



Review Article

Advancing Yak Breeding in China: Harnessing Genetic Resources and Marker-Assisted Selection for Improved Production Traits

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ABSTRACT

Yak breeding plays a crucial role in sustaining livestock production and ensuring the livelihoods of communities in the mountainous regions of China. With the aim of improving production traits in yaks, this study explores the potential of harnessing genetic diversity and marker-assisted selection (MAS) techniques. The genetic diversity of yak populations is a valuable resource that can be tapped into to enhance desirable traits such as meat quality, milk yield, disease resistance, and adaptability to harsh environments. This study emphasizes the importance of conducting comprehensive genetic characterization of yak populations across different regions in China to identify unique genetic variations and breed-specific traits. Furthermore, the integration of MAS techniques can facilitate the selection of superior individuals for breeding programs. By identifying and utilizing genetic markers associated with desired traits, breeding strategies can be optimized, resulting in accelerated genetic improvement. Various molecular markers, such as single nucleotide polymorphisms (SNPs), microsatellites, and candidate genes, can aid in the identification of economically important traits in yaks. The availability of high-throughput genotyping technologies and advanced statistical models further support the efficient implementation of MAS in yak breeding programs.

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NJ, CL, MZK and W-DB designed the study and wrote the manuscript. The sources data were collected by NJ, RM, SU, CL, MZK, W-DB, YM, GS, MS, ZZ, D-ZL, QU, MKS, and SN. The manuscript was reviewed and edited by all authors. All authors were informed and agreed to publish the manuscript.

Key words

Yak, Genetic resources, China, Genetic markers, Copy number variations, Production traits, Genomics

INTRODUCTION

The domestic yak (*Bos grunniens*) and Wild yak (*Bos mutus*) holds great significance in Tibetan culture, serving as a vital resource for local communities residing in high-altitude regions (Gao *et al.*, 2022). These yaks provide essential commodities like meat, milk, transportation, fuels, and hides to sustain the livelihoods of the people living in these challenging environments. Several studies,

including [Jia *et al.* \(2019, 2020\)](#) have highlighted the crucial role played by yaks in Tibetan culture.

The domestic yak is believed to have descended from the wild yak (*Bos mutus*), with the Qinghai Province in China recognized as a primary center for yak domestication. This region possesses a wide range of yak genetic resources and unique yak populations and breeds due to its distinct geographical location, complex plateau climate, and extensive breeding history. Studies conducted by [Guo *et al.* \(2006\)](#), [Ma \(2018, 2022\)](#), and the [National Committee of Animal Genetic Resources \(2021\)](#) have shed light on the rich genetic diversity of yaks in Qinghai Province. Studying yak genetics and breeding has dual benefits: Supporting local animal husbandry development and contributing to the understanding of animal and human adaptation to the plateau, where yaks are the main local livestock species providing essentials and income for herders. Advances in animal genetics and breeding technology have led to the widespread use of molecular markers such as SNP, indel, and SVs in improving and selecting economically valuable traits in livestock, with SNP being particularly popular due to its richness, high polymorphism, and reproducibility. Indel, characterized by insertions or deletions of segments smaller than 50 bp, offers the advantage of convenience and efficiency in detection compared to SNP, making it a valuable tool in genetic analysis and research.

It is widely recognized that many production traits and diseases in animals are influenced by multiple genes ([van Rheenen *et al.*, 2019](#)). Traditional methods have proven insufficient in effectively improving production performance and disease control in animals. Consequently, current research in animal science is primarily focused on identifying markers and elucidating the underlying mechanisms that govern these phenotypes ([Goddard and Hayes, 2009](#)). Various genetic approaches, such as RNA-sequencing ([Khan *et al.*, 2020](#); [Augustino *et al.*, 2020](#); [Liu *et al.*, 2022](#)), whole-genome sequencing, mapping of quantitative trait loci (QTL) ([Uemoto *et al.*, 2021](#)), candidate gene analysis ([Yang *et al.*, 2016](#)), and genome-wide association studies (GWAS) ([Wang *et al.*, 2022](#); [Kai-Yuan *et al.*, 2022](#)), have been employed to identify key genes or their polymorphisms that are associated with production traits and disease resistance in animals ([Ma *et al.*, 2021](#); [Khan *et al.*, 2023](#)).

The utilization of markers for milk quality, production traits, disease resistance ([Khan *et al.*, 2022](#); [Yang *et al.*, 2023](#)), thermo-tolerance, fertility, and carcass quality in cattle plays a critical role in enhancing their health and productivity ([Khan *et al.*, 2022](#)). Similarly, several GWAS studies have been conducted in yaks to identify genetic markers and their associations with production traits,

including growth traits ([Jia *et al.*, 2020](#)), body weight ([Wang *et al.*, 2022](#); [Liu *et al.*, 2023](#); [Jiang *et al.*, 2022](#)). Additionally, transcriptomic analysis has been employed to identify potential genes associated with various traits in yaks, such as reproductive traits ([Lan *et al.*, 2014](#); [Zhou *et al.*, 2022](#); [Zhang *et al.*, 2022](#); [Pei *et al.*, 2023](#); [Chen *et al.*, 2022](#)), milk production traits ([Wu *et al.*, 2020](#); [Cao *et al.*, 2022](#)), and meat production traits ([Wang *et al.*, 2020](#); [Ma *et al.*, 2023](#)). These markers facilitate targeted selection and breeding programs aimed at optimizing production and reducing infection risks in yaks. Thus, in this review, we focus on the available yak breeds in China, their biodiversity, and the genetic markers associated with various productive and reproductive traits.

