Wide-genome selective analysis of Boer goat to investigate the dynamic heredity evolution under different domestic stages

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April 16, 2024

Abstract

Boer goats, as kemp in meat-type goats, are selected and bred from African indigenous goats under a long period of artificial selection. Their advantages in multiple economic traits, particularly their plump growth, have attracted worldwide attention. Here, we displayed the wide-genome selective sweep of South Africa indigenous goat (AF), African Boer (BH), and Australian Boer (AS) to investigate the hereditary basis of artificial selection in different domesticated stages. A total of 18321865 SNPs and 9784 autosomal CNVs were identified, 573 candidate genes are screened by top 5% of both parameters (πrate and FST) for BH vs AF; 502 candidate genes were obtained from AS vs BH based on SNP data. Regarding CNV data, 24 candidate genes were annotated from top 1% CNVs (FST[?]0.511719) based on BH vs AF, and 23 were annotated from top 1% (FST[?]0.609523) CNVs in AS vs BH. A mount of identified candidate genes was related to reproduction, metabolism, growth, and development according to GO and KEGG annotation. Furthermore, these candidate genes related to the metabolism of fatty acids, minerals, and vitamins confirmed that raising level led to the rapid co-evolution of the metabolism and environment of Boer goats. Specifically, we found a series of non-synonymous mutations from the coding region of NF1 have significant allele frequency different between populations that was related to muscle development. This study provided valuable genomic resources for exploring the evolutionary history of Boer goats and genetic improvement of goats. It also helped us elucidate the genetic basis behind artificial selection in domestic animals.

INTRODUCTION

Following the advances of high-throughput sequencing technology, the scientific community has widely explored relative heredity basis with adaptability and economic phenotype of animals using wide-genome selective analysis strategy (WGSA)(Bovo et al., 2020; Fawcett et al., 2019; Lan et al., 2018). In particular, a series of candidate genes related to domestication and artificial selection of domestic animal was determined. For example, the mutation genotype pattern located in the promoter region of *PDGFD* may be the cause of fat deposition in the tail of sheep(Li et al., 2020); the AHR gene related to female reproduction is under strong positive selection during the domestication of pigs(Zhu et al., 2017). An 8-kb sequence spanning the *AMY2B*locus showed signals of selection of key roles in starch digestion and fat metabolism (Axelsson et al., 2013).

Furthermore, many studies displayed the WGSA to investigate the key genes of environmental adaptability (Chebii et al., 2020) and multiple economic traits (Guan et al., 2021; Kim et al., 2019) in goats, as well as their population migration (Bertolini, Servin, et al., 2018), phylogeny, and domestic history (Bertolini, Cardoso, et al., 2018). For instance, a study found that *MUC6* gene mutation in goats can improve the antiparasitic ability of their gastrointestinal tract to ensure that they have more adaptability to the human environment in the domestication stage (Zheng et al., 2020).

According to relevant reports, the indigenous goat accounted for more than 63% of total stock in South Africa,

and it displayed remarkable contribution to local livestock husbandry. Moreover, high-performance breeds under artificial selection appeared with the transformation of small-scale production systems to large-scale commercial agriculture (Mdladla, Dzomba, Huson, & Muchadeyi, 2016). Boer goat is a world-famous meat-type goat breed that underwent long-term artificial selection from African indigenous animals(Malan, 2000). Up to date, many countries have introduced Boer goats to improve local breeds and achieved excellent benefit. Therefore, the genetic basis of artificial selection in the improvement of economic traits can be elucidated by investigating the genomic genetic divergence between Boer goats with different domestic stages and African indigenous goats.

In this study, we displayed the WGSA analysis among African indigenous, South African Boer, and Australian Boer goats with wide-genome sequencing data to identify the inheritance shake by artificial selection during their domestication stage. Results were valuable for future molecular-assisted breeding and genetic improvement of goats.

MATERIALS AND METHODS

Animals, genome sequencing, and data acquisition

The experiment was carried out in strict accordance with the guidelines of the International Cooperation Committee of Animal Welfare on the care and use of experimental animals.

Genomic DNA of ten African Boer goats (BH) were supplied by Sokoine University of Agriculture (SUA) of Tanzania. Sequencing libraries of all samples were constructed by using NEBNext® MLtra DNA library preparation kit (Illumina®, 15026486 Rev. C, US) and wide-genome sequencing was performed by Illumina NovaSeq 6000 ×Ten platform (BGI,China). The high depth genome datasets of total 30 Australian Boer goats (AS) and 30 African indigenous goats (AF) were obtained from our previous study(Yang et al., 2021) and NCBI SRA database(PRJNA671542), respectively(Table S1).

