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Advancements in copy number variation screening in herbivorous livestock genomes and their association with phenotypic traits

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Copy number variations (CNVs) have garnered increasing attention within the realm of genetics due to their prevalence in human, animal, and plant genomes. These structural genetic variations have demonstrated associations with a broad spectrum of phenotypic diversity, economic traits, environmental adaptations, epidemics, and other essential aspects of both plants and animals. Furthermore, CNVs exhibit extensive sequence variability and encompass a wide array of genomes. The advancement and maturity of microarray and sequencing technologies have catalyzed a surge in research endeavors pertaining to CNVs. This is particularly prominent in the context of livestock breeding, where molecular markers have gained prominence as a valuable tool in comparison to traditional breeding methods. In light of these developments, a contemporary and comprehensive review of existing studies on CNVs becomes imperative. This review serves the purpose of providing a brief elucidation of the fundamental concepts underlying CNVs, their mutational mechanisms, and the diverse array of detection methods employed to identify these structural variations within genomes. Furthermore, it seeks to systematically analyze the recent advancements and findings within the field of CNV research, specifically within the genomes of herbivorous livestock species, including cattle, sheep, horses, and donkeys. The review also highlighted the role of CNVs in shaping various phenotypic traits including growth traits, reproductive traits, pigmentation and disease resistance etc., in herbivorous livestock. The main goal of this review is to furnish readers with an up-to-date compilation of knowledge regarding CNVs in herbivorous livestock genomes. By integrating the latest research findings and insights, it is anticipated that this review will not only offer pertinent information but also stimulate future investigations into the realm of CNVs in livestock. In doing so, it endeavors to contribute to the enhancement of breeding strategies, genomic selection, and the overall improvement of herbivorous livestock production and resistance to diseases.

KEYWORDS

copy number variation, herbivorous livestock, phenotypes, genome, molecular markers

1 Introduction

China, renowned as one of the earliest nations to engage in livestock domestication (1), has a rich history of nurturing herbivorous livestock, including cattle, sheep, horses, and donkeys. This ancient practice has played a pivotal role in fulfilling diverse human needs, ranging from the procurement of essential animal-derived products such as meat, eggs, milk, and leather to harnessing domesticated animals for laborious tasks (2). Over time, the scope of domestication has expanded to encompass a multitude of applications. Throughout this evolutionary process, natural and artificial selection mechanisms have yielded an array of domestic animal breeds characterized by varying traits (3), including phenotypic attributes, economic characteristics, environmental adaptability, and resistance to diseases. Nonetheless, the intricate genetic underpinnings responsible for these disparities remain incompletely elucidated.

In recent years, the exploration of genomic variation has emerged as a central focus of scientific inquiry in the fields of animal production and health regulation, as evidenced by numerous studies (4–10). This emphasis on genetic variation holds significant significance in our quest to comprehend the intricate interplay between genetic diversity and a wide array of phenotypic and economic traits exhibited by animals (11–13). Furthermore, it serves as a robust theoretical foundation for elucidating genetic mechanisms and advancing the field of molecular breeding. Since the introduction of genomic selection, a range of livestock species, including sheep, goats, cattle, and horses, have undergone genotyping to assess their suitability for important economic traits, as demonstrated by previous studies (14–16). Up to this point, single nucleotide polymorphisms (SNPs) have been the primary focus of genomic research within the animal breeding community (17, 18). Significant strides have been made in establishing a solid genetic foundation for enhancing production and disease resistance in animals (18, 19). However, it is worth noting that despite these advancements, ~25% of the identified copy number variants (CNVs) exhibit no significant linkage disequilibrium with any SNP, leading to the conclusion that CNVs harbor genetic information that cannot be solely elucidated through SNP analysis (20).

CNVs are heritable chromosomal structural variations, characterized by deletions or insertions exceeding 50 base pairs (21). Notably, CNVs encompass a larger proportion of the genome compared to SNPs (22, 23). Consequently, CNVs are being proposed as an additional reservoir of information to elucidate the genetic variance underlying complex traits that may not be fully accounted for by SNPs alone (20). To date, several methodologies have been commonly employed for CNV detection, including comparative genome hybridization, extracting CNV data from SNP arrays, and whole-genome sequencing (WGS) approaches (24–26). Notably, recent research endeavors have delved into the investigation of the association between CNV in specific genes and a variety of phenotypic traits in animals, including growth characteristics in cattle (27, 28), goats (29–31), sheep (32) and horses (33–38). These studies have also extended their focus to examine the link between CNVs and other vital phenotypes, such as reproduction traits (39, 40) and disease resistance (7, 41). These studies have unveiled CNV as a key player linked to diverse facets of phenotypic diversity and economic traits in animal realms.

The confluence of two pivotal trends, the rising prevalence of molecular markers in livestock breeding and the maturation of microarray and sequencing technologies, necessitates a contemporary and comprehensive review of the burgeoning body of research on CNVs. This review paper seeks to illuminate the intrinsic value and biological ramifications of CNV in the landscape of genetic variation, with a particular focus on its potential as a potent molecular marker in the realm of livestock breeding. Through this approach, our review aims to introduce fresh viewpoints regarding genetic diversity and molecular breeding. Thus, in current review, we have focused on the progress of CNV screening methods in genomes of various herbivorous livestock including cattle, horses, donkeys, sheep and goat. In addition, we have briefly evaluated the association of CNVs in genes with different phenotypic traits including growth traits, reproductive traits, pigmentation, disease resistance, and environmental adaptability, etc., in cattle, horses, sheep and goat. The overall progress in screening CNVs within livestock genomes is summarized in Figure 1 (32–35, 37, 42–70).

