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Research Article

Genome-wide CNV analysis reveals variants associated with high-altitude adaptation and meat traits in Qaidam cattle

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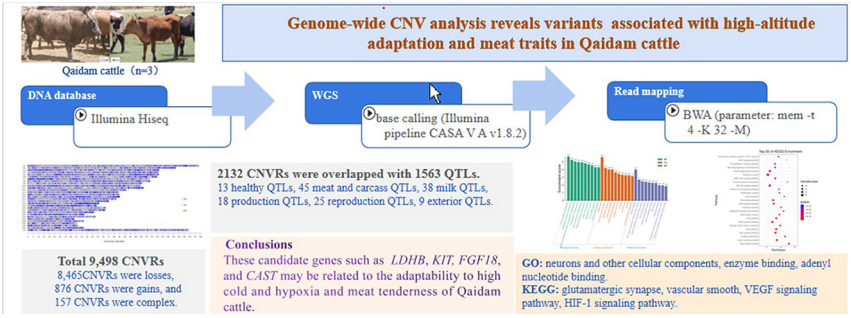
GRAPHICAL ABSTRACT



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ABSTRACT

Background: Qaidam cattle are local breeds that habitats in northwest China. It has many excellent characteristics, such as high cold and roughage tolerance, low oxygen adaptability, and tender meat quality. Copy number variation (CNV) can induce phenotypic changes in animals by a variety of effects, and thus affects the biological functions of the animals. To explore the molecular mechanism of its adaptation to extreme cold weather and muscle fat development, the CNV variations in the genome of three Qaidam cattle were detected by whole-genome sequencing, in this study.

Results: A total of 16,743 CNVs and 9498 copy number variable regions (CNVRs) were obtained after the screening, which accounts for 2.18% of the bovine genome. The CNVR length detected ranged from 0.3 KB to 10.77 KB, with a total length of 58.17 MB and an average length of 6.12 KB/ CNVR. Through functional enrichment of CNVR related genes, LDHB, and ME1 genes were screened as the key genes for Qaidam cattle to adapt to the cold and low oxygen environments, whereas KIT and FGF18 genes might be related to the coat color and growth. In the CNVR overlapped with QTLs, variation in CAPN1 and CAST genes might be closely related to the tender meat quality of Qaidam cattle.

Conclusions: Therefore, this study provides new genetic insights on the environmental adaptability and important economic traits of Qaidam cattle.

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1. Introduction

Qaidam cattle are unique species that are distributed around the Qaidam basin in Qinghai province. Qinghai yellow cattle belong to the Mongolian cattle category [1]. In modern times, they are influenced by the Central Asian zebu cattle, the Kazakh cattle, Qinchuan cattle, and Simmental cattle, and also introduced dairy cattle blood to different degrees [2]. Qaidam cattle have the characteristics of strong disease resistance and strong adaptability to low oxygen plateau. The altitude of the Qaidam cattle production area is in the range of 2800~3000 m, and their living environment is relatively cold. The annual average temperature is 3.0~6.5°C, with a large difference in temperature between day and night, dry climate, and less rain. The coat color of Qaidam cattle varies; after long-term cultivation and domestication, they have formed a solid, compact, rectangular body, as shown in Fig. 1.

Because of long-term natural grazing, the meat quality of these cattle is fine and tender, has a high lean meat rate and obvious marbling pattern, but the meat production rate remained low [3]. To improve the meat production of Qaidam cattle, crossbreeding was carried out by introducing different beef breeds [4]. However, the molecular genetic mechanism of the superior traits of Qaidam cattle has not been elucidated.

With the rapid application of high-throughput technologies, especially chips and next-generation sequencing technologies, many forms of genetic variations were found in the genomes of living organisms. Previously, a large number of single nucleotide polymorphisms (SNPs) found in the human genome were thought to be the main causes of the genetic and phenotypic diversity of organisms. In recent years, the copy number variations (CNVs) have been widely taken into consideration by researchers [5,6,7]. CNV is defined as the deletion or repetition of a genome copy number, ranging from 50 bp to several Mb in length [8,9]. There are four forms of CNV formation mechanism: nonallelic homologous recombination (NAHR), nonhomologous end-joining (NHEJ), fork stalling and template switching (FoSTeS), and L1-mediated retrotransposition [10] that are responsible for the occurrence of most of the CNVs. However, studies have shown that CNVs cause substantial phenotypic changes through multiple effects such as gene dosage, gene fusion, gene interruption, and position effects [11]. CNV fragments are large in length, ubiquitous in genomes, and cover a wider range of genomes than SNP mutations, and so they have broader prospects in studying the animal genomes and application of breeding [12]. As a new type of genomic structural variation, after detection of CNV in humans [7], it was also found in other species such as mice [13], drosophila melanogaster [14], pig [15], chicken [16], sheep [17], and cattle [18]. In humans, CNV is associated with many common diseases, such as autism spectrum disorder (ASD) [19] and deletion of the APOBEC3 gene that increases the risk of breast cancer [20]. In domestic animals, it has been proved that CNV is closely related to animal reproduction, along with the production and occurrence of many major diseases. Methenyltetrahydrofolate synthetase domain (MTHFSD) in the CNV region plays an important role in pig reproduction by regulating the metabolism of MTHFS mRNA [21]. Luo et al. [22] found 45 CNVs in chickens with different susceptibility to Marek's disease, 28 of which may be involved in immune response and cell proliferation. Bickhart et al. [23] have detected several quantitative trait loci (QTLs) related to cattle growth and meat quality by genome-wide sequencing technology, and this indicated that CNVs affecting the individual phenotypic differences were widely present in the genome. Silva et al. [24] found that two CNVRs were proximal to glutathione metabolism genes that were previously associated with meat tenderness in Nelore cattle. Some studies have also confirmed that CNV variation is closely related to the adaptability of animals to high-altitude environments [25,26]. These studies indicate that many CNVs are associated with important economic benefits of livestock.