Read filtering, alignment, and variant calling

The quality controlled and filtered raw sequencing reads (RSR) were obtained by fastp (v0.20.1), which is a method used to obtain high quality reads (HQRs). The HQRs were mapped to *Capra hircus*reference genome (ARS1) using Burrows-Wheeler Aligner (v.0.7) with default parameters. Single nucleotide polymorphism (SNP) variants were called and annotated by GATK (v.3.7) and SAMtools (v.1.3). The copy number variations (CNVs) were identified using CNVcaller software (X. Wang et al., 2017) with parameters as SILHOUETTE SCORE [?] 0.6, MAF [?] 0.05, 4 Kb-size sliding window and 2 Kb-size step.

Diversity, phylogenetic, and population genetic analyses

Neighbor-joining phylogenetic network was constructed by VCF2Dis (https://github.com/BGI-shenzhen/VCF2Dis) and Phylip (https://github.com/topics/phylip), and visualization performed by iTOL online tool (https://itol.embl.de/). Principal component analysis (PCA) was estimated and graphics visualized by GCTA (https://github.com/cooljeanius/gcta) and R program (ggplot2 package), respectively. Linkage disequilibrium (LD) was performed using Pop LDdecay software(https://github.com/BGI-shenzhen/Pop LDdecay).

Genome-wide selective sweep analysis and gene annotation

Both WGSA of SNPs and CNVs analysis were performed with two groups, as follows: (1) 10 African Boer goats (case) versus 30 African indigenous individuals (control); and (2) 30 Australian Boer goat (case) versus 10 African Boer goats (control). For the SNPs dataset, the pairwise fixation index (F_{ST}) and π ratio (πcase/πcontrol) were calculated with 40 kb sliding windows and 20 kb step size using vcftools(v.0.1.16). Candidate genes were annotated by the intersection of the both parameters with top 5% threshold windows. For the CNV dataset, the F_{ST} was calculated on the basis of absolute copy number (CN) to identify different CNV profiles between case and control within each group. The overlapping genes from top 5% divergence CNV regions were defined as the candidate genes for annotation. Additionally, candidate genes were

subjected to gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) with KOBAS 3.0(http://kobas.cbi.pku.edu.cn/).

Bioinformatics and data analysis of single key candidate gene

Haplotype reconstruction of candidate gene was displayed with phase method by DnaSP6 software http://www.ub.edu/dnasp/). Linkage disequilibrium (LD) pattern of intercepted gene region was performed by using LDBlockShow (*https://anaconda.org/bioconda/ldblockshow*).

RESULTS

A total of 18321865 SNPs were obtained from 70 animals, most frequency of SNPs is located in the intergenic region (66.79%) and intron region (26.66%). On the contrary, the least frequency of SNPs is distributed in 3'UTR (0.32%) and 5' UTR (0.07%). In particular, 66485 (56.2541%) of 118,187 SNPs located in the exon region were synonymous mutations, 50725 (42.9193%) were non-synonymous mutations, and 977 (0.8266%) SNPs were located on start/ stop codon region (Table S2).

The phylogenetic network revealed that all populations were divided into single linkage (Figure 1A), respectively, which corresponded to that from the PCA pattern (Figure 1B). Analysis result of LD (r^2) showed the highest mean LD and the slowest decay in the AS population. In contrast, the lowest mean LD and the fastest decay in AF population (Figure 1C) are shown. Coincidentally, the highest nucleic acid diversity (ND) of wide genome is AF in comparison with BH and AS (Figure 1D).

The WGSA result of group 1 (BH VS AF) (Table S3) revealed that the strongest F_{ST} window was located on Chr25 (27020001bp-27060000bp, F_{ST}=0.836582)**,** and the strongest window with $\vartheta\pi$ rate was located on Chr 15 (32300001bp -32340000bp, $\vartheta\pi$rate=0.001356). A total of 1604 intersected selection windows were screened by top 5% (F_{ST}>0.315896 and -Log10 ($\vartheta\pi$ratio)>0.344995) of both parameters (Figure 2A). A total of 573 candidate genes were extracted from intersected windows at the gene overlapping region (exon, intron, and 3/5' UTR).