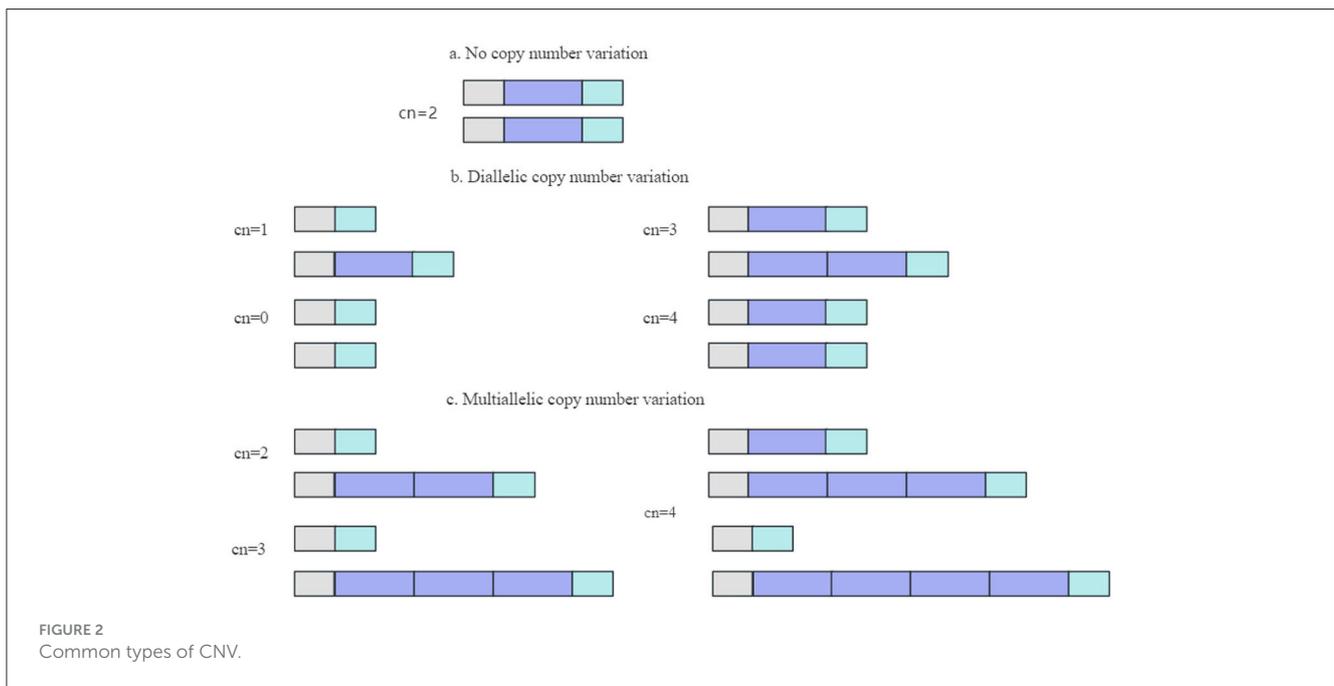
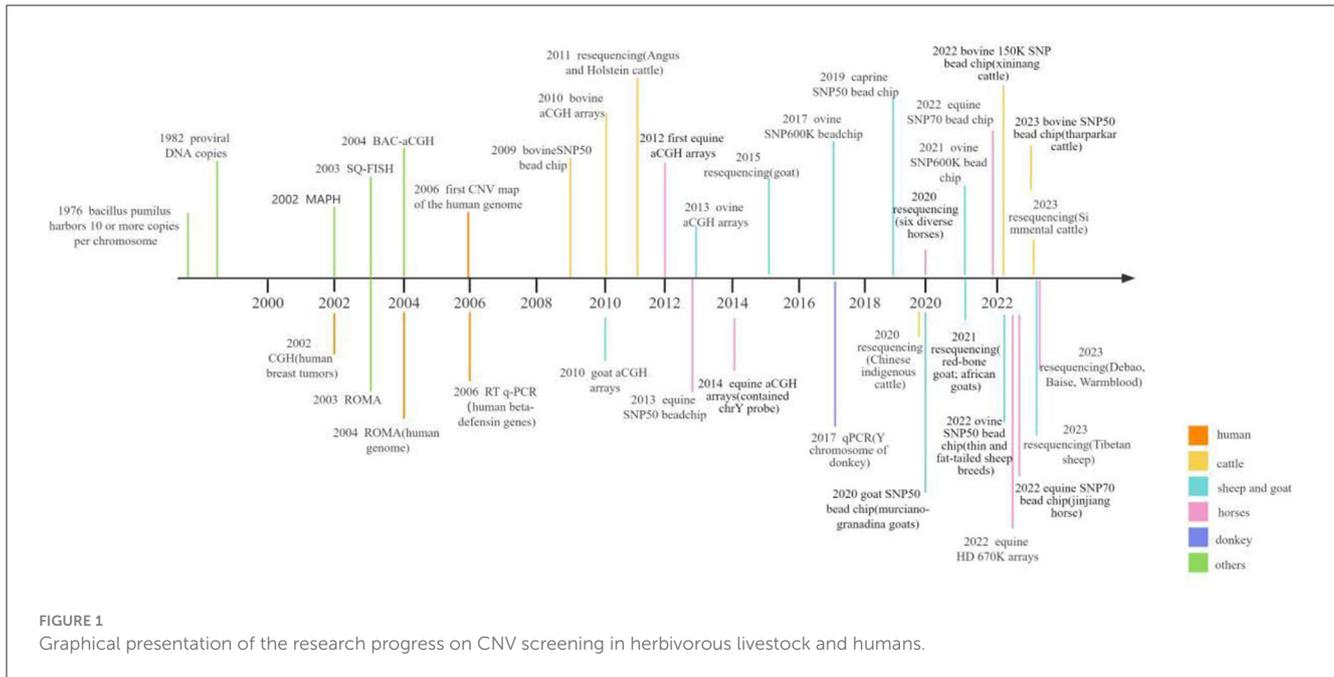
2 Overview of CNV biology

2.1 CNV definition

A CNV, typically resulting from genome rearrangement, refers to the amplification or reduction in the copy number of a large genome segment of 1 kb or greater in length, primarily demonstrated via sub-microscopic deletions and duplications (50, 71). The common variant forms of CNV are illustrated in Figure 2 (72).

Several nearby CNVs and partially overlapping CNVs in the same genomic region can be merged into a single CNV segment (73). CNVs play a vital role in genomic structural variation (SV) (74). The number of base pairs regulated by CNVs is over five times greater than the number regulated by single nucleotide variants (SNVs) in each individual. Each CNV is correlated more than three times with one genome-wide association signal and fifty times with expression quantitative trait loci (eQTL) compared to SNVs (75). Furthermore, CNVs have been recognized for its significant influence on the evolution of phenotypic diversity, disease resistance, and evolutionary processes in organisms (76, 77).

It is widely recognized that CNVs are common in the genomes of plants, animals, and humans (78), but there is no final conclusion on the mechanism of CNV formation. According to existing studies, three primary formation mechanisms may be involved: (1) Non-allelic homologous Recombination, NAHR: Rearrangements occurring between homologous chromosomes of an individual's genomic DNA during meiosis can lead to duplications, deletions, inversions, and translocations (79, 80). (2) Non-homologous end-joining, NHEJ: A mechanism of genomic rearrangement that occurs during the period of DNA double-strand break repair and that can result in numerous simple CNVs (79, 80). (3) Replication fork stalling and template Switching, FoSTeS: Refers to the stalling of DNA replication forks which causes the lagging strand to break away from the DNA template and switch to other replication forks to continue DNA replication



synthesis. This can lead to DNA duplications or deletions and the emergence of a significant number of CNVs. Consequently, the formation of complex structural CNVs may be attributed to this phenomenon (80, 81).

2.2 CNV detection methods

2.2.1 Chip technology

Array comparative genomic hybridization (aCGH) has proven to be an efficient technique for the identification of CNVs at a genome-wide level (82–84). The fundamental principle of CGH

involves labeling the DNA under analysis and control DNA with distinct fluorescent dyes. Subsequently, these treated DNAs are hybridized to standard chromosomes, and a digital fluorescence imaging system is employed to scan them, with a priority on fluorescence intensity ratios (85, 86). The aCGH is a microarray technology that utilizes two types of microarrays depending on the probes used during fabrication: Bacterial Artificial Chromosome CGH microarrays and Oligonucleotide Probe CGH microarrays. These aCGH microarray probes cover the entire genome and exhibit exceptional sensitivity, accuracy, and resolution, facilitating high-throughput screening. Previous research has provided robust support for the credibility of the experimental data generated by CGH (87, 88).

TABLE 1 Summary of CNVs and identification methods performed in cattle.