Hence, in this study, the molecular mechanism of strong adaptability to cold and low oxygen environments and excellent meat quality were analyzed. Through high-throughput sequencing technology, the CNV in the genome was detected and the pathways or genes related to stress resistance and meat development in Qaidam cattle were searched. This has great significance in expanding the genetic information resources of this species and protects excellent breeds in the future.

2. Materials and methods

2.1. Animals and DNA database

The samples selected for this study include three Qaidam cattle and the blood samples were collected from the Zongjia town, Dulan County, Haixi Mongolian-Tibetan Autonomous Prefecture, Qinghai Province (36°44′ N, 96°47′ E). Approximately 5 ml of venous blood was collected from the necks of two cows and one bull, and the blood samples were coded as V346227, V347862, and O718844. All experiments involving animals were conducted in accordance with the Regulations for the Administration of Affairs Concerning Experimental Animals that were published by the Ministry of Science and Technology of China in 2004.

DNA samples of 80 μl were extracted by the TIANamp Blood DNA kit (TIANGEN, Beijing, CA) and the purity of DNA was detected by Nanodrop. The TruSeq library construction kit was used to construct the library. Subsequently, Qubit2.0 was used for preliminary

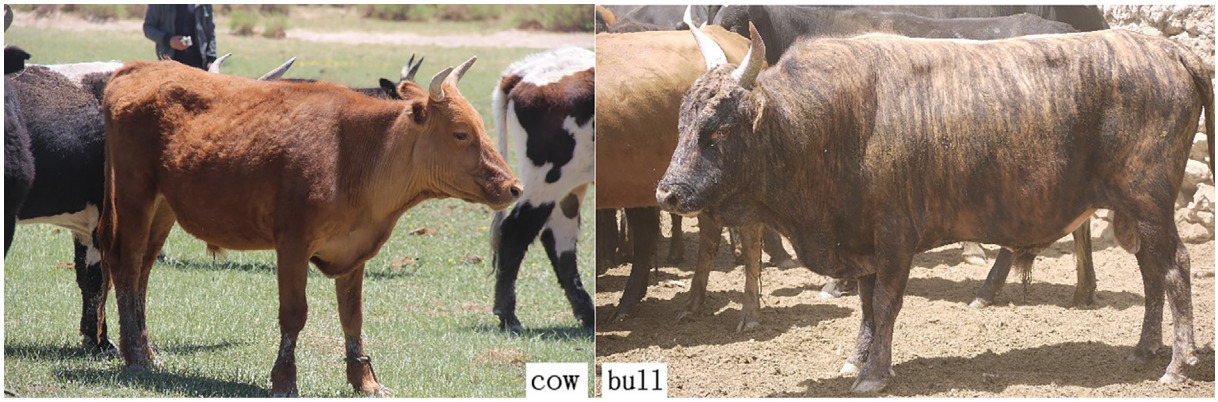

Fig. 1. The appearance characteristics of Qaidam cattle.

quantification and the library was diluted to 1 ng/μl. The insert size of the library was then detected by Agilent 2100. After the expectation of the insert size has been met, the effective concentration of the library was accurately quantified by Q-PCR (effective concentration > 2 nM), to ensure the quality of the library. The library was then sequenced by Illumina Hiseq.

2.2. Whole-genome sequencing (WGS) and quality control (QC)

The original imaging data generated by the sequencing machine were converted into sequence data through base calling (Illumina pipeline CASA V A v1.8.2), and then, subjected to QC to remove the unusable reads: (1) the reads containing the Illumina library construction adapters; (2) the reads containing more than 10% unknown bases (N bases); and (3) the reads with more than 50% of low-quality bases on one end (sequencing quality value≦5).

2.3. Read mapping

The sequencing reads were aligned to the reference genome using BWA [27] (parameter: mem -t 4 -K 32 -M) with default parameters. Subsequent processing, including the removal of duplicates, was performed using SAMtools and PICARD [28] Reference genome download address: ftp://ftp.ensembl.org/pub/release-88/fasta/bos_taurus/dna/.

2.4. CNV detection and annotation

Potential deletions and duplications by different reading coverage depths on the genome were detected by CNVnator V0.3 (parameter: - call 100) [29]. The CNVs were combined from three samples into CNVRs and the combined standard is 1 bp overlap [30]. The combined CNVRs were classified into those that appeared in only one individual and those that appeared in two individuals. Gene annotation was carried out for the CNVRs that appeared in two individuals, and the structure and function of detected mutations were annotated by ANNOVAR 2013 August 23.