GENETIC RESOURCES AND BIODIVERSITY OF YAK IN CHINA

The available genetic resources of yak have been summarized in [Table I](#). Genetic diversity, a key component of biological diversity, plays a significant role in biological evolution, species differentiation, population maintenance, and adaptation to changing habitats. Some researchers, such as [Li *et al.* \(2023\)](#), have emphasized the importance of genetic diversity in various biological processes. The development of electrophoresis and sequencing technologies provides opportunities to accurately evaluate the genetic diversity of yak populations at the molecular level. Since the late 1990s, random amplified polymorphic DNA (RAPD), amplified fragment length polymorphism (AFLP), sequence-related amplified polymorphism (SRAP), and simple sequence repeat (SSR) markers have been used to evaluate the molecular genetic diversity of yaks ([Ma *et al.* 2013](#)).

Recent investigations into the Y-chromosomal and maternal genetic diversity of wild and domestic yaks in the Qinghai Province have yielded notable findings. Studies conducted by [Ma *et al.* \(2018, 2022\)](#), [Wang *et al.* \(2021\)](#), and [Li *et al.* \(2022\)](#) have demonstrated the presence of substantial genetic diversity, weak phylogeographic structures, and multiple origins within these yak populations. Furthermore, the development of a high-quality reference genome for yaks, known as BosGru3.0 (GCA_005887515.2), using advanced long-read sequencing technology, has significantly enhanced our ability to investigate genomic diversity, ascertain population structures, and determine phylogenetic relationships among different yak breeds and populations at the genomic level. This breakthrough has also facilitated the identification of the genetic foundations underlying complex traits exhibited by yaks. Studies conducted by

Table I. Summary of genetic resources available in China.

| Breeds or genetic resources | Location | References |
|---|---|-----------------------------|
| Tianzhu white yaks | Lanzhou (China) | Bao <i>et al.</i> , 2022 |
| Maiwa yak | Qinghai Province, China | Cai <i>et al.</i> , 2015 |
| Ashidan yaks | Qinghai Province, China | Dai <i>et al.</i> , 2022 |
| Tianzhu white yak, Qinghai-Plateau yak, Xinjiang yak, Gannan yak, Datong Yak | Gansu, China | Ding <i>et al.</i> , 2012 |
| Ashidan yaks | Qinghai Province, China | Ge <i>et al.</i> , 2019 |
| Datong yak, Gannan yak, polled yak, Tianzhu white yak, plateau yak | Qinghai and Lanzhou provinces, China | Goshu <i>et al.</i> , 2018a |
| Chinese Datong yaks | Qinghai Province, China | Goshu <i>et al.</i> , 2018b |
| Chinese Datong yaks | Qinghai province, China | Goshu <i>et al.</i> , 2019a |
| Datong yaks, Polled yaks, Tianzhu yaks, Gannan yaks | Qinghai Province, China | Goshu <i>et al.</i> , 2019b |
| Chinese Datong yaks | Lanzhou province, China | Goshu <i>et al.</i> , 2020 |
| Chinese indigenous yak | Qinghai Province, China | Gui <i>et al.</i> , 2021 |
| Gannan yaks | Gansu Province, China | Hu <i>et al.</i> , 2019 |
| Ashidan yaks | Qinghai-Tibet Plateau (China) | Huang <i>et al.</i> , 2021 |
| Jiali, Pali, Sibü yaks | Qinghai-Tibet Plateau (China) | Jiang <i>et al.</i> , 2022 |
| Ashidan yaks | Qinghai Province, China | Li <i>et al.</i> , 2022b |
| Jiulong yak, Zhongdian yak | Sichuan province, China | Liu <i>et al.</i> , 2011 |
| Ashidan yaks | Qinghai Province, China | Liu <i>et al.</i> , 2022 |
| Tianzhu white yaks | Lanzhou (China) | Meng <i>et al.</i> , 2022 |
| Datong yaks | Qinghai Province, China | Peng <i>et al.</i> , 2020 |
| Ashidan yaks | Qinghai Province, China | Ren <i>et al.</i> , 2022 |
| Gannan yak | Gansu, China | Shi <i>et al.</i> , 2019 |
| Datong yak, Xueduo yak, Huanhu yak, Gannan yak, Tianzhu White yak, Niangya yak, Leiwuqi yak, Sibü yak, Muli yak, Jiulong yak, Maiwa yak, Zhongdian yak, Bazhou yak, Ashidan yak | Qinghai-Tibet Plateau (China) | Wang <i>et al.</i> , 2015 |
| Maiwa yaks | Sichuan and Qinghai-Tibet Plateau (China) | Wang <i>et al.</i> , 2022 |
| Tianzhu white yaks | Lanzhou (China) | Wang <i>et al.</i> , 2023 |
| Pali, Gannan, Tianzhu White yaks | China | Wu <i>et al.</i> , 2015 |
| Datong yak | Qinghai Datong, China | Wu <i>et al.</i> , 2020 |
| Gannan yaks | Gansu Province, China | Yan <i>et al.</i> , 2014 |
| Tianzhu white yak , Tibetan yaks | Lanzhou and Tibet (China) | Yang <i>et al.</i> , 2019 |
| Maiwa, Jiulong, Jinchuan, Changtai | Sichuan Province, China | Yang <i>et al.</i> , 2021 |
| Gannan yaks | Gansu Province, China | Zhang <i>et al.</i> , 2021 |
| Tianzhu | Gansu Province, China | Zhang <i>et al.</i> , 2021 |
| Jiali yak, Sibü yak, Cawula yak | Tibet province, China | Zhang <i>et al.</i> , 2022b |
| Jiali yak, Sibü yak, Cawula yak | Tibet province, China | Zhang <i>et al.</i> , 2022b |
| Ashidan yaks | Qinghai Province, China | Zhang <i>et al.</i> , 2022c |
| Jiulong yak | Sichuan (China) | Zheng <i>et al.</i> , 2011 |
| Wild yak | Tibet province, China | Wang <i>et al.</i> , 2011; |
| Zhongdian | Yunan (China) | Wu <i>et al.</i> , 2016; |
| Xinjiang, Bazhou | Xinjiang (China) | Liu <i>et al.</i> , 2023 |
| Tianzhu, Gannan | Gansu, China | |
| Maiwa, Jiulong, Jinchuan, Changtai | Sichuan, China | |
| Qilian, Huanhu, Gaoyuan, Datong | Qinghai, China | |
| Zhongba, Senza, Cuona, Sangsang, Sangri, Sibü, Riduo, Pali, Nierong, Longzi, Leiwuqi, Kangbu, Lijia, Jiangda, Gongbujiangda, Baqing, Dingqing, Tibet alpine, Nianya, Muli | Tibet, China | |
| Tianzhu, Menyuan and Huzhu | Qinghai-Tibet, China | Luo <i>et al.</i> , 2022 |

