Animal 19 (2025) 101466

Contents lists available at ScienceDirect

Animal
The international journal of animal biosciences

Detecting the footprint of selection on the genome of Girgentana goat, a popular ancient breed

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ARTICLE INFO

Article history:
Received 18 July 2024
Revised 10 February 2025
Accepted 10 February 2025
Available online 17 February 2025

Keywords:
Candidate genes
Haplotypes
Local breed
Selection
Single nucleotide polymorphism markers

ABSTRACT

Girgentana goats are an ancient breed with distinctive morphological, adaptive, and production traits, making this population an interesting model for studying the genetic architecture underlying these traits. These special features result from natural and human-mediated selection. In this study, we aimed to detect potential signatures of selection in the Girgentana genome by combining the following statistical methods: the integrated haplotype score (**iHS**), the standardised log-ratio of the integrated site-specific extended haplotype homozygosity test between pairs of populations (**Rsb**), the runs of homozygosity (**ROH**) islands and the population differentiation index ($\mathbf{F_{ST}}$). A composite dataset of 206 Girgentana and 334 animals from 13 goat populations across Northern and Southern Italy was analysed. All animals were genotyped using an Illumina Goat medium-density BeadChip. Multidimensional scaling and neighbour-joining analyses revealed a clear separation of the three major clades, coinciding with Girgentana, Northern, and Southern Italian goats. Twelve regions putatively under selection were detected using iHS and Rsb, whereas 16 hotspot regions were identified using F_{ST} and ROH. Notably, a candidate region on chromosome 01 was consistently identified in all four tests. This region, along with other candidate regions, includes several genes associated with adaptive immunity, reproduction, and body size traits. The Girgentana breed showed signals of ongoing selection in a region of chromosome 6 encompassing several milk quality genes, such as caseins (*CSN2*, *CSN1S2*, and *CSN3*). Our study provides a glimpse into the genomic regions harbouring genes that presumably affect the desired features of Girgentana. This highlights the importance of ancient breeds in providing essential genetic traits for adapting livestock to increasing climate change challenges.

Implications

The present investigation on Girgentana goats aimed to deepen our knowledge of its genomic structure. The results showed that Girgentana is one of the most isolated Italian goat breeds. We identified several selection signatures associated with body size, reproduction, immune resistance, and other environmental adaptation traits, emphasising unique genomic characteristics and distinctive selection signals of this breed. This study addresses the aspects of safeguarding local genetic resources and exploiting the related production systems.

Introduction

Local breeds are important reservoirs of genetic diversity and are adapted to a wide range of climatic conditions. Therefore, they are an attractive model for understanding the genetic basis of specific traits under selection (Bertolini et al., 2018; Onzima et al., 2018; Ben-Jemaa et al., 2020). In Italy, diverse climatic and topographical conditions, together with socioeconomic factors, have resulted in several goat breeds that are well-adapted to local

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https://doi.org/10.1016/j.animal.2025.101466
1751-7311/

environments (Cortellari et al., 2021; Dadousis et al., 2021), leading to a large reservoir of biodiversity.

Girgentana is an ancient autochthonous breed from Sicily Island (southern Italy) that is primarily raised under a semi-extensive production system. This breed is categorised as endangered (FAO Domestic Animal Diversity Information System, https://www.fao.org/dad-is/en/), and approximately, 1 500 animals are officially registered in the herdbook. The most impressive morphological feature of this breed is its large helical horns (Fig. 1). This breed is characterised by a defined genetic structure (Negrini et al., 2012) and is well-known for its disease resistance, adaptability, and milk production traits (Criscione et al., 2016; Mastrangelo et al., 2016).

Selection signatures are defined as a reduction, elimination, or change in genetic variation in genomic regions adjacent to causative variants in response to natural or artificial selective pressures (Qanbari and Simianer, 2014). These regions may contain genetic variants that could influence breed-specific traits such as morphology, production, and adaptation to different production systems and environments (Saravanan et al., 2020). Therefore, their identification can be conveniently used to locate genes exerting a selective advantage or disadvantage and therefore guide the rational management of livestock.

High-throughput genomic techniques have enabled the screening of large parts of the genome to detect signatures of selection (Sabeti et al., 2007). Therefore, several analytic methods have been proposed to detect genomic footprints, such as the standardised log-ratio of the integrated site-specific extended haplotype homozygosity (**EHH**) test between pairs of populations (**Rsb**) (Tang et al., 2007), the integrated haplotype score (**iHS**) (Voight et al., 2006), the population differentiation index ($\mathbf{F_{ST}}$) (Weir and Cockerham, 1984), and the runs of homozygosity islands (Gibson et al., 2006).

Studies using genome-wide single nucleotide polymorphisms (**SNPs**) in goat species have identified genomic regions under selection for different traits such as thermotolerance, body size and development, production, and reproduction traits (e.g. Wang et al., 2016; Brito et al., 2017; Bertolini et al., 2018; Guo et al., 2018; Peng et al., 2024). These findings suggest that selective sweeps are key evolutionary forces shaping phenotypic plasticity in livestock. This adaptability is especially important for species raised in harsh climates, such as goats, where phenotypic plasticity helps them respond to short-term environmental changes. Understanding the molecular bases of these adaptations is crucial for sustainable livestock production, conservation, and genetic improvement.

In this study, we performed, for the first time, a whole-genome scan for selection signatures in the Girgentana goat breed using multiple approaches. A comparative genome-wide analysis of Northern and Southern Italian goats allowed us to identify several candidate regions putatively under selection related to important economic-functional traits, that may provide the basis for appropriate selection and conservation plans for the breed.

Material and methods

Sampling, genotyping and quality control

Blood samples were collected from 184 Girgentana goats on different farms in Sicily (Southern Italy), an island in the Mediterranean Sea. The Illustra Blood Genomic Prep Mini Spin kit (GE Healthcare, Little Chalfont, UK) was used to extract genomic DNA. An Illumina Goat IGGC 65 K v2 BeadChip containing 59 727 SNPs (Illumina, San Diego, CA, USA) was used to genotype all animals. We combined these newly generated data with genotypes available from a previous study (Cortellari et al., 2021) including individuals belonging to 13 Italian breeds (five from Southern Italy and eight from Northern Italy) and 59 Girgentana animals. Prior to merging the data for analysis, PLINK ver. 1.9 software (Chang et al., 2015) was used to separately perform quality control for the Girgentana, Southern Italian, and Northern Italian breeds. A relatedness test was conducted between the individuals using PLINK ver. 1.9 software (Chang et al., 2015). The software calculates a relationship index called PIHAT, which reflects the extended haplotypes shared between individuals. One individual from any pair showing a PIHAT score ≥ 0.25 was removed from further analysis. The chromosomal coordinates of the markers were assigned to the ARS1 genome assembly (Assembly GCA_001704415.1). Markers assigned to unmapped contigs were filtered out, and SNPs located on autosomes were considered. Additionally, SNPs with call rates < 90%, minor allele frequencies < 1%, and individuals with > 10% missing genotypes were excluded. The filtered genotypes from each dataset (Girgentana, Southern Italian, and Northern Italian breeds) were merged, resulting in a final panel of 48 193 common SNPs genotyped in 540 individuals (Table 1).

Genetic diversity and population relationships

Girgentana were used to investigate the following genetic diversity indices: observed ($\mathbf{H_O}$) and expected ($\mathbf{H_E}$) heterozygosity, inbreeding coefficient ($\mathbf{F_{IS}}$), and average minor allele frequencies. All metrics were computed using PLINK software.

Population relationships among all goat breeds were investigated by performing multidimensional scaling analysis on pairwise identity-by-state distances implemented in PLINK. Moreover, a Neighbour-Joining tree based on allele-sharing distances was visualised using SplitsTree ver. 6.3.20 (Huson and Bryant, 2006).

Identification of selection signatures

The selection signatures were explored using four different approaches. We computed (i) the iHS statistic method within the Girgentana breed and (ii) the Rsb statistic for each of the two pairwise comparisons: Girgentana vs Northern Italy and Girgentana vs Southern Italy. Both the metrics were implemented using the *rehh* package in R (Gautier and Vitalis, 2012). FastPHASE software ver. 1.4 (Scheet and Stephens, 2006) was used to reconstruct the haplotypes from the genotyped SNPs. Because fastPHASE relies on haplotype clusters whose size should be set a priori, we used the toolkit implemented in *imputeqc* R package (Khvorykh and Khrunin, 2020) to estimate the optimal number of haplotype clusters (K) required for haplotype phasing. In the present study, K = 20 provided the best imputation quality because this value corresponded to the lowest imputation error rate for 5% of the masked data (Fig. S1) and was then used as the number of clusters in fastPHASE. Both EHH-based tests defined candidate regions as those containing at least three neighbouring SNPs exceeding the threshold $-\log10(P\text{-value}) = 3$ within non-overlapping 2-Mb sliding windows. We focused on clusters of neighbouring SNPs because they are more powerful to look for windows of consecutive SNPs that contain numerous extreme iHS scores rather than treating each SNP separately (Voight et al., 2006).