To compare the CNVRs identified in the present study with reported QTL locations, a cattle QTL dataset was downloaded from the animal QTL database website (https://www.animalgenome.org/cgi-bin/QTLdb/BT/index) [31]. An overlap of at least 1 bp between our CNVRs and the QTL dataset was determined using the Bedtools [32] intersect with default settings. Since the confidence intervals of some QTLs of the downloaded dataset were too long to be used to compare, the QTLs with confidence intervals greater than 10 Mb were discarded and any two or more QTLs that had greater than 50% overlapped confidence intervals were merged into a larger QTL. Moreover, to compare our CNV detection results with several previous CNV analyses conducted in chicken breeds and lines, the overlap of CNVs between our study and others using an overlap length of at least 1 bp was determined using the Bedtools intersect with default settings.

3. Results

3.1. Evaluation of sequencing results

The Raw data of the three Qaidam cattle samples were 386.915 G and the filtered clean data were 385.856 G. The Raw data of each sample was sufficient, which ranged from 112,334.244 M to 139,234.107 M. The sequencing quality was high (Q20≧96.69%; Q30≧93.29%), and the GC content was between 44.86% and 45.28% with normal distribution, as shown in Table 1.

The size of the reference genome was 2670.42 Mb and the comparison results were found to be normal. The comparison rate was between 98.04% and 98.90% in all the samples. The average coverage depth of the reference genome (excluding N region) was between 27.47x and 39.09x and the 1X coverage (with at least one base coverage) was over 99.39%.

3.2. Genome-wide detection of CNVRs

A total of 16,743 CNVs were found in these three Qaidam cattle. The CNVs that existed in at least two individuals were overlapped and merged into CNVRs, and the 16,743 detected CNVs were condensed into 9498 CNVRs (Table S1). Among these, 8465 CNVRs were losses (deletions), 876 were gains (duplications), and 157 were complex (which included both loss events and gain events) (Fig. 2). The ratio of loss events to gain events was 9.66:1.

The size of the identified CNVRs ranged from 0.3 KB to 10.77 KB. The total length detected was 58.17 MB with losses and gains of 40.94 MB and 9.56 MB, respectively (Table 2). The average length of each CNVR was 6.12 KB. Almost 90% of the CNVRs ranged from 0 to 10 KB in size, 9.31% ranged from 10 to 50 KB, and larger than 50 KB were relatively rare (Fig. 3).

3.3. CNVRs annotation

As shown in Fig. 4, more than half of the CNVRs were in the intergenic region, 20.83% of the variants in the intronic region, 15.71% in the exonic region, and relatively few were in the upstream and downstream 1 KB regions.

According to the bovine genome information published by the NCBI, the CNVR information detected was located on the Qaidam cattle genome and assisted in constructing the CNVR chromosome

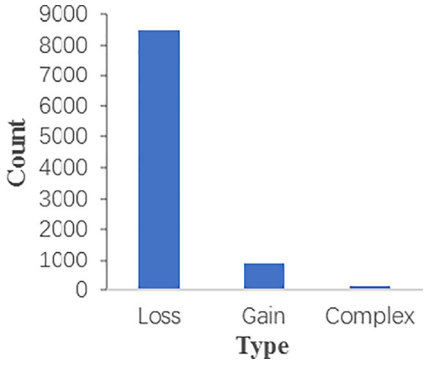

Fig. 2. The different types of CNVRs summary statistics results in Qaidam cattle.

Table 1
The sequencing quality and depth information of Qaidam cattle.

Sample	Raw Base (bp)	Clean Base (bp)	Effective Rate (%)	Total Reads	Mapping Rate (%)	Average Depth (%)
V346227	112334244300	112087604700	99.78	747250698	98.90	27.47
O718844	135346345500	134911079700	99.68	899407198	98.16	38.52
V347862	139234107300	138857005200	99.73	925713368	98.04	39.09

Table 2
The summary statistics and size distributions information of CNVRs in Qaidam cattle.

CNVR summary statistics	Total	Loss	Gain	Complex
Number of CNVRs	9498(100%)	8465(89.13%)	876(9.22%)	157(1.65%)
Total length (Mb)	58.17	40.94	9.56	7.68
Average length per CNVR (Kb)	6.12	4.84	10.91	48.92
<10 Kb	8455(89.02%)	7799	613	43
≥10 Kb to < 50 Kb	884(9.31%)	566	243	75
≥50 Kb to < 100 Kb	89(0.94%)	54	16	19
≥100 Kb to < 500 Kb	68(0.71%)	44	4	20
≥500 Kb to < 1 Mb	1(0.01%)	1	0	0
≥1Mb	1(0.01%)	1	0	0

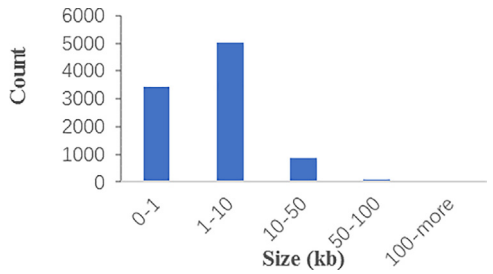

Fig. 3. The length and frequency distribution of differential CNVRs in Qaidam cattle.