Qiu *et al.* (2012), Ji *et al.* (2021), and Zhang *et al.* (2021) have leveraged the BosGru3.0 reference genome to explore the genetic diversity of yaks, uncover their population structure, and delve into the genetic underpinnings of intricate traits. Recently, the examination of maternal genetic diversity in wild and domestic yak breeds/populations, specifically Qinghai-Plateau, Huanhu, Xueduo, and Yushu yak, was conducted based on nucleotide variants of mitogenomes. The findings indicated that both domestic and wild yak from Qinghai display a broad spectrum of maternal variability, with a weak genetic differentiation observed among the indigenous yak populations in Qinghai. However, each indigenous yak breed in Qinghai possesses unique maternal genetic information (Li *et al.*, 2022). Regarding the phylogeny of maternal origins in yaks, both wild yak and domestic yak from Qinghai can be classified into three distinct maternal lineages (Lineages I, II, and III), representing three potential maternal origins. However, only a small number of wild and domestic yak individuals carry Lineage III (Li *et al.*, 2022).

Runs of homozygosity (ROH) have become a crucial metric for assessing inbreeding levels and genetic diversity patterns in livestock populations (Xia *et al.*, 2021). A recent study conducted by Li *et al.* (2023) observed notable variations in the distribution of ROHs among nine yak breeds/populations. The study revealed that the Geermu and wild yak populations exhibited low frequencies of ROHs, suggesting their habitats are located far from human settlements and have experienced minimal artificial intervention. Conversely, among the other domestic yak breeds/populations, the Datong yak demonstrated the highest counts and lengths of ROHs, followed by Yushu, Huanhu, Tongde, Huzhu white, Xueduo, and Qilian yak (Li *et al.*, 2023).

In a study conducted by Ji *et al.* (2021), it was demonstrated that wild yak populations had undergone a genetic bottleneck, a phenomenon characterized by a reduction in genetic variation. Surprisingly, despite this bottleneck event, the genomic diversity of wild yak remained comparatively higher than that of domestic yak. This contradicts the findings of Qiu *et al.* (2015), who concluded that the genomic nucleotide diversity of domestic yak slightly exceeded that of wild yak. According to their research, the value for domestic yak was 0.0014, while wild yak exhibited a slightly lower value of 0.0013. Similarly, Chai *et al.* (2020) discovered that the genomic diversity of wild yak, with a value of 0.0012, was lower than that observed in specific domestic yak breeds or populations, ranging from 0.0010 to 0.0016. These contrasting findings highlight the complexity of genomic diversity patterns in wild and domestic yak and underscore the need for further investigation and analysis.

GENETIC MARKERS ASSOCIATED WITH PRODUCTION TRAITS IN YAK

Genetic markers are specific sequences of DNA that can be used to identify and locate genes or other segments of DNA within the genome. These markers can be variations in the DNA sequence, such as single nucleotide polymorphisms (SNPs), or structural variations, such as insertions or deletions.

Copy number variations (CNVs) in genes

Copy number variations (CNVs) refer to structural variations in the genome that involve the duplication or deletion of larger DNA segments, including entire genes (Hastings *et al.*, 2009). CNVs can have significant impacts on gene expression levels and functional diversity, thus influencing various traits in organisms, including production traits in livestock species (Bickhart *et al.*, 2012) such as yak (Dutreuil *et al.*, 2022). Several studies have investigated CNVs in the yak genome and their associations with production traits, and are summarized in Table 1. Huang *et al.* (2021) investigated the copy number variation (CNV) of the *HPGDS* gene in the Ashidan yak breed and its association with growth traits. The study found that Ashidan yaks with a higher copy number of the *HPGDS* gene had higher body weight, chest circumference, and hip circumference than those with a lower copy number. The researchers suggest that *HPGDS* gene could be a potential genetic marker for selecting breeding yaks with better growth traits. Zhang *et al.* (2022) explored the CNV of the SRY-like box genes (*SOX5* and *SOX8*) in the yak and their relationship with growth traits. The study identified two different CNVs of the *SOX5* and *SOX8* genes in yaks, and found that yaks with a higher copy number of the *SOX5* gene had larger chest circumference, body length, and body weight, while those with a higher copy number of the *SOX8* gene had higher body weight, chest circumference, and hip circumference. The authors suggest that these genes could be potential genetic markers for selecting breeding yaks with better growth traits. Dai *et al.* (2022) focused on the CNV of the aromatic hydrocarbon receptor (*AHR*) gene in Ashidan yaks and its association with growth traits. The study found that Ashidan yaks with a higher CNV of the *AHR* gene had higher body weight, chest circumference, and hip circumference than those with a lower CNV. In a study conducted by Ge *et al.* (2019), it was discovered that cell adhesion molecule 2 (*CADM2*) is expressed widely in the brain and adipose tissue and plays a role in regulating body weight through the central nervous system. The researchers identified two copy number variations (CNVs) in the *CADM2* gene that were associated with growth traits in Chinese Ashidan yak.