References	Methods	Species	Samples	CNV number	CNVR number
Matukumalli et al. (51)	BovineSNP50 BeadChip	6	576	79	-
Liu et al. (52)	Bovine aCGH arrays	3	90	1041	229
Bae et al. (98)	BovineSNP50 BeadChip	1	265	885	368
Fadista et al. (22)	Bovine aCGH arrays	4	20	-	304
Stothard et al. (23)	Resequencing	2	2	790	-
Bickhart et al. (99)	Resequencing	3	6	1265	-
Zhang et al. (100)	Bovine aCGH arrays	15	29	-	605
Da Silva et al. (101)	Bovine HD Genotyping Bead Chip, Resequencing	1	1717	68007	7319
Zhou et al. (102)	BovineHD Genotyping BeadChip	1	528	191	-
Liu et al. (60)	Resequencing	1	14	-	1344
Mei et al. (63)	Resequencing	8	75	-	11486
Butty et al. (26)	BovineHD Beadchip, Genome Profiler Bovine 150 K, Genome Profiler Bovine HD, BovineSNP50 Beadchip	1	96	-	52/36
Butty et al. (24)	BovineHD Beadchip, Genome Profiler Bovine 150K, Genome Profiler Bovine HD, BovineSNP50 Beadchip, Genome Profiler Bovine 50K	1	5845	23256	1645
Zhou et al. (67)	Bovine 150K SNP BeadChip	1	403	-	38/33
Kooverjee et al. (103)	Resequencing	3	5	-	355
Kumar et al. (69)	BovineSNP50 BeadChip	1	72	693	447
Sun et al. (104)	Resequencing	1	30	-	2944

Single nucleotide polymorphism (SNP) microarray technology represents another effective method for detecting CNVs. SNP microarray technology requires only a single hybridization, thus obviating the need for the simultaneous double hybridization of two DNA samples with probes. It determines the genomic copy equivalents of each locus by comparing variations in signal intensities between the samples being tested (89). A SNP microarray demonstrates remarkable stability and high resolution, enabling the detection of diverse forms of CNVs, including sub-microscopic deletions, duplications, and more (90). In comparison to Comparative Genomic Hybridization, SNP microarrays offer the advantage of simultaneously detecting CNVs while determining their genotypes and revealing heterozygous deletions. This approach is not only more cost-effective but also facilitates large-scale CNV testing (91). Several software and programs are currently available for CNV detection using chip technology, including CNVPartition, PennCNV, and QuantiSNP. A study revealed through genome sequencing of horses that the optimal order of performance for the three assays was CNVPartition, PennCNV, and QuantiSNP (92). Furthermore, the combination of PennCNV and QuantiSNP exhibited improved accuracy in CNV detection.

2.2.2 Sequencing technology

As gene sequencing technology has matured, numerous tools and software have been developed to enhance the efficiency and precision of copy number variant detection. Next-generation sequencing (NGS) has emerged as the most commonly used

method for detecting CNVs in recent years (93), with Illumina's Solexa/HiSeq technology being a prominent representative. Second-generation sequencing technology aims to synthesize and sequence DNA simultaneously. Fluorescent signals are excited by lasers and recorded using optical equipment. These recorded signals are then converted into bases using computer technology. Second-generation sequencing methods are not limited to target sequences hybridized with primer probes and can identify genome-wide CNVs, structural variants, and other variations (94). In the current landscape, four primary strategies and methods are employed for detecting variants in NGS data: paired-end mapping (PEM), split-read (SR), read depth (RD), and *de novo* assembly (AS), in addition to a combined approach based on the above four methods. Compared to microarray-based methods, next-generation sequencing technology offers advantages in terms of speed, resolution, cost-effectiveness, and reproducibility (95–97). Furthermore, widely used sequencing technologies for identifying CNVs, software including CNVnator, CNVpytor, CNVcaller, and ERDS have been documented.

3 Overview of screening methods for CNVs in herbivorous livestock genomes

3.1 Cattle genome

Cattle ranching represent a promising industry with substantial economic, ecological, and social implications. The diversity of

cattle breeds, including Holstein for dairy production, Charolais for beef, and regionally adapted yaks and buffaloes, caters to a wide range of human needs. CNVs assume significant importance in the exploration of phenotypic traits and adaptation to various environments, shedding light on the domestication origins of these animals. As dietary preferences evolve toward beef with higher protein and lower fat content, copy number variation regions (CNVRs) have been found to be associated with cattle carcass traits, offering theoretical support for future breeding endeavors. In recent years, numerous investigations have identified CNVs within the bovine genome. Table 1 provides a comprehensive summary of some of these studies. Consistently, a study identified a total of 79 CNV loci across six distinct cattle breeds, employing the BovineSNP50 BeadChip (51). Notably, 10 CNVs were found to overlap with those previously identified through aCGH data. Similarly another study conducted an extensive genome-wide analysis of CNVs in 90 modern domesticated cattle, uncovering over 200 potential CNVRs (52). In addition, this high-quality bovine CNV map fills critical gaps in current genome-wide association and selection studies based on SNP genotyping. Previous studies generated genome-wide CNV maps for cattle using the BovineSNP50 BeadChip and aCGH arrays, respectively (22, 98). Similarly, Kumar et al. (69) pioneered CNV detection in Indian Tharparkar cattle, identifying a total of 8881 CNVs, which were subsequently filtered down to 693 CNVs and merged into 447 CNVRs, representing ~2.17% of the cattle genome. Utilizing a purebred Angus cow as a reference, a study documented 605 CNVRs through a genome-wide analysis of CNVs in comparative genomic crossbreeding arrays of 29 Chinese domestic bulls (100). Detailed distribution maps of these CNVRs were constructed on their respective genomes. In a consistent manner, Kooverjee et al. (103) conducted a comprehensive investigation, wherein they successfully identified a total of 355 CNVRs in a cohort of five crossbred cows. This identification was accomplished through the utilization of the Panelcn.MOPS software. Notably, these CNVRs exhibited an average length of 9318 base pairs, collectively representing ~0.15% coverage of the bovine genome. Previous studies employed different platforms for genotyping Holstein cattle, followed by CNV analysis, to investigate the impact of genotype array density on CNV detection, thereby contributing to our understanding of genetic variation in Holstein cattle (24, 26). Accordingly, Sun et al. (104) harnessed sequencing technology to sequence the entire genome of Simmental bulls, detecting 2944 CNVRs, which were subsequently subject to genetic analysis, revealing associations with reproduction, immunity, and fertility. These findings constitute a valuable molecular breeding resource for cattle. A study analyzed common CNV regions in Xinjiang brown cattle and compared differences between the ARS and UMD reference genomes, suggesting the ARS reference genome's superior effectiveness in CNV detection (102). Likewise, previously studies conducted on CNVs in the bovine genome utilizing the BovineHD Genotyping BeadChip (38, 102). Conversely, studies undertook an analysis of CNVs in the bovine genome through sequencing technologies (23, 63, 99, 105).

