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Investigation of selection signatures of dairy goats using whole-genome sequencing data

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Abstract

Dairy goats, a livestock species with a long history of milk production, are essential for the economic advancement of nations, particularly in regions experiencing growth. In this study, we gathered whole-genome resequencing data of 58 goats, including 34 dairy goats and 24 wild goats (Bezoar), to explore the selection signatures linked to milk production traits using ROH (Runs of homozygosity), CLR (composite likelihood ratio), Fst (Fixation index), XP-EHH (Ex-tended haplotype homozygosity across populations) and XP-CLR(Cross-population composite likelihood ratio test) methods. Analysis of five tests of selection signatures for dairy goats revealed a total of 210 genes, with 24 genes consistently identified in at least two approaches. These genes are associated with milk fat, milk protein, and fat yield. Gene enrichment analysis highlighted important GO and KEGG pathways related to milk production, such as the "acyl-CoA metabolic process", "glycerolipid biosynthetic process", "cellular response to fatty ac-id", "hormone metabolic process", "Galactose metabolism". Additionally, genes linked to repro-duction, immune response, and environmental adaptation were identified in dairy goats. The findings from our study offer profound understanding into the critical economic features of dairy goats and offer practical guidance for the improvement and development of crossbreeding initiatives across different dairy goat breeds.

Keywords Goat, Milk production traits, Selection signatures, Dairy goats

Introduction

The agricultural progress of the Neolithic era was facilitated by the domestication of animals and plants. Around 10,000 years ago, goats were one of the first livestock to be tamed in the Zagros Mountains of the Fertile Crescent region [1]. In the beginning, goats were predominantly used for their meat. Nevertheless, after approximately 5,000 years, humans began to extract other materials from goats, including wool, hides, and milk [2]. As agricultural civilization progressed, humans started selectively breeding goat breeds based on the specific products they desired, such as milk [3]. This early practice of goat breeding marked the beginning of goat domestication. Dairy goats are particularly important in the livestock industry as they provide humans with nutritious milk, as well as meat, wool, and hide. These goats play a vital role

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in animal husbandry globally, with over 200 dairy goat breeds totaling 220 million individuals found worldwide [2]. Through extensive artificial selection, modern dairy goats have been bred to emphasize milk production characteristics. Certain dairy goat breeds like Saanen, Alpine, and Toggenburg are well-known for their high milk yield, averaging 900 kg in 305 days. In contrast, Indian Beetal goats produce 200 kg of milk in 190 days [2]. This highlights the significant impact of human intervention in shaping the milk production capabilities of dairy goats over time.

Throughout history, goats have been referred to as the "poor man's cow." In the Neolithic era, humans began domesticating small herds of goats primarily for their milk, as goats produce milk earlier than cows [4]. Goat's milk is packed with nutrients and is frequently easier to digest compared to cow's milk, making it a great option for those with allergies or intolerances to cow's milk [5]. Its unique protein composition also makes it ideal for producing soft and moist cheeses [6]. However, goat milk is more costly than cow's milk due to its lower yield. While newborn goats depend on goat milk for growth, mother goats often struggle to feed multiple offspring, leading to lower survival rates and impeding the industry's progress [2]. Therefore, identifying genes associated with milk production traits is crucial to breed goats with higher milk yields.

The genetic material of domesticated animals has been shaped by both natural and human-driven selection processes. It is crucial to identify the markers of selection in order to understand the distinct traits of various breeds and reveal the genetic influences of the selection pressures they have faced [7–9]. Milk production traits are of great importance economically and are fundamental criteria for selective breeding in dairy goats. Previous research has investigated the genes that may influence milk production traits in different breeds of goats and sheep, such as the Guanzhong dairy goat breed [10], Canadian Alpine and Saanen dairy goats [11], Assaf sheep [12], and Churra sheep [13]. Nonetheless, these studies have predominantly relied on SNP arrays, which have constraints in SNP coverage and depth, along with potential biases in chip design.

In this study, we gathered whole-genome resequencing data from 58 goats, including 34 dairy goats from Europe and Africa (such as Saanen, Alpine, and Toggenburg dairy goats) and 24 wild goats (Bezoar), to examine the genetic markers linked to milk production characteristics. Our study aimed to investigate the genetic relationships and population structure of dairy goat breeds, as well as to detect regions of homozygosity (ROH) within these breeds. By utilizing five statistical methods (ROH, CLR, Fst, XP-EHH, and XP-CLR), we were able to pinpoint selection signals related to milk production traits in dairy goat populations. These discoveries will offer valuable insights for dairy goat breeding programs.

Materials and methods

Sample collection

The study download 34 whole-genome sequencing data of dairy goats originating from Europe and Africa. These included dairy goats from the Netherlands (NLCH, $n=3$), Switzerland (SWCH, $n=10$), France (FRCH, $n=5$), Tanzania (TASCH, $n=15$), and Kenya (KETCH, $n=1$). Furthermore, data from 24 wild goats (Bezoar) were also download from previous studies to analyze selection signatures related to milk production traits. Details of the samples are provided in TableS1.

Read alignment, variant annotation, and genetic structure

We utilized BWA v0.7.15 [14], a bioinformatics tool, to align the paired-end reads from 58 goat samples to the most current goat reference genome, ARS1 (GCF_001704415.1). Subsequently, we used the Genome Analysis Toolkit's HaplotypeCaller (version 3.7) [15] and the Analysis of next-generation Sequencing Data (ANGSD, version 0.918) [16] for the purpose of detecting single nucleotide polymorphisms (SNPs) across all the samples. The selection criteria for including sites were those that exhibited biallelic polymorphism as identified by both the Genome Analysis Toolkit's HaplotypeCaller and ANGSD. These sites were required to have a quality score above 50 and less than 10% missing data. The specific filter parameters were as indicated [2]: SNPs with a Quality by Depth (QD) of under 2.0, missing rates (Miss) equal to or greater than 0.1, and minor allele frequencies (MAF) below 0.05. We used Beagle software to phase the identified SNPs in goats, following the method outlined by Browning [17]. ANNOVAR was employed to annotate all SNPs, based on the GFF file of the goat reference genome ARS1 [18]. Plink [19–21] was employed to perform principal component analysis (PCA) based on filtered SNPs. The Bayesian clustering analysis was conducted using STRUCTURE v2.3.4 [22], with 50,000 iterations and a burn-in phase. Different K values from 2 to 4 were examined. Estimation of the effective population size (Ne) was conducted through the utilization of SNeP v1.1, with reference to the ped and map files [23].

Runs of homozygosity (ROH) and inbreeding coefficient

The sliding runs method in the R package detectRUNS was utilized to identify ROHs in all goats [23]. In order to conduct the analysis, the following parameters were necessary: (1) a minimum of 20 consecutive SNPs within a run of homozygosity (ROH), (2) a ROH length of at least 250 kb, (3) no more than a 1 Mb gap between consecutive

homozygous SNPs, (4) only one opposite genotype allowed in the run, and (5) a maximum of one missing genotype permitted. After calculating the total ROH values per goat, they were categorized into five groups based on ROH estimates: 0–4 Mb, 4–8 Mb, 8–16 Mb, 16–32 Mb, and above 32 Mb [20]. The study focused on determining the length categories of ROH and the distribution of ROH across each autosome when assessing each breed. It was essential to opt for the consecutive method over the sliding window approach to ensure that ROH shorter than the designated 20 SNP window were not mistakenly detected [24].