A significant effect of CNV2 ($p < 0.05$) was observed on body weight at 6 months, with the gain-type copy number variation showing superior performance compared to other variants, resulting in increased body weight at 6 months ($p < 0.05$). This study represents the first exploration into the function of CADM2-CNVs and their association with growth traits in animals.

Furthermore, a related study conducted by Ren *et al.* (2022) reported that heat shock factor 1 (HSF1)-CNV exhibited a significant association with body length ($p < 0.05$) and a highly significant association with withers height ($p < 0.01$) in 18-month-old Ashidan yaks. Additionally, the relative expression of HSF1 in the heart and muscle tissues was found to be significantly higher than in other tissues ($p < 0.01$). Liu *et al.* (2022) investigated the association between copy number variations (CNVs) in the casL-like protein 2 (*MICALL2*) and monoacylglycerol O-acyltransferase 2 (*MOGAT2*) genes and growth traits in Ashidan yaks. The study found that Ashidan yaks with higher CNVs of the *MICALL2* gene had larger chest circumference and body weight, while those with higher CNVs of the *MOGAT2* gene had larger hip circumference and body weight. Consequently, Huang *et al.* (2021) investigated the impact of copy number variation (CNV) in the *HPGDS* gene on the growth traits of Ashidan yaks. Significant correlations were found between HPGDS-CNV and body weight and body length at different ages. Individuals with gain copy number type showed better performance in these traits (Huang *et al.*, 2021).

Consistently, Wang *et al.* (2023) identified a novel structural variation (SV) in the *GHR* gene and its association with growth traits in yaks. The study found that yaks with a higher copy number of the SV in the *GHR* gene had larger chest circumference, hip circumference, and body weight. The authors suggest that this SV could be a potential genetic marker for selecting breeding yaks with better growth traits. Similarly, another study documented the copy number variations (CNVs) of the glypican1 (*GPC1*) gene in five domestic yak breeds [Polled yak (Qinghai province), Tianzhu white yak (Gansu province, Tianzhu Tibetan autonomous county, China), Plateau Yak (Qinghai province, northern and southern Qinghai, China), Datong Yak (Qinghai province, Datong Yak Farm in Qinghai, China), Gannan yak (Gansu province, bordering Sichuan and Qinghai, China)] and their association with growth traits and gene expression (Goshu *et al.*, 2019a). The researchers utilized real-time quantitative PCR (qPCR) for data analysis. They found that loss and normal copy number types of *GPC1* were significantly associated with body height, weight, length, and chest girth compared to gain of copy number types. The study also revealed a negative correlation between DNA copy numbers and

mRNA transcription levels of *GPC1*, suggesting that *GPC1* CNVs could influence mRNA transcription levels in skeletal muscles, ultimately affecting quantitative growth traits (Goshu *et al.*, 2019a). Accordingly, a study investigated the copy number variation (CNV) of the choline kinase beta (*CHKB*) gene in Chinese domestic yak breeds and its impact on gene expression and growth traits. The researchers found that normal CNV of the *CHKB* gene was significantly associated with greater chest girth and body weight in Datong yaks across different age groups (Goshu *et al.*, 2019b). A previous study utilizing next-generation sequencing demonstrated that the cholinergic receptor muscarinic 3 (*CHRM3*) gene is located within copy number variable regions (CNVRs) in yak populations, which overlap with quantitative trait loci (QTL) associated with meat quality and growth (Goshu *et al.*, 2020). In addition, they found that the gain CNV type in the *CHRM3* gene was strongly associated ($P < 0.05$) with various growth traits in both six-month-old and five-year-old Datong yaks. The gain CNV type was more prevalent than the loss and normal types across all yak breeds. Notably, the *CHRM3* gene copy number exhibited a highly significant ($P < 0.0012$) and moderately negative correlation with mRNA transcription levels in the skeletal muscle of Chinese Datong yaks (Goshu *et al.*, 2020). Consistently, a study focused on the association between copy number variations (CNVs) of the kruppel-like factor 6 (*KLF6*) gene and growth traits in Chinese domestic yak breeds, found that *KLF6* CNVs were prevalent in yak populations and correlated with mRNA expression levels in skeletal muscles. They further revealed a negative relationship between DNA copy numbers of *KLF6* and gene expression, suggesting that *KLF6* CNVs play a significant role in determining growth traits in yak breeds (Goshu *et al.*, 2018).

Single nucleotide polymorphisms in genes

A study focused on analyzing the Ankyrin 1 (*ANK1*) gene in yak and identified a total of nine single-nucleotide polymorphisms (SNPs) (Hu *et al.*, 2021). Out of these SNPs, four were found in the coding region, and three SNPs (c.179 C/A, c.250 G/C, and c.313 C/T) were predicted to cause amino acid changes (p. Ala 60 Glu, p. Asp 84 His, and p. Pro 105 Ser). Additionally, certain SNPs were observed in the promoter region, specifically within or in close proximity to potential transcription factor binding sites. Some SNPs were found in promoter regions, potentially affecting gene expression. Certain SNP combinations were associated with increased hot carcass weight, decreased drip loss rate, and decreased Warner-Bratzler shear force, indicating that *ANK1* gene variations could serve as useful biomarkers for improving yak meat

quality. Consistently, an experimental trial documented *T2416C*, *T3490C*, and *A7500G* variants of the *GHR* gene, *T1387C* in *GHSR* and *A757 G* and *T949C* in Maiwa yak. The above identified SNPs in *GHR*, *GH*, and *GHSR* were significantly associated with cannon circumference and body weight in Maiwa yak (Hai *et al.* 2017). Similarly, another study identified four SNPs (g.6256 C > T (c.298 C > T), g.96284 G > A (c.3090 G > A), g.24791 A > G (c.706 A > G) and g.29121 A > G (c.979 A > G) in *ACSL1* genes that were significantly associated with milk fat trait in cattleyak situated in Sichuan province, China.

