

Review

Deciphering Adaptive Potential and Performance Traits in Cattle through Integrative Genomic Approaches

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ABSTRACT

Genomic tools and techniques have revolutionized our understanding of the genetic basis of adaptation and economically important traits in cattle and helped us to achieve sustainability in livestock breeding. This review highlights the amalgamation of genome-wide association studies (GWAS) and selection signature analyses to reveal candidate genes and genomic regions affecting disease resistance, productivity, climate resilience, and reproductive performance in cattle. The use of high-density SNP arrays and next-generation sequencing techniques, like ddRAD-Seq and GBS has transformed the detection of trait-associated loci and selection footprints. Case studies across diverse cattle populations, including Indian, African, and temperate ruminants, have revealed critical genomic regions bearing genes like *HSPA1B*, *EPAS1*, *DGAT1*, and *BoLA*, which are associated with immunity, thermotolerance, and economic performance. In addition to this, this paper highlights the urgent need to conserve India's native cattle breeds and also advocates for proper *in situ* conservation strategies. The integration of molecular markers in GWAS and selection signature analyses have allowed precision breeding and improved the accuracy of candidate gene identification, facilitating genomic selection for climate resilience and productivity. This study also underlines the significance of genomically informed breeding programs in enhancing future livestock sustainability.

Keywords: Genome-Wide Association Studies (GWAS), Cattle Adaptation and Productivity, Climate Resilience, NGS, Selection Signature

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INTRODUCTION

Natural selection, domestication, and artificial selection have all increased genetic variance across breeds. Certain genetic regions that influence behaviour, reproduction, production performance, body conformation, environmental adaptation, and disease resistance are subject to these selection pressures. Natural selection favours advantageous mutations or alleles essential to an individual's survival within a population (Nielsen *et al.*, 2005). Over time, genomics has become increasingly utilized in livestock breeding. The ability to identify unique genetic patterns left by selection in the genome has been greatly enhanced thanks to developments in high-throughput sequencing and SNP genotyping technologies. A key aspect of modern livestock genomics is identifying genetic regions associated with adaptability and productivity traits in cattle. Breeding techniques can be improved by knowing the genetic makeup of these features. Understanding the genetic foundation of these traits helps enhance breeding tactics, productivity, and resistance to environmental stressors. Genome-wide association studies make finding genetic variations, typically single-nucleotide polymorphisms, or SNPs, that are connected to particular economic traits.

By screening the genomes of large populations, researchers can discover common genetic markers associated with certain phenotypic characteristics, such as disease susceptibility, height, weight, or milk yield in cattle. Analysis of selection signatures reveals genomic areas subject to positive selection, which could result from artificial selection for desired traits or past or present adaptations to environmental stresses. In the meantime, GWAS offers a high-resolution understanding of genotype-phenotype relationships by linking specific genetic variations to phenotypic characteristics. By combining these two approaches, scientists can identify loci essential for evolutionary and selection processes and influence phenotypic variation. In cattle populations, linkage disequilibrium (LD), adequate population size (N_e), genetic diversity, population structure, and selection signatures are studied using SNP chips of various densities (Hayes *et al.*, 2009; Gautier *et al.*, 2010; Qanbari *et al.*, 2011). Furthermore, research on evolution, selection, domestication, speciation, and admixture has been facilitated by SNP chips (Decker *et al.*, 2016). Even without a reference genome, sequence-based genotyping is enabled by next-generation sequencing (NGS) (Kobayashi *et al.*, 2016). Researchers can

connect candidate genes under selection to phenotypes by using the detection of selection signatures as a supplementary method to genome-wide association studies (GWAS). Such findings support the application of genomic selection (Chen *et al.*, 2016). While genetic diversity studies evaluate the level of divergence among cattle breeds or populations, investigations of selection signatures provide additional insight into the genetic underpinnings of diversification. Finding the genes causing variations in economically significant features requires identifying these selection signatures (Cesarani *et al.*, 2018).

Status of Indian Cattle Breeds and their Conservation

India, the third-richest country in biodiversity in Asia, is a treasure trove of indigenous cattle genetic resources. With a total cattle population of 194.2 million, India is home to 53 registered indigenous cattle breeds, constituting a significant proportion of the total cattle population (DAHDF 2020). However, the indigenous cattle population is declining at an alarming rate, posing a threat to these breeds' genetic diversity and sustainability. One of the primary reasons for this decline is the fragmentation of agricultural lands and the mechanization of farming practices. The reduced reliance on bullocks for draught purposes has led to the neglect of many indigenous draught breeds, pushing them toward extinction. Additionally, the introduction of high-yielding exotic breeds for crossbreeding, aimed solely at enhancing milk production, has overshadowed the tremendous potential of indigenous breeds. These native breeds, known for their adaptability and survivability in harsh climatic conditions, have been undervalued in the race for higher milk yields.