The genomic inbreeding coefficient assesses genomic segments found in runs of homozygosity (ROH), highlighting regions where chromosome copies are of identical descent due to recent ancestral coalescence, with a scale from 0 to 1 [25]. The coefficient of inbreeding (FROH) for each goat was calculated using ROH, as described by [26]: FROH = LROH/Lauto. LROH denotes the total length of runs of homozygosity (ROHs) in an individual's genetic profile, while Lauto represents the cumulative length of autosomal regions covered by single nucleotide polymorphisms (SNPs) in the goat genome, estimated at 2.46 GB [27].

Selection signatures of dairy goats

Investigation of selection signatures for dairy goats involved estimating the occurrence of ROH throughout the genome. The proportion of SNP occurrences was calculated for dairy goats in order to identify genomic regions with a high frequency of ROH. These findings were then visually displayed on chromosomes using Manhattan plots generated using the qqman package of R [25]. The determination of selected regions for each breed was guided by the ROH value, focusing on peaks that represent the top 1% of SNP markers [19]. Moreover, the investigation employed CLR method [26] to pinpoint selection signatures resulting from the artificial selection of milk traits. The computational analysis of CLR values for genomic sites in non-overlapping 50 kb windows was carried out utilizing SweepFinder2 [27]. The top 1% of windows identified by this method are considered potential signal candidates [28].

Selection signatures between dairy and wild goats

Furthermore, in order to pinpoint potential selection signatures throughout the genome, Fst, XP-EHH, and XP-CLR tests were utilized to examine the differences between dairy goats and wild goats. Utilizing VCFtools [29], Fst values were determined through a sliding 30-kb window with a step size of 25 kb to uncover selection signatures [30]. Furthermore, we used the command "-xpehh" [31] under window size 30 k setting in selscan v1.2.0a software [32] to identify the signatures of selection in dairy goats compared with wild goats. Subsequently, we carried out the XP-CLR test using XP-CLR software with non-overlapping 30 kb windows [33]. The top 1% windows from each method were chosen as candidate signals. Furthermore, we compared the selection signals between European and African goats using the Fst and XP-EHH methods.

Functional annotation and GO enrichment

After identifying candidate signals using five methods that exceeded the designated threshold, gene functional annotations were retrieved from BioMart on the Ensembl Genome Browser (https://www.ensembl.org/biomart/martview) [34], utilizing the goat reference genome (ARS1.2) [35]. Subsequently, gene functions and protein domains were determined through the literature database of PMC. Enriched Gene Ontology (GO) terms were identified using the Metascape database [36], with a significance threshold set at $P < 0.05$.

Conservation and EHH analysis of ACSS2 gene

In order to confirm the conservation of the ACSS2 gene, we conducted sequence alignment of the ACSS2 gene from goats, sheep, and cattle in the MEGA software [37]. In addition, genes subject to recent strong selection are expected to exhibit high extended haplotype homozygosity (EHH) values due to limited recombination events over a short period. Following this premise, EHHS tests were conducted on two groups (milk and Bezoar goats) to ascertain the selection signals of ACSS2 genes using rehh packages of R software. Our approach compares the decay of EHH of an individual SNP site (EHHS), rather than EHHA, between populations. EHHS is defined as the decay of identity of haplotypes starting from the tested SNP [38]. EHHS covers the candidate region from 63,780,001 bp to 63,810,001 bp on chromosome 13, encompassing 34 SNPs. The SNP located in the middle of chromosome 13 at position 63,802,064, referred to as the tested SNP (13chr63802064snp), serves as the focal point.

Results

Genome sequence mapping, SNPs and population structure

A total of 58 whole-genome data samples were integrated, encompassing dairy goats from Europe and Africa along with wild goats (Bezoar). The average sequence depth for these 58 goat genomes was 16.91×, with an average alignment rate of 99.6% covering 92.72% of the reference genome (Table S1). After mapping and SNP calling, a total of 41,439,258 SNPs were identified from the 58 goat samples. To establish the genetic and evolutionary

relationship among the 58 goat samples, principal component analysis (PCA) and population structure analysis were utilized. The results revealed a division into two groups: dairy goats and wild goats (Bezoar) (Fig. 1).

ROH statistics and effective population size

The total number of runs of homozygosity (ROH) segments in Africa, Europe, and Bezoar goats were 677, 966, and 1431, respectively, with average counts per individual of 42.31, 53.66, and 59.65, respectively (TableS2). Mean total ROH lengths ranged from 244.20 Mb in Bezoar goats to 271.27 Mb in Africa goats (TableS2). The maximum ROH lengths found in Africa, Europe, and Bezoar goats were 839.81 Mb, 830.82 Mb, and 777.18 Mb, respectively(TableS2, and Fig. 2 A). Long ROH segments (8–16 Mb) and (16–32 Mb) were present in all studied goats (Fig. 2B). The frequency of long ROH segments in Africa and Europe goats was higher than in Bezoar goats. The mean inbreeding coefficient (FROH) values for Africa, Europe, and Bezoar goats were 0.073, 0.079, and 0.182, respectively (Fig. 2C). The effective population size (Ne) of Africa, Europe, and Bezoar goats was evaluated over 995 generations, with Bezoar goats showing the highest Ne value at 7650 in generation 995, while Africa exhibited the lowest at 4467 and a decreasing trend in Ne estimates over time was observed (Fig. 2D).

Signal selection within a group of dairy goats

To identify areas characterized by a high frequency of ROH, also known as ROH hotspots, which are crucial for selection, the percentage of SNP occurrences was examined for each breed and plotted according to their positions on autosomes. Manhattan plots were employed to visualize the distribution of ROH in the four goat breeds (Fig. 3A). The application of the top 1% SNP threshold led to the identification of 17 ROH hotspots containing 56 genes (TableS3). Eight genes were associated with milk production traits, including milk yield (HTR3C and