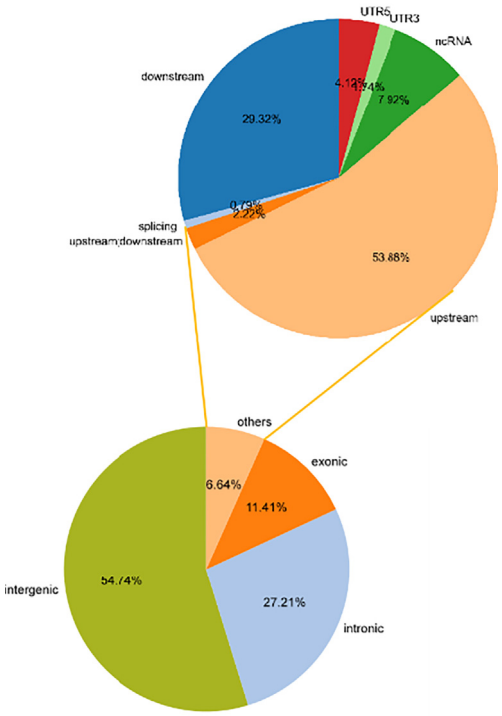

Fig. 4. The proportion of CNVRs in different functional regions of the chromosome.

map as shown in Fig. 5 (based on Bovine UMD3.1 assembly). The circos plot is shown in Fig. 6. CNVRs cover 2.18% of the bovine genome. Gene localization to CNVR was performed using the BioMart tools, and a total of 3880 genes were annotated in the CNVRs detected (which excluded the intergenic, upstream, and downstream regions) with 1471 protein-coding genes. Although CNVRs were identified in all the chromosomes, the number and proportion of chromosomes covered by CNVRs varied considerably (Table S2). The number of CNVRs on CHR X was found to be the highest with 671, covering 3.93% of its sequences. Next, the chromosomes with more CNVRs were CHR 5, CHR 7, CHR 3, and CHR 1, which contained 499, 469, 447, and 422 CNVRs, respectively. In CHR 12, the total length of the CNVR was 4100.6 KB, and the average length of each CNVR was 19.34 KB. CHR24 has the lowest total length of all CNVRs among the autosomes, only 478.5 KB, with an average length of 2.99 KB, which covered only 0.77% of its sequences. Thus, CHR24 contains smaller segment variations.

3.4. Enrichment analysis

Gene Ontology (GO) divides the function of a gene into three parts: cellular component (CC), molecular function (MF), and biological process (BP). Enrichment analysis was performed on 1655 genes from the annotated genes. The online websites g: Profiler and Kobas were used to make GO terms and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways analyses (Table S3 and Table S4). These genes are mainly concentrated in the synaptic structure, neurons, and other cellular components. In terms of molecular function, the genes showed significant enrichment in enzyme binding, guanyl-nucleotide exchange factor activity, adenyl nucleotide binding, ATP binding, and other functions. The biological processes are mainly concentrated in the development of the nervous system (Fig. 7). The results of pathway enrichment analysis of the screened genes showed that the main pathways of enrichment included glutamatergic synapse, calcium signaling pathway, circadian entrainment, Rap1 signaling pathway, focal adhesion, vascular smooth, muscle contraction, MAPK signaling pathway, axon guidance, and dopaminergic synapse. Most of these pathways are involved in the olfactory, nervous system, muscle development, and hypoxic adaptation (Fig. 8).

3.5. QTLs overlapping with identified CNVRs

A total of 2132 CNVRs were overlapped with 1563 QTLs, which involved a total of 148 traits and 6 trait categories, accounting for 22.45% of all the total CNVRs (Table S5). QTLs were divided into six categories: healthy QTLs, meat and carcass QTLs, milk QTLs, production QTLs, reproduction QTLs, and exterior QTLs. The number of traits involved in each QTL category was 13, 45, 38, 18, 25, and 9, respectively. The health QTLs were mainly related to respiratory diseases and resistance to ticks in the cattle. The longissimus muscle area, shear force, intramuscular fat, and carcass weight were related to meat and carcass QTLs. The main factors related to milk QTLs were milk yield, milk fat percentage, whey protein content, and fatty acid content in milk, while those associated with the production of QTLs were body weight, feed efficiency, and feed conversion ratio. For reproductive QTLs, it was mainly related to calving ease and conception rate. For exterior QTLs, the main traits showed association with muscularity.