Genome window-based analysis using the average F_{ST} according to the method described by Weir and Cockerham (1984) was performed using VCFtools v. 0.1.12b (Danecek et al., 2011). A total of 4 936 windows of 1 Mb with steps of 500 kb were tested by computing the average F_{ST} based on the SNPs overlapping the window. The top 0.996 mean F_{ST} of the percentile distribution with at least four SNPs in a window was considered statistically significant (Bertolini et al., 2022).

Fig. 1. Specimens of Girgentana goats.

Table 1
Goat datasets: Population's full name (breed), acronymous (code), number of individuals after quality control and origin area.

Breed	Code	N	Group
Girgentana	GIR	206	–
Argentata dell'Etna	ARG	48	Southern
Derivata di Siria	DDS	32	
Maltese	MAL	16	
Messinese	MES	24	
Nicastrese	NIC	24	
Bionda dell'Adamello	BIO	24	Northern
Livio-Lariana	LIV	24	
Nera di Verzasca	NVE	19	
Orobica	ORO	23	
Roccaverano	RCC	28	
Valdostana	VAL	24	
Vallesana	VLS	24	
Val Passiria	VPS	24	

Abbreviations: N = number of individuals.

Finally, runs of homozygosity for the Girgentana breed were investigated using PLINK v1.9 software (Chang et al., 2015), applying the sliding-window approach. The parameters used to define an runs of homozygosity were set as reported by Cortellari et al. (2021), by changing the number of SNP per 1 000 kb from two to one. The top 0.999 SNPs in the percentile distribution of the homozygosity range were used to identify runs of homozygosity islands.

Gene annotation an enrichment analysis

Genomic coordinates for all the identified regions were checked for annotated genes in the *Capra hircus* genome assembly (ARS1) using BioMart tool of Ensembl (https://www.ensembl.org/info/data/biomart/index.html). Gene lists were examined for significant overrepresentation of genes with particular functional categories using the open-source database for annotation, visualisation, and integrated discovery (**DAVID**) version 2021 (https://david.ncifcrf.gov) (Sherman et al., 2022). The DAVID software uses thousands of annotation terms for several categories, such as Gene Ontology, Biological Process, Gene Ontology Molecular Function, and InterPro Domains, to examine gene lists for enriched processes and functions. An adjusted false discovery rate *P*-value < 0.1 was used as a criterion for the statistical significance of enrichment.

We used the *R* package Genomic Annotation in Livestock for positional candidate LOci (**GALLO**) (Fonseca et al., 2020), to search for quantitative trait loci and perform enrichment analysis. Regions 250 kb downstream and upstream were considered (Manca et al., 2020). Adjusted *P*-values were calculated based on Bonferroni correction (adjusted *P*-value < 0.05).

Results

Following quality control procedures, 540 individuals (Table 1) genotyped for 48 193 SNPs distributed over 29 autosomes were used for downstream analysis. After filtering for the Girgentana goat breed, 206 individuals were counted.

Genetic diversity and population relationships

Genetic diversity indices are presented in Table 2. Girgentana displayed moderate variability, with an observed heterozygosity (H_O) of 0.363, expected heterozygosity (H_E) of 0.371, F_{IS} of 0.020, and minor allele frequencies of 0.285.

Multidimensional scaling analysis showed a clear separation of the three clades coinciding with the Girgentana, Northern Italian, and Southern Italian breeds, based on the first two dimensions (Fig. 2a). More detailed information on the relationships and patterns of divergence was obtained by neighbour-joining based on allele-sharing distances (Fig. 2b), which confirmed the genetic isolation of the Girgentana breed from the other two groups.

Identification of selection signatures

We first performed an iHS analysis to detect the signatures of positive selection within Girgentana. iHS scores were computed for each SNP over the whole genome using 412 estimated Girgentana haplotypes per autosome. The results revealed three regions with extended homozygosity on *Capra hircus* chromosomes (CHI) 1, 5 and 6, in the Girgentana breed (Fig. 3a). These regions underwent a sudden drop in nucleotide diversity and showed clear selec-

Table 2
Genetic diversity indices for Girgentana goat breed. Observed (H_O) and expected (H_E) heterozygosity, inbreeding coefficient (F_{IS}) and average minor allele frequency (MAF).

Breed	$H_O \pm SD$	$H_E \pm SD$	$F_{IS} \pm SD$	MAF ± SD
Girgentana	0.363 ± 0.113	0.371 ± 0.130	0.020 ± 0.076	0.285 ± 0.135

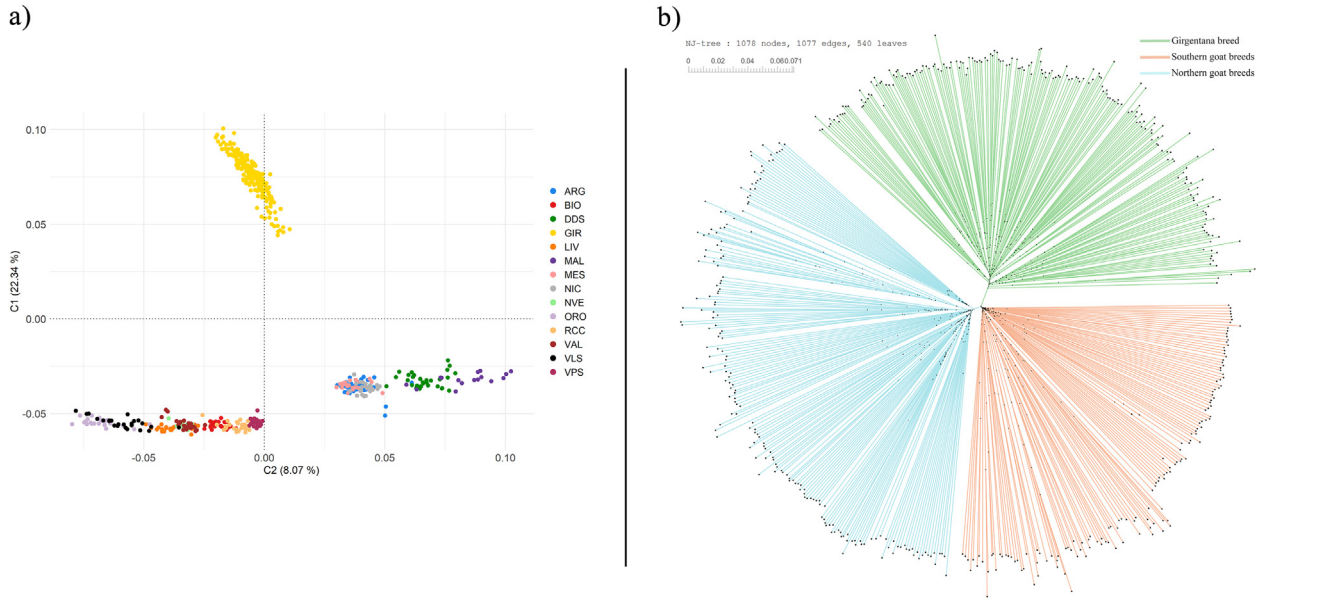

Fig. 2. Genetic relationship based on (a) the multidimensional scaling (MDS) analysis and (b) Neighbour-Joining tree based on Allele Sharing Distances for all the goat Italian breeds. For a full definition of breeds, see Table 1.

tion patterns, especially for CHI01 (110–112 Mb) (Fig. S2). Regions with the highest iHS for the Girgentana were located on CHI06 from 85.9 to 87 Mb and on chromosome 5 from 38.8 to 39.5 Mb. We identified 40 protein-coding genes that overlapped with these three regions (Table 3).

We subsequently investigated haplotype-extension patterns using the standardised log-ratio of the integrated site-specific EHH test between pairs of populations (Rsb). Given that we were primarily interested in identifying signatures of selection that were specific to the Girgentana breed, we focused on the comparison between Girgentana and Northern Italian breeds and Girgentana and Southern Italian breeds. In our study, extremely positive Rsb values indicated longer haplotypes in Girgentana, suggesting that selection occurred in this breed. In total, 10 candidate regions were identified in each of the two comparisons: Girgentana/Northern Italian breed (Fig. 3b) and Girgentana/Southern Italian breed (Fig. 3c). Among these, nine candidate regions resulting in underselection in Girgentana were common between the two comparisons. Chromosome 1 had the largest peak and number of statistically significant SNPs for both comparisons with more than 57% of the markers exceeding the significance threshold (Table 4). Moreover, the outlier SNPs within this candidate region, located between 103.5 and 107.8 Mb, have the highest Rsb values for both comparisons. The region with the second-highest proportion of outlier SNPs was CHI07 from 22 to 28 Mb, with more than 30% of the SNPs exceeding the significance threshold (Table 4).