3.2 Sheep and goat genomes

Sheep products, encompassing mutton meat, milk, wool, and cashmere, are of considerable significance within the sheep industry. They not only enhance the quality of life for individuals but also contribute substantially to industrial development, augment the incomes of farmers and herdsman, and provide high-quality fertilizers for farmland, among other advantages. Genomic selection technology has emerged as a pivotal approach in sheep breeding. Current research has unveiled associations between CNVs and various traits in sheep, including growth characteristics, wool color, cashmere quality, disease resistance, and reproduction.

Numerous studies focused on mapping CNVs within the sheep genome have significantly enriched our understanding of genomic variations in sheep. Table 2 provides a comprehensive summary of research pertaining to CNVs in the sheep genome. A study identified a total of 238 CNVRs and establishing a CNV map in the genomes of three distinct sheep breeds using the sheep SNP50K microarray (54). Consequently, Ma et al. (106) investigated CNVs in the genomes of eight sheep breeds using the sheep SNP50K microarray, identifying 111 CNV regions from 160 sheep and mapping the distribution of CNVRs across autosomal chromosomes. Consistently, total of 13,347 CNVs based on sequencing data from six domesticated goats and two wild goats were detected (56). While another experimental trial employed high-density sheep SNP microarrays to identify 371, 301, and 66 autosomal CNVRs within the genomes of big-tailed frigid sheep, Altai sheep, and Tibetan sheep, respectively (107). This endeavor resulted in the creation of the first high-resolution sheep CNV map, offering a valuable resource for comprehending genomic variation in sheep. In continuity, Yang et al. (108) identified 24,558 CNVs from 2,254 sheep across various geographic regions worldwide, culminating in 619 CNV regions with a combined length of 197 megabases (Mb). This encompasses 6.9% of the sheep genome and establishes a comprehensive CNV map that can assist in genome annotation for sheep. In addition, Igoshin et al. (111) detected 4,527 CNVs among 354 sheep representing 16 Russian indigenous breeds. Gene function enrichment analysis revealed significant impacts of CNVs on olfactory perception and immunity within 12 of the breeds. In line, Taghizadeh et al. (68) identified 328 and 187 CNVRs in fat-tailed and thin-tailed sheep breeds, respectively. These CNVRs were found to be located within or overlapping with 790 known sheep genes, covering ~73.85 Mb of the sheep genome. Previous report conducted a genome-wide analysis on 48 beach sheep, documented 1,296 CNV regions and constructed a CNVs map of the Tan sheep genome, thereby complemented the data on CNVs in the Chinese sheep genome (59). While another study identified 6,286 CNVs in a total of 1,023 sheep representing 50 different breeds worldwide, employing the pennCNV tool. The results unveiled differences in CNVs among populations across different geographic regions (60). Furthermore, a study reported 42 CNVs from 120 samples representing five dairy goat breeds and established significant associations between two CNVs (CNV5 and CNV25) and two milk production traits (109). Consequently, Guan et al. (62) detected 1,461 regions of

CNV within the Spanish dairy goat genome, with an average length of 196.89 kilobases (kb). The total length of all CNV regions accounted for 3.9% of the autosomal genome, leading to the creation of a CNV map. Previous study has identified 127 CNVRs in four breeds of goats, covering ~11.39 Mb of the bovine genome, thereby establishing the first CNVR map for goats (70). In addition, a study reported 1,217 CNVRs in 67 sheep breeds worldwide (66). Furthermore, a study identified 4,769 high-quality CNVRs in 47 sheep breeds globally, subsequently generating CNV maps. Additionally, they investigated the influence of solar radiation on CNVs within sheep genomes (66). Consistently, a study employed resequencing to detect CNVs in two Tibetan sheep breeds, ultimately identifying 368 distinct CNVRs, which may contribute to determining population disparities (32). Yuan and co-authors were the first to utilize resequencing technology to establish a CNV map of Chinese fine-wool sheep and analyzed the overlap of CNVRs with several quantitative trait loci related to economic traits, providing vital insights for the future improvement of fine-wool sheep (110). Consistently previous studies employed resequencing to analyze the genomic CNVs of Mile red-boned goats and African goats, respectively (64, 65). These findings facilitated a deeper understanding of the genetic traits of these animals. Consequently, another study identified a total of 702 CNVs in 120 dairy goats, resulting in the creation of a CNVR map, which promises to be beneficial for further research on the association between CNVs and phenotypic variations (13).

3.3 Horses genome

China's horse industry has experienced remarkable growth owing to the country's rapid social and economic development, coupled with continuous improvements in living standards. Consequently, equestrian sports have gained significant popularity as leisure and recreational activities within the nation. The maturation of microarray and sequencing technologies has played a pivotal role in the identification of equine CNVs. These CNVs are of paramount importance for the study of equine trait variations, disease prevention and treatment, exploration of genetic diversity, tracing the origins of domestication, and the development of new equine breeds.

In recent years, the substantial progress in microarray and sequencing technologies has facilitated the detection of CNVs. Researchers from both domestic and international institutions have undertaken extensive investigations into equine genome CNV identification, with select research findings summarized in Table 3. Doan et al. (53) were the pioneers in reporting CNVs within equine genomes. They identified 775 CNV regions in 16 horses using an aCGH microarray, demonstrating the significant impact of CNVs on biological phenotypic diversity. Subsequently, in an effort to detect CNVs in both normal horses and Przewalski horses, Ghosh et al. (55) prepared an aCGH microarray that also included a Y chromosome probe. They successfully detected 258 CNVRs in autosomes, chrX, and chrUn, but none were found in chrY. Notably, the majority of these CNVRs were associated with genes related to sensory perception, the immune system, and reproduction (55). Previous study meticulously described

the mapping of CNVs in Chinese horses using high-resolution array Comparative Genomic Hybridization (aCGH), a highly effective method for genome-wide CNV detection in animals (114). Consequently, Kader et al. (57) through whole-genome analysis of CNVs in 96 horses representing three Chinese breeds: Debo Shorthorn, Mongolian horse, and Yili horse. Their work identified a total of 287 CNVs, which were combined to form 122 CNV regions (CNVRs) with sizes ranging from 199 base pairs to 2,344 kilobases. Consistently, a study reported 15,041 CNVs and 5,350 CNVRs in 222 Friesian horses, creating a distribution map of CNVRs within the equine genome (115). Similarly, a recent study performed an analysis of CNV in 469 horses from four Korean breeds, uncovering 843 CNVRs that overlapped with 7.2% of the reference genome for horses (33). Furthermore, they constructed an autosomal map of CNVRs in horses. In addition, Laseca et al. (34) analyzed high-density SNP genotyping data from 654 horses, identifying a total of 19,902 CNV segments and 1,007 CNV regions, with CNVs covering 4.4% of the equine genome.

A study utilized gene chips to identify CNVs in 1,755 horses representing eight breeds. Their findings revealed that the size of CNV regions varied from 1 kilobase to 21.3 megabases (116). Consequently a study revealed an average total of 1,540 CNVs per horse through whole-genome resequencing of six horses representing six different breeds. Their results suggested that a reduction in the number of LATH copies might be linked to the development of endurance in horses (61). While a recent study by Choudhury et al. (37) leveraged resequencing data for Debao (DB), Baise (BS), and Warmblood (WB) horses to identify CNVs and create a CNVR map of the equine genome. Their research indicated that differential CNVRs may influence the phenotypic characteristics of different breeds.