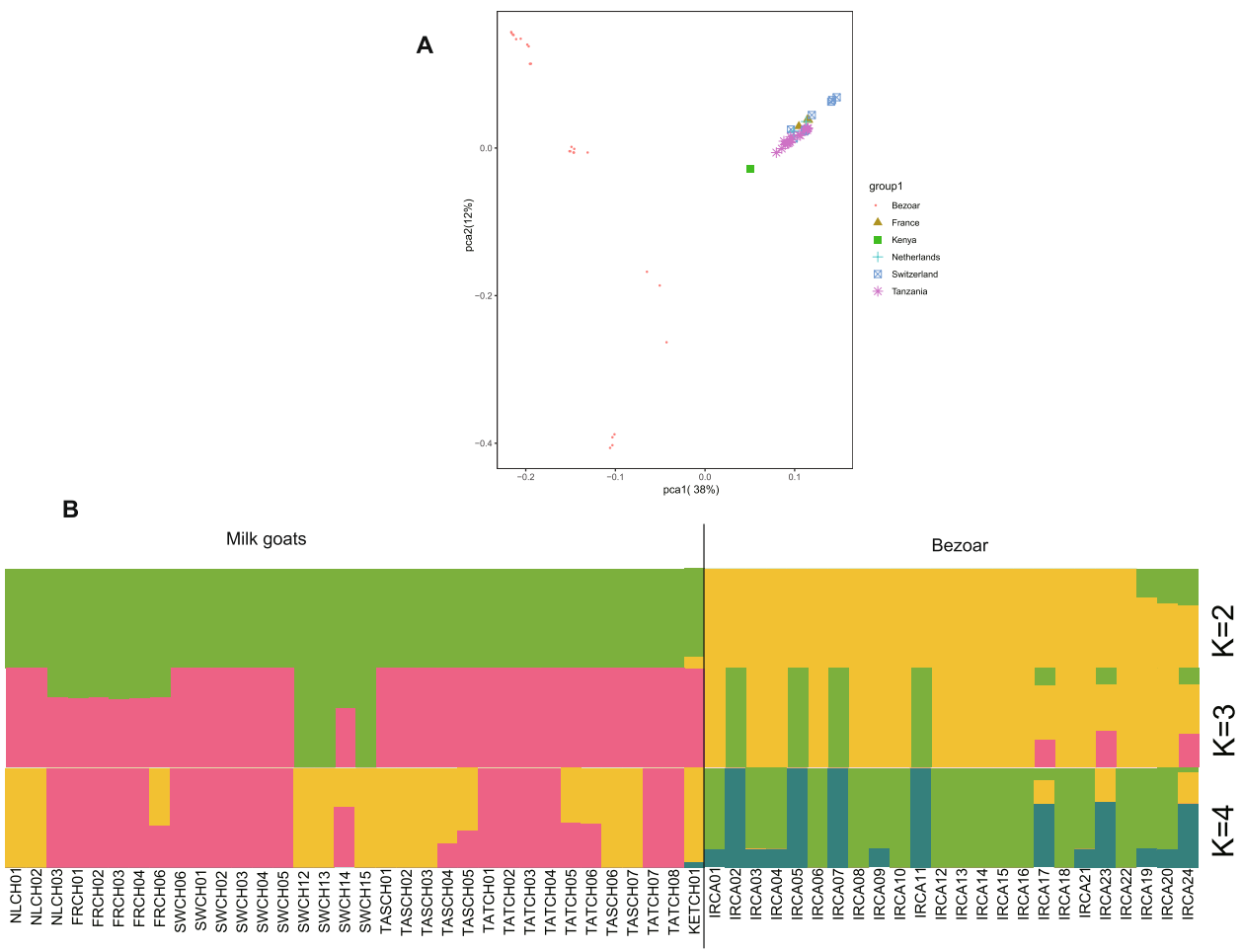


Fig. 1 Population genetic structure of dairy goats and wild goats. **A** principal component analysis (PCA) for dairy goats and wild goats. Breeds are presented in different colors, and each point represents one sample. **B** estimated population structure displayed with individual Q-matrix (K = 2–5)

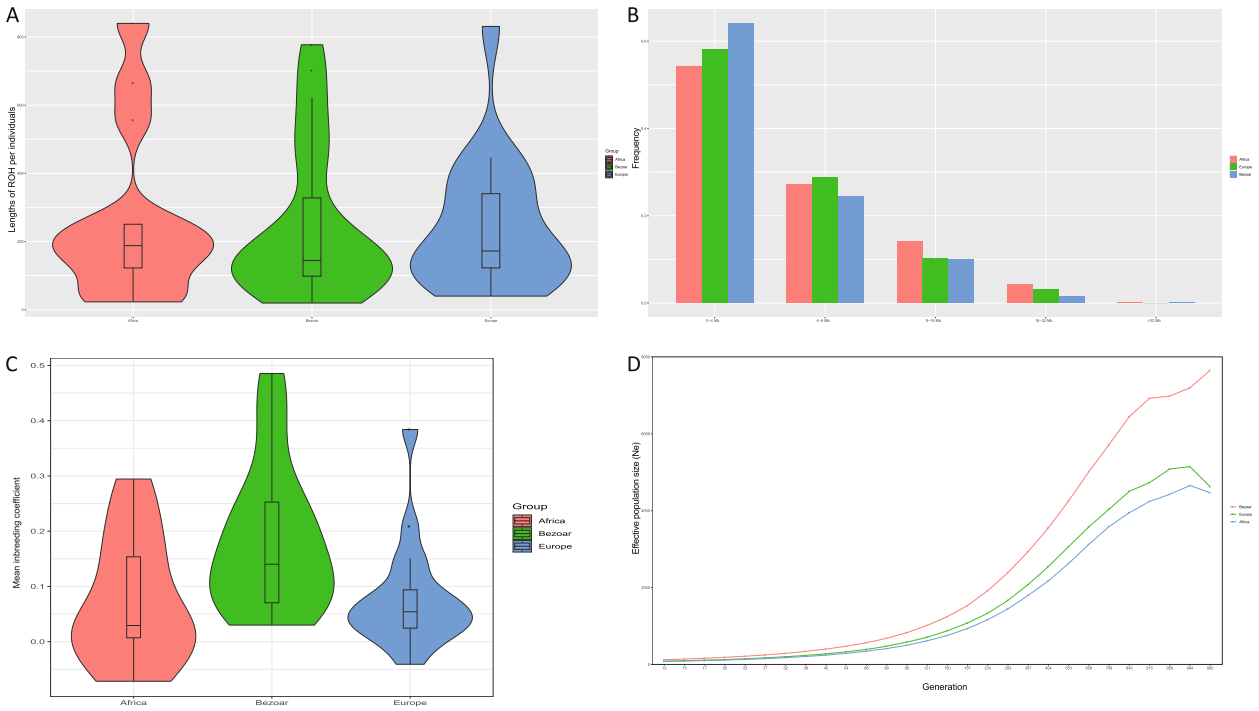


Fig. 2 ROH analysis and effective population size (Ne). **A** distribution of the lengths of ROH in Africa dairy goats, Europe dairy goats and Bezoar goats. **B** The proportion of runs of homozygosity (ROH) segments in each length category. **C** Mean inbreeding coefficient of Africa dairy goats, Europe dairy goats and Bezoar goats. **D** Effective population size (Ne) trends of Africa dairy goats, Europe dairy goats and Bezoar goats