CANDIDATE GENES ASSOCIATED WITH PRODUCTION TRAITS IN YAK

Candidate genes refer to specific genes that are selected as potential candidates for involvement in a particular trait, disease, or biological process based on prior knowledge or preliminary evidence. Several methods including RNA-seq, microarray, and GWAS studies are utilized to identify candidate genes.

Milk production traits in Yak

Xia *et al.* (2018) conducted a study utilizing quantitative reverse transcription polymerase chain reaction (RT-qPCR) to investigate the gene expression profile associated with yak milk synthesis. Notably, up-regulation of genes involved in various aspects of fatty acid (FA) metabolism was observed during lactation. These included genes responsible for FA uptake from blood (*LPL*, *CD36*), intracellular FA transport (*FABP3*), activation of long- and short-chain FAs (*ACSS1*, *ACSS2*, *ACSL1*), de novo synthesis (*ACACA*), desaturation (*SCD*), triacylglycerol (*TAG*) synthesis (*AGPAT6*, *GPAM*, *LPIN1*), lipid droplet formation (*PLIN2*, *BTN1A1*, *XDH*), ketone body utilization (*BDH1*, *OXCT1*), and transcriptional regulation (*THRSP*, *PPARGC1A*). In particular, the study found that intracellular de novo FA synthesis (*ACSS2*, *ACACA*, and *FABP3*) and TAG synthesis (*GPAM*, *AGPAT6*, and *LPIN1*) exhibited higher levels of activation compared to dairy cows, suggesting coordinated regulation within the gene network controlled by SERBF1 during milk fat synthesis. However, genes involved in lipid droplet formation (*PLIN2*, *XDH*, and *BTN1A1*) exhibited lower expression levels compared to dairy cows, where their regulation is primarily governed by the PPARG regulator. These findings provide valuable insights into the unique mechanisms of milk fat synthesis in yaks compared to dairy cows. Consequently, in a recent study conducted by Xia *et al.* (2023), a comprehensive transcriptome analysis was carried out on yak mammary tissue throughout the entire lactation cycle, revealing the differential expression

of more than 6000 genes. Remarkably, significant changes in gene expression were observed particularly at the onset and conclusion of lactation. The investigation identified several key genes (*ABCG2*, *MTHFR*, *PPAR*, *ENPP3*, *SPP1*, *RPS15*, *RPS23*, *UXT*, *TP53*, *FARP1*, *DGATI*, *SLC1A5*, *LPL*, *FABP3*, *SCD1*, *AGPAT6*, *CSN3*, and *BDH1*) associated with lactation, with functional implications in lipid metabolism, amino acid metabolism, protein synthesis, and glycan biosynthesis. Additionally, the study emphasized the downregulation of genes related to cell cycle regulation and immune response during lactation, suggesting a controlled morphological change and reduced immune hyper-response within the mammary gland. Understanding the genetic makeup of yaks is crucial, and a comparative analysis between early lactation (ELS) and mature lactation (MLS) stages uncovered 25 expressed sequence tags (Wu *et al.*, 2020). Further, their expression analysis confirmed significant up-regulation of 9 genes, including *LAO1* and *COL1A1*, in yak mammary tissue at ELS compared to MLS. Notably, certain milk fat genes exhibited earlier expression peaks in yaks than in dairy cows, and MYC is implicated in regulating *COL1A1*, *CD44*, *SPARC*, *FASN*, and *GPAM* (Wu *et al.*, 2020).

In a study conducted by Wu *et al.* (2020), the underlying mechanism was investigated by employing RNA sequencing to analyze the long non-coding RNA (lncRNA) transcriptome in mammary tissue samples from yak at two distinct physiological stages: lactation (LP) and the dry period (DP). The research findings highlighted that differentially expressed lncRNAs (DELs) were associated with target genes involved in lactation-related pathways, including ECM-receptor interaction, PI3K-Akt signaling pathway, biosynthesis of amino acids, and focal adhesion. Furthermore, these candidate genes were found to be associated with milk yield and quality traits.

Meat production traits in Yak

Transcriptomic analysis conducted on yak fed with total mixed rations (TMR) demonstrated that upregulation of *ACSL1* and *ACACB* genes significantly enhanced the synthesis and deposition of fat during the fattening process (Liu *et al.*, 2021). Conversely, the expression of *SLC7A8*, *ATP1A4*, *ATP1A1*, *SLC3A2*, and *CPA3* genes showed regulatory effects on proteolysis, resulting in its attenuation. These results showed that fattening with TMR enhanced the meat yield and quality in yak by regulating *SLC7A8*, *ATP1A4*, *ATP1A1*, *SLC3A2*, *CPA3*, *ACSL1* and *ACACB* genes in yak. Furthermore, a study focused on the genetic construction of body size among yak breeds using a genome-wide association study (GWAS) (Liu *et al.*, 2023). The pCMLM method, incorporating habitat-based clustering, was employed to analyze five body size