The GO analysis results showed that 534 of 573 genes were enriched in 3033 GO terms, and 264 were significantly enriched (corrected$P$ <0.05). A large number of growth trait-related GO terms were identified, such as tissue development (GO:0009888); muscle fiber development (GO:0048747), and fibroblast growth factor binding (GO:0017134). In addition, 43 reproduction-related terms were also identified, such as positive regulation of intracellular estrogen receptor signaling pathway (GO:0033148), gonad development (GO:0008406), and sperm-egg recognition (GO:0035036). KEGG analysis results showed that a total of 239 genes were enriched in 270 KEGG pathway, including 33 pathways were significantly enriched (corrected$P$ <0.05). Specifically, the amount of genes enriched in the following environmental information processing pathways are high: FoxO signaling pathway, Ras signaling pathway, TGF-beta signaling pathway; Energy metabolism related pathways: Nitrogen metabolism, oxidative phosphorylation, development and regeneration, axon guidance, thyroid hormone synthesis, digestive system, gastric acid secretion, salivary secretion, endocrine system, oxytocin signaling pathway, GnRH signaling pathway, and estrogen signaling pathway (Table S4).

Subsequently, the result of WGAS in group 2 (AS vs BH) using SNP dataset revealed that the highest F_{ST} divergence window was located on Chr2 (FST=0.948729), and the strongest window with $\vartheta\pi$ rate was located on Chr6 ($\vartheta\pi$rate>0.00444257). A total of 1704 intersection selection signal windows were obtained by top 5% (F_{ST}>0.464566 and -Log10($\vartheta\pi$ratio)> 2.35236572) of two parameters (Figure 2B). A total of 502 candidate genes were extracted from the intersected windows at the gene overlapping region.

The GO analysis result showed that a total of 481 of 502 genes were enriched in 2748 GO terms and 191 genes were annotated in 253 known KEGG pathways (Table S5). It was similar to the GO and KEGG enrichment in the rich multiple categories of group 1, such as those with 108 GO terms and 7 KEGG pathways related to growth and development and 57 GO terms and 6 KEGG pathways related reproduction. Interestingly, according to the results of gene functional enrichment of selected genes at two different domestic stages, outstanding visible divergence in digestion and metabolism-related KEGG pathways was found (Table 1).

Notably, 23 parallel genes (eg., *ARMC9* , *CPNE8* ,*DNER* , *GABRA5* , *SOS1, NF1*) under selection in both groups were identified. Particularly, the LD pattern of NF1 gene (Figure 3A) showed piecemeal compactness from AF to AS, thereby implying that NF1 gene is continuously selected during the different domestic stages with 140 SNPs from NF1 gene region in our dataset. In addition, 8 SNPs located in coding region (5 synonymous mutations and 3 non-synonymous mutations) were reconstructed, and 8 haplotypes (H) of NF1 gene were obtained. The network of haplotype results (Figure S1) of 18 haplotypes of NF1 showed that H_2 is shared within three populations, and 13 haplotypes (H_6 to H_18) were private in the AF population. The most frequently distributed in H_1 was AS. Other AS sporadic distributions are in H_2, H_3, and H_4. The genotype distribution of 8 coding SNPs (S1-S8) (Figure 3B) and Amino acid changes caused by 3 non-synonymous mutations (S2, S3, S8) (Figure 3C) showed visible differences in genotype frequency between populations.

Regarding the CNV dataset, a total of 9784 autosomal CNVs were identified from 70 individuals, and the most number (MNR) of CNVs was from CHR7. The distribution of different types of CNV in each Chromosome is shown in Figure 4.

The WGAS result of group 1 (Table S6) based on CNV dataset revealed that the largest signal of F_{ST} (F_{ST}=1) was located at Chr 8_12783501-12786000bp and Chr 18_42235001-42237500bp, and 24 candidate genes (e.g., *PLA2G4A* , *KCNK2*) were annotated from 45 top 1% CNVs (F_{ST} [?]0.511719) (Figure 5A). In the results of KEGG (Table S7), 12 of 45 genes were enriched into 57 KEGG signaling pathways, such as reproductive pathways (ovarian steroidogenesis [*PLA2G4A*] related to reproduction, cortisol synthesis and secretion, GnRH signaling pathway[*PLA2G4A*], oxytocin signaling pathway[*PLA2G4A*], and TGF-beta signaling pathway[*BMPR1B*]). For GO terms, 21 of 45 genes were enriched into 303 GO terms, such as regulation of cell population proliferation (*PLA2G4A, FER*), smooth muscle contraction, and chondrocyte development(*BMPR1B*).

In addition, WGAS result of group 2 (Table S8) showed that the largest signal is located at Chr 12_14845001-14850000bp and Chr 12_14856501-14918000bp (F_{ST}=0.944547), and 23 candidate genes were annotated from 56 strong selective CNVs within the top 1% CNVs (F_{ST}[?]0.609523) (Figure 5B). Fourteen of 23 genes were enriched to 60 KEGG signaling pathways (Table S10), seven of which were related to reproduction pathways and annotated, such as steroid biosynthesis (*HSD17B7*), steroid hormone biosynthesis (*HSD17B7*), and cortisol synthesis and secretion (*EDNRA, WNT9A*). Twenty-one genes were enriched into 283 GO terms, such as skeletal system development (*MMP16*), embryonic skeletal joint development (*WNT9A*), and cellular response to growth factor stimulus (*BMPR1B*).