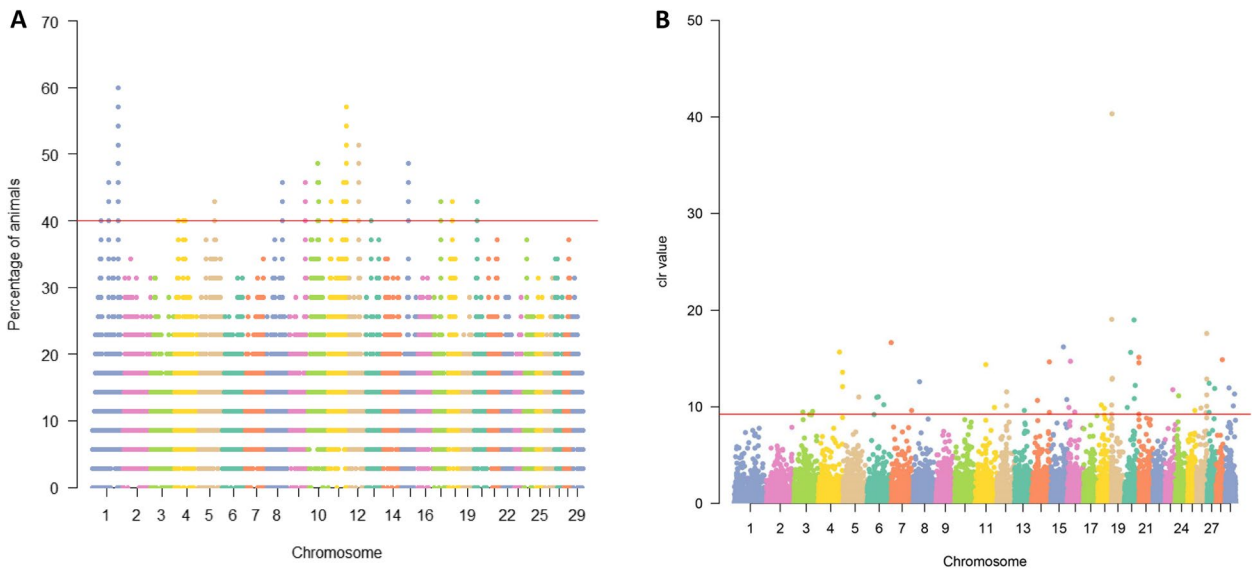
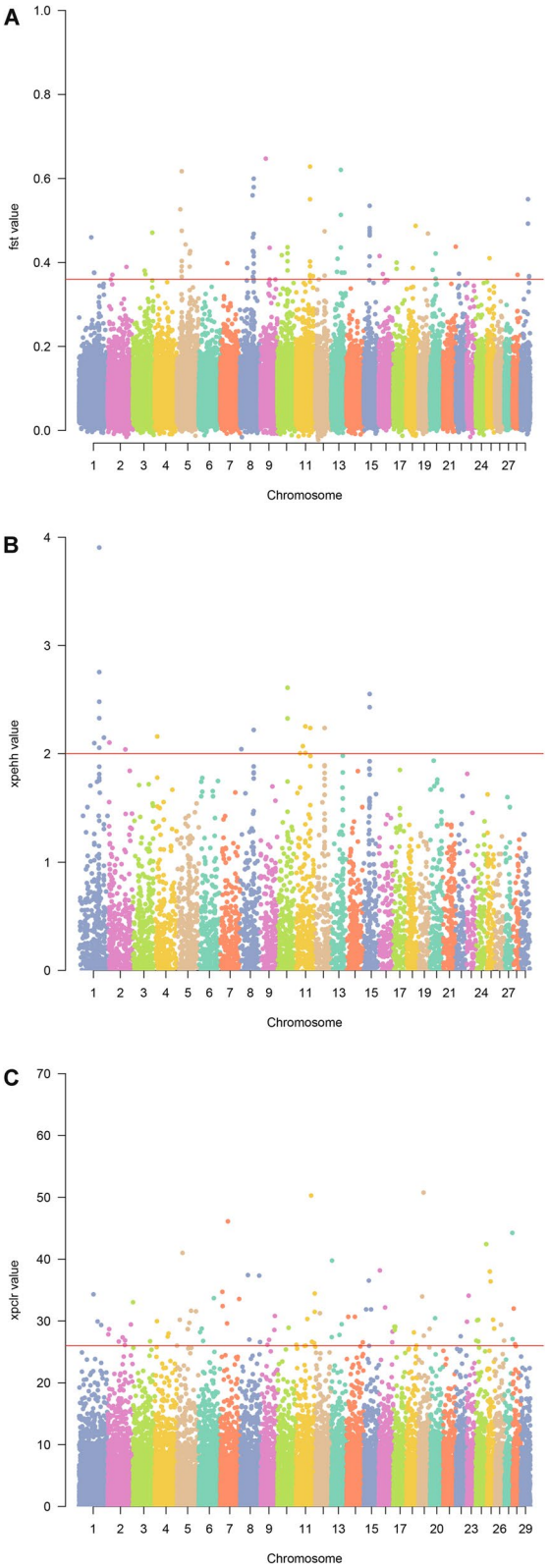


Fig. 3 Manhattan plots of signal selection based on ROH and CLR methods in dairy goats. **A** manhattan plot of signal selection based on ROH. The x-axis is the autosome number and the y-axis shows the frequency (%) at which each SNP was observed in ROH across individuals. **B** manhattan plot of signal selection based on CLR methods. The x-axis is the autosome number and the y-axis shows clr value

VPS13C), milk fat (ATF7, NFX1, UBE2R2, and ABTB2), and milk traits (ACSS2 and ITFG1). Moreover, several crucial genes associated with fertility (STAG1, PCCB, DENND1A, and ECE2), immune response (IL2 and IL21), and environmental adaptation (PARP4, ZMYM5, PSPC1, GJB2, and ADAMTS6) were also identified.



◀ **Fig. 4** Identification of selective signals based on comparing dairy goats and wild goats. **A** manhattan plot of signal selection based on Fst methods. The x-axis is the autosome number and the y-axis shows Fst value. **B** manhattan plot of signal selection based on XP-EHH methods. The x-axis is the autosome number and the y-axis shows xpehh value. **C** manhattan plot of signal selection based on XP-CLR methods. The x-axis is the autosome number and the y-axis shows xpclr value

Additionally, the dairy goats' genomic regions associated with selection were detected using CLR test (see Fig. 3B). We pinpointed the top 1% of SNP as candidate regions, resulting in the identification of 23 regions encompassing 51 genes (TableS4). Seven genes, including AMPD1, NRAS, ACSS2, DGAT2, DNAJC24, FA2H, and GHR, have been identified as being linked to milk production. Additionally, genes associated with fecundity (SYCP1, TSHB, DENND1A, and ADAM18) and follicle development (LHX2) were also discovered. Among these genes, two genes (ACSS2 and DENND1A) were detected by ROH and CLR tests.