traits in 31 yak breeds (Liu *et al.*, 2023). They found six significant markers associated with height were identified, and four candidate genes (*FXYD6*, *SOHLH2*, *ADGRB2*, and *OSBPL6*) were implicated (Liu *et al.*, 2023). The study highlights the effectiveness of pCMLM in cases where traditional CMLM clustering groups are suboptimal and provides valuable insights into the gene localization of body size traits in yak breeds. In a study, RNA-sequencing was utilized to compare subcutaneous fat thickness in yaks under stall feeding (SF) and graze feeding (GF) (Xiong *et al.*, 2023). SF yaks exhibited enhanced fat deposition capacity, accompanied by significant differences in abundances of triglycerides (TGs), phosphatidylethanolamines (PEs), diglycerides (DGs), sphingomyelins (SMs), and phosphatidylcholine (PC) in subcutaneous fat. Differential gene expression analysis revealed the involvement of the cGMP-PKG signaling pathway and specific genes (*INSIG1*, *ACACA*, *FASN*, *ELOVL6*, *SCD*, *AGPAT2*, and *DGAT2*) in lipid metabolism and triglyceride synthesis (Xiong *et al.*, 2023). These findings contribute valuable insights for yak genetic breeding and promoting healthy feeding practices. Consistently, another study investigated the expression patterns of myostatin (*MSTN*) and calpastatin (*CAST*) genes, negative regulators of skeletal muscle growth, in highland yaks (*Bos grunniens*) (Zheng *et al.*, 2011). mRNA levels of *MSTN* and *CAST* were assessed in various yak tissues, with a focus on longissimus muscle, using semi-quantitative and real-time quantitative RT-PCR. They also examined meat quality traits such as intramuscular fat content, tenderness, and pH in different age groups of yaks and adult Yellow cattle. Their findings revealed tissue-specific expression of *MSTN* and *CAST*, higher levels in longissimus muscle compared to adipose tissue, and lower mRNA levels in yak calves than in adult yaks. Additionally, yak longissimus muscle exhibited lower intramuscular fat content compared to cattle, despite their smaller body size, suggesting differences in muscle expression and composition between adult yaks and yak calves when compared to yellow cattle (Zheng *et al.*, 2011).

Hair follicle and coat color development

A comprehensive study conducted by Bao *et al.* (2022) focused on investigating the genetic mechanisms that contribute to variations in hair length within the Tianzhu white yak breed in China. The researchers employed advanced genomic sequencing techniques to analyze the genomes of both long-haired Tianzhu white yaks (LTWY) and normal Tianzhu white yaks (NTWY). Additionally, they utilized various statistical methods to identify specific genetic loci and genes associated with long-haired traits.

The findings of the study revealed the presence of two significant hotspots on chromosome 6, characterized by the presence of genes such as *FGF5*, *CFAP299*, *ATP8A1*, *SLC30A9*, *SHISA3*, and *TMEM33*. Functional enrichment analysis further elucidated the involvement of multiple signaling pathways, including Ras, MAPK, PI3K-Akt, and Rap1, in the regulation of hair length differences. Moreover, the study highlighted the role of *ACOXL*, *PDPK1*, *MAGEL2*, and *CDHI* as genes associated with hair follicle development, thereby providing novel genetic insights into the mechanisms underlying LTWY hair growth (Bao *et al.*, 2022). In a related study, Meng *et al.* (2022) discovered associations between hair growth and hair follicle development in Tianzhu White yaks. This research identified *ASTN2*, *ATM*, *COL22A1*, *GK5*, *SLIT3*, *PM20D1*, and *SGCZ* as genes linked to these traits. These findings contribute to a broader understanding of the genetic factors involved in hair-related characteristics in the Tianzhu white yak breed. Furthermore, a separate investigation focused on the hair follicle cycle and RNA editing in Tianzhu white yaks. This study identified a total of 54,707 adenosine-to-inosine (A-to-I) RNA editing sites, which resulted in alterations in known genes as well as changes in target genes of microRNAs. Differential RNA editing was found to be associated with crucial processes such as skin development, hair growth, and the hair follicle cycle. Genes involved in peroxisome, metabolic, Notch, and PPAR signaling pathways, along with specific genes including *FAS*, *APCDD1*, *WVVOX*, and *LEPR*, were suggested to play significant roles in hair follicle development. These findings shed new light on the regulation of RNA editing and its impact on hair growth and the hair follicle cycle in Tianzhu white yaks. The genes associated with reproductive traits and related information are given in Table II.

Reproductive traits

Wang *et al.* (2023) conducted a comprehensive single-cell RNA sequencing (scRNA-seq) study on spermatogenesis in sexually mature yak, revealing six somatic cell types and various germ cells. Pseudo-timing analysis demonstrated the common progenitor origin of Leydig and myoid cells in yaks. Functional enrichment analysis highlighted significant involvement of cAMP, PI3K-Akt, MAPK signaling pathways, and ECM receptor interactions in testicular somatic cells. Candidate marker genes for spermatogonial stem cells and sertoli cells were identified, offering potential applications in *in-vitro* culture and identification of yak spermatogonial stem cells (Wang *et al.*, 2023). Consequently, in a recent study, the

Table II. Genetic markers associated with production traits in Yak.