Table 5 shows the overlapping genomic regions highlighted by the F_{ST} approach for both Girgentana vs Northern Italian breeds and Girgentana vs Southern Italian breeds. A total of ten top windows distributed across six chromosomes were detected, with an average F_{ST} ranging between 0.149 (CHI07) and 0.251 (CHI12).

Finally, we relied on the occurrence of high-frequency runs of homozygosity (runs of homozygosity islands) to assess the potential regions under selection in the Girgentana genome. This analysis led to the identification of 250 outlier SNPs grouped into six runs of homozygosity islands on CHI01, CHI12, CHI18, and CHI27, and included 136 annotated coding genes (Table 6).

Enrichment analysis

We found no significant enrichment of any biological processes in the list of genes retrieved using the iHS and runs of homozygosity approaches. By contrast, the 145 protein-coding genes overlapping with Rsb candidate regions (Table 4) witnessed, amongst others, a highly statistically significant process with the UP_KW_Molecular_Function, related to bacteriolytic enzyme activity (False discovery rate adjusted *P*-value = 3.98 $^{*}10^{-13}$, Supplementary Table S1). Similarly, DAVID analysis based on the F_{ST} results revealed an enriched cluster associated with the immune response (Immunoglobulin V-set domain and T cell receptor) (Supplementary Table S1). Thirteen quantitative trait locis linked to nine traits were found to overlap within the candidate genomic regions detected using the iHs, Rsb, F_{ST} and runs of homozygosity approaches (Supplementary Table S2). Among these, only two quantitative trait locis associated with teat number were significant (adjusted *P*-value < 0.05).

Congruence among selection signals

A single overlap in genomic regions that showed evidence of selection signatures identified by all four methods occurred on CHI01 (from 110 to 111 Mb). This region encompasses eight coding genes. Rsb, F_{ST}, and runs of homozygosity highlighted a short common region in CHI01 harbouring two genes (*VEPH1* and *PTX3*). Our results also highlighted several regions that were identified between two out of the four approaches used in the present study.

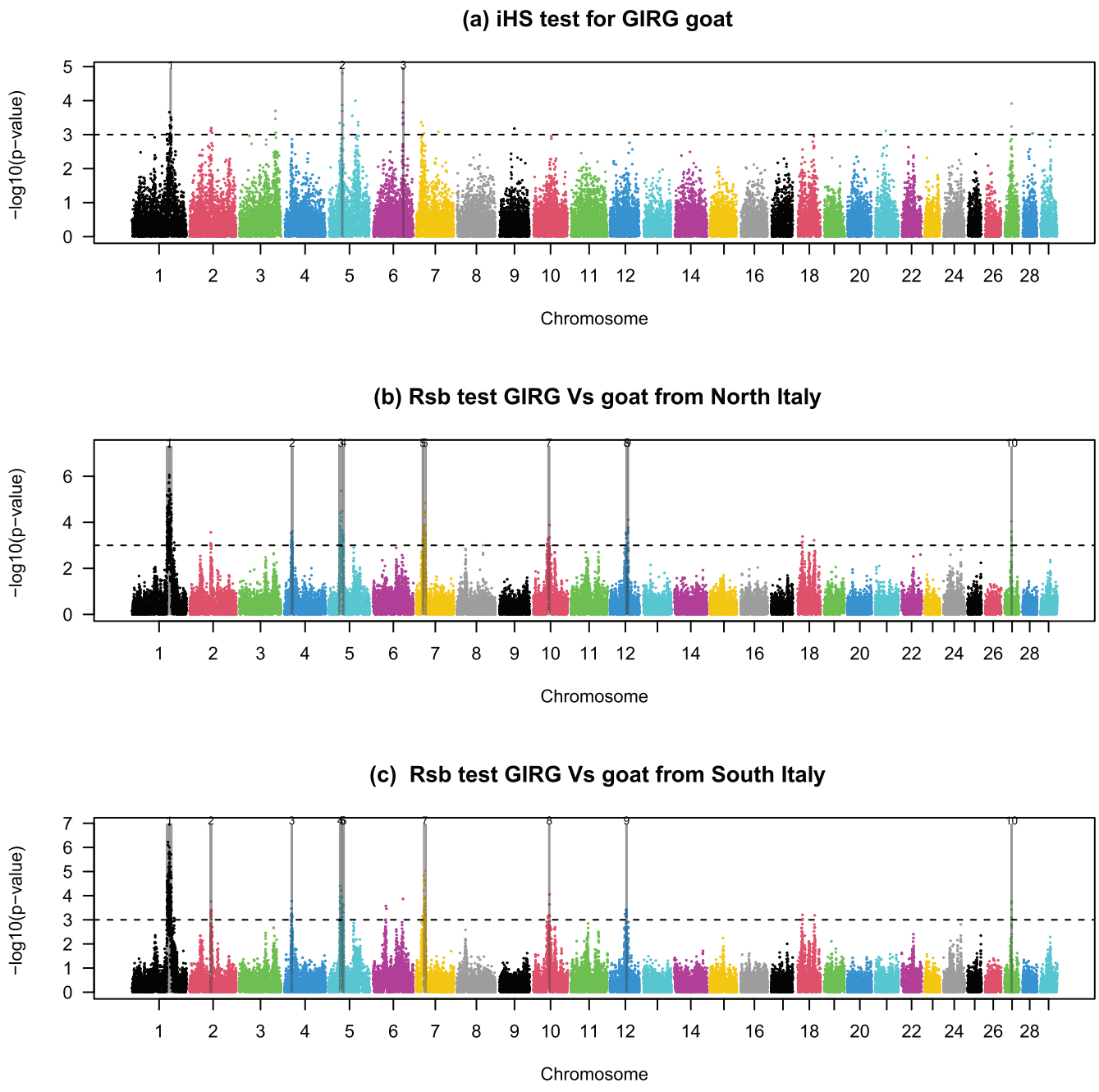

Fig. 3. Manhattan plot of the: (a) genome-wide integrated haplotype score (iHS) analysis for Girgentana goat breed; (b) Rsb test for Girgentana vs Northern Italy and (c) Rsb test for Girgentana vs Southern Italy. Horizontal dashed lines mark the significance threshold applied to detect the outlier SNPs–log10 (*P*-value) = 3. Abbreviations: GIRG = Girgentana; Rsb = standardised log-ratio of the integrated site-specific extended haplotype homozygosity (EHH) test between pairs of populations.

Table 3
Putative signatures of selection for iHS test in the Girgentana goat breed. The candidate regions have been identified among those containing at least three neighbouring SNPs exceeding the threshold –log10(*P*-value) = 3 within non-overlapping 2-Mb sliding windows. Each candidate region is described by its Start and End positions, the number of SNPs (nSNPs) and the percentage of SNPs exceeding the significance threshold (EXTR_MRK).

CHI	Start (bp)	End (bp)	nSNPs	EXTR_MRK	Genes
1	110 000 000	112 000 000	36	11.11	*CCNL1*[1], *LEKR1*[1], *ENSCHIG00000010147*[1], *ENSCHIG00000023809*[1], *TIPARP*[1], *SSR3*[1], *KCNAB1*[1], *ENSCHIG00000025482*[1], *ENSCHIG00000020039*[2], *GMPS*[2], *SLC33A1*[2], *C3orf33*[2], *PLCH1*[2]
5	38 000 000	40 000 000	39	7.69	*YAF2*[2], *GXYLT1*[2], *PDZRN4*[2], *ENSCHIG00000019720*[2], *CNTN1*[2], *MUC19*[2]
6	86 000 000	88 000 000	64	7.81	*CSN2, CSN1S2, ODAM, CSN3, CABS1, ENSCHIG00000025315, AMTN, AMBN, ENAM, JCHAIN, UTP3, RUFY3, GRSF1, MOB1B, DCK, SLC4A4, ENSCHIG00000016138, GC, NPFFR2, ENSCHIG00000011194, ADAMTS3,*

Abbreviations: CHI = *Capra hircus* chromosome; iHS = integrated haplotype score; nSNPs = number of single nucleotide polymorphisms.
[1] Genes identified by four approaches.
[2] Genes identified by at least two approaches.

Table 4
Overlapping genomic regions for Rsb test in the comparison between the Girgentana vs Northern and Girgentana vs Southern goat breeds. The candidate regions have been identified among those containing at least three neighbouring SNPs exceeding the threshold −log10(*P*-value) = 3 within non-overlapping 2-Mb sliding windows. Each candidate region is described by its Start and End positions, the number of SNPs (nSNPs) and the percentage of SNPs exceeding the significance threshold (EXTR_MRK).