Signal selection between dairy and wild goats

Fst, XP-EHH, and XP-CLR tests were employed to identify potential selection signatures across the genome to compare dairy goats with wild goats. These tests successfully identify signatures containing alleles that are either almost fixed or completely fixed. The threshold for identifying outliers was established at the top 0.1% of windows. Through the Fst test, 55 genes were pinpointed that are associated with various traits (Fig. 4A and TableS5), including milk production (SP7, NCKAP1L, PDE1B, PPP1R1A, ATF7, NFX1, VPS13C, LARP4B, PRPF6, and ACSS2), fatty acid synthesis (PFDN5 and PANK3), reproduction (ITGA5, CHMP5, DENND1A, and AAAS), and lipid metabolism (AP2M1and RPTOR), as well as immune response (IRAK3), neural function or behavior (STIM1 and RRM1). The XP-EHH test identified 36 genes by focusing on the top 1% of windows (Fig. 4B and TableS6). Among these genes, seven genes were found to be related to milk traits (UBE2R2, B4GALT1, VPS13C, ACSS2, PITRM1, SPIDR, and FCHSD2). Additionally, genes associated with reproduction (TET2, IFT88, and SPEF2), energy and regulation activities (FBXO8), environmental adaptation (RHOG), and disease resistance (NHSL1 and ARHGEF17) were also pinpointed (TableS5). Through the XP-CLR test, a total of 41 genes were uncovered by analyzing the top 1% of windows (Fig. 4C and TableS7). Among these genes, four were found to be crucial for milk production (RFX4, ACSS2, GDPD5, and RBM19). Furthermore, genes associated with litter size and nipple numbers (LRP1B), immune response (GALNT8 and SBF2), brown adipose (ABHD8

and GOLGA7B), cold tolerance (ZNF536), and coat color (EXOC2) were also pinpointed.

Among these genes, ACSS2 genes were identified by five methods (ROH, CLR, Fst, XP-EHH, and XPCLR), while DENND1A genes were detected by three methods (ROH, CLR, Fst). ROH, Fst, and XPEHH identified STIM1 and VPS13C genes. Additionally, ten genes (ZMYM2, PSMD2, DVL3, ABCF3, AP2M1, PUM2, NFX1, ATF7, CHMP5, and EIF4G1) were detected by ROH and Fst. Furthermore, nine genes (B4GALT1, PGAP2, NUDT6, RHOG, IFT88, UBE2R2, NOL6, CRYL1, and IL17D) were identified by ROH and XPEHH (Fig. 6A and TableS10).

Signal selection between Africa and Europe goats

Fst and XP-EHH tests were employed to identify selection signatures within the genomes of African and European goats. 74 genes and 69 genes were identified based on the top 0.1% of windows by Fst and XP-EHH methods, respectively (TableS8 TableS9, and Fig. 5). Five genes (TBC1D23, TOMM70, ADGRG7, TFG, and DPH6) were tested by both methods (TableS8 and

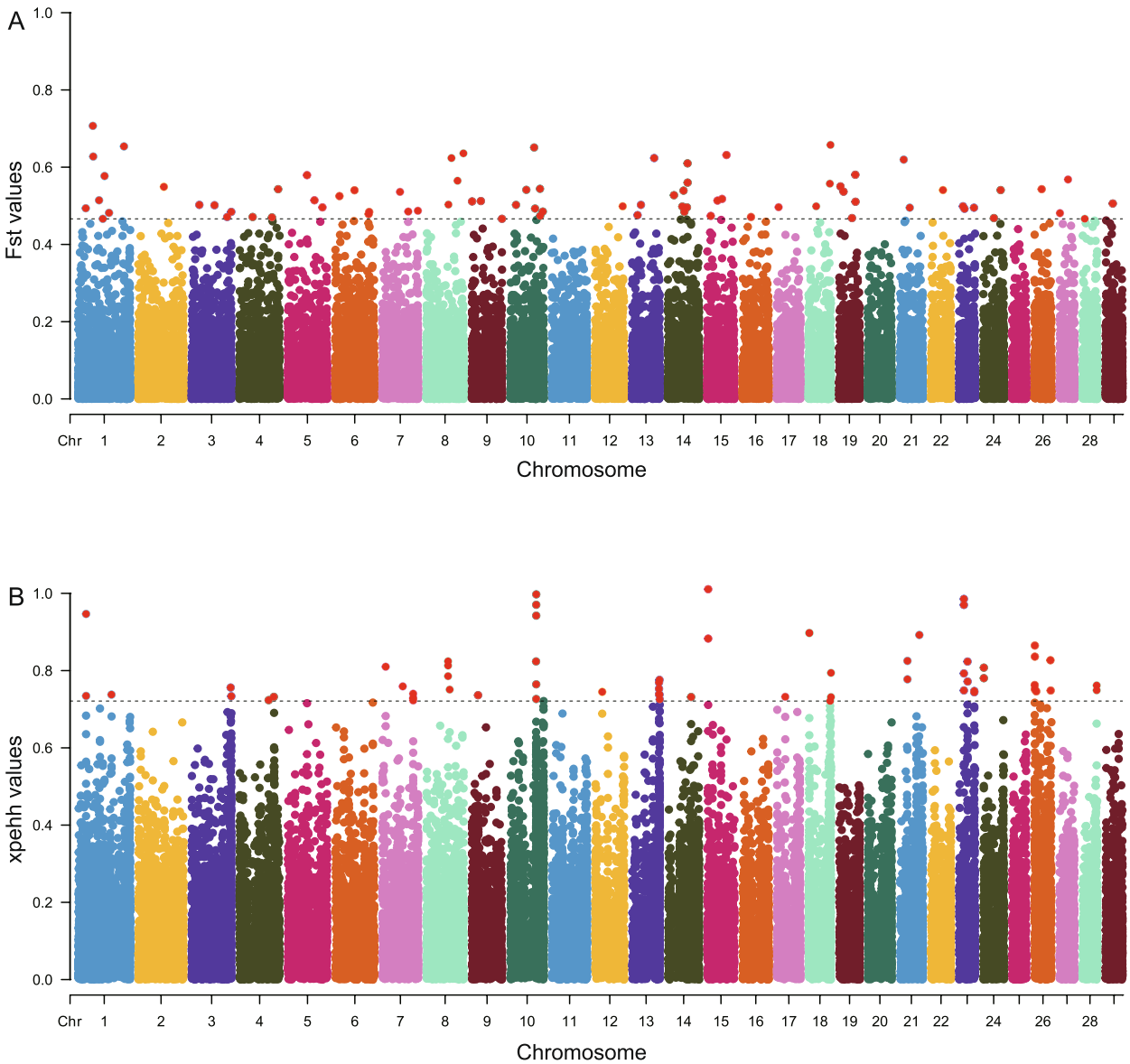


Fig. 5 Selective signals between Africa and Europe dairy goats. **A** manhattan plot of signal selection based on Fst methods. The x-axis is the autosome number and the y-axis shows Fst value. **B** manhattan plot of signal selection based on XP-EHH methods. The x-axis is the autosome number and the y-axis shows xpehh value