| Genes | Associated traits | Breed | Country | References |
|--|---|--|--------------------------------------|-----------------------------|
| <i>FGF5, CFAP299, ATP8A1, SLC30A9, SHISA3, TMEM33, COXL, PDPK1, MAGEL2, CDH1</i> | Associated with metabolism, hair growth and hair-follicle development | Tianzhu white yaks | Lanzhou (China) | Bao <i>et al.</i> , 2022 |
| <i>MC4R</i> | Improved metabolism and Growth traits | Maiwa yak | Qinghai Province, China | Cai <i>et al.</i> , 2015 |
| <i>AHR</i> | Growth traits | Ashidan yaks | Qinghai Province, China | Dai <i>et al.</i> , 2022 |
| <i>LPL</i> | Carcass traits and fat deposition | Tianzhu white yak, Qinghai-Plateau yak, Xinjiang yak, Gannan yak, Datong Yak | Gansu, China | Ding <i>et al.</i> , 2012 |
| <i>CADM2</i> | Body weight and growth traits | Ashidan yaks | Qinghai Province, China | Ge <i>et al.</i> , 2019 |
| <i>CHKB, KLF6, GPC1 and CHRM3</i> | Meat quality and growth traits | Datong yak, Gannan yak, polled yak, Tianzhu white yak, plateau yak | Qinghai and Lanzhou provinces, China | Goshu <i>et al.</i> , 2018a |
| <i>KLF6</i> | Modulate gene transcription and growth traits | Chinese Datong yaks | Qinghai Province, China | Goshu <i>et al.</i> , 2018b |
| <i>GPC1</i> | Growth traits | Chinese Datong yaks | Qinghai province, China | Goshu <i>et al.</i> , 2019a |
| <i>CHKB</i> | Meat production and quality | Datong yaks, Polled yaks, Tianzhu yaks, Gannan yaks | Qinghai Province, China | Goshu <i>et al.</i> , 2019b |
| | | Chinese Datong yaks | Lanzhou province, China | Goshu <i>et al.</i> , 2020 |
| <i>GHI</i> | Growth-related traits | Chinese indigenous yak | Qinghai Province, China | Gui <i>et al.</i> , 2021 |
| <i>GH, GHR and GHSR</i> | Body weight | Maiwa yaks | Sichuan, Tibet province (China) | Hai <i>et al.</i> , 2017 |
| <i>DGAT2</i> | Carcass and meat quality traits | Gannan yaks | Gansu Province, China | Hu <i>et al.</i> , 2019 |
| <i>HPGDS</i> | Growth traits | Ashidan yaks | Qinghai-Tibet Plateau (China) | Huang <i>et al.</i> , 2021 |
| <i>GRK4</i> | Body growth and development | Jiali, Pali, Sibu yaks | Qinghai-Tibet Plateau (China) | Jiang <i>et al.</i> , 2022 |
| <i>SOX6</i> | Growth and development Immune function and neurogenesis | Ashidan yaks | Qinghai Province, China | Li X <i>et al.</i> , 2022 |
| <i>DGAT1 K232A</i> | Milk Quality Traits Milk fat percentage and fatty acid profiles | Jiulong yak, Zhongdian yak | Sichuan province, China | Liu <i>et al.</i> , 2011 |
| <i>MICALL2 MOGAT2</i> | Body weight, length, and height. Mitochondrial protein targeting and exhibits predicted stress fiber colocalization | Ashidan yaks | Qinghai Province, China | Liu <i>et al.</i> , 2022 |

Table continued on next page.....

| Genes | Associated traits | Breed | Country | References |
|--|---|--|---------------------------------|-----------------------------|
| <i>ASTN2, ATM, COL22A1, GK5, SLIT3, PM20D1, SGCZ</i> | Associated with metabolism, hair growth and hair-follicle development | Tianzhu white yaks | Lanzhou (China) | Meng <i>et al.</i> , 2022 |
| <i>TLR2</i> | Body's immune regulation mechanism | Datong yaks | Qinghai Province, China | Peng <i>et al.</i> , 2020 |
| <i>HSF1</i> | Heat stress regulation and maximizes heat shock protein (HSP) expression. Growth traits (withers height, body weight, chest girth, and body length) | Ashidan yaks | Qinghai Province, China | Ren <i>et al.</i> , 2022 |
| <i>FASN</i> | Milk Regulation i.e., milk fat percentage and total milk solid percentage | Gannan yak | Gansu, China | Shi <i>et al.</i> , 2019 |
| <i>GHR</i> | Growth traits | Datong yak, Xueduo yak, Huanhu yak, Gannan yak, Tianzhu White yak, Niangya yak, Leiwuqi yak, Sibuyak, Muli yak, Jiulong yak, Maiwa yak, Zhongdian yak, Bazhou yak, Ashidan yak | Qinghai-Tibet Plateau (China) | Wang F <i>et al.</i> , 2023 |
| <i>MFSD14A, SASS6, TRMT13, LRRC39, DBT, NCAM2, TFPI, BPTF, KPNA2</i> | Growth and development traits | Maiwa yaks | Sichuan, Tibet province (China) | Wang <i>et al.</i> , 2022 |
| <i>UCHL1, ZPBP, ACRV1, ACTL7B, HOOK1, TEX35, CAPZA3, HEMGN, TEX29, SPATA19, TKTL1, SOX9, WFDC2 VWF, CD34, PALMD, CIQA, CSF1R, CYP11A1, IGFBP5, INHBA, LGALS3, ACTA2, MYH11, TAGLN, FHL2 NKG7 SYCP1, MEIOB, SYCP2, SYCE1, DMRTC2, ZPBP, SPATA16</i> | yak spermatogenesis and the development of various types of cells in the testis, | Tianzhu white yaks | Lanzhou (China) | Wang X <i>et al.</i> , 2023 |
| <i>EPAS1</i> | High Altitude Polycythemia, higher hemoglobin concentration | Pali, Gannan, Tianzhu White yaks | China | Wu <i>et al.</i> , 2016 |
| <i>MyHC</i> | Muscle tissues of domestic yak, Improved meat quality | Datong yak | Qinghai Datong, China | Wu <i>et al.</i> , 2020 |
| <i>PPP2R2B and TBLR1</i> | Extra thoracolumbar vertebral and meat production traits | Jinchuan yak | Sichuan, China | Wang Y <i>et al.</i> , 2020 |
| <i>Dmrt7</i> | Sexual development Male yak fertility | Gannan yaks | Gansu Province, China | Yan <i>et al.</i> , 2014 |
| <i>PDCD1, NUP210, ABCG8, NEU4, COL4A1, RTP5, LOC102287650, D2HGDH, HDAC11</i> | Associated with coat color and metabolism | Tianzhu white yak, Tibetan yaks | Lanzhou and Tibet (China) | Yang <i>et al.</i> , 2019 |
| <i>SORBS1</i> | Milk fat regulation | Maiwa, Jiulong, Jinchuan, Changtai | Sichuan Province, China | Yang <i>et al.</i> , 2021 |
| <i>WNT5A, HOXC13, DLX3, FOXN1, OVOL1, FER, ELMO1, PCOLCE, HOXC13</i> | Hair follicle development | Gannan yaks | Gansu Province, China | Zhang <i>et al.</i> , 2021 |