Nine CNVs were identified (as shown in Table 2) from the top 1% interacted CNV and annotated in three genes (*BMPR1B, PLA2G4A* , and*KCNK2*) in both domestic stages (Figure 5C). Furthermore, we noticed that the other three CNVs (V1: Chr 14_54973001-54976000bp, V2: Chr5_96856001-96858500bp, and V3: Chr 13_63248501-63382000bp) had large genetic divergence between different domestic stages of Boer goat (Figure 5D), and three genes (*ADCYAP1R1, ETV6, ASIP*) were annotated. The duplicate-type allele of CNV of V1 accounted for 16%, 35%, and 55% in AF, BH, and AS, respectively; the missing-type CNV of V2 accounted for from 0 (AF) to 50% (AS). The great frequency of changes of the duplicate-type CNV (Chr 13_63248501-63382000bp) located at ASIP ranged from 15% (AF) to 98% (AS).

DISCUSSION

In this study, the ND of both Boer goat populations was lower than that of African indigenous goat. The higher LD linkage within the AS population indicated that the frequency of the dominant genotype is gradually fixed at different domestic stages as humans expected during the artificial selection process (Chai et al., 2020; Gray et al., 2009; Rao et al., 2008). The phylogenetic and PCA pattern relationship of three populations was inconsistent with their geographic location, which implied that artificial selection can retouch domestic animal genome greatly and rapidly.

Boer goat was initially selected and bred from AF goats and has a superior economic phenotype and fecundity (Brand, Van Der Merwe, Hoffman, & Geldenhuys, 2018; Malan, 2000). Interestingly, 23 genes were identified

to undergo selection in both breeding stages of Boer goat, which was widely confirmed to be involved in the various biological functions, such as reproduction, growth, and metabolism.

Despite that a series of metabolism-related (MRD) genes were found in the two domestication stages of BH and AS, the genes and their MRD pathways were different. For example, in terms of amino acid metabolism, nine pathways related to amino acid metabolism were enriched and were involved in digestion and absorption of 17 essential and non-essential amino acids in the stages of AF to BH. Only four MRD pathways were enriched. Eight kinds of amino acids were involved in the stage of BH to AS. The feeding conditions of AF are generally decayed and irresponsible (Rumosa Gwaze, Chimonyo, & Dzama, 2009). The BH has undergone scientific selection and breeding in the commercial system with improved living conditions and medical security. Corresponding changes have been made in the environmental adaptation, metabolism, and other hereditary traits of Boer goats. Furthermore, the differences in the ecological environment of the habitat, breeding standards, and improved raising level in AS led to the rapid co-evolution of the metabolism and environment of Boer goats. This was also confirmed by a large number of candidate genes related to the metabolism of fatty acids, minerals, and vitamins, as identified in AS VS BH. In fact, the co-evolution between the metabolic inheritance and the integrated living environment in animals has been universally confirmed (Cole et al., 2020; Ohgushi, 2016; Z. Wang et al., 2015).

Particularly, some candidate genes related to metabolism have attracted our attention. *TRPM7* is a key regulator of mammalian systemic Mg (2+) homeostasis (Ryazanova et al., 2010) and a constitutive active channel that is highly permeable to divalent cations (Zheng et al., 2020). Studies have shown that whole body balance of Zn^{2+}, Mg^{2+}, and Ca^{2+} were heavily dependent on *TRPM7* channel in the intestine. When the *TRPM7* function loosened in the intestine, the mice showed severe Zn^{2+} deficiency (Mittermeier et al., 2019). Niemann-Pick C1-Like 1 (*NPC1L1*) was widely verified to be a cholesterol import protein and mediated intestinal cholesterol absorption (Garcia-Calvo et al., 2005). It also participated in intestinal absorption of fat-soluble vitamins (Takada et al., 2015).*ALAS1* (5-aminolevulinic acid synthase) is the rate-limiting enzyme for the synthesis of porphyrin and heme. It can be quickly adjusted to meet the metabolic needs in cells(Degenhardt, Väisänen, Rakhshandehroo, Kersten, & Carlberg, 2009). Porphyrin and metalloporphyrin are the main composition of life pigments, such as chlorophyll (a magnesium-containing metalloporphyrin) and heme (iron protoporphyrin)(Leeper, 1987). The heme is used to form hemoglobin in red blood cells, myoglobin in muscle cells, cytoChrome P-450, mitochondrial cytoChrome, and other hemoglobin in liver cells (Besur, Hou, Schmeltzer, & Bonkovsky, 2014). As a heme analog, the chlorophyll iron can increase the concentration of iron, whereas chlorophyll and metal chlorophyll derivatives can bind to environmental toxins(Zhong, Bird, & Kopec, 2021). In particular, the systemic activities of chlorophyll derivatives involved in various biological functions included the regulation of oxidative stress and xenobiotic metabolism system to the prevention of cancer (Hayes & Ferruzzi, 2020). Therefore, the capture of these genes implied that the metabolic and physiological functions of Boer goats are continuously affected by the selective breeding process.