Ironically, while India overlooks its indigenous breeds, countries like the USA and Australia have utilized them for crossbreeding purposes (Feliuss *et al.*, 2014). For instance, the Girolando breed in Brazil is a successful dairy breed developed by crossing the Indian Gir with Brazilian Holstein. Such international demand has led to the export of indigenous breeds, resulting in the loss of their native breeding tracts and a subsequent reduction in genetic diversity.

Several indigenous cattle breeds in India are now on the verge of extinction. According to the ICAR-National Bureau of Animal Genetic Resources (NBAGR), population sizes categorize breeds into normal (>25,000), insecure (15,000–25,000), vulnerable (5,000–15,000), endangered (2,000–5,000), and critical (<2,000) status (Srivastava *et al.*, 2019). Conservation efforts become imperative when the breeding population falls below 5,000 females. Breeds like Vechur (Kerala), Punganur (Andhra Pradesh), and

Krishna Valley (Karnataka) are critically endangered, while others like Bargur (Tamil Nadu), Siri (West Bengal), and Ponwar (Uttar Pradesh) are in vulnerable or insecure status (Animal Husbandry Statistics, 2013).

In terms of milk quality, indigenous breeds outshine exotic ones. Their milk contains higher levels of total solids, fats, proteins, and essential nutrients like amino acids and vitamins. For example, Malnad Gidda milk is particularly rich in health-promoting compounds (Ashokan *et al.*, 2021). The beta-lactoglobulin content in indigenous milk boosts human immunity, while its lower sterol content makes it healthier. These attributes highlight the immense value of indigenous breeds in supporting sustainable food systems.

The Indian government has initiated several conservation measures, such as establishing the National Animal Gene Bank, which has preserved over 1,20,000 doses of semen from breeds like Hariana, Tharparkar, and Punganur (Joshi *et al.*, 2013). Gaushalas, pinjrapoles, and incentive programs under NBAGR's Network Programme encourage farmers to conserve indigenous breeds. However, the most effective strategy is *in situ* conservation preserving these breeds within their native breeding tracts with active participation from livestock owners and stakeholders.

Given the challenges posed by climate change and global warming, the adaptive traits of Indian cattle breeds have become indispensable for sustainable agricultural production. Conserving the genetic diversity of these breeds ensures the availability of resilient options to meet changing environmental conditions and resource constraints.

Utilization of Genetic Markers in Livestock Genomics

Molecular markers have played a pivotal role in advancing our understanding of genetic variation, adaptation, and productivity traits in cattle. Before the advent of molecular tools, cattle genetic diversity was primarily assessed using morphological traits and pedigree information, often supported by ethnographic and local knowledge (Nivsarkar *et al.*, 2000; Joshi *et al.*, 2001). Early genetic studies also utilized biochemical markers such as blood group polymorphisms and allozyme systems during the 1970s, which provided preliminary insights into population structure but lacked resolution and genome-wide coverage (Nei, 1987; Altshuler *et al.*, 2000). The shift towards DNA-based markers began with the use of restriction fragment length polymorphisms (RFLPs), random amplified polymorphic DNA (RAPD), amplified fragment length polymorphism (AFLP), and variable number of tandem repeats (VNTR), including microsatellites or simple

sequence repeats (SSRs) (Yaro *et al.*, 2017). Among these, microsatellites became the most widely used in the 1990s due to their high polymorphism, codominant nature, and broad genome distribution (Fredholm and Winterø, 1996; Bowling *et al.*, 1997; Canon *et al.*, 2001; Delgado *et al.*, 2012; Eusebi *et al.*, 2017; Ginja *et al.*, 2019). They were employed extensively for parentage verification, breed identification, genetic diversity studies, and quantitative trait loci (QTL) mapping in cattle (Kumar *et al.*, 2003; Pandey *et al.*, 2006; Panigrahi *et al.*, 2024). Microsatellite marker-based diversity analyses provided a baseline for the development of more advanced marker systems and laid the groundwork for genome-wide studies in cattle. However, limitations such as low throughput, scoring difficulties, and limited genome coverage prompted the transition to more robust marker systems.