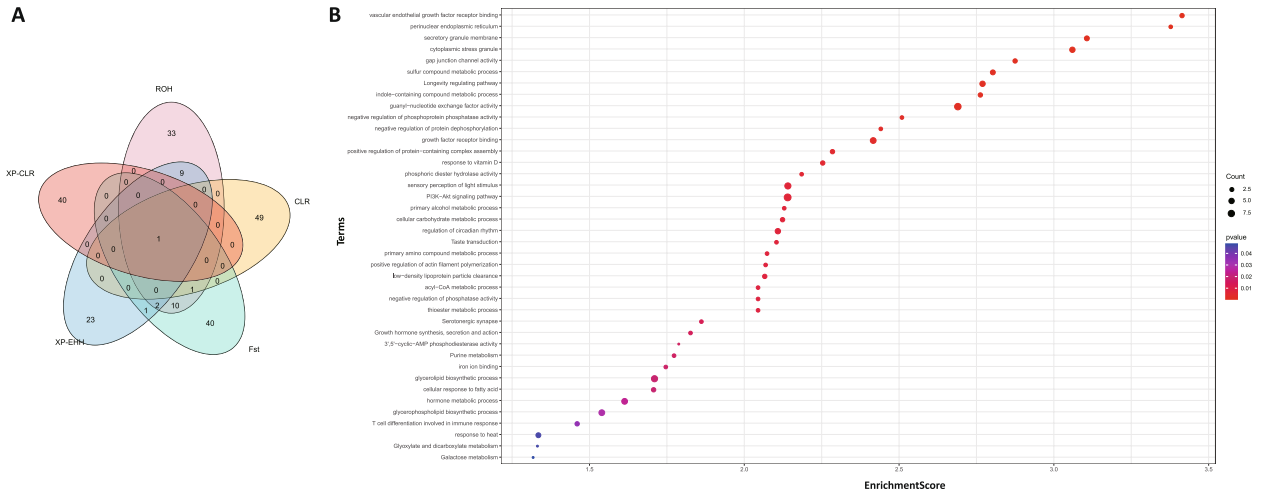


Fig. 6 Venn diagram for genes identified by ROH, CLR, Fst, XP-EHH, and XP-CLR methods (**A**) and top 40 GO and KEGG terms identified based on candidate genes (**B**)

TableS9). These genes may related to carcass and growth traits (TBC1D23), cashmere traits (TOMM70), immune responses (ADGRG7), disease resistance (TFG), and seasonal patterns (DPH6). These genes may have significant implications in adapting to local environments.

GO enrichments and selection signals of the ACSS2 gene

Using ROH, CLR, Fst, XPEHH, and XPCLR methods, 210 genes were pinpointed, with 24 genes consistently identified across at least two approaches. Afterwards, we utilized the metascape database to analyze the genes and uncovered various biological terms and pathways associated with milk characteristics, environmental adaptation, and immune response (Fig. 6B and TableS11). One notable finding was that the GO term "Vascular endothelial growth factor receptor binding" was the most significant molecular function (MF), with three genes (VEGFC, ITGA5, and CCDC88A) linked to milk traits. Additionally, two cell component (CC) enrichments, "perinuclear endoplasmic reticulum" and "secretory granule membrane," were identified as important GO terms related to milk traits. These enrichments included six genes (DGAT2, GDPD5, B4GALT1, NCKAP1L, NRAS, and VPS13C) that are associated with milk traits. Key biological processes such as "sulfur compound metabolic process," which involve ACSS2, B4GALT1, DGAT2, and GHR genes, as well as "negative regulation of phosphoprotein phosphatase activity," which includes NCKAP1L and PPP1R1A genes, play a crucial role in milk production. Additionally, processes like "acyl-CoA metabolic process" (involving ACSS2 and DGAT2 genes), "cellular response to fatty acid" (involving DGAT2, P2RY6, and TNC genes), "hormone metabolic process" (including ECE2, TSHB, RPE65, DGAT2, GHR, and TIPARP genes), and "glycerophospholipid biosynthetic process" (involving PGAP2, FGF2, PTDSS2, PITPNM1, ETNPPL, and ABHD8 genes) are also essential for milk production. Moreover, important KEGG enrichments were identified, such as "Growth hormone synthesis, secretion, and action" (which includes GHR and NRAS genes), "Purine metabolism" (involving AMPD1 and PDE1B genes), "Glyoxylate and dicarboxylate metabolism" (involving the ACSS2 gene), and "Galactose metabolism" (involving the B4GALT1 gene), all of which play a significant role in influencing milk traits. Furthermore, several important Gene Ontology (GO) terms related to environmental adaptation were discovered. These include terms such as "sensory perception of light stimulus" which involve genes GJA3, RPE65, WDR36, PCDH15, CABP4, CABP2, and RORB. Other GO terms identified were "Regulation of circadian rhythm" with genes PSPC1, MAGEL2, HNF4A, MTA1, and RORB, and "Response to heat" with genes EIF2B5, TCIM, AAAS, and RPTOR. Additionally, GO terms associated with immune response were also found, such as "T cell differentiation involved in immune response" with genes IL2, IL21, and TSC1, and "PI3K-Akt signaling pathway" with genes IL2, FGF2, NRAS, GHR, VEGFC, ITGA5, RPTOR, TNC, and TSC1. In addition, based on the DNA sequence alignment results, the ACSS2 gene exhibits a high level of conservation in goats, sheep, and cattle, indicating its significance in regulating the characteristics of dairy products (Fig. 7A). Furthermore, EHH analysis of the ACSS2 gene showed elevated EHHS values in dairy goats in comparison to wild goats, elucidating its role in artificial selection for dairy production (Fig. 7B).