Table continued on next page.....

| Genes | Associated traits | Breed | Country | References |
|---|---|---------------------------------|-------------------------|-------------------------------|
| <i>DELS</i> | Muscle growth and development | Tianzhu | Gansu Province, China | Zhang <i>et al.</i> , 2021 |
| <i>ACSL1</i> | Milk yield, milk fat content, milk protein percentage | Jiali yak, Sibü yak, Cawula yak | Tibet province, China | Zhang Q <i>et al.</i> , 2022b |
| <i>GHSR</i> | Growth and development traits | Jiali yak, Sibü yak, Cawula yak | Tibet province, China | Zhang <i>et al.</i> , 2022b |
| <i>SOX5, SOX8</i> | Withers height and chest girth | Ashidan yaks | Qinghai Province, China | Zhang <i>et al.</i> , 2022c |
| <i>MSTN, CAST</i> | Body height, height at hip cross, and chest width index | Jiulong yak | Sichuan (China) | Zheng <i>et al.</i> , 2011 |
| <i>FST, CYP11A1, PIK3R1, PIK3R2</i> | Follicular development | Ashidan yaks | Qinghai (China) | Xu <i>et al.</i> , 2020 |
| <i>COL1A2, NR4A1, THBS2, PTGS2, SCARB1, STAR, WNT2B</i> | Follicular growth, ovulation, and hormone metabolism. | Gannan yaks | Gansu (China) | Guo <i>et al.</i> , 2021 |
| <i>ACSL1, ACACB, SLC7A8, ATP1A4, ATP1A1, SLC3A2, CPA3</i> | Improve growth and fat in meat | Gannan yaks | Gansu (China) | Liu <i>et al.</i> , 2021 |

Hematopoietic prostaglandin D synthase (*HPGDS*), SRY-like box genes (*SOXs*); CasL-like protein 2 (*MICAL2*); monoacylglycerol O-acyltransferase 2 (*MOGAT2*); Aromatic hydrocarbon receptor (*AHR*); melanocortin 4 receptor (*MC4R*); growth hormone receptor (*GHR*); Diacylglycerol acyltransferase-2 (*DGAT2*); Kruppel-like factor 6 (*KLF6*); Cell adhesion molecule 2 (*CADM2*); sorbin and SH3 domain-containing 1 (*SORBS1*)

researchers investigated the transcriptome profile of the corpus luteum (CL) in Maiwa yak at different stages: Early (EYCL), middle (MYCL), and late (LYCL). Furthermore, the study found that PGRMC1 and PI3K-Akt pathway were significantly associated with steroidogenesis in yak (Yang *et al.*, 2023).

CONCLUSIONS

In conclusion, our exploration of the genetic resources and biodiversity of yak in China has shed light on the remarkable richness and potential that this species holds. Through our research, we have underscored the importance of conserving and leveraging these genetic resources to ensure the long-term survival and sustainable utilization of yaks. The findings presented in this study have deepened our understanding of the genetic diversity within yak populations, which can serve as a valuable foundation for future breeding programs and conservation efforts. Recognizing the unique genetic variations among different yak breeds allows for targeted selection of desirable traits, such as improved milk production, adaptation to harsh environments, and disease resistance. Moreover, we have highlighted the significant advancements in molecular breeding techniques for yaks. The utilization of molecular markers and genomic tools has revolutionized the breeding process, enabling more precise selection and faster genetic improvement. These technologies have the potential to accelerate the development of superior yak breeds with enhanced productivity, resilience, and adaptability. The integration of genetic knowledge and molecular breeding strategies holds great promise for the yak industry in

China and beyond. By harnessing the available genetic resources and biodiversity, we can not only enhance yak production but also contribute to the livelihoods of local communities and the conservation of this iconic species. However, it is crucial to emphasize the importance of sustainable and responsible breeding practices. While genetic advancements offer tremendous opportunities, they must be balanced with ethical considerations, ensuring the welfare and well-being of yaks throughout the breeding process. Conservation efforts should also prioritize the preservation of natural habitats and traditional yak husbandry systems, which have shaped the genetic diversity we observe today.

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Date availability statement

All the data is available in the submitted manuscript.

Informed consent

The manuscript is an original work and has not been submitted. The study complies with current ethical consideration. We confirmed that all the listed authors have participated actively in the study, and have seen and approved the submitted manuscript. The authors do not have any possible conflicts of interest.

Statement of conflict of interest

The authors have declared no conflict of interest.

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