A series of reproduction-related genes was identified in both domestication stages. For example, *KIT* is verified to be involved in mammalian oocyte growth and follicular development (Moniruzzaman, Sakamaki, Akazawa, & Miyano, 2007). A lack of *KIT* can lead to the loss of oocytes. In the ovaries of rodents, *KIT* displayed an important role in the migration, proliferation, and survival of primordial germ cells (Sakata et al., 2003). In addition, the retinoic acid (RA) was confirmed to essential for mammalian spermatogenesis (Clagett-Dame & Knutson, 2011; Wolgemuth & Chung, 2007). The Rol dehydrogenase encoded by the retinol dehydrogenase 10 (*RDH10*) can oxidize vitamin A to retinal and then transformed it into RA. RA may trigger the initiation of spermatogonia differentiation and meiosis via the regulation of FSH signals in the testis (Khanehzad, Abbaszadeh, Holakuyee, Modarressi, & Nourashrafeddin, 2021). In addition, many studies have shown that *BMPR1B* is associated with litter size in animals (Ahlawat et al., 2016; Tang et al., 2018; Y. Wang et al., 2019). It is the main gene that affects the ovulation rate and litter size in sheep (Çelikeloğlu et al., 2021; Shokrollahi & Morammazi, 2018; Wen et al., 2021). In addition, a series of studies have confirmed that the*BMPR1B* can affect follicular development and ovulation (Zhang et al., 2020) and cause ovarian insufficiency(Renault et al., 2020). These genes may directly affect the fertility of Boer goats

under strong artificial selective pressure at different stages of Boer goat domestication.

Subsequently, excellent growth performance is one of the important goals of Boer goat breeding. Therefore, investigating the selective genes between different breeding stages of Boer goats may help elucidate the genetic basis of muscle development (Yang et al., 2021). Notable, some genes identified from this study attracted our attention. For example, as an essential for maintaining skeletal muscle mass and protein homeostasis, the *RBFOX2* was confirmed to control the fusion of myoblasts in myogenesis by coordinating the alternative splicing of Mef2d and Rock2(Singh et al., 2014). Many evidences supported that the*FGF18* as member of FGF subfamily, plays a role in variety of tissues development, including lungs, limb buds, palate, bones, central nervous system, and hair follicles(Hagan et al., 2019). Studies have confirmed that *FGF18* is necessary for normal cell proliferation and differentiation in the process of osteogenesis and chondrogenesis (Ohbayashi et al., 2002).

NF1 had been widely proven to be a key regulator of muscle development and metabolism. A study found that the mice with muscle-specific gene (*NF1* muscle [-/-]) knockout could not thrive, and their newborns died. At the same time, a direct link was verified between *NF1* and mitochondrial fatty acid metabolism (Sullivan et al., 2014). The inactivation of *NF1* in myocardium with developing stage can lead to myocardial fibrosis, hypertrophy, and progressive myocardial dysfunction. Furthermore, the Ras-GAP neurofibrillary protein was encoded by *NF1* gene. Mutations in its coding region can negatively regulate Ras signaling by neuro-fibrin and then lead to neurofibromatosis type 1, thereby showing clinically obvious skeletal muscle deficiency (Stevenson et al., 2006). In addition, studies have confirmed that the reduction or absence of neurofibrin expression level could result in functional damage in a variety of tissue cells, such as osteoblasts, osteoclasts, chondrocytes, fibroblasts, and vascular endothelial cells (Kossler et al., 2011). Therefore, neurofibrin plays a vital role in the growth process of the animal, including embryonic development, the development of the skeletal system, and the formation and maintenance of muscle (Elefteriou et al., 2006; Kolanczyk et al., 2007).