3.6. Comparison with previous studies of bovine CNVRs

To further confirm the accuracy of the CNVRs screened in this study, the research on the screening of CNVRs for other cattle

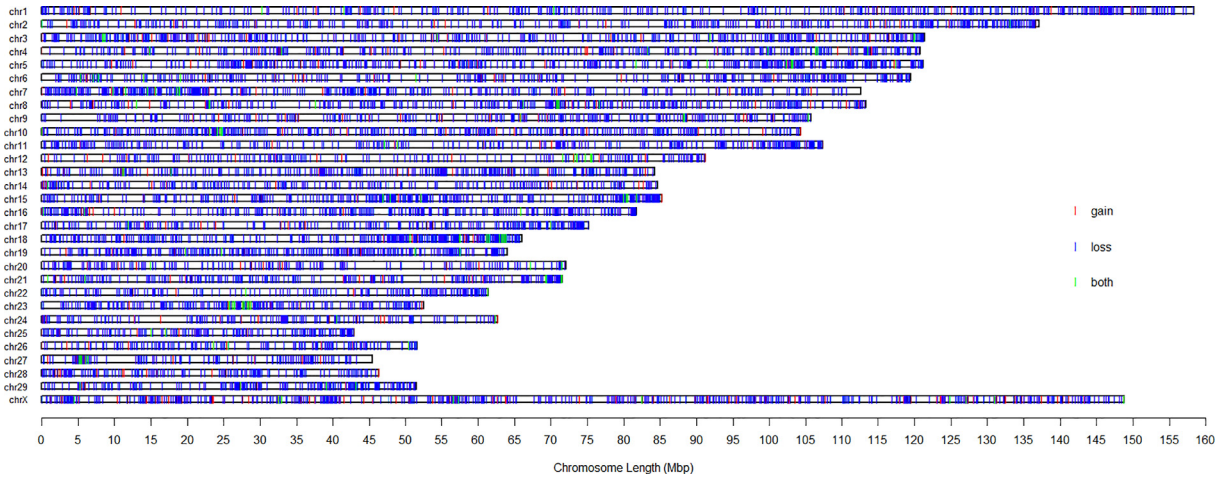

Fig. 5. Distribution of gain, loss, and both CNVRs detected across the Qaidam cattle genome (based on UMD3.1).

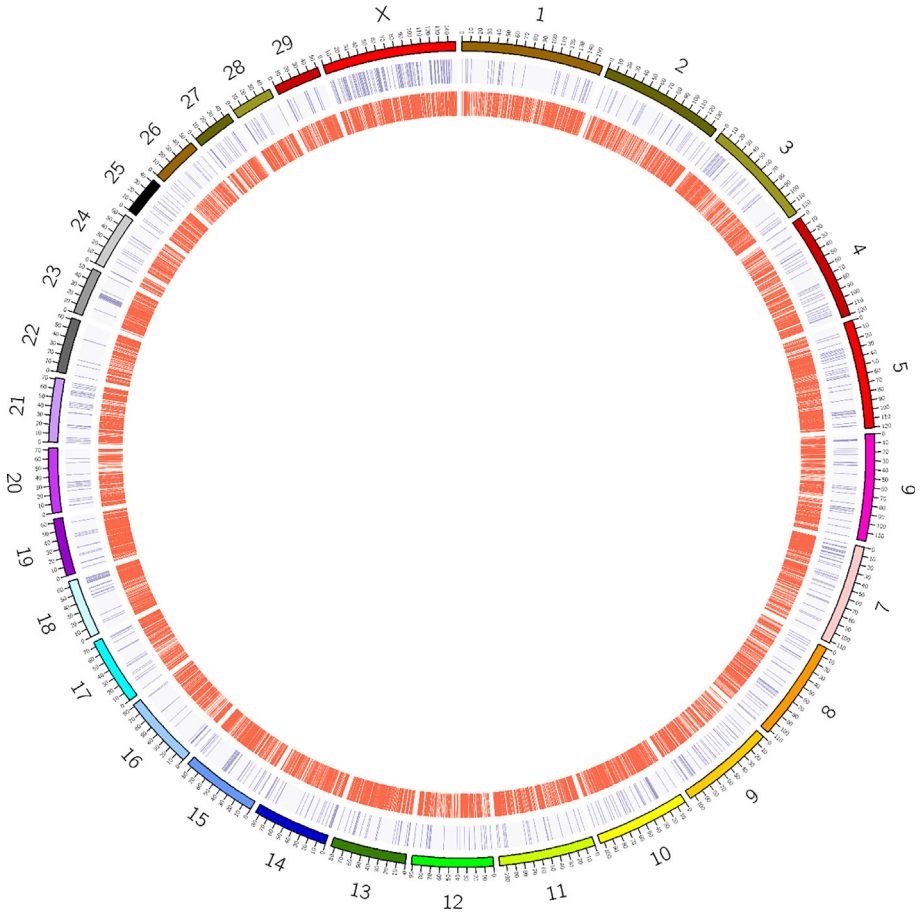

Fig. 6. Circos plot of CNVR distributions in Qaidam cattle. Plots on different tracks, from outside to inside, represent gain events and loss events, respectively.

breeds by different platforms (Bovine HD SNP chip and CGH chip) was compared and then analyzed. In this article, 12 studies on CNVs of cattle reported from 2012 to 2020 were selected [24,33,34,35,36,37,38,39,40,41,42,43] (Table 3). In these 12 studies, different methods, different breeds, and different number of experimental samples (20–1682 samples) were used for detecting the CNVRs of cattle. Three studies are used to detect the CNVRs by CGH chip containing 6.3 million probes and 10 studies are used to detect CNVRs by Bovine HD SNP chip among them. More than 500 CNVRs were detected in 10 studies in the cattle genomes of different breeds. Based on the overlap analysis of 9498 CNVRs of Qaidam cattle and the CNVRs reported in the above literature, the overlapping numbers of CNVRs detected in this study and those obtained from the other studies ranged from 30 to 2000, with the overlapping proportions ranging from 0.39% to 19.74%. The difference in the number and proportion of overlap might be greatly related to the selection of cattle breeds, different detection methods, and the number of samples.