CHI	Start (bp)	End (bp)	nSNPs	EXTR_MRK	Genes
1	100 000 000	114 000 000	275	57.10	*BCHE, SLITRK3*[2], *ENSCHIG00000016725*[2], *SI*[2], *ENSCHIG00000011051*[2], *ENSCHIG00000023820, OTOL1, SPTSSB, NMD3, ENSCHIG00000026689, ENSCHIG00000020415, ENSCHIG00000014679, PPM1L, ENSCHIG00000022304, ARL14, KPNA4, TRIM59, SMC4, IFT80*[2], *C3orf80*[2], *ENSCHIG00000021362*[2], *ENSCHIG00000009835*[2], *IL12A*[2], *ENSCHIG00000018805*[2], *SCHIP1*[2], *IQCJ*[2], *ENSCHIG00000014424*[2], *MFSD1*[2], *RARRES1*[2], *GFM1*[2], *LXN*[2], *MLF1*[2], *ENSCHIG00000011968*[2], *SHOX2*[2], *VEPH1*[2], *PTX3*[2], *CCNL1*[1], *LEKR1*[1], *ENSCHIG00000010147*[1], *ENSCHIG00000023809*[1], *TIPARP*[1], *SSR3*[1], *KCNAB1*[1], *ENSCHIG00000025482*[1], *ENSCHIG00000020039*[2], *GMPS*[2], *SLC33A1*[2], *C3orf33*[2], *ENSCHIG00000011194*[2], *PLCH1*[2], *MME, ENSCHIG00000017243, GPR149, DHX36, ARHGEF26*
4	22 000 000	24 000 000	47	19.15	*AKR1B1, SLC35BL, ENSCHIG00000017125, ENSCHIG00000025857, LRGUK, ENSCHIG00000024010, ENSCHIG00000012890, ENSCHIG00000018200, ENSCHIG00000001384, EXOC4, CHCHD3, PLXNA4*
5	32 000 000	36 000 000	70	31.43	*VDR, HDAC7, SLC48A1, RAPGEF3, ENSCHIG00000018045, RPAP3, ENSCHIG00000013454, PCED1B, AMIGO2, SLC38A4, SLC38A2, SLC38A1, ENSCHIG00000011733, SCAF11, ARID2, ANO6*[2], *ENSCHIG00000023172*[2], *DBX2*[2], *NELL2*[2], *TMEM117*
5	38 000 000	40 000 000	39	15.38	*YAF2*[2], *GXYLT1*[2], *PDZRN4*[2], *ENSCHIG00000019720*[2], *CNTN1*[2], *MUC19*[2]
5	42 000 000	44 000 000	46	13.04	*PTPRR, PTPRD, KCNMB4, CNOT2, MYRFL, RAB3IP, LRRC10, CCT2, FRS2, ENSCHIG00000020628, ENSCHIG00000020882, YEATS24, ENSCHIG00000027096, ENSCHIG00000024463, ENSCHIG00000022325, ENSCHIG00000006608, ENSCHIG00000010988, ENSCHIG00000004867, ENSCHIG00000022881, ENSCHIG00000020710, S-LZ, CPSF6*
7	22 000 000	28 000 000	110	31.82	*MEF2C, TMEM161B, ENSCHIG00000009148, ENSCHIG00000011671, CCNH*[2], *RASA1*[2], *ENSCHIG00000026992*[2], *ENSCHIG00000018614, EDIL3, HAPLN1, VACN, XRCC4, ENSCHIG00000010267, ENSCHIG00000012625, TMEM167A*
10	46 000 000	48 000 000	36	8.33	*WDR72, UNC13C*
12	46 000 000	48 000 000	40	17.50	*PCDH9, ENSCHIG00000004535*
27	20 000 000	22 000 000	36	11.11	*TNKS*[2], *ENSCHIG00000024143*[2], *PPP1R3B*[2], *ERI1*[2], *MFHAS1*[2], *ENSCHIG00000023645*[2], *CLDN23*[2], *PRAG1, LONRF1, TRMT9B, DLC1*

Abbreviations: Rsb = standardised log-ratio of the integrated site-specific extended haplotype homozygosity (EHH) test between pairs of populations; CHI = *Capra hircus* chromosome; SNP = single nucleotide polymorphisms; nSNPs = number of single nucleotide polymorphisms.
[1] Genes identified by four approaches.
[2] Genes identified by at least two approaches.

Table 5
The top overlapping genome windows regions for F_{ST} test in the comparison between the Girgentana vs Northern and Girgentana vs Southern goat breeds.

CHI	Start (bp)	End (bp)	nSNPs	mean_Fst	Gene
1	109 500 001	110 500 000	13	0.222	*VEPH1*[2], *PTX3*[2], *CCNL1*[1], *LEKR1*[1], *ENSCHIG00000010147*[1], *ENSCHIG00000023809*[1], *TIPARP*[1]
1	110 000 001	111 000 000	18	0.220	*CCNL1*[1], *LEKR1*[1], *ENSCHIG00000010147*[1], *ENSCHIG00000023809*[1], *TIPARP*[1], *SSR3*[1], *KCNAB1*[1], *ENSCHIG00000025482*[1], *ENSCHIG00000020039*[2]
5	34 500 001	35 500 000	19	0.171	*ANO6*[2], *ENSCHIG00000023172*[2], *DBX2*[2], *NELL2*[2]
7	23 500 001	24 500 000	14	0.149	*CCNH*[2], *RASA1*[2], *ENSCHIG00000026992*[2]
10	78 000 001	79 000 000	6	0.171	*ENSCHIG00000017339, ENSCHIG00000013389, ENSCHIG00000012600, ENSCHIG00000014547, ENSCHIG00000017647, ENSCHIG00000012575*
12	43 500 001	44 500 000	11	0.251	–
12	44 000 001	45 000 000	16	0.215	–
12	49 500 001	50 500 000	18	0.192	*ATP12A*[2], *RNF17*[2], *CENPJ*[2], *PARP4*[2], *MPHOSPH8*[2], *PSPC1*[2], *ZMYM5*[2]
18	13 000 001	14 000 000	14	0.193	*GSE1*[2], *GINS2*[2], *C16orf74*[2], *ENSCHIG00000001129*[2], *EMC8*[2], *ENSCHIG00000012976*[2], *IRF8*[2], *FOXF1*[2], *ENSCHIG00000017834*[2], *MTHFSD*[2], *FOXC2*[2], *FOXL1*[2]
18	20 500 001	21 500 000	20	0.193	*SIAH1, LONP2, ABCC1, ABCC12, PHKB, ENSCHIG00000010050, ITFG1*

Abbreviations: F_{ST} = population differentiation index; CHI = *Capra hircus* chromosome; nSNPs = number of single nucleotide polymorphisms.
[1] Genes identified by four approaches.
[2] Genes identified by at least two approaches.

These include two regions on CHI05 at position 38–40 Mb (jointly identified by iHS and Rsb; Tables 3 and 4) and at position 34.5–35.5 Mb (jointly identified by Rsb and F_{ST}; Tables 4 and 5), CHI07 from 23.5 to 24.5 Mb (jointly identified by Rsb and F_{ST}; Tables 4 and 5), CHI12 from 49.5 to 50.5 Mb and CHI18 from 13 to 14 Mb (jointly identified by F_{ST} and runs of homozygosity; Tables 5 and 6), and CHI27 at position 20–21 Mb (jointly identified by Rsb and runs of homozygosity; Tables 4 and 6).

Discussion

Goats were among the first species to be domesticated as livestock (Boyazoglu et al., 2005). Following human migration and colonisation, domesticated goats progressively showed several features distinct from their wild ancestors, such as a decline in body size, a more docile temperament, and a wide variety of coat colours (Dong et al., 2015). Furthermore, natural selection in various environments and human-mediated selection for production traits, such as milk, meat, wool, or leather, have led to a diverse variety of populations (Galal, 2005). Understanding how selection has shaped the genomic diversity of ancient breeds may help understand the traits that have been targeted over time, thereby providing a practical framework to guide genetic improvement practices.

Genetic diversity and population relationships

We first assessed the genetic variation in the Girgentana breed. Heterozygosity estimates were comparable to those observed in other Italian goat breeds (Nicoloso et al., 2015). We used the F_{IS} to measure the extent of non-random mating (inbreeding) within the Girgentana breed. The values show high variability which is reflected in the wide dispersion of individual inbreeding values.

Table 6
Runs of homozygosity islands (ROH) identified in the Girgentana goat breed. The top 0.999 SNPs of the percentile distribution were considered to identify the ROH islands.