Accidentally, two nervous system-related genes (*EVI2A* and*OMG*) were found to be located in the intron of *NF1* when we scanned deeply into the *NF1* genome region. Evidence confirmed that *EVI2A* is one factor that causes schizophrenia (Mladinov et al., 2016), and genomes missing from *NF1* regions that covered*EVI2A* gene were found in a large number of learning disabilities patient with neurofibromatosis type 1 patients (Kayes et al., 1994). Moreover, the oligodendrocyte myelin glycoprotein, which is expressed by neurons and oligodendrocytes, can inhibit neuronal differentiation of neural progenitor cells (Li et al., 2009), and it is associated with autism in children (Vourc'h et al., 2003). The continuous optimization of the growth performance of Boer goats may be related to the continuous selection of *NF1* in the different breeding stages of Boer goats. However, we were convinced that the emotional dependence of animal on humans (EDAH) is the most important contribution to domestication. EDAH prompts animals to come in contact easily with human and adapt to more large-scale gregariousness with social insensitivity, which was also the key fundamental condition for the domestication of animals (Herbeck & Gulevich, 2019). Therefore, these two nervous system-related genes (EVI2A and OMG) were selected in the artificial selection process of Boer goat, suggesting that they may affect the emotional cognition of animals and help them easily adjust to humans.

Regarding the CNV results, we also found that some candidate genes are related to reproduction, growth and development. K(2P) channel protein (*KCNK2*) was verified to be expressed in the ovaries, testes, oocytes, embryos, and sperm of cattle and mice and promoted germ cell development (Hur et al., 2012). The activity of endometrial phospholipase PLA2 (*PLA2G4A*) was associated with the development of follicular cycle (Ababneh & Troedsson, 2013), and *PLA2G4A*stimulates the culture of bovine granulocytes (GC) with increasing*PLA2G4A* mRNA and protein, when cows ovulate (Diouf et al., 2006). The 7-hydroxysteroid dehydrogenase type 7 enzyme (*HSD17B7*) converts weak estrogen into potent estradiol and plays a vital role in embryonic development and fetal survival role (Shehu et al., 2011).

MMP16 is a key regulator of chondrocyte ECM, and some studies suggested that the miR-193b-3p can promote the synthesis of chondrocyte sheet ECM by inhibiting *MMP16 (Chen et al., 2019)* , and reducing*MMP16* can inhibit proliferation and migration of smooth muscle cells in blood vessels (Sun et al., 2020).

WNT9A was confirmed to be a conserved regulator of zebrafish and human hematopoietic development (Richter et al., 2018) and also related to skeletal development (Weissenböck et al., 2019). Some evidence supported that inhibiting *WNT9A* transcription and downstream signals would activate Wnt signals to guide eMSC differentiation and save ectopic cartilage phenotype caused by excessive Pdgfra activity (Bartoletti, Dong, Umar, & He, 2020).

Many studies showed that *ASIP* plays a major role in the determination of mammalian coat color (Henkel et al., 2021; Trigo et al., 2021). Specifically, variants of *ASIP* was associated with coat color and phenotype pigmentation in various livestock (Almathen, Elbir, Bahbahani, Mwacharo, & Hanotte, 2018). Theoretically, a previous study suggested that more ASIP duplication reduced the production of eumelanin and promoted the outward appearance of domestic breeds with lighter coats (Dong et al., 2015). Therefore, the frequency of duplicate-type allele of CNV (CHR13:63228709-63249542bp) within*ASIP* gene region gradually increased from AF to AS, which can help us understand the molecular heredity basis of specific coat color and pigmentation phenotype in Boer goat.

Finally, the process of animal domestication starts from captive animals that are taken in by humans to provide a stable breeding state according their requirements (Brooker & Feeney, 2019). Domestication resulted in outstanding changes in these animals, physiologically and phenotypically (Brooker & Feeney, 2019; Lord, Larson, Coppinger, & Karlsson, 2020). This is a powerful proof of the co-evolution between animal hereditary and feeding environment and artificial selection in domestic production.

Conclusion

This study provided valuable genomic resources for exploring the evolutionary history of Boer goats and genetic improvement of goats. It also helped us elucidate the genetic basis behind artificial selection in domestic animals.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This research was funded by Chongqing Natural Science Foundation (cstc2021jcyj-msxmX0013) and the National Natural Science Foundation of China grant number No. 31172195.

Author contributions

Ying Yuan, Guang-Xin E, Cheng-Li Liu conceived and designed the experiments. Ying Yuan, Bai-Gao Yang, Wei-Yi Zhang, Yong-Meng He, Hao-Yuan Zhang, Lu Xu analyzed the data. Ying Yuan, Guang-Xin E analyzed the data and wrote the paper. Hang-Xing Ren, Gao-Fu Wang provided funding and Yong-Fu Huang read and approved the manuscript.