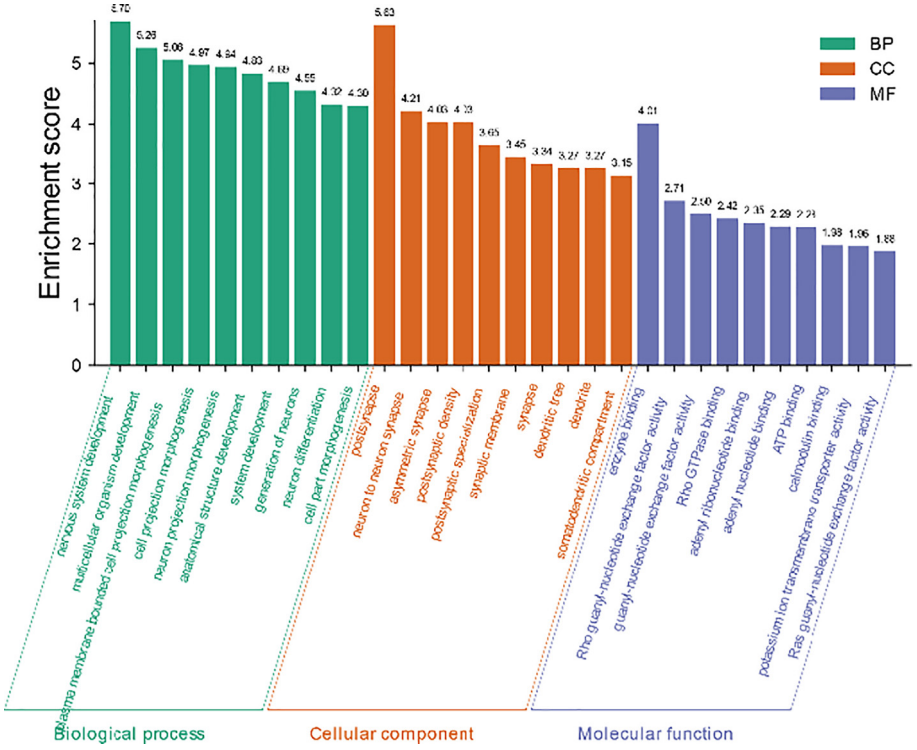

Fig. 7. Functional enrichment analyses results of coding genes in CNVRs.

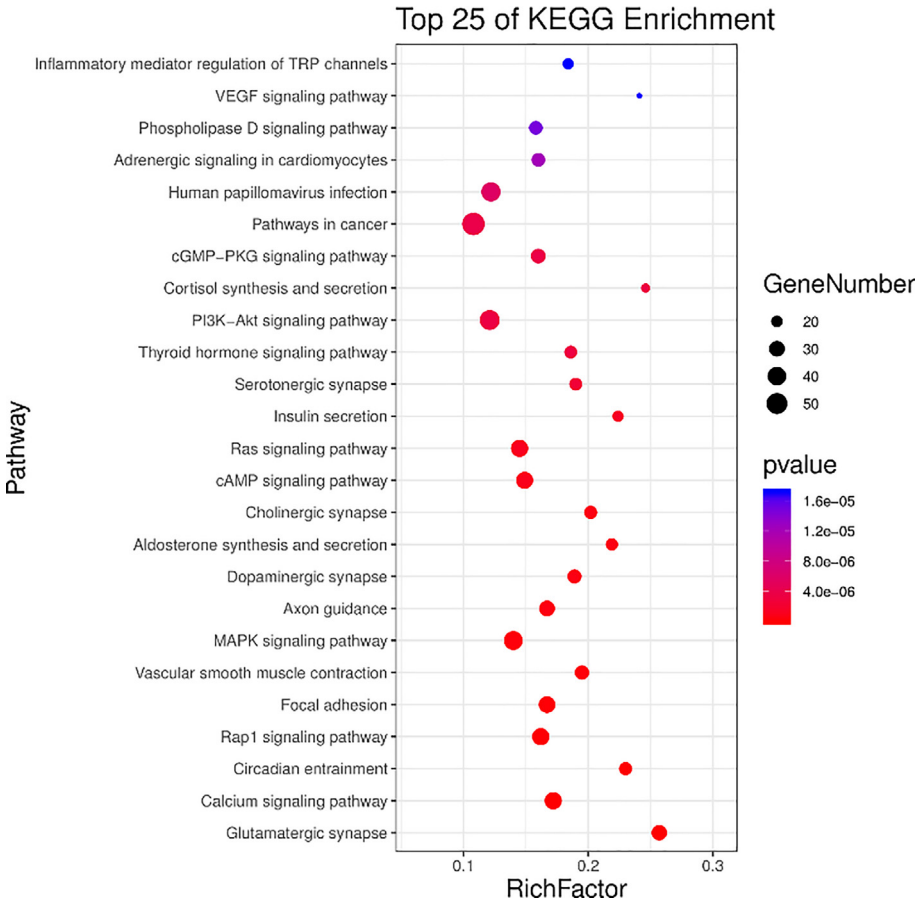

Fig. 8. Top 25 enrichment pathway analyses results of coding genes in CNVRs.