CHI	Start (bp)	End (bp)	nSNPs	Genes
1	101 323 092	103 365 326	38	*SLITRK3*[2], *ENSCHIG00000016725*[2], *SI*[2], *ENSCHIG00000011051*[2]
1	106 720 153	110 964 225	81	*IFT80*[2], *C3orf80*[2], *ENSCHIG00000021362*[2], *ENSCHIG00000009835*[2], *IL12A*[2], *ENSCHIG00000018805*[2], *SCHIP1*[2], *IQCJ*[2], *ENSCHIG00000014424*[2], *MFSD1*[2], *RARRES1*[2], *GFM1*[2], *LXN*[2], *MLF1*[2], *ENSCHIG00000011968*[2], *SHOX2*[2], *VEPH1*[2], *PTX3*[2], *CCNL1*[1], *LEKR1*[1], *ENSCHIG00000015405*[1], *ENSCHIG00000010147*[1], *TIPARP*[1], *SSR3*[1], *KCNAB1*[1], *ENSCHIG00000025482*[1]
12	49 190 233	51 519 415	47	*ATP12A*[2], *RNF17*[2], *CENPJ*[2], *PARP4*[2], *MPHOSPH8*[2], *PSPC1*[2], *ZMYM5*[2], *ZMYM2, GJA3, GJB2, GJB6, CRYL1, IFG88, IL17D, EEF1AKMT1, XP04, LATS2, ENSCHIG00000020953, SAP18, ENSCHIG00000017508, SKA3, TRNAE-UUC, MRPL57, ZDHHC20, ENSCHIG00000013087, MICU2, FGF9*
18	12 989 973	14 367 383	22	*GSE1*[2], *GINS2*[2], *C16orf74*[2], *ENSCHIG00000011295*[2], *EMC8*[2], *ENSCHIG00000012976*[2], *IRF8*[2], *FOXF1*[2], *MTHFSD*[2], *FOXC2*[2], *FOXL1*[2], *ENSCHIG00000022152, FBX031*
18	35 967 886	36 862 118	18	*CBFB, B3GNT9, TRADD, FBXL8, HSF4, NOL3, KIAA0895L, EXOC3L1, E2F4, ELMO3, ENSCHIG00000019793, LRRC29, TMEM208, FHOD1, SLC9A5, PLEKHG4, KCTD19, LRRC36, TPPP3, ZDHHC1, HSD11B2, ATP6V0D1, FAM65A, AGRP, CTCF, CARMIL2, ACD, PARD6A, ENKD1, GFOD2, RANBP10, TSNAXIP1, CENPT, THAP11, ENSCHIG00000024970, NUTF2, EDC4, NRN1L, PSKH1, PSMB10, LCAT, SLC12A4, DPEP3, DPEP2, DDX28, DUS2, NFATC3*
27	17 451 106	20 969 806	44	*WRN, PURG, ENSCHIG00000008011, TEX15, PPP2CB, UBXN8, GSR, GTF2E2, SMIM18, RBPM5, DCTN6, MBOAT4, LEPROTL1, SARAF, ENSCHIG00000026850, DUSP4, ENSCHIG00000025550, TNKS*[2], *ENSCHIG00000024143*[2], *PPP1R3B*[2], *ERI1*[2], *MFHAS1*[2], *ENSCHIG00000023645*[2], *CLDN23*[2]

Abbreviations: CHI = *Capra hircus* chromosome; SNP = single nucleotide polymorphisms; nSNPs = number of single nucleotide polymorphisms.
[1] Genes identified by four approaches.
[2] Genes identified by at least two approaches.

A similar finding was reported by Cortellari et al. (2021). This is most likely attributable to differences in inbreeding management practices between flocks.

The results from the genetic relationships corroborate previous reports, suggesting that Girgentana is one of the most isolated Italian goat breeds, with the highest degree of differentiation from its Italian counterparts (Negrini et al., 2012; Nicoloso et al., 2015; Cortellari et al., 2021). The presence of screw-shaped horns similar to those of the wild markhor and the highly divergent mitochondrial DNA haplotypes (Sardina et al., 2006) suggest an Asian origin and a direct descent from *C. falconeri* (Ajmone-Marsan et al., 2014). This, together with the distinctive phenotypic traits that contributed to preserving the breed from indiscriminate crossbreeding, likely led to this genomic divergence.

Investigating the existence of fixed and ongoing selective sweeps in Girgentana genome

In total, 12 genomic regions that were potentially under selection were identified using two complementary EHH-derived statistics. Most of these (nine candidate regions) were detected using the Rsb test, indicating that the largest number of selective sweeps in Girgentana had already reached fixation. Two of the three other regions identified using the iHS test were also detected using the Rsb statistic. In contrast, the third region, a 2-Mb long region located on CHI06, was only detected by iHS, suggesting the presence of several intermediate-frequency variants within this region which are under ongoing selection. Notably, this region has previously been identified as being potentially under selection in different goat breeds (Bertolini et al., 2018; Kumar et al., 2018). The most significant variants within the candidate region on CHI06 were scattered over a ~1-Mb interval, particularly between 85 946 764 bp and 86 946 899 bp. Importantly, this interval encompasses a group of genes associated with milk production and composition traits, such as *CSN2, CSN1S2* and *CSN3* for casein content (Caroli et al., 2006) and other genes, including *AMBN, AMTN, ENAM, MOB1B, DCK, and SLC4A4*. The latter has been shown to be associated with milk production traits in Alpine and Saanen dairy goats (Massender et al., 2023). Finally, three genes (*GC, NPFFR2*, and *ADAMTS3*) within this selection signature showed highly significant SNPs affecting milk yield in Holstein cattle (Jiang et al., 2019). These findings suggest that genes associated with milk production traits in CHI06 are mainly targeted by ongoing selection in the Girgentana breed.

Congruence among selection signals

In the present study, we used various tests to identify candidate genomic regions that could explain the divergent selection between Girgentana and other Italian goat breeds. These tests allowed the detection of different signals across different timescales. For example, runs of homozygosity islands typically reflect recent selective sweeps within populations, whereas outlier intervals identified by EHH-based approaches such as iHs tend to identify regions where selection occurs further back in evolutionary time (Bertolini et al., 2024). This may explain the low degree of overlap between approaches.

Because the four tests can detect various patterns of selection, even if several regions are only detected by one test, they can still be real selection targets. Additionally, the use of multiple tests provides a complete view of the selection signals for a given breed (Saravanan et al., 2020). Simultaneous detection of a genomic region using multiple approaches enhances its potential importance (Ben-Jemaa et al., 2020). Similarly, other studies reported that combining several methods can significantly increase the ability to detect true selection signals (Qanbari and Simianer, 2014; Vatsiou et al., 2016).

In this study, outlier SNPs were identified based on cut-off values derived from a posteriori empirical distribution rather than a priori theoretical distributions. While applying False discovery rate or Bonferroni corrections to outlier SNPs identified through empirical distributions is a commonly used approach, congruence among different methods can also be a valid alternative to get valuable insights, helping to distinguish false positives from true signals of selection (Fustier et al., 2017).

We found a 1-Mb region (CHI01 from 110 to 111 Mb) that overlapped among the four approaches. Interestingly, this region showed a sudden decrease in nucleotide diversity (Fig. S2). This region contains several genes, many of which (*CCNL1, TIPARP, SSR3,* and *KCNAB1*) are common with selection signatures reported for native pig breeds and are mainly associated with molecular binding in biological regulation and metabolic processes (Szmatoła et al., 2020). *LEKR1* and *CCNL1* are associated with reduced birth weight in humans (Andersson et al., 2011) and were found within selection signatures in Angus, a breed that has recently been selected to reduce birth weight to alleviate dystocia (Ramey et al., 2013). The Girgentana census has declined by nearly 90% in the past 40 years, pushing this breed towards extinction, partly because of a sharp decline in fresh goat milk consumption

(Mastrangelo et al., 2016). This demographic decline has led to an increase in inbreeding, probably leading to a significant reduction in the birth weight and height of withers. Therefore, the presence of body size-related genes within the genomic regions that were shown to be under selection could be expected. In this regard, the *SHOX2* (short stature homeobox 2) (identified by Rsb and runs of homozygosity) and the *VEPH1* (Ventricular Zone Expressed PH Domain Containing 1) (identified by Rsb, F_{ST}, and runs of homozygosity approaches) genes (Tables 4, 5, and 6) are involved in regulating growth and overall body size in mammals (Zhang et al., 2018; Zhang et al., 2021).

Two candidate regions detected by the runs of homozygosity islands overlapped with the candidate genomic regions from the F_{ST} analysis. These include CHI18 (13–14 Mb) and CHI12 (49 51 Mb). Notably, the latter was close to a candidate region detected using the Rsb test (CHI12, from 46 to 48 Mb). The runs of homozygosity island on CHI12 identified in our study coincided with the selection signals detected in Italian Garfagnina (Dadousis et al., 2021), a mixture of Italian, Spanish, and French goat breeds (Serranito et al., 2021) and Barki goats (Kim et al., 2016; Sallam et al., 2023). The presence of a common runs of homozygosity island among geographically distant breeds suggests a shared evolutionary response to environmental challenges. runs of homozygosity islands have been extensively studied in the goat genome and candidate genes associated with production traits, immune responses, and environmental adaptation (e.g. Bertolini et al., 2018; Cortellari et al., 2021; Mastrangelo et al., 2021; Signer-Hasler et al., 2022).