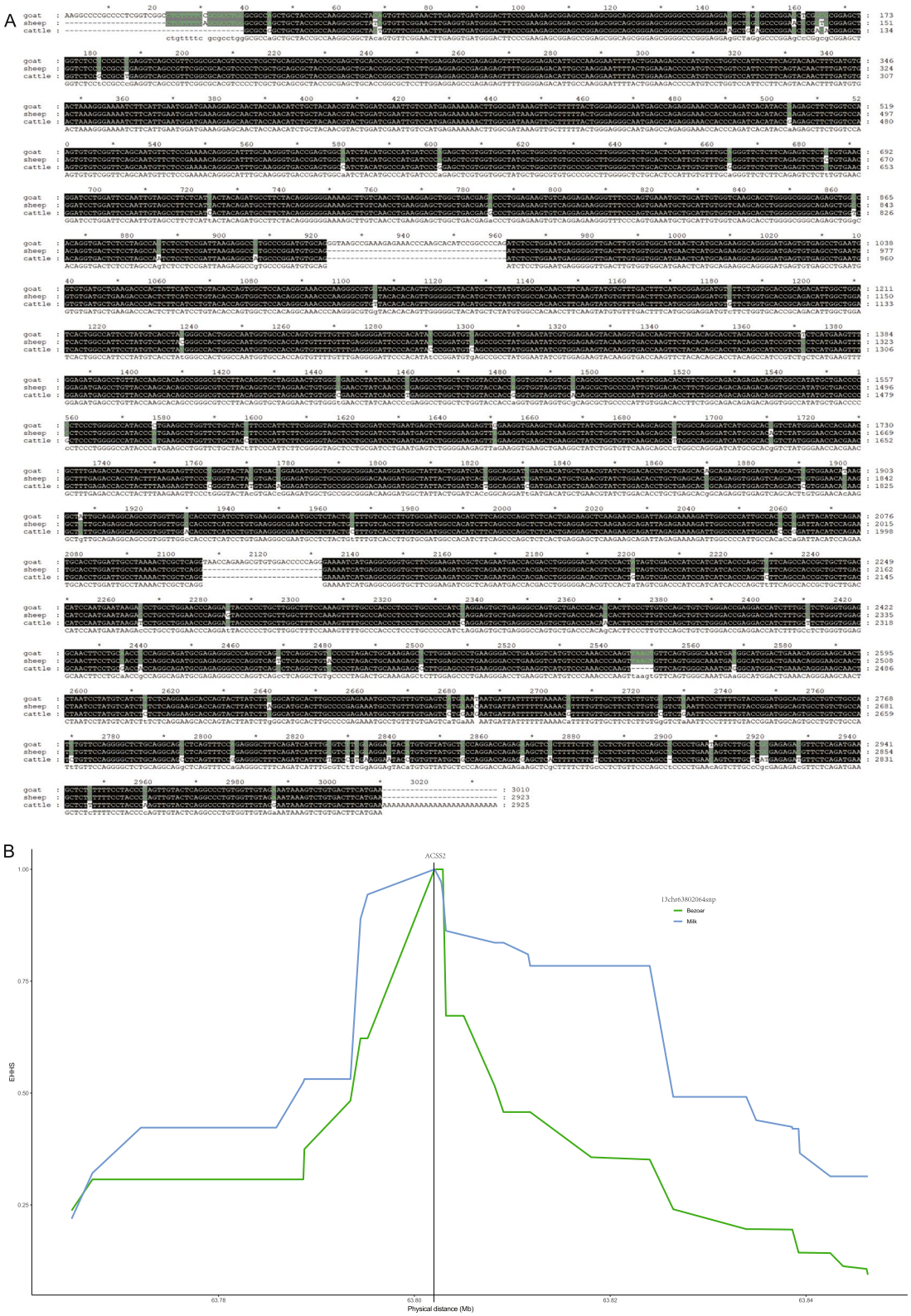


Fig. 7 DNA Sequence Alignment and EHH Analysis of ACSS2 gene. **A** DNA Sequence Alignment of ACSS2 gene in goat, sheep and cattle. **B** the EHH decay plot for ACSS2 gene between dairy and Bezoar goats based on candidate region from, 63,780,001 bp to and 63,810,001 bp on chromosome 13

Discussion

The widespread dispersal of dairy goats around the world, driven by human migration and agricultural trade, has led to their presence in various climates and living conditions. This has been particularly beneficial for low and middle-income farmers, who rely on dairy goats for their livelihoods. In Europe, there are over 187 goat breeds, with many high-yield dairy breeds such as Saanen, Alpine, Toggenburg, and Nubian. However, in developing countries, some dairy goat breeds have low milk production, which poses challenges for economic growth. Therefore, studying the genetic relationships and specific traits of dairy goat breeds, as well as identifying genes related to milk production, is crucial for improving dairy goat breeding programs. This study focuses on analyzing selection signals in dairy goat populations using whole genome re-sequencing data from 58 goats (34 dairy goats and 24 wild goats). The population structure analysis indicates a clear distinction between domestic dairy goats and wild goats, with two distinct genetic clusters (Fig. 1). Domestic dairy goats from Africa and Europe show less differentiation, suggesting a shared genetic background in the domestication process. Comparing domestic dairy goats with wild goats can help identify genes associated with milk quality, environmental adaptation, reproductive, immune response, and disease resistance that have evolved during the domestication process. By comparing runs of homozygosity (ROH) among African dairy goats, European dairy goats, and wild goats, we observed that African dairy goats exhibit longer ROH segments and higher ROH counts (Fig. 2A and B). In addition, compared to FNW, HG, LS, and THB breeds, African and European dairy goats show an elevated ROH number and longer ROH segments. These results may be attributed to the recent artificial selection of dairy traits. Wild goats (Bezoar) exhibit higher mean inbreeding coefficients, which can be attributed to their smaller population size and lack of genetic exchange with other goat breeds. In contrast, dairy goats are the result of long-term hybridization and artificial selection between local and commercial breeds. Furthermore, results of the effective population sizes also indicate a rapid decline in the population of wild goats (Bezoar). PCA analysis indicated that wild goats exhibit a relatively homogeneous population structure, distinct from African and European goats without evidence of admixture or genetic exchange.

Milk production traits play an important role in the economic viability of dairy goats and also serve as their defining characteristics. These traits, influenced by minor polygenes, are categorized as quantitative traits. Key indicators of milk production traits include milk yield, milk protein, and fat yield, as well as milk protein and fat content [37]. Milk fat, an essential natural fat, plays a key role in milk composition, consisting of 99% milk triglycerides [38]. These triglycerides are mainly produced by mammary epithelial cells (MECs) and blood, and their synthesis and transfer involve multiple pathways, such as de novo fatty acid synthesis, fat droplet formation, and fatty acid uptake and transport [2]. This study revealed that 10 genes (ATF7, ABTB2, ACSS2, DGAT2, DNAJC24, FA2H, ITFG1, NFX1, RFX4, and UBE2R2) are linked to milk fat synthesis (TableS3-S7). For example, DGAT2 is essential for the final step of triacylglycerol (TAG) biosynthesis in the Kennedy pathway and can significantly impact milk production and fat content in goats [39, 40]. ACSS2 gene detected by five methods in this study (Fig. 6A), is involved in lipogenesis by converting acetate into acetyl-CoA (TableS10), a process regulated by SREBP1 and crucial for ruminant milk fat synthesis [41]. Additionally, we confirm the selection of the ACSS2 gene between dairy and wild goats through EHHS analysis, and compare the conservation of this gene in goats, sheep, and cattle (Fig. 7). All these results collectively validate the crucial role played by the ACSS2 gene in the characteristics of goat milk.

In addition, goat milk proteins possess unique biologically active components that affect the milk properties and impact numerous aspects of human nutrition. Goat milk contains less lactose and higher alkalinity than cow milk [42]. In this study, we have pinpointed several genes (LARP4B, SPIDR, NCKAP1L, PITRM1, and GHR) that may play a role in the synthesis of milk proteins (Table S3-S7). For example, LARP4B is a member of a protein family that is evolutionarily conserved and is involved in RNA metabolism and translation. This protein family is made up of five sub-families, with one being a genuine La protein and the other four being La-related protein (LARP) sub-families. It is suggested that LARP4B may enhance amino acid transport as a cytoplasmic protein [43]. The activation of the GHR gene leads to improved functionality of mammary gland cells, ultimately contributing to higher milk output in buffaloes [44], dairy cows [45], and sheep [46].

