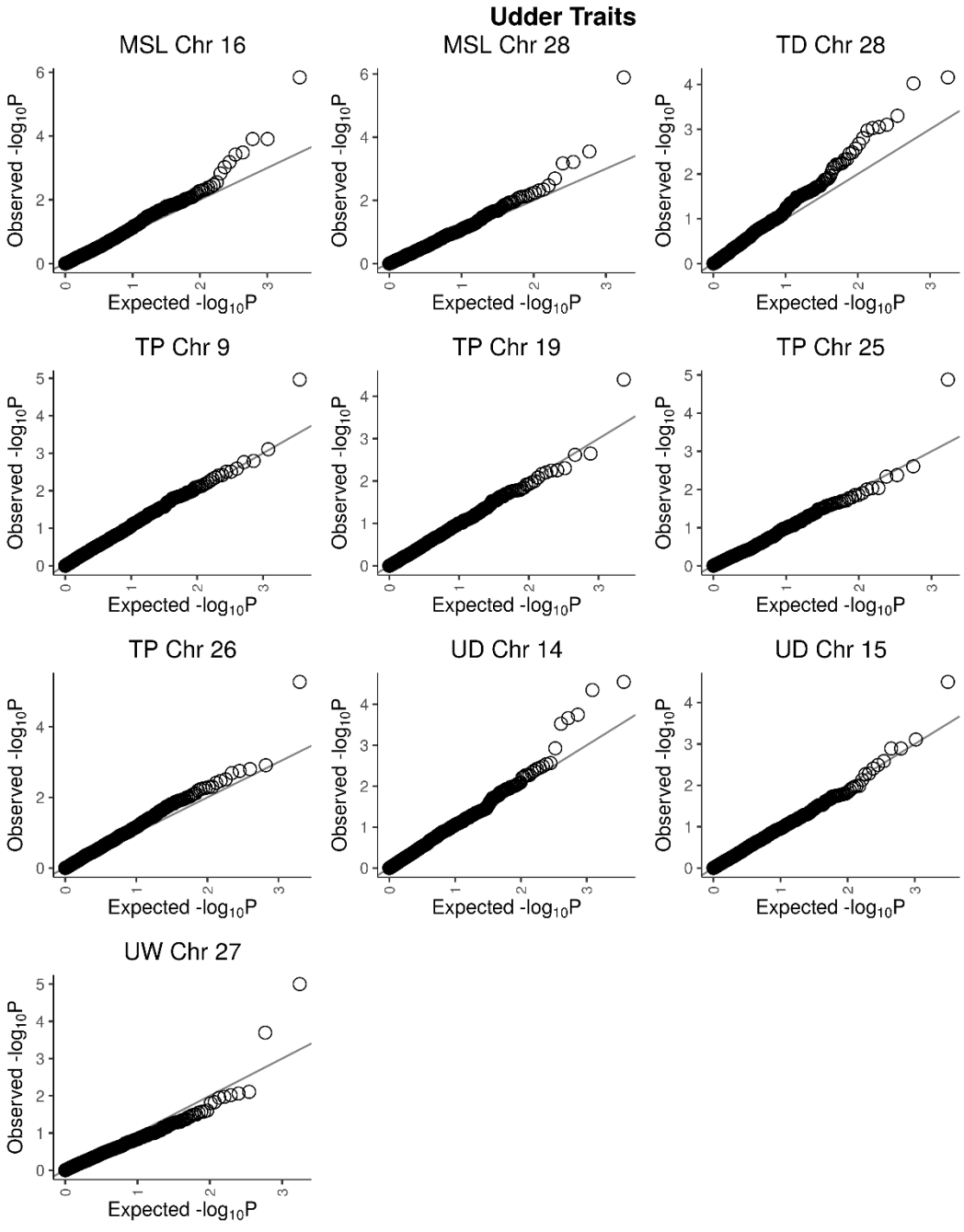
**Supplementary Figure 5**. Manhattan plots depicting negative $\log_{10}$ *P*-values (*y*-axis) of the associations at the chromosome-wide level between SNPs and body morphology traits plotted against the genomic location of each SNP marker (*x*-axis). Only chromosome hosting significant associations are shown (*q*-value < 0.05).The following abbreviations have been used, **ANG**, angularity; **BD**, body depth; **BQ**, bone quality; **CW**, chest width; **HT**, height; **RA**, rump angle; **RW**, rump width.