Biological function of the genes within regions identified as putatively being under selection

Local breeds, such as Girgentana goats, have adapted to various environments over time and have developed adaptive characteristics that increase their fitness in harsh environments or resistance to diseases (Kim et al., 2016). Consistently, several genes found within our candidate regions were part of an immune response that provided adaptability to multiple stressors in the Girgentana environment. In addition to a significant overrepresentation of genes related to bacteriolytic enzyme activity and the Immunoglobulin V-set domain (found in immunoglobulin light and heavy chains), other immunity-related genes located within our candidate regions were identified. For instance, the three genes, *IL12A, GFM1,* and *PTX3,* located in the relevant candidate region on CHI01, play roles in innate and adaptive immunity (Trinchieri, 1998; Camozzi et al., 2006; O'Gorman et al., 2009), whereas a common region jointly identified by F_{ST} and runs of homozygosity on CHI18 spanned *IRF8,* a gene linked to the immune response (Ben-Jemaa et al., 2020). In CHI05, the region identified using the two EHH-derived statistics (Tables 3 and 4) overlapped with two genes (*YAF2* and *GXYLT*) associated with paratuberculosis resistance in cattle (Mwacharo et al., 2019). These two genes have been previously reported to be located within the runs of homozygosity islands in Sicilian goats (Mastrangelo et al., 2021). The presence of several annotated genes involved in host defence and immune response (*IL17D*) and in the local adaptation of small ruminants (*ATP12A, CENPJ, PARP4, PSPC1, ZMYM5, PSPC1, and GJB2*) (Chessari et al., 2024) within the runs of homozygosity island on CHI12 points towards an adaptive role of this region in the goat genome.

Notably, temperature appears to have played a central role in the adaptation processes of goat breeds (Bertolini et al., 2018). Here, we identified *RASA1* (a candidate region of CHI07) as a regulator of blood and lymphatic vessel growth in adult mice and humans. This gene was surrounded by the two most significant SNPs in the Rsb test, which were identified as outlier markers in F_{ST} analysis. *RASA1* induced-deficiency results in lymphatic vessel disorders characterised by hyperplasia and leakage (Lapinski et al., 2012), which can affect the vasodilation and dissipation of excess body heat through the skin (de Oliveira et al., 2024). The *RASA1* gene was also found within the signals of selection linked to thermal stress in cattle (Freitas et al., 2021). Furthermore, a genome-wide association study revealed that several SNPs within this gene had the largest effect on body temperature variation in beef cattle during climatic stress (Howard et al., 2014). We identified several other genes involved in various aspects of environmental adaptation in livestock, including *TNKS* (Yurchenko et al., 2018), *CLDN23* (Zhang et al., 2022), *HSF4* (Archana et al., 2017), and *PCDH9* (Serranito et al., 2021). Among the candidate genes underlying the outlier windows, several are associated with reproductive functions such as *IFT80, MLF1* and *GPR149* located within the candidate region on CHI01 (Edson et al., 2010; Ortega et al., 2022; Gonçalves et al., 2023), *TSN* which overlaps with the candidate region on CHI02 (Serrano et al., 2021), *AKR1B1* (Yang et al., 2016), *LRGUK* (Yuan et al., 2022), *EXOC4* (He et al., 2021) which overlaps with the candidate region on CHI04, and *ABCC1* on CHI18 (La et al., 2019). The different typologies of genes identified in these selective sweeps suggest that both natural and artificial selection contributed to the modelling of the Girgentana goat genome.

Conclusions

The results from our various tests corroborated previous reports suggesting that the Girgentana breed retains distinctive genetic characteristics of Italian caprine heritage. The breeding scheme and conservation programme currently applied to Girgentana are aimed at preserving milk production aptitude, local adaptation, and morphological traits. This was partially reflected in our results, which, in line with the breeding history of this popular local goat, allowed the identification of several putative regions encompassing many genes that play key roles in these traits. Maintaining these traits is fundamental to preserving this reservoir of genetic diversity and maximising the ability of this traditional livestock system to adapt to changing environments. This study did not identify the genes involved in horn patterning, likely because of the relatively low coverage of the Goat medium-density BeadChip. Clearly, increasing SNP density would help identify additional candidate regions.

Supplementary material

Supplementary Material for this article (https://doi.org/10.1016/j.animal.2025.101466) can be found at the foot of the online page, in the Appendix section.

Ethics approval

Blood samples were collected in compliance with the European rules [Council Regulation (EC) No. 1/2005 and Council Regulation (EC) No. 1099/2009] during routine health controls by the public veterinary service. Moreover, the animal study protocol was approved by the Bioethics Committee of the University of Palermo: protocol code UNPA-CLE–98597.

Data and model availability statement

None of the data were deposited in an official repository. Information can be made available from the authors upon request.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author(s) did not use any AI and AI-assisted technologies.

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Declaration of interest

None.

Acknowledgements

None.

Financial support statement

This research was financed by Co.Ri.A.L, Conservazione Risorse Animali Locali. PSR Sicilia 14/20–Operazione 10.2b "Conservazione delle risorse genetiche animali in agricoltura". Project number IRIS PRJ-0717, CUP G72C21000580009, and by A.R.C.A.S. "Azioni per il recupero dei Caratteri Autoctoni in Sicilia" PSR Sicilia 14/20–Operazione 10.2b "Conservazione delle risorse genetiche animali in agricoltura", CUP G79J21003850009.

References

Ajmone-Marsan, P., Colli, L., Han, J.L., Achilli, A., Lancioni, H., Joost, S., Crepaldi, P., Pilla, F., Stella, A., Taberlet, P., Boettcher, P., Negrini, R., Lenstra, J.A., 2014. The characterization of goat genetic diversity: towards a genomic approach. Small Ruminant Research 121, 58–72.

Andersson, E.A., Harder, M.N., Pilgaard, K., Pisinger, C., Stančáková, A., Kuusisto, J., Grarup, N., Faerch, K., Poulsen, P., Witte, D.R., Jorgensen, T., Vaag, A., Laakso, M., Pedersen, O., Hansen, T., 2011. The birth weight lowering C-allele of rs900400 near LEKR1 and CCNL1 associates with elevated insulin release following an oral glucose challenge. PLoS One 6, e27096.

Archana, P.R., Aleena, J., Pragna, P., Vidya, M.K., Abdul Niyas, P.A., Bagath, M., Krishnan, G., Manimaran, A., Beena, V., Kurien, E.K., Sejian, V., Bhatta, R., 2017. Role of heat shock proteins in livestock adaptation to heat stress. Journal of Dairy, Veterinary & Animal Research 5, 13–19.

Ben-Jemaa, S., Mastrangelo, S., Lee, S.H., Lee, J.H., Boussaha, M., 2020. Genome-wide scan for selection signatures reveals novel insights into the adaptive capacity in local North African cattle. Scientific Reports 10, 19466.

Bertolini, F., Servin, B., Talenti, A., Rochat, E., Kim, E.S., Oget, C., Palhiere, I., Crisa, A., Catillo, G., Steri, R., Amills, M., Colli, L., Marras, G., Milanesi, M., Nicolazzi, E., Rosen, B.D., Van Tassell, C.P., Guldbrandtsen, B., Sonstegard, T.S., Tosser-Klopp, G., Stella, A., Rothschild, M.F., Joost, S., Crepaldi, P., AdaptMap, C., 2018. Signatures of selection and environmental adaptation across the goat genome post-domestication. Genetics Selection Evolution 50, 1–24.

Bertolini, F., Moscatelli, G., Schiavo, G., Bovo, S., Ribani, A., Ballan, M., Bonacini, M., Prandi, M., Dall'Olio, S., Fontanesi, L., 2022. Signatures of selection are present in the genome of two close autochthonous cattle breeds raised in the North of Italy and mainly distinguished for their coat colours. Journal of Animal Breeding and Genetics 139, 307–319.

Bertolini, F., Schiavo, G., Bovo, S., Ribani, A., Dall'Olio, S., Zambonelli, P., Gallo, M., Fontanesi, L., 2024. Signatures of selection analyses reveal genomic differences among three heavy pig breeds that constitute the genetic backbone of a dry-cured ham production system. Animal 18, 101335.

Boyazoglu, J., Hatziminaoglou, I., Morand-Fehr, P., 2005. The role of the goat in society: past, present and perspectives for the future. Small Ruminant Research 60, 13–23.

Brito, L.F., Kijas, J.W., Ventura, R.V., Sargolzaei, M., Porto-Neto, L.R., Canovas, A., Feng, Z., Jafarikia, M., Schenkel, F.S., 2017. Genetic diversity and signatures of selection in various goat breeds revealed by genome-wide SNP markers. BMC Genomics 18, 229–249.

Camozzi, M., Rusnati, M., Bugatti, A., Bottazzi, B., Mantovani, A., Bastone, A., Inforzato, A., Vincenti, S., Bracci, L., Mastroianni, D., Presta, M., 2006. Identification of an antiangiogenic FGF2-binding site in the N terminus of the soluble pattern recognition receptor PTX3. The Journal of Biological Chemistry 281, 22605–22613.