Data availability

The sequence data has been deposited at NCBI with the accession number PRJNA671542, PRJNA770516.

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Table 1 The visible divergence of KEGG pathways related digestion and metabolism at two different domestic stages

Table 2 The list of 9 CNVs were identified from the top 1% and overlapped genes in the both domestic stages.

Figure legends

Figure 1 Genomic characteristic of the three goat breeds. (A) Neighbor-joining (NJ) tree of the 70 individuals based on the matrix of Hamming genetic distance. (B) Plots of the first and the second principal components for the 70 individuals. (C) The boxplot indicates the distribution of nucleotide diversity (pi) of each breed. (D) Genome-wide average linkage disequilibrium decay in each breed.

Figure 2 Wide-genome selective sweep analysis for SNPs in AF VS BH goats using a π ratio of

nucleotide diversity ($\pi_{case}/\pi_{control}$) and pairwise fixation index (F_{ST}). (Manhattan map of F_{ST}, Manhattan map of $\pi_{case}/\pi_{control}$, and the top 5% intersection of sweep windows between F_{ST} and $\pi_{case}/\pi_{control}$.) (A). Wide-genome selective sweep analysis for SNPs in AS VS BH goats using a π ratio of nucleotide diversity ($\pi_{case}/\pi_{control}$) and pairwise fixation index (F_{ST}). (Manhattan map of F_{ST}, Manhattan map of $\pi_{case}/\pi_{control}$, and the top 5% intersection of sweep windows between F_{ST} and $\pi_{case}/\pi_{control}$.) (B).

Figure 3 The diversity of *NF1* gene in each breed (A)the LD pattern of NF1 gene from AF to AS;(B)the genotype distribution of 8 coding SNPs (S1-S8); (C) the visible differences of amino acid changes caused by 3 non-synonymous mutations (S2, S3, S8) from AF to AS.

Figure 4 The distribution of different types of 9784 autosomal CNVs in each Chromosome from 70 individuals.

Figure 5 (A)Manhattan map of wide-genome selective sweep analysis for CNVs in AF VS BH goats using pairwise fixation index (F_{ST}); (B) Manhattan map of wide-genome selective sweep analysis for CNVs in AS VS BH goats using pairwise fixation index (F_{ST}) (C); the candidate genes from top 1% interacted CNV in different domestic stages and three genes (*BMPR1B, PLA2G4A* , and *KCNK2*) in both domestic stages; (D) genetic divergence of three genes (*ADCYAP1R1, ETV6, ASIP*) in different domestic stages of goat.

Supporting information

Figure S1 The network of haplotype results of 18 haplotypes of NF1

Table S1 Basic information and data reads-depth of 70individuals.

Table S2 SNP mutation types and numbers from 70 goat individuals.

Table S3 Genome-wide selective signal analysis of 70 individual goats and annotated candidate genes by SNP-based FST and πratio.

Table S4 Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis of candidate genes from top 5% intersection of sweep windows between FST and πcase πcontrol in group1 based on SNP datas.

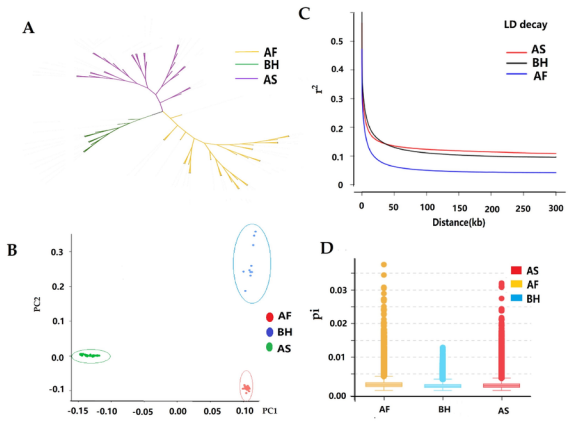
Table S5 Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis of candidate genes from top 5% intersection of sweep windows between FST and πcase πcontrol in group2 based on SNP datas.

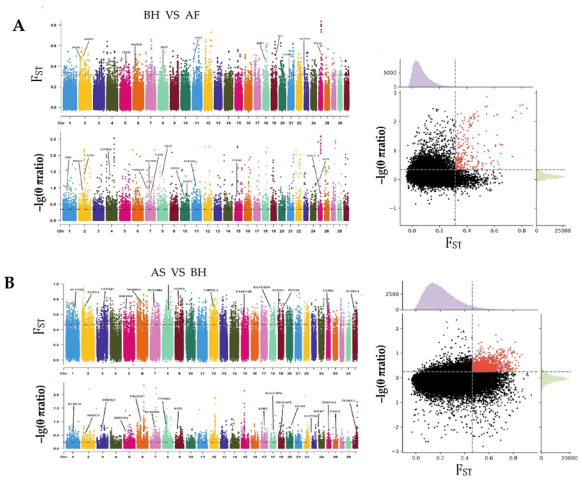
Table S6 wide-genome selective analysis result of group 1 based on CNV dataset.