3.4 Donkey genome

The donkey industry has emerged as a significant contributor to the growth of the livestock sector in recent years. However, the detection of CNVs within the genetic variations of the donkey genome, both in China and internationally, remains a relatively understudied area. In a study conducted by Han, a cohort comprising 263 native Chinese donkeys representing 13 breeds from eight provinces and regions was employed to identify CNVs in five Y chromosome genes of donkeys (CUL4BY, ETSTY1, ETSTY4, ETSTY5, and SRY) through quantitative Polymerase Chain Reaction (qPCR) analysis (58). While studies related to Single Nucleotide Polymorphisms (SNPs) have been reported, studies focusing on CNVs in donkeys are limited. Consistently, another study detected ~7 million SNPs in 126 domestic donkeys and made a noteworthy discovery that black or chestnut coat color was attributed to a 1 base pair deletion downstream of the TBX3 gene (117). This deletion led to reduced gene expression and its inhibitory effect on pigmentation. In addition to SNPs, CNVs represent crucial genetic resources. They possess distinct advantages, including their ubiquitous presence in the genome, extensive coverage, and relative ease of detection compared to SNPs (50, 118).

TABLE 2 Summary of CNVs and identification methods performed in sheep and goat.

References	Methods	Species	Samples	CNV number	CNVR number
Fontanesi et al. (70)	aCGH	4	9	161	127
Liu et al. (54)	Ovine SNP50 BeadChip	3	50	3624	238
Ma et al. (106)	Ovine SNP50 BeadChip	8	160	173	111
Dong et al. (56)	Resequencing	2	8	13347	-
Zhu et al. (107)	Ovine HD 600K SNP arrays	3	110	-	738
Ma et al. (59)	Ovine SNP600K BeadChip	1	48	5190	1296
Yang et al. (108)	Ovine SNP50 BeadChip	68	2111	24588	619
Liu et al. (105)	CaprineSNP50 BeadChip	50	1023	6286	978
Kang et al. (109)	CaprineSNP50 BeadChip	5	120	42	-
Guan et al. (62)	Goat SNP50 BeadChip	1	1036	-	1461
Di Gerlando et al. (13)	GoatSNP50 BeadChip	4	120	702	75
Yuan et al. (110)	Resequencing	3	32	1747604	7228
Salehian-Dehkordi et al. (66)	Ovine SNP600K BeadChip	67	2059	18152	1217
He et al. (64)	Resequencing	2	72	5862	-
Nandolo et al. (65)	Resequencing	34	82	253553	6231
Igoshin et al. (111)	Ovine Infinium HD SNP BeadChip	16	354	4527	1450
Taghizadeh et al. (68)	OvineSNP50 Beadchip	3	192	815	515
Salehian-Dehkordi et al. (112)	Ovine SNP600K BeadChip	47	695	39145	4769
Shi et al. (32)	Resequencing	2	20	60429	4927

The continued advancement of sequencing technology promises to greatly facilitate the identification of CNVs within the donkey genome.

The subsequent section offers insights into potential reasons why CNVs have been relatively overlooked in donkey research:

1. Donkeys predominantly serve as working animals in many parts of the world. Consequently, researchers may prioritize the study of genetic markers associated with phenotype traits in species other than donkeys.
2. Initially, copy number variation was primarily detected using gene chips, which were less readily available for donkeys compared to other livestock species such as cattle, sheep, and horses. In recent years, the development of sequencing technology and the completion of whole-genome sequencing for donkeys have created favorable conditions for the detection of CNVs within the donkey genome.
3. Funding for research pertaining to donkeys may be comparatively constrained when compared to other livestock species like cattle and sheep. Consequently, researchers may face challenges in securing adequate resources for the study of CNVs in donkeys.
4. In many parts of the world, the commercial value of donkeys is primarily linked to their performance as working animals, rather than their utility for products such as milk or meat. As a result, there may be limited commercial interest in investigating CNVs in donkeys.

4 Gene ontology analysis for genes overlapping CNVRs

To identify genes that may be influenced by CNVRs within the genome, an annotation analysis of genes associated with CNVRs revealed that olfactory-related functions, specifically olfactory transduction and olfactory receptor activity, were frequently affected. This observation aligns with previous findings in various species, including cattle (119), sheep (62, 111), horses (34, 115, 120) and humans (121–123), where genes affected by copy number variation have shown enrichment for olfactory-related functions. In the case of humans, the sense of smell is considered a minor aspect of overall health and may not be closely linked with adaptation. Consequently, human olfactory receptor (OR) genes tend to evolve neutrally (121). However, in the animal kingdom, the sense of smell holds paramount importance as it plays a vital role in locating food, identifying harmful substances, avoiding predators, selecting mates, and ensuring long and healthy survival and reproduction (124). Consistently, a study proposed that olfactory receptors also play a role in appetite regulation and feeding efficiency in mammals. Hence, alterations in these receptors may lead to individual differences in feed intake, body weight, and body composition (125). Additionally, CNVRs have been found to intersect with Quantitative Trait Loci (QTL) associated with various factors such as morphology, disease resistance, and more. This intersection serves as a fundamental foundation for the examination of phenotypic diversity. Variations in CNVR frequency among different breeds have been identified in CNVR

TABLE 3 Summary of CNVs and identification methods performed in horses.

References	Methods	Species	Samples	CNVs	CNVRs
Doan et al. (53)	aCGH arrays	15	16	2368	775
Dupuis et al. (113)	Equine SNP50 bead-chip array	4	477	2797	478
Metzger et al. (92)	Equine SNP50 bead-chip array	17	717	50	-
Ghosh et al. (55)	aCGH arrays	16	38	-	258
Wang et al. (114)	aCGH arrays	6	6	700	353
Kader et al. (57)	Equine SNP70 bead-chip array	3	96	287	122
Schurink et al. (115)	Equine genotyping array	1	222	15041	5350
Solé et al. (116)	Equine genotyping array	8	1755	18800	939
Al Abri et al. (61)	Resequencing	6	6	1540	-
Kim et al. (33)	Equine SNP70 bead-chip array	4	469	-	843
Laseca et al. (34)	Equine high-density 670K	1	654	19902	1007
Wang et al. (35)	Equine SNP70 bead-chip array	10	70	577	239
Choudhury et al. (37)	Resequencing	3	26	18974	4279

tests involving animals from various regions (52, 111, 126). These variations can be attributed to breed domestication and environmental adaptation.

5 CNVs and their association with phenotypic traits in herbivorous livestock

It has been well-established that genomic CNVs exert an impact on an organism's phenotype through various mechanisms, including changes in gene dosage, modulation of gene expression, modulation of gene transcriptional regulators, and positional effects (127). The association of CNVs in genes and their association with various phenotypic traits (growth traits, reproductive traits, pigmentation, and diseases resistance) in herbivorous livestock (cattle, sheep, goat, and horses) have been summarized in Table 4.