Caroli, A., Chiatti, F., Chessa, S., Rignanese, D., Bolla, P., Pagnacco, G., 2006. Focusing on the goat casein complex. Journal of Dairy Science 89, 3178–3187.

Chang, C.C., Chow, C.C., Tellier, L.C., Vattikuti, S., Purcell, S.M., Lee, J.J., 2015. Second-generation PLINK: rising to the challenge of larger and richer datasets. GigaScience 4, 1–16.

Chessari, G., Criscione, A., Marletta, D., Crepaldi, P., Portolano, B., Manunza, A., Cesarani, A., Biscarini, F., Mastrangelo, S., 2024. Characterization of heterozygosity-rich regions in Italian and worldwide goat breeds. Scientific Reports 14, 3.

Cortellari, M., Bionda, A., Negro, A., Frattini, S., Mastrangelo, S., Somenzi, E., Lasagna, E., Sarti, F.M., Ciani, E., Ciampolini, R., Marletta, D., Liotta, L., Ajmone Marsan, P., Pilla, F., Colli, L., Talenti, A., Crepaldi, P., 2021. Runs of homozygosity in the Italian goat breeds: impact of management practices in low-input systems. Genetics Selection Evolution 53, 1–11.

Criscione, A., Bordonaro, S., Moltisanti, V., Marletta, D., 2016. Differentiation of South Italian goat breeds in the focus of biodiversity conservation. Small Ruminant Research 145, 12–19.

Dadousis, C., Cecchi, F., Ablondi, M., Fabbri, M.C., Stella, A., Bozzi, R., 2021. Keep Garfagnina alive. an integrated study on patterns of homozygosity, genomic inbreeding, admixture and breed traceability of the Italian Garfagnina goat breed. PLoS One 16, e0232436.

Danecek, P., Auton, A., Abecasis, G., Albers, C.A., Banks, E., DePristo, M.A., Handsaker, R.E., Lunter, G., Marth, G.T., Sherry, S.T., McVean, G., Durbin, R., Genomes Project Analysis, G., 2011. The variant call format and VCFtools. Bioinformatics 27, 2156–2158.

de Oliveira, L.F., Veroneze, R., Sousa, K.R.S., Mulim, H.A., Araujo, A.C., Huang, Y., Johnson, J.S., Brito, L.F., 2024. Genomic regions, candidate genes, and pleiotropic variants associated with physiological and anatomical indicators of heat stress response in lactating sows. BMC Genomics 25, 467.

Dong, Y., Zhang, X., Xie, M., Arefnezhad, B., Wang, Z., Wang, W., Feng, S., Huang, G., Guan, R., Shen, W., Bunch, R., McCulloch, R., Li, Q., Li, B., Zhang, G., Xu, X., Kijas, J. W., Salekdeh, G.H., Wang, W., Jiang, Y., 2015. Reference genome of wild goat (capra aegagrus) and sequencing of goat breeds provide insight into genic basis of goat domestication. BMC Genomics 16, 431–442.

Edson, M.A., Lin, Y.N., Matzuk, M.M., 2010. Deletion of the novel oocyte-enriched gene, Gpr149, leads to increased fertility in mice. Endocrinology 151, 358–368.

Fonseca, P.A.S., Suarez-Vega, A., Marras, G., Canovas, A., 2020. GALLO: An R package for genomic annotation and integration of multiple data sources in livestock for positional candidate loci. GigaScience 9, 1–9.

Freitas, P.H.F., Wang, Y., Yan, P., Oliveira, H.R., Schenkel, F.S., Zhang, Y., Xu, Q., Brito, L.F., 2021. Genetic diversity and signatures of selection for thermal stress in cattle and other two bos species adapted to divergent climatic conditions. Frontiers in Genetics 12, 604823.

Fustier, M.A., Brandenburg, J.T., Boitard, S., Lapeyronnie, J., Eguiarte, L.E., Vigouroux, Y., Manicacci, D., Tenaillon, M.I., 2017. Signatures of local adaptation in lowland and highland teosintes from whole-genome sequencing of pooled samples. Molecular Ecology 26, 2738–2756.

Galal, S., 2005. Biodiversity in goats. Small Ruminant Research 60, 75–81.

Gautier, M., Vitalis, R., 2012. rehh: an R package to detect footprints of selection in genome-wide SNP data from haplotype structure. Bioinformatics 28, 1176–1177.