Table 3
The comparison results of our study with 12 previous bovine CNVs studies.

Study	Platform	Breed	Sample	CNVR count	CNVR length (percentage)	Overlapping CNVR count	Overlapping percentage	Reference genome
Zhou et al. [33]	BovineHD	1	1682	4562	186 Mb (7.5%)	1005	10.58%	UMD3.1
Yang et al. [34]	BovineHD	8	157	3356	148.0 Mb (5.8%)	934	9.83%	UMD3.1
Bickhart et al. [35]	CGH	8	75	1853	87.5 Mb (3.1%)	893	9.40%	UMD3.1
Hou et al. [36]	BovineHD	27	674	3438	146.9 Mb (5.8%)	212	2.23%	Btau 4.0
Jiang et al. [37]	BovineHD	1	96	367	42.7 Mb (1.6%)	273	2.87%	UMD3.1
Wu et al. [38]	BovineHD	1	792	263	35.5 Mb (1.4%)	131	1.38%	UMD3.1
Silva et al. [24]	BovineHD	1	723	2649	170.6 Mb (6.8%)	1077	11.34%	UMD3.1
Sasaki et al. [39]	BovineHD	1	791	861	43.7 Mb (1.7%)	379	3.99%	UMD3.1
Upadhyay et al. [40]	BovineHD	5	149	923	61.1 Mb (2.5%)	385	4.05%	UMD3.1
Liu et al. [41]	CGH	1	47	1043	46.8 Mb (2.06%)	691	7.28%	UMD3.1
Zhang et al. [42]	Bovine HD	25	375	5818	379.95 Mb (14.34%)	1875	19.74%	UMD3.1
Fadista et al. [43]	CGH	4	20	304	22 Mb (0.68%)	37	0.39%	Btau4.0

4. Discussion

CNV is shown to be highly correlated with appearance [44], meat quality [24,45], production [46], reproduction [24], and other traits of domestic animals [47]. Research on CNVs in the genome has been conducted on a large scale. This is the first study to detect CNVs of Qaidam cattle by whole genome sequencing. In this study, a total of 9498 CNVRs were detected in Qaidam cattle, which accounted for 2.18% of the reference genome. The length of CNVR detected ranged from 0.3 KB to 10.77 KB and the average length was about 6 KB. The number of deletion types was much higher than insertion types. Most CNVRs are located in intergenic regions, with the largest number located on chromosome X. CHR 5, CHR 7, CHR 3, and CHR 1 also contain a large proportion of CNVRs. Compared with the other 12 studies, the total number of overlapping CNVRs detected in this study is 7892, ranging from 37 to 1875, with an overlap ratio between 0.39% and 19.74% (Table 2). In these overlapped CNVRs, the number of CNVRs located on CHR 15, 5, and 6 is more, and the number located on CHR 20, 22, and 24 is less. This showed a great relationship with the selected sample species. Among them, the research conducted by Zhang et al. [42] has demonstrated the highest overlap ratio, reaching about 1/5. The breeds tested in this study are Chinese local yellow cattle breeds and yak. Qaidam cattle, naturally have the highest genetic similarity as that of Chinese local yellow cattle breeds. Secondly, yak, as a typical species living in a cold and low oxygen environment, has been adapted to the harsh environment for a long time. Qaidam cattle, as a breed of cattle that lives at high altitudes, also have similar genetic variations to that of yaks, to enhance environmental adaptability. In the research results, we found some CNVRs unique to Qaidam cattle, such as CNVR1951, CNVR2285, CNVR3380, CNVR5021, CNVR8394, and CNVR8778, which were closely related to the unique economic traits of Qaidam cattle.

Qaidam cattle have been living in the cold north for a long time. Their coat is thick and long, and their muscle fat deposition is strong, indicating that they have adapted to the local cold and low oxygen environment. CNVs in the genome of Qaidam cattle were detected and the genes located in the CNVR regions were analyzed by Go and KEGG analyses. Some key pathways and genes involved in stress, heat production, metabolism, and other biological processes were found, and this might explain the genetic mechanism of adaptability and fat metabolism in Qaidam cattle.

Compared with animals living in low-altitude areas, animals living in high-altitude areas causes a series of physiological and pathological changes in the hypoxic environment [48]. After a long period of environmental adaptation, they have experienced physiological, molecular, and cellular changes through oxidative metabolism and signal transduction pathways, and gradually acquired the unique ability to adapt to the hypoxic environment [49]. These in turn enhance the oxygen-carrying capacity of the blood by increasing the mass of red blood cells, respiration rate, and blood volume [50]. In our study, KEGG analysis of these genes showed significant enrichment in the pathways related to hypoxic adaptation, such as vascular smooth muscle contraction (bta04270), VEGF signaling pathway (bta04370), and HIF-1 signaling pathway (bta04066) (Table S4).