The introduction of single nucleotide polymorphisms (SNPs) and SNP arrays transformed cattle genomics by offering high-resolution, high-throughput, and cost-effective genotyping tools. SNPs are the most abundant and evenly distributed genetic markers in the genome, found in both coding and non-coding regions, making them ideal for large-scale studies such as genome-wide association studies (GWAS) and selection signature analyses (Panigrahi *et al.*, 2022; Panigrahi *et al.*, 2023). The Illumina BovineSNP50 BeadChip and the higher-density BovineHD 777K array (Matukumalli *et al.*, 2009) have been widely applied in both *Bos taurus* and *Bos indicus* populations for detecting genomic regions associated with economically important traits. However, SNP arrays are not without limitations. The major concern is ascertainment bias, as the SNPs included in commercial arrays are often discovered in a limited number of reference populations, mostly European breeds, leading to underrepresentation of rare or population-specific alleles in indigenous breeds. To overcome these biases and to capture the full spectrum of genomic variation, sequencing-based techniques such as whole genome sequencing (WGS) and reduced representation sequencing (RRS) approaches have emerged. RRS techniques, including genotyping-by-sequencing (GBS) (Elshire *et al.*, 2011), restriction site-associated DNA sequencing (RADseq) (Miller *et al.*, 2007), and double digest RADseq (ddRAD) (Peterson *et al.*, 2012), utilize restriction enzymes to target specific genomic regions, reducing genome complexity while allowing deep coverage of informative loci. These approaches minimize repetitive regions and enhance the discovery of novel SNPs with reduced ascertainment bias, proving effective in genetic studies of various livestock species. ddRAD, in particular, has been widely adopted for population structure analysis, SNP discovery, and trait association

studies, especially in resource-limited settings due to its cost-effectiveness and scalability (Heffelfinger *et al.*, 2014; Davey *et al.*, 2011; Wang *et al.*, 2012). These molecular marker platforms, from microsatellites to high-density SNP arrays and NGS-based techniques, have become indispensable in detecting genomic regions under selection, identifying candidate genes for traits such as heat tolerance, milk yield, feed efficiency, disease resistance, and facilitating precision breeding. Collectively, these advancements in molecular marker technologies have significantly enhanced our capacity to explore genomic variation in cattle, guiding the development of informed breeding programs and contributing to the long-term sustainability and resilience of livestock genetic resources (Baumung *et al.*, 2004; Mukherjee *et al.*, 2019; Nayee *et al.*, 2018; Dixit *et al.*, 2021; Okou *et al.*, 2007).

Approaches for Identifying Trait-Associated Genomic Loci

There are two primary approaches to exploring genes responsible for phenotypic traits. The top-down approach involves genetic analyses aimed at identifying genes associated with traits of interest. This approach in population genomics includes methods such as association studies, candidate gene studies, linkage disequilibrium (LD) mapping, and the identification of quantitative trait loci (QTL) (Potkin *et al.*, 2009). However, this method requires prior knowledge of genes or genomic regions related to the target trait (Gu *et al.*, 2009). In contrast, the bottom-up approach begins at the molecular level and works upward to connect genetic variations to phenotypes, using statistical inferences and population-level data (Barrera-Redondo *et al.*, 2020). The bottom-up approach for detecting selection signatures employs various indicators, including linkage or gametic disequilibrium (LD), genetic differentiation, and patterns in the site frequency spectrum (SFS) (Qanbari *et al.*, 2010). Population genomics, in this context, is guided by two fundamental assumptions: (1) Demographic events and evolutionary history similarly influence all neutral loci. (2) Loci under selection exhibit atypical or distinctive patterns of genetic variation compared to neutral loci (Luikart *et al.*, 2003).

Selection signatures

The “hitchhiking approach” of Maynard Smith refers to studying the evolution of genetic traits linked to a selectively advantageous allele. This approach involves tracking the spread of the favourable allele throughout a population and the genetic characteristics that “hitchhike” along with it (Smith and Haigh, 1974). A selective sweep is a process in which a beneficial

mutation becomes fixed in a population due to positive selection. This results in a region of the genome associated with the advantageous mutation becoming fixed (i.e., all individuals carry the exact version of the gene), reducing genetic variation and elevating linkage disequilibrium in that region (Pennings and Hermisson, 2006).

A “hard selective sweep” is a process in which a new favourable allele (a gene variant) becomes fixed in a population due to intense selective pressure. This reduces genetic variation in a specific locus (region of DNA) and the near fixation of the favourable allele in the population (Pritchard *et al.*, 2010). In a “soft sweep, Multiple haplotypes with beneficial mutations may simultaneously increase in frequency. It may

occur either due to genetic variation or by recurrent mutation or migration, and tends to contribute to the fixation of alleles at multiple origins (Pennings and Hermisson, 2006). When these polygenic alleles do not complete fixation, the resulting haplotype pattern corresponds to several partial selection signatures or “partial sweeps”. These polygenic alleles are not entirely fixed, and the resulting haplotype pattern comprises several partial selection signatures or multiple partial sweeps (Pritchard *et al.*, 2010). Reducing or eliminating a harmful allele through purifying or negative selection leads to decreased genetic diversity at linked loci, a phenomenon referred to as “background selection” (Charlesworth, 1993). Fig. 1 illustrates the detailed chronology of a selective sweep.