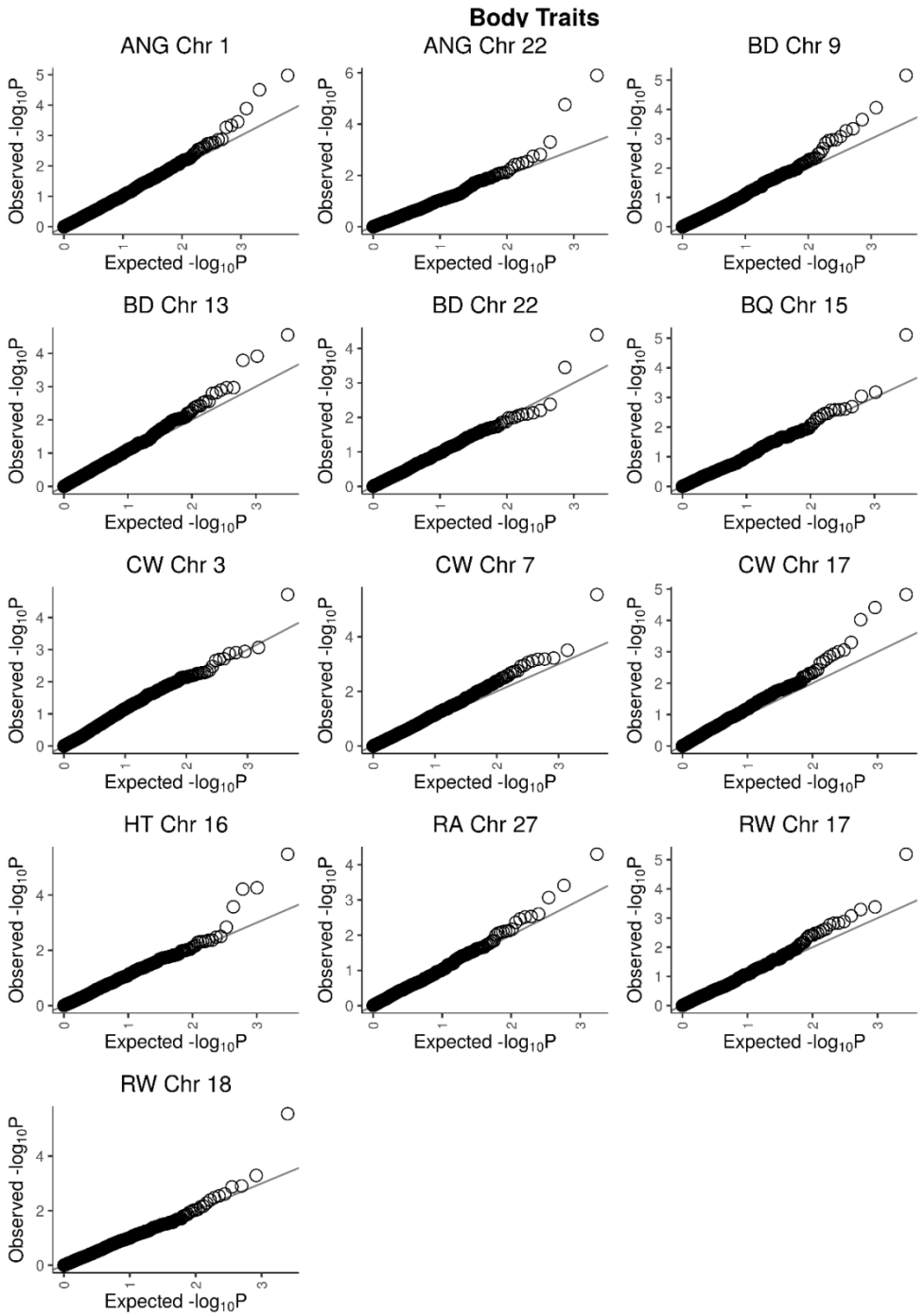
**Supplementary Figure 6.** Manhattan plots depicting negative $\log_{10}$ *P-values* (*y*-axis) of the associations at the chromosome-wide level between SNPs and leg traits plotted against the genomic location of each SNP marker (*x*-axis). Only chromosomes hosting significant associations are shown (*q*-value < 0.05). The following abbreviations have been used, **MOB**, mobility; **RLR**, rear legs rear view; **RLS**, rear legs side view.



**Supplementary Figure 7**. Quantile-Quantile plots showing the expected distribution of the -$\log_{10}$ *P*-values (*x*-axis) compared to the observed -$\log_{10}$ *P*-values (*y*-axis) in the GWAS performed at the chromosome wide level for udder traits.The mean lambda (λ) inflation factor was 1.060 ± 0.201. The following abbreviations have been used, **MSL**, medial suspensory ligament; **TD**, teat diameter; **TP**, teat placement; **UD**, udder depth; **UW**, udder width.



**Supplementary Figure 8**. Quantile-Quantile plots showing the expected distribution of the -$\log_{10}$ *P*-values (*x*-axis) compared to the observed -$\log_{10}$ *P*-values (*y*-axis) in the GWAS performed at the chromosome wide level for body traits. The mean lambda (λ) inflation factor was 1.090 ± 0.113. The following abbreviations have been used, **ANG**, angularity; **BD**, body depth; **BQ**, bone quality; **CW**, chest width; **HT**, height; **RA**, rump angle; **RW**, rump width.



**Supplementary Figure 9.** Quantile-Quantile plots showing the expected distribution of the -$\log_{10}$ *P*-values (*x*-axis) compared to the observed -$\log_{10}$ *P*-values (*y*-axis) in the GWAS performed at the chromosome wide level for leg traits goats. The mean lambda (λ) inflation factor was 1.098 ± 0.272. The following abbreviations have been used, **MOB**, mobility; **RLR**, rear legs rear view; **RLS**, rear legs side view.