Although most mammals have enough oxygen to maintain their resting metabolism at high altitudes, the amount of oxygen is often insufficient to support normal physiological activities. Therefore, there are other ways in which animals compensate the lack of energy caused by low oxygen levels. For example, hypoxia increases metabolic pathways, such as glycolysis. Lactate dehydrogenase B (LDHB) catalyzes the mutual conversion of pyruvate and lactic acid during insufficient oxygen supply, and glycolysis or gluconeogenesis in the liver is upregulated, thus enhancing the adaptability to the hypoxic environment [51,52]. Therefore, the increase of LDHB involving glycolysis might enhance the adaptability of Qaidam cattle to hypoxic conditions. For mammals living at high altitudes, these animals are not only continuously affected by hypoxia, but also need extra metabolism and subcutaneous fat to maintain the body temperature when exposed to extremely low ambient temperatures. Metabolic pathways (bta01100), with a key gene of ME1, were found to be involved in adipogenesis. The malic enzyme encoded by the ME1 gene is responsible for oxidative decarboxylation of malic acid to pyruvate, generating NADPH, which is necessary for de novo synthesis of fatty acids [53]. In addition, the level of ME1 reflects the lipophilic activity of adipose tissue [53]. Many studies have shown that polymorphism of the ME1 gene showed close relation to fat synthesis and metabolism in animals [54,55,56,57].

In addition, the genes KIT and FGF18 are shown to be related to coat growth and color. Proto-oncogenec-kit (KIT) gene is a proto oncogene that determines the color of animal skin and villi by regulating melanin deposition [58]. The KIT gene of cattle is located on chromosome 6 and it produces a white phenotype when the gene mutates. The different positions of its allele on the chromosome can also make the skin and hair of the animals show different types of white spots [59]. At present, many studies have confirmed that the KIT gene plays an important role in regulating the coat color of the cattle [60,61,62]. Qaidam cattle have a mixed coat color, which is also one of its characteristics, and this might be related to the variation of the KIT gene. Fibroblast growth factors (FGFs) are involved in the morphogenesis of hair follicles and regulation of the hair growth cycle [63]. FGF18 might affect the hair follicle cells by inducing the hair papilla cells to secrete other cytokines or growth factors or affect the blood circulation of the hair follicle by acting on vascular endothelial cells, and indirectly regulate the hair growth cycle [64,65]. Similar to Yanbian cattle [66], the hair of Qaidam cattle is long and dense, which might be formed during the process of long-term domestication to resist the cold. FGF18 might be an important regulator that stimulate hair growth.

In this study, the CNVRs were examined from the BOVINE QTL database. In 2132 CNVRs, 1536 QTLs involving 6 types of traits were

identified. Some CNVRs overlap with bovine QTLs, showing high correlations with important economic traits. Genes LCORL and XKR4 (located in CNVR2285 and CNVR5021) were overlapped with carcass weight QTLs; ADRB3 (located in CNVR8394) overlapped with intramuscular fat QTLs; CAPN1 (located in CNVR8777 and CNVR8778) overlapped with intramuscular fat and juiciness QTLs; and CAST (located in CNVR2950) overlapped with shear QTLs (Table S5).

Studies have reported that LCORL gene variation is closely related to the growth and carcass traits of the cattle [67,68], whereas the XKR4 gene is related to body size and feed intake of cattle [69]. Porto et al., [70] have shown that variation of the XKR4 gene was related to the thickness of hip fat. (3) - β-adrenergic receptors (ADRB3) belong to the class of G protein-coupled receptors and are mainly involved in mediating metabolic effects, especially lipolysis and thermogenesis in the adipose tissue [71]. ADRB3 is associated with intramuscular fat content and fatty acid composition in pigs [72], the carcass composition, and the meat quality of sheep [73].

Meat tenderness is an important symbol of beef quality and is influenced by marbling, juicy, and flavor. The protease μ-calpain (CAPN1) and its inhibitor calpastatin (CAST) proteins can be used as genetic markers of beef tenderness [74]. CAPN1/CAST is an endogenous calcium-dependent protease system that mediates the proteolysis of critical myofibrin during the postmortem storage of refrigerated carcasses and meat lumps [75]. CAPN1 is responsible for the breakdown of myofibrin and meat tenderness [76], whereas CAST inhibits μ- and m-calain activity, which regulates postmortem proteolysis. Studies have shown that SNPs in the CAPN1 gene are associated with beef marbling levels [77] Several studies have shown the effect of genetic markers in CAPN1 on beef tenderness [78,79,80,81]. The tenderness of Qaidam beef was an important characteristic and it is speculated to be related to the CNV variation of CAPN1 and CAST genes.

5. Conclusions

A total of 9498 CNVRs were detected in the genomes of three Qaidam cattle, with a total length of 58.17 MB, and this accounted for 2.18% of the bovine genome. Some interesting pathways and genes were identified in the results, such as metabolic pathways, gene LDHB, ME1, KIT, FGF18, CAPN1, and CAST. These candidate genes may be related to the adaptability to high cold and hypoxia, and meat tenderness of Qaidam cattle. Hence, the results of this study might provide valuable insights into the molecular mechanisms of plateau adaptation and the potential genomic basis of its important economic traits, along with genetic information for the breeding improvement of Qaidam cattle.

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Conflict of interest

The authors declare no conflict of interest.

Supplementary material

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