Gibson, J., Morton, N.E., Collins, A., 2006. Extended tracts of homozygosity in outbred human populations. Human Molecular Genetics 15, 789–795.
Gonçalves, J.D., Ferraz, J.B.S., Meirelles, F.V., Nociti, R.P., Oliveira, M.E.F., 2023. An exploratory data analysis from ovine and bovine RNA-seq identifies pathways and key genes related to cervical dilatation. Animals (basel) 13, 1–18.
Guo, J., Tao, H., Li, P., Li, L., Zhong, T., Wang, L., Ma, J., Chen, X., Song, T., Zhang, H., 2018. Whole-genome sequencing reveals selection signatures associated with important traits in six goat breeds. Scientific Reports 8, 10405.
He, Y., Zhou, X., Zheng, R., Jiang, Y., Yao, Z., Wang, X., Zhang, Z., Zhang, H., Li, J., Yuan, X., 2021. The association of an SNP in the EXOC4 gene and reproductive traits suggests its use as a breeding marker in pigs. Animals (basel) 11, 1–13.
Howard, J.T., Kachman, S.D., Snelling, W.M., Pollak, E.J., Ciobanu, D.C., Kuehn, L.A., Spangler, M.L., 2014. Beef cattle body temperature during climatic stress: a genome-wide association study. International Journal of Biometeorology 58, 1665–1672.
Huson, D.H., Bryant, D., 2006. Application of phylogenetic networks in evolutionary studies. Molecular Biology and Evolution 23, 254–267.
Jiang, J., Ma, L., Prakapenka, D., VanRaden, P.M., Cole, J.B., Da, Y., 2019. A large-scale genome-wide association study in U.S. Holstein cattle. Frontiers in Genetics 10, 412.
Khvorykh, G.V., Khrunin, A.V., 2020. imputeqc: an R package for assessing imputation quality of genotypes and optimizing imputation parameters. BMC Bioinformatics 21, 304–318.
Kim, E.S., Elbeltagy, A.R., Aboul-Naga, A.M., Rischkowsky, B., Sayre, B., Mwacharo, J. M., Rothschild, M.F., 2016. Multiple genomic signatures of selection in goats and sheep indigenous to a hot arid environment. Heredity 116, 255–264.
Kumar, C., Song, S., Dewani, P., Kumar, M., Parkash, O., Ma, Y., Malhi, K.K., Yang, N., Mwacharo, J.M., He, X., Jiang, L., 2018. Population structure, genetic diversity and selection signatures within seven indigenous Pakistani goat populations. Animal Genetics 49, 592–604.
La, Y., Zhang, X., Li, F., Zhang, D., Li, C., Mo, F., Wang, W., 2019. Molecular characterization and expression of SPP1, LAP3 and LCORL and their association with growth traits in sheep. Genes (Basel) 10, 616.
Lapinski, P.E., Kwon, S., Lubeck, B.A., Wilkinson, J.E., Srinivasan, R.S., Sevick-Muraca, E., King, P.D., 2012. RASA1 maintains the lymphatic vasculature in a quiescent functional state in mice. The Journal of Clinical Investigation 122, 733–747.
Manca, E., Cesarani, A., Gaspa, G., Sorbolini, S., Macciotta, N.P.P., Dimauro, C., 2020. Use of the multivariate discriminant analysis for genome-wide association studies in cattle. Animals (basel) 10, 1–15.
Massender, E., Oliveira, H.R., Brito, L.F., Maignel, L., Jafarikia, M., Baes, C.F., Sullivan, B., Schenkel, F.S., 2023. Genome-wide association study for milk production and conformation traits in Canadian Alpine and Saanen dairy goats. Journal of Dairy Science 106, 1168–1189.
Mastrangelo, S., Tolone, M., Montalbano, M., Tortorici, L., Di Gerlando, R., Sardina, M. T., Portolano, B., 2016. Population genetic structure and milk production traits in Girgentana goat breed. Animal Production Science 57, 430–440.
Mastrangelo, S., Di Gerlando, R., Sardina, M.T., Sutera, A.M., Moscarelli, A., Tolone, M., Cortellari, M., Marletta, D., Crepaldi, P., Portolano, B., 2021. Genome-wide patterns of homozygosity reveal the conservation status in five Italian goat populations. Animals (basel) 11, 1–11.
Mwacharo, J., Elbeltagy, A.R., Kim, E.S., Aboul-Naga, A.M., Rischkowsky, B., Rothschild, M.F., 2019. Intra-population SNP analysis identifies signatures for grazing stress tolerance in Egyptian local goats. Presented at the World Congress on Genetics Applied to Livestock Production (WCGALP), 11–16 February 2019, Auckland, New Zealand.
Negrini, R., D'Andrea, M., Crepaldi, P., Colli, L., Nicoloso, L., Guastella, A.M., Sechi, T., Bordonaro, S., Ajmone-Marsan, P., Pilla, F., 2012. Effect of microsatellite outliers on the genetic structure of eight Italian goat breeds. Small Ruminant Research 103, 99–107.
Nicoloso, L., Bomba, L., Colli, L., Negrini, R., Milanesi, M., Mazza, R., Sechi, T., Frattini, S., Talenti, A., Coizet, B., Chessa, S., Marletta, D., D'Andrea, M., Bordonaro, S., Ptak, G., Carta, A., Pagnacco, G., Valentini, A., Pilla, F., Ajmone-Marsan, P., Crepaldi, P., Italian Goat, C., 2015. Genetic diversity of Italian goat breeds assessed with a medium-density SNP chip. Genetics Selection Evolution 47, 1–10.
O'Gorman, G.M., Park, S.D., Hill, E.W., Meade, K.G., Coussens, P.M., Agaba, M., Naessens, J., Kemp, S.J., MacHugh, D.E., 2009. Transcriptional profiling of cattle infected with Trypanosoma congolense highlights gene expression signatures underlying trypanotolerance and trypanosusceptibility. BMC Genomics 10, 207–228.
Onzima, R.B., Upadhyay, M.R., Doekes, H.P., Brito, L.F., Bosse, M., Kanis, E., Groenen, M.A.M., Crooijmans, R., 2018. Genome-wide characterization of selection signatures and runs of homozygosity in Ugandan goat breeds. Frontiers in Genetics 9, 318.
Ortega, M.S., Bickhart, D.M., Lockhart, K.N., Null, D.J., Hutchison, J.L., McClure, J.C., Cole, J.B., 2022. Truncation of IFT80 causes early embryonic loss in Holstein cattle associated with Holstein haplotype 2. Journal of Dairy Science 105, 9001–9011.
Peng, W., Zhang, Y., Gao, L., Shi, W., Liu, Z., Guo, X., Zhang, Y., Li, B., Li, G., Cao, J., Yang, M., 2024. Selection signatures and landscape genomics analysis to reveal climate adaptation of goat breeds. BMC Genomics 25, 420–433.
Qanbari, S., Simianer, H., 2014. Mapping signatures of positive selection in the genome of livestock. Livestock Science 166, 133–143.
Ramey, H.R., Decker, J.E., McKay, S.D., Rolf, M.M., Schnabel, R.D., Taylor, J.F., 2013. Detection of selective sweeps in cattle using genome-wide SNP data. BMC Genomics 14, 1–18.
Sabeti, P.C., Varilly, P., Fry, B., Lohmueller, J., Hostetter, E., Cotsapas, C., Xie, X., Byrne, E.H., McCarroll, S.A., Gaudet, R., Schaffner, S.F., Lander, E.S., International HapMap, C., 2007. Genome-wide detection and characterization of positive selection in human populations. Nature 449, 913–918.
Sallam, A.M., Reyer, H., Wimmers, K., Bertolini, F., Aboul-Naga, A., Braz, C.U., Rabee, A.E., 2023. Genome-wide landscape of runs of homozygosity and differentiation across Egyptian goat breeds. BMC Genomics 24, 573–589.
Saravanan, K.A., Panigrahi, M., Kumar, H., Bhushan, B., Dutt, T., Mishra, B.P., 2020. Selection signatures in livestock genome: a review of concepts, approaches and applications. Livestock Science 241, 104257.
Sardina, M.T., Ballester, M., Marmi, J., Finocchiaro, R., van Kaam, J.B., Portolano, B., Folch, J.M., 2006. Phylogenetic analysis of Sicilian goats reveals a new mtDNA lineage. Animal Genetics 37, 376–378.
Scheet, P., Stephens, M., 2006. A fast and flexible statistical model for large-scale population genotype data: applications to inferring missing genotypes and haplotypic phase. The American Journal of Human Genetics 78, 629–644.
Serranito, B., Cavalazzi, M., Vidal, P., Taurisson-Mouret, D., Ciani, E., Bal, M., Rouvellac, E., Servin, B., Moreno-Romieux, C., Tosser-Klopp, G., Hall, S.J.G., Lenstra, J.A., Pompanon, F., Benjelloun, B., Da Silva, A., 2021. Local adaptations of Mediterranean sheep and goats through an integrative approach. Scientific Reports 11, 21363.
Serrano, M., Ramon, M., Calvo, J.H., Jimenez, M.A., Freire, F., Vazquez, J.M., Arranz, J. J., 2021. Genome-wide association studies for sperm traits in Assaf sheep breed. Animal 15, 100065.
Sherman, B.T., Hao, M., Qiu, J., Jiao, X., Baseler, M.W., Lane, H.C., Imamichi, T., Chang, W., 2022. DAVID: a web server for functional enrichment analysis and functional annotation of gene lists (2021 update). Nucleic Acids Research 50, W216–W221.
Signer-Hasler, H., Henkel, J., Bangerter, E., Bulut, Z., VarGoats, C., Drogemuller, C., Leeb, T., Flury, C., 2022. Runs of homozygosity in Swiss goats reveal genetic changes associated with domestication and modern selection. Genetics Selection Evolution 54, 1–11.
Szmatoła, T., Jasielczuk, I., Semik-Gurgul, E., Szyndler-Nędza, M., Blicharski, T., Szulc, K., Skrzypczak, E., Gurgul, A., 2020. Detection of runs of homozygosity in conserved and commercial pig breeds in Poland. Journal of Animal Breeding and Genetics 137, 571–580.
Tang, K., Thornton, K.R., Stoneking, M., 2007. A new approach for using genome scans to detect recent positive selection in the human genome. PLoS Biology 5, e171.
Trinchieri, G., 1998. Interleukin-12: a cytokine at the interface of inflammation and immunity. Advances in Immunology 70, 83–243.
Vatsiou, A.I., Bazin, E., Gaggiotti, O.E., 2016. Detection of selective sweeps in structured populations: a comparison of recent methods. Molecular Ecology 25, 89–103.
Voight, B.F., Kudaravalli, S., Wen, X., Pritchard, J.K., 2006. A map of recent positive selection in the human genome. PLoS Biology 4, e72.
Wang, X., Liu, J., Zhou, G., Guo, J., Yan, H., Niu, Y., Li, Y., Yuan, C., Geng, R., Lan, X., An, X., Tian, X., Zhou, H., Song, J., Jiang, Y., Chen, Y., 2016. Whole-genome sequencing of eight goat populations for the detection of selection signatures underlying production and adaptive traits. Scientific Reports 6, 38932.
Weir, B.S., Cockerham, C.C., 1984. Estimating F-Statistics for the analysis of population structure. Evolution 38, 1358–1370.
Yang, L., Yao, X., Li, S., Chen, K., Wang, Y., Chen, L., Zhang, L., 2016. Expression of genes associated with luteolysis in peripheral blood mononuclear cells during early pregnancy in cattle. Molecular Reproduction & Development 83, 509–515.
Yuan, Y., Yang, B., He, Y., Zhang, W., E, G., 2022. Genome-wide selection signal analysis of Australian Boer goat by insertion/deletion variants. Russian Journal of Genetics 58, 1504–1512.
Yurchenko, A.A., Daetwyler, H.D., Yudin, N., Schnabel, R.D., Vander Jagt, C.J., Soloshenko, V., Lhasaranov, B., Popov, R., Taylor, J.F., Larkin, D.M., 2018. Scans for signatures of selection in Russian cattle breed genomes reveal new candidate genes for environmental adaptation and acclimation. Scientific Reports 8, 12984.
Zhang, B., Chang, L., Lan, X., Asif, N., Guan, F., Fu, D., Li, B., Yan, C., Zhang, H., Zhang, X., Huang, Y., Chen, H., Yu, J., Li, S., 2018. Genome-wide definition of selective sweeps reveals molecular evidence of trait-driven domestication among elite goat (Capra species) breeds for the production of dairy, cashmere, and meat. GigaScience 7, 1–11.
Zhang, C.L., Liu, C., Zhang, J., Zheng, L., Chang, Q., Cui, Z., Liu, S., 2022. Analysis on the desert adaptability of indigenous sheep in the southern edge of Taklimakan Desert. Scientific Reports 12, 12264.
Zhang, Y., Xue, X., Liu, Y., Abied, A., Ding, Y., Zhao, S., Wang, W., Ma, L., Guo, J., Guan, W., Pu, Y., Mwacharo, J.M., Han, J., Ma, Y., Zhao, Q., 2021. Genome-wide comparative analyses reveal selection signatures underlying adaptation and production in Tibetan and Poll Dorset sheep. Scientific Reports 11, 2466.