5.1 CNVs associated with growth and reproductive traits in herbivorous livestock

CNVs have been extensively studied in various livestock species, including cattle, sheep, donkey and horses, and its association with important growth, reproduction, and fertility traits has been documented. This comprehensive review discusses key findings and contributions from various research studies in these livestock species. In cattle, Yang et al. (131) identified CNV in the cytochrome P-450 4A11 (CYP4A11) gene, which was associated with increased growth. Multiple copies of CYP4A11 were found to promote the differentiation of 3T3-L1 cells into adipocytes, potentially leading to increased fat deposition. Previous studies investigated SERPINA3-1 and GAL3ST1 gene CNVs in different Chinese cattle breeds, revealed associations with growth traits such as body height, body weight, and rump width (146, 180). These

genes hold promise as candidate genes for Chinese cattle breeding. Correspondingly, Hu et al. (139) analyzed CCDC39 gene CNVs and their impact on body length and hip width, noting significant effects, particularly in the Pinan (PN) breed. Additionally, Shi et al. (128) found a correlation between leptin gene CNV and various phenotypic traits, including body weight, body height, body length, and brisket circumference, in multiple cattle breeds.

In sheep, Zhu et al. (107) identified adiposity-related genes, including PPARA, RXRA, KLF11, ADD1, FASN, PPP1CA, and PDGFA, in CNV regions of fat-tailed sheep. These genes were associated with fat deposition, with individuals carrying copy number deletions exhibiting higher body weight. Similarly, a recent study by Wang et al. (155) documented a significant correlation between CNV in the KAT6A gene and body height and hip width in Hu sheep (HU). They also found that CNV3 duplicates were associated with higher body height and weight. Yang et al. (153) highlighted the BAG4 gene's role in regulating body height in sheep and its potential as a molecular marker for molecular breeding. Feng et al. (156) discovered that CNVs of the PIGY gene significantly impacted body weight, chest circumference, and tube circumference in sheep. Additionally, Xu et al. (29) found that CNV types of the CCSER1 gene were correlated with body weight and heart girth traits in Guizhou white goats (GZW).

Horses were also subject to CNV studies. Consistently, Metzger et al. (92) conducted a genome-wide analysis of CNVs and their association with equine body height traits. They identified deleted regions in ECA1, ECA8, and ECA9, which were significantly linked to equine body height. While Kim et al. (33) reported CNVRs with overlapping quantitative trait loci (QTLs) associated with equine body height in Jeju riding horses and Hanra horses. These findings provided valuable insights into the genetic factors influencing equine body height.

In the context of fertility, CNVs have also been explored. Consistently, a deletion in the intronic region of the SPAG16 gene has been identified in bulls with poor sperm motility (PSM), suggesting its potential role in bull fertility (104). A comprehensive

TABLE 4 Summary of CNVs in genes and their association with phenotypic traits in herbivorous livestock.

Genes (CNVs)	Phenotypes	Biological effect	Species	References
Changes in the CNV region within the LEPR intron 3	Growth traits	Body weight, body height, body length, and brisket circumference	Cattle	(128)
Myosin heavy chain 3 (MYH3)-CNV		Skeletal muscle development		(129)
Mitogen-activated protein kinase 10 (MAPK10)-CNV		Body weight ($P < 0.05$), body height and chest girth		(130)
CYP4A11-CNV		Lipid deposition		(131)
Guanylate binding protein 2 (GBP2)-CNV		Body height, body length, heart girth, hip width, rump length		(132)
Insulin-like growth factor 1 receptor (IGF1R)-CNV		Associated with body weight and body height of Jinnan cattle and was significantly linked with body height and hucklebone width of Qinchuan cattle		(133)
Kupple like factor 3 (KLF3)-CNV		Body mass and heart girth		(134)
Potassium inwardly-rectifying channel, subfamily J 12 (KCNJ12)-CNV (1&2)		Significant association with the body length, chest circumference, body weight, rump length		(135)
MLLT10-CNV		Hip width, rump length, hucklebone width, and cannon bone circumference		(136)
Uanylate-binding protein 6 (GBP6)-CNV		Associated with body weight, cannon circumference and chest circumference		(137)
(CNV1: 3600 bp, including exon 2–11; CNV2: 4800 bp, including exon 21–22) of the CLCN2 gene		Cannon circumference, body slanting length, chest girth, and body weight		(138)
CCDC39- CNV (Normal, deletion, duplication)		body length, hip width, heart girth and cannon bone, and circumference		(139)
PLA2G2A-CNV (Normal, Deletion)		Height at sacrum, heart girth and body height, chest depth		(140)
SYT11-CNV		Significantly correlated with body length, cannon circumference, chest depth, rump length, and forehead size of Yunling cattle, and was significantly correlated with the bodyweight of Xianan cattle		(141)
Mitochondrial fusion protein (MFN1)-CNV		Significant correlation with hucklebone width, hip width, height at sacrum, chest width and rump length		(142)
DYNC1I2-CNV (Duplication and deletion)		Associated with height at hip cross, body length, chest width and hucklebone width, chest depth		(143)
WW domain binding protein 1-like (WBP1L)-CNV		Associated with heart girth, rump length and body weight (Pinan cattle), withers height, rump length, body length, chest depth and BW of (Jiexian cattle)		(144)
MUC19-CNV		Correlated with hip width, height at hip cross and withers height, body length, and huckle bone width		(145)
SERPINA3-1-CNV		Body height		(12)
GAL3ST1- CNV (deletion)		Body weight		(146)
VAMP7-Duplication		Body growth trait (height at the hip cross)		(147)
ZNF679-CNV		Body size and length		(148)
CNVRs harbored genes (PPARA, RXRA, KLF11, ADD1, FASN, PPP1CA, PDGFA, and PEX6)		Fat deposition	Sheep	(107)
Src homology 2 domain containing E (SHE)-CNV		Correlated to body length, circumference of cannon bone, heart girth, chest width and high at the cross		(149)
ORMDL sphingolipid biosynthesis regulator 1 (ORMDL1)-CNV		Body weight, body height, body length, chest depth, and height of hip cross		(150)
KMT2D-CNV		Body length, withers height, hip width		(151)
TOP2B-CNV		Body length, chest circumference, canon circumference and height of hip cross		(152)

(Continued)

TABLE 4 (Continued)