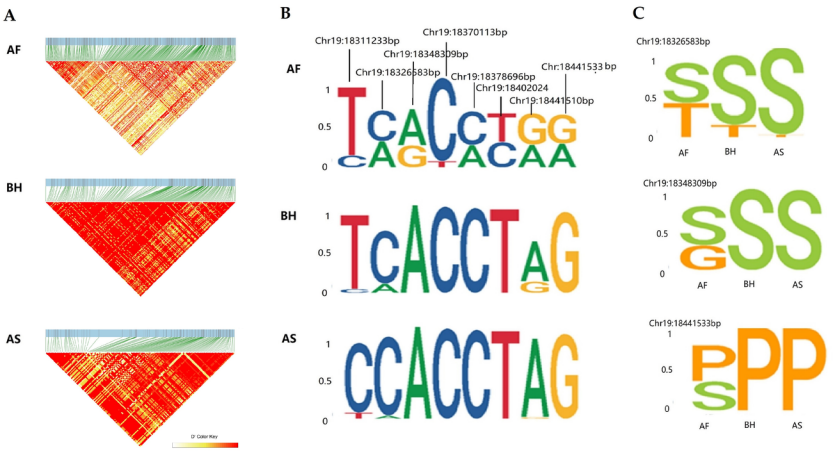
Table S7 Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis of candidate genes from top 1% intersection of sweep windows between F_{ST} in group1 based on CNV datas.

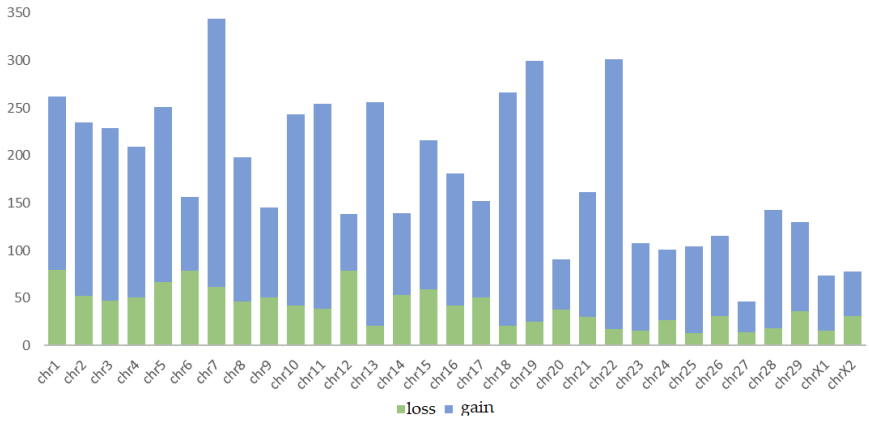
Table S8 wide-genome selective analysis result of group 2 based on CNV dataset.

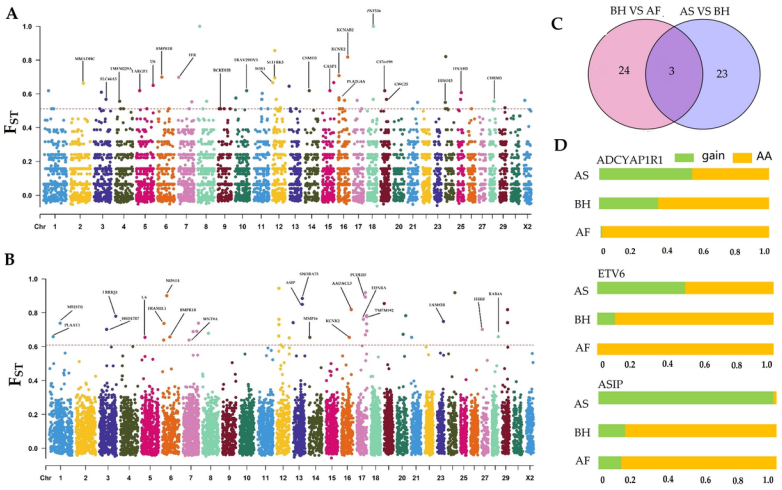
Table S9 Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis of candidate genes from top 1% intersection of sweep windows between F_{ST} in group2 based on CNV datas.











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