Furthermore, we have also pinpointed genes associated with milk production traits (B4GALT1, HTR3C, VPS13C, PRPF6, FCHSD2, ITFG1, RBM19, and PPP1R1A) (TableS3-S7). For example, The B4GALT1 gene encodes the catalytic part of the enzyme lactose synthase, responsible for lactose synthesis in the mammary gland, and is potentially associated with milk production traits in dairy cows [47]. The serotonin receptor HTR3C is necessary for the signaling of serotonin, a neurotransmitter that is essential for the regulation of milk synthesis in the epithelium of the mammary gland [48]. PRPF6 plays a crucial role in the regulation of the androgen receptor (AR) by interacting with its N-terminus, thereby boosting

AR-mediated transactivation. This function is closely linked to milk production in cows [49]. PPP1R1A has been found to have a significant association with growth and milk quality traits [50] through its regulation of insulin secretion [51].

Epidermal growth factor (EGF) plays a crucial role in the development and maintenance of mammary gland morphology, according to Accornero et al. [52]. EGF receptors are located in the rapidly growing mammary ductal region and the surrounding stromal cell area. Activation of EGF receptors triggers multiple intracellular signaling pathways related to cell proliferation and survival. This study discovered significant GO terms, specifically vascular endothelial growth factor receptor binding (GO: 0005172) (TableS11), that play a crucial role in the lactation process of dairy goats. In addition, Hormones and cytokines are important signaling molecules that regulate cellular metabolism in multicellular organisms. research studies have shown that the uptake of glucose by mammary epithelial cells is influenced by the developmental stage of the mammary gland and the nutritional status, indicating that this process is regulated by lactogenic hormones such as prolactin and growth hormone [53]. The pathways identified in this study, such as growth hormone synthesis, secretion, and action (hsa04935) (TableS11), could be crucial in understanding milk traits associated with lactation [54]. Furthermore, the synthesis of lactose, using glucose as a precursor, takes place in the Golgi apparatus cisternae of mammary epithelial cells. Lactose is synthesized in the Golgi apparatus cisternae and transferred to the apical membrane of epithelial cells through secretory vesicles, and during this process, water enters the secretory vesicles containing lactose due to the osmotic effect of lactose. Therefore, lactose synthesis has a direct impact on milk production [47]. Consequently, pathways associated with lactose metabolism, and glucose metabolism may also affect milk products. This research indicates that there may be a connection between the acyl-CoA metabolic process (GO: 0006637), crucial for glucose metabolism, and the development of goat milk flavor [55]. Additionally, the galactose metabolism pathway (hsa00052) involving the B4GALT1 gene, linked to milk production traits [47], may also play a role (TableS11).

Dairy goats, being seasonal breeding animals, possess certain genes associated with reproduction. In this research, several genes linked to reproduction were discovered. For example, STAG1 and PCCB, two crucial genes associated with embryonic development, have undergone long-term balancing selection following domestication [19]. ECE2 was detected in cashmere goats related to Fertility and embryo development [56]. The absence of the CHMP5 gene, essential for embryogenesis, leads to early embryonic lethality in mice [57]. TSHB is a key element of thyroid-stimulating hormone (TSH) that influences the biological specificity and synthesis rate of TSH. Additionally, it is closely associated with the photoperiod of seasonal reproduction in mammals [58]. BIRC6 has been shown to play a role in follicle development in broilers, as well as early embryonic development and fertility in Bos indicus [56].

Furthermore, intramammary infections and mastitis are known to cause a decrease in milk production and quality in dairy goats. This research has pinpointed several genes related to the immune system and disease resistance. For example, IRAK3 is an essential player in the Toll-like receptor (TLR) signaling pathway, responsible for regulating immune responses. Its primary role is to serve as a negative regulator of TLR signaling, ensuring that the innate host defense mechanisms are adjusted to prevent prolonged and excessive inflammation [59]. GALNT8 plays a role in both innate and acquired immune responses, as well as cytokine signaling, all of which are essential for defending sheep from parasitic invasion [60]. In sheep, ARHGEF17 has been pinpointed as a gene that may impact serum levels of immunoglobulin A (IgA), a key marker for resistance against gastrointestinal nematodes [61]. NHSL1 plays a role in metabolism and has been correlated with subclinical ketosis and resistance to gastrointestinal nematodes in mature sheep [61]. Additionally, this gene has been associated with protection against tick parasites [62], indicating its importance in improving environmental adaptation [63]. Additionally, as dairy goats are found in various environmental conditions, genetic adaptations to their surroundings have been retained through both natural evolution and selective breeding. Genes associated with environmental adaptation have been identified. For example, ADAMTS6 is implicated in porcine growth traits and has a connection to high-altitude adaptation in Chinese sheep [64]; ZNF536 has been identified as a significant gene associated with cold tolerance in Chantecler chickens [65]. In goat breeds, PARP4, ZMYM5, PSPC1, and GJB2 were identified as high altitude-related genes in previous reports [66]. In the comparison between European and African dairy goats, it is evident that selection signals in these regions are predominantly associated with adapting to local environments. Factors such as cashmere traits (TOMM70), immune responses (ADGRG7), disease resistance (TFG), and seasonal patterns (DPH6) play a crucial role in this regard. The disparities in climate between Africa and Europe are the main contributing factor. Africa's climate is characterized by arid conditions, high temperatures, and a prevalence of various livestock diseases, whereas Europe

experiences a more humid, rainy climate with lower average temperatures.

Conclusion

In this study, we utilized whole-genome resequencing data to investigate the selection signatures in dairy goats and pinpoint traits specific to dairy goats such as milk production, reproductive abilities, environmental adaptation, and immune traits. Additionally, we discovered that the ACSS2 gene, identified by five methods, may be specific to dairy goats in certain regions. These findings offer valuable insights into the key economic traits of dairy goats and can serve as a helpful resource for improving and establishing crossbreeding programs for different dairy goat breeds.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12864-025-11437-9.

Supplementary Material 1.

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Authors' contributions
W.F.P drafted the manuscript. Y.Y.Z., L.G. and S.P.W. contributed to Read alignment, variant annotation, and genetic structure. M.T.L. and E.R. S. analyzed the runs of dairy goats' homozygosity (ROH). X.K.L., B.L. and Y.X.Z. performed selection signatures of dairy goats. Y.F.G., M.Y.W., Y.M.Z, Z.H.W, and Y.H., performed the analysis of selection signatures between Africa and Europe goats. G.Y.L., Y.F.G, M.S.Y., S.H.F., and L.H. improved the manuscript and prepared Figs. 1–7. All authors read and approved the final manuscript.

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Data availability
The data used in this manuscript are available from Goat VariationDB (GGVD) databases (http://animal.omics.pro/code/index.php/GoatVar).

Declarations

Ethics approval and consent to participate
All goats were handled following the guidelines established by the Council for Animal Welfare of China. The protocols for sample collection and animal handling have been approved by the Faculty of Animal Policy and Welfare Committee of Zhoukou Normal University (ZKNU, Protocol number, ZKNU-2024014).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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