Genes (CNVs)	Phenotypes	Biological effect	Species	References
BAG4 -CNV		Body height, body slanting length, body height and hip cross height		(153)
TOP2B-CNV		Body length, chest circumference, canon circumference and height of hip cross		(152)
LRRFIP1-CNV		Chest width, rump breadth and circumference of cannon, larger heart girth		(154)
KAT6A-(CNV1, CNV2, CNV3)		Body height and body length		(155)
PIGY- CNV		Body weight, chest circumference, and tube circumference		(156)
Myosin light chain kinase-4(MYLK)-CNV		Body weight, body length and body height	Goat	(157)
Opn4-CNV		Body weight in Guizhou white goat Body length in Guizhou black goat		(158)
SNX29 gene-CNV ADCY1-CNV		Meat production traits		(159)
CADM2-CNV (Deletion)		Withers height and body length		(160)
Sorting nexin 29 (SNX29)-CNV		Body length, body height, heart girth, chest width, canon circumference		(161)
Myogenic differentiation 1 (MyoD1)-CNV		Body weight, height at hip cross, heart girth and hip width		(30)
A-kinase-anchoring protein 13 (AKAP13)-CNV		Body height and body length, chest depth, chest circumference, and cannon circumference		(162)
Pleomorphic adenoma gene 1 (PLAG1)-CNV		Body weight, heart girth, height at hip cross, and hip width		(163)
CCSER1-CNV (deletion)		Body weight and heart girth traits		(29)
Deleted regions on ECA1, ECA8 and ECA9.		Body height	Horses	(92)
23 CNVRs with overlapping QTLs associated with equine body height		Body height		(33)
A deletion in the intronic region of the SPAG16 gene	Reproductive traits	Bull-fertility traits (sperm motility)	Cattle	(104)
CNV of ZNF280BY		Negative correlation with the percentage of normal sperm and sperm concentration		(164)
CNVs of the bovine HSFY and ZNF280BY		Correlated negatively with testis size, while positively with sire conception rate.		(165)
CNV of ZNF280BY		Negatively correlated with testis size	Hu sheep	(166)
SMAD2		Litter size and semen quality	Goat	(40)
Sorting nexin 29 (SNX29)-CNV (Indel)		Litter size and fertility		(167)
Protein phosphatase 3 catalytic subunit alpha (PPP3CA)-CNV		Litter size and semen quality		(168)
PRP1 and PRP6 have CNV mutations in the HF group		Litter size		(169)
CNVs in regions of the Y chromosome		Male development and equine fertility	Horses	(170)
An 1155 bp deletion in the ASIP gene		Coat color darkening		(171)
2,809 bp LINE-1 insertion in ASIP gene		White coat color		(172)
ASIP-CNV (Duplication)		Light coat color	Goat	(56)
ASIP- CNV		White coat colour		(173)
1 Mb CNV affect EDNRA gene		White coat color		(174)
13.42kb duplication upstream of ASIP		Non-classic swiss markings		(175)

(Continued)

TABLE 4 (Continued)

Genes (CNVs)	Phenotypes	Biological effect	Species	References
A 4.6 kb duplication in intron 6 of STX17		Gray phenotype	Horses	(176)
A deletion including exon 3 of the ED1 gene	Disease resistance	Anhidrotic Ectodermal Dysplasia	Cattle	(177)
Low relative expression levels of KIF2A and PHKG2		Disease resistance	Sheep	(106)
CNVs in CCL1, CCL2, CCL8, CCL11, NOS2, TNF, CSF3, and STAT3 genes		Resistance to natural <i>Haemonchus contortus</i> infections		(41)
CNVR33, CNVR65, and CNVR7 overlap with immune system-related genes		Strong resistance to infectious diseases	Goat	(13)
CNVRs located in the MHC region of ECA20		Insect bite hypersensitivity	Horses	(115)
A pure deletion of the AKR1C gene		Disorders of sexual development		(55)
CNV in GRIK4, IFNLR1, and LOC102275985	Environmental adaptability	High-altitude adaptation	Cattle	(178)
CNV in LDHB and ME1		Cold and low oxygen environments		(179)
CNV changes affect in ALKBH5, NARFL genes		Plateau acclimatization	Sheep	(107)
CNVR is significantly correlated with solar radiation		Solar radiation		(112)
Genes associated with hemoglobin binding located on CNVRs		Harsh plateau environment	Horses	(114)
Changes in NFKBIA, SOCS4, HSPA1A, and IL6 genes located in the CNVR		High temperatures and humidity		(35)

analysis documented CNVs in Laoshan dairy goat populations with differing fertility levels and showed that CNV mutations in PRP1 and PRP6 genes, which affect mammalian fertility (169). A study investigated CNVs in Y chromosome-specific regions in male horses, identifying potential genes linked to stallion fertility and contributing to our understanding of equine male development and fertility (170). These studies collectively underscore the significance of CNVs in shaping various traits in cattle, sheep, and horses, from growth and fat deposition to fertility. The identification of specific genes and regions associated with these traits holds promise for selective breeding programs and further genetic research in these livestock species.

5.2 Pigmentation

The role of CNVs in determining coat color and disease resistance in cattle, horses, and sheep has been the subject of extensive scientific investigation. In this discussion, we will delve into various studies that have shed light on the influence of CNVs on these traits in these livestock species. A study reported two sequence translocations between chromosomes 6 and 29 in Belgian Blue and Swiss Brown cattle, affecting the KIT gene, leading to color-sidedness (181). Similarly another study reported that a deletion of 1155 bp within the ASIP gene in Nellore cattle results in dark hair color in specific regions by elevating melanin production (171). Furthermore, a 2,809 bp LINE-1 insertion in the ASIP gene causing a white coat color phenotype by impeding melanin production has been identified in buffalo (172). Consequently a study postulated that a 4.6 kb duplication within intron 6 of the

STX17 gene leads to a pronounced upregulation of both STX17 and NR4A3 gene expression (176). This heightened gene expression subsequently instigates the proliferation of melanocytes, ultimately culminating in the manifestation of a gray coat phenotype in affected horses. Furthermore, it is noteworthy that horses harboring this mutant phenotype exhibit a gradual transition in hair color from gray to white as they advance in age. In a similar vein, previous investigations encompassed genomic analyses of feral and domestic goat populations, which unveiled the intriguing revelation that 13 genes situated within CNV regions overlap with the comprehensive roster of cloned color genes provided by the European Society for Pigment Cell Research (ESPCR) (56). Moreover, these investigations substantiated the substantial impact of CNVs within the ASIP gene on the lightening of coat color in domestic goat breeds, employing rigorous resequencing analyses. A subsequent inquiry brought to light the potential influence of CNVs on the ASIP gene, which may, in turn, lead to the emergence of a white coat color phenotype in the Girgentana and Saanen goat breeds, as corroborated by Fontanesi et al. (173). A recent report presented compelling evidence demonstrating the significant association between a 13.42 kb repeat sequence located upstream of the ASIP gene and non-classic Swiss markings in goats, utilizing CNV assays and quantitative Polymerase Chain Reaction (qPCR) techniques (175). This finding further underscores the pivotal role of CNVs in shaping coat color patterns in goats. Furthermore, Menzi et al. (174) unraveled the involvement of the EDNRA gene, situated within a 1 Mb CNV region on chromosome 17, in potentially attenuating melanism among Boer goats. Notably, an elevation in the copy number within this CNV region could potentially lead to a reduction

in skin pigmentation, thereby culminating in the manifestation of a white-spotted phenotype. In summary, these comprehensive investigations collectively shed light on the intricate interplay between CNVs and the genetic determinants of coat color diversity in horses and goats, providing valuable insights into the underlying genetic mechanisms governing these phenotypic variations.

5.3 Disease resistance

The CNVs hold significant potential to influence disease resistance in livestock species, including cattle, sheep, and horses. Notably, Liu et al. (52) conducted an exhaustive investigation in cattle, uncovering multiple CNVs that play pivotal roles in crucial biological processes such as drug detoxification, innate and adaptive immunity, as well as receptor and signal recognition. In the context of cattle, it is worth highlighting the association between CNVs and disease susceptibility. For instance, Drögemüller et al. (177) reported that a deletion encompassing exon 3 of the ED1 gene has been linked to anhidrotic ectodermal dysplasia, underscoring the critical role of CNVs in disease vulnerability. Furthermore, a study reported CNVs in 18 candidate genes (TERT, NOTCH1, SLC6A3, CLPTM1L, PPAR α , BCL-2, ABO, VAV2, CACNA1S, TRAF2, RELA, ELF3, DBH, CDK5, NF2, FASN, EWSR1 and MAP3K11) which were associated with milk somatic cells count and mastitis resistance in dairy cattle (182). Consistently, another study reported that CNVs in ZNF496 and NLRP3 were significantly associated with resistance to gastrointestinal nematodes in Angus cattle (129).

Shifting our focus to small ruminants, Di Gerlando et al. (13) embarked on an exploration of Sicilian goat breeds. Their study unveiled intriguing findings, as CNVR33, CNVR65, and CNVR7 were found to overlap with genes closely associated with the immune system. This discovery offers a potential explanation for the remarkable resistance of these goat breeds against infectious diseases. In the case of Florida Native sheep, Estrada-Reyes et al. (41) delved into the genetic underpinnings of resistance against gastrointestinal nematodes. Their meticulous investigation revealed that 14 CNVs exhibited overlaps with QTLs associated with gastrointestinal nematode resistance. Moreover, these CNVs demonstrated significant correlations with fecal egg count (FEC), suggesting a potential influence of CNVs on parasite resistance in these sheep. Ma et al. (106) conducted an extensive study encompassing 160 Chinese sheep breeds, leading to the identification of 111 CNV regions. Their functional analysis highlighted an enrichment of CNV regions with genes closely linked to environmental responses. Notably, 17 candidate genes emerged from this analysis, primarily associated with specific diseases, metabolic processes, and development. Particularly intriguing was the observation of lower relative expression levels of KIF2A and PHKG2 in domestic sheep breeds compared to introduce sheep breeds, implying enhanced disease resistance within modern Gansu sheep breeding populations.

In the equine domain, Schurink et al. (115) undertook a thorough investigation into CNVs within Friesian horses. Their research unveiled a staggering 15,041 CNVs identified across 222 individuals. Importantly, this study integrated genome-wide

association study (GWAS) leveraging both SNPs and CNVs data. A significant finding was the association between CNV regions situated in the major histocompatibility complex (MHC) region of ECA20 and insect bite hypersensitivity (IBH) in Friesian horses. Notably, approximately half of the horses included in the study were afflicted by this condition. Consistently, Ghosh et al. (55) conducted a comprehensive genomic analysis encompassing healthy horses representing 16 distinct breeds. Their investigation identified 258 CNV regions. Notably, the study extended its inquiry to horses exhibiting sexual developmental impairments, wherein they identified a pure deletion of the AKR1C gene in two male pseudohermaphrodites. This discovery suggests a potential association between this gene deletion and the observed abnormalities.

5.4 Environmental adaptability

A comparative examination of CNVs in herbivorous livestock originating from diverse regional breeds has illuminated the potential influence of CNVs on their environmental adaptability. A performed a comprehensive investigation into the differential distribution of CNVs within yak populations hailing from the Tibet and Gansu regions (178). Their study identified seven candidate CNVs, specifically annotating three genes (GRIK4, IFNLR1, and LOC102275985) enriched in five well-established signaling pathways that play pivotal roles in the animals' acclimatization to their environments and various physiological functions. Of particular note is the regulation of physiological processes in hypoxic environments. This research significantly contributes to our understanding of the molecular mechanisms underlying the high-altitude environmental adaptability of yaks. Qaidam cattle, known for their adaptation to cold and low-oxygen environments, underwent genomic analysis by Guo et al. (179). This study identified LDHB and ME1 as potential key genes influencing the cattle's remarkable adaptability to such harsh conditions.

Tibetan sheep, native to high-altitude plateaus, were investigated by Zhu et al. (107), who identified 66 CNVRs associated with their plateau acclimatization. Notably, α -ketoglutarate-dependent dioxygenase alkB homolog 5 (ALKBH5) and nuclear prelamin A recognition factor-like (NARFL) were found to be associated with plateau adaptation within the identified CNVRs. A study performed by Salehian-Dehkordi et al. (112) documented CNVs in 47 sheep breeds. Their research revealed 155 CNVs highly significantly correlated with various environmental parameters, with 35 CNVRs showing significant correlations with solar radiation. Moreover, genes overlapping with CNVs, such as B3GNTL1, UBE2L3, TRAF2, GTF2F1, and IGFALS, were significantly correlated with climatic variables, further emphasizing the role of CNVs in environmental adaptation.

In the equine domain, Wang et al. (114) utilized aCGH to identify CNVs in six horse breeds, uncovering a total of 700 CNVs. These CNVs were classified into 353 CNVRs, and their genetic examination revealed specific genes associated with hemoglobin binding, suggesting a potential influence on horses' adaptability to the challenging plateau environment. The Jinjiang horse, an indigenous breed exclusive to the southeastern coast of China and

adapted to high temperatures and humidity, was the focus of a study by Wang et al. (35). They identified 229 genes that overlapped with CNVRs, with four specific candidate genes (NFKBIA, SOCS4, HSPA1A, and IL6) highlighted due to their strong correlation with cellular thermal acclimatization.

6 Conclusions

Common herbivorous livestock, like cattle and sheep, are vital to human daily life due to their significant contributions to meat and dairy production, playing crucial roles in animal husbandry. Recently, China has seen remarkable growth in its equine and donkey industries, driven by advancements in science, technology, and societal progress, establishing themselves as emerging specialties within the livestock sector. Therefore, investigating CNVs within the genomes of these animals holds profound importance. Advancements in microarray and sequencing technologies, along with decreasing sequencing costs, have provided a robust foundation for identifying and studying CNVs. These CNVs, characterized by extended mutant fragment lengths and their substantial impact on genes, represent a formidable genetic resource for exploring genetic variations in livestock and poultry. Extensive research focusing on CNVs in herbivore genomes has unequivocally demonstrated the pivotal role CNVs play in shaping phenotypic diversity, influencing economic traits, enhancing disease resistance, and facilitating environmental adaptation. Researchers worldwide have dedicated their efforts to elucidating the connection between CNVs and phenotypic differences as well as diseases in livestock and poultry. These findings offer compelling support for exploring the potential applications of CNVs as genetic markers in regulation of various productive and disease resistance traits. Consequently, CNVs emerge as a promising avenue for augmenting genetic diversity and expediting molecular breeding strategies in common herbivorous livestock, including cattle, sheep, horses, and donkeys. In conclusion, CNVs represent a valuable and dynamic field of study poised to make a lasting impact on the genetic improvement of herbivorous livestock species, ultimately benefiting both human society and the global livestock industry.

Author contributions

XL: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Software, Writing—original draft, Writing—review & editing. WCh: Methodology, Writing—review & editing, Data curation, Formal analysis. BH: Writing—review & editing, Investigation, Software.

XW: Investigation, Software, Writing—review & editing, Data curation, Formal analysis. YP: Data curation, Software, Writing—review & editing, Conceptualization. XZ: Data curation, Software, Writing—review & editing, Investigation. WCha: Software, Writing—review & editing, Formal analysis, Methodology. MK: Methodology, Writing—review & editing, Conceptualization, Project administration, Supervision, Writing—original draft. CW: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing—original draft, Writing—review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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