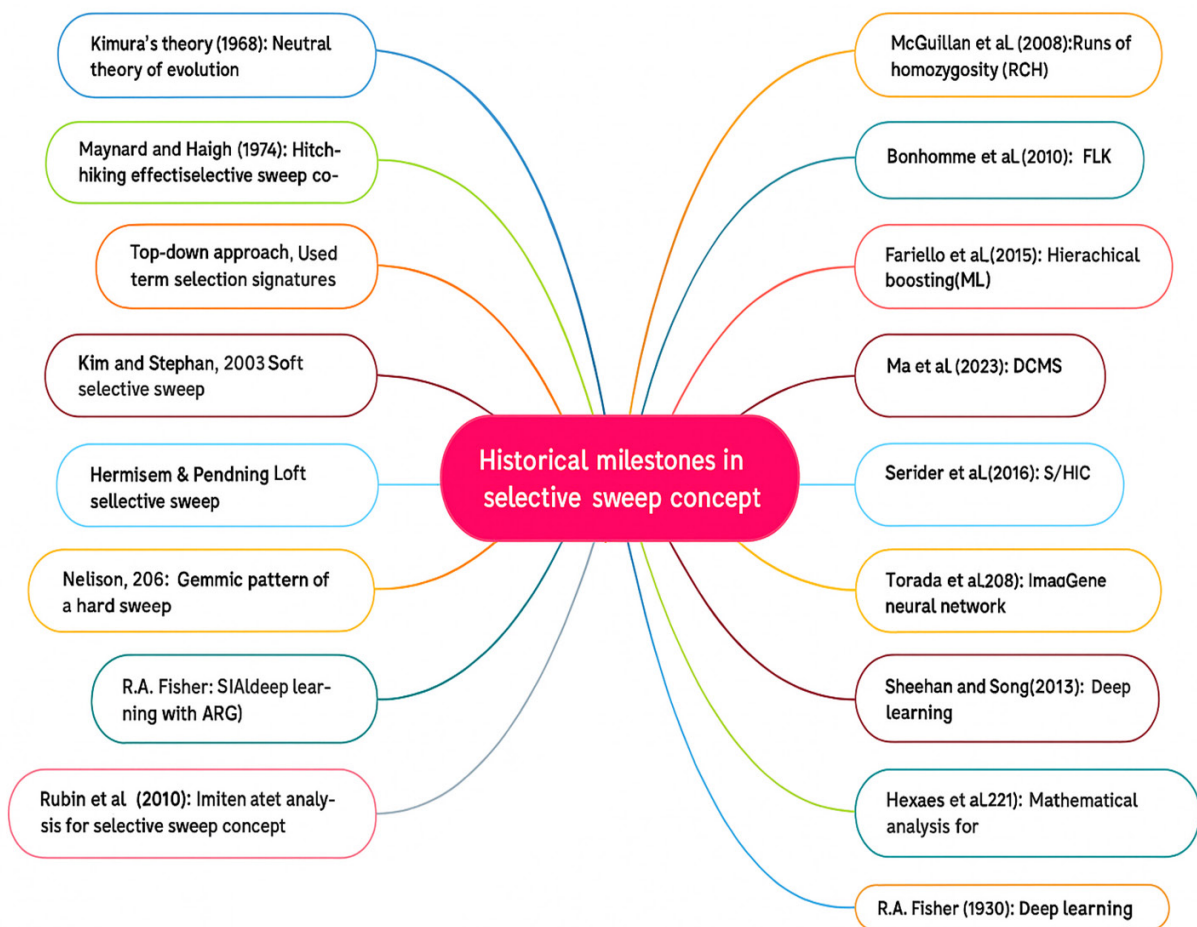


Fig. 1: Chronological Representation of a Selective Sweep Event.

Methods to Detect Signatures of Selection

The detection of selection signatures involves testing the hypothesis of neutral evolution using statistical and population-genomic approaches. These methods can be broadly classified into three categories of analysis:

Intraspecific Variation-Based Methods

These approaches rely on patterns of genetic variation within a single species to identify deviations from neutrality that may indicate selection. Common tests include Tajima’s D, Fu and Li’s D, Extended Haplotype Homozygosity (EHH), and Integrated Haplotype Score (iHS), which detect excesses of rare alleles, long

haplotypes, or reduced diversity in genomic regions under selection.

Interspecific Comparative Methods

These methods focus on genetic divergence between species to identify loci subjected to historical selection pressures. Examples include the dN/dS ratio (Ka/Ks), which compares nonsynonymous to synonymous substitution rates, and the McDonald-Kreitman (MK) test, which contrasts polymorphism within species and divergence between species to infer selection.

Combined Polymorphism-Divergence Approaches

These integrative techniques utilize both intraspecific polymorphism and interspecific divergence data for a more comprehensive detection of adaptive evolution. Approaches like the Hudson-Kreitman-Aguadé (HKA) test and Composite Likelihood Ratio (CLR) methods evaluate the combined signals of selection from multiple sources of genetic data.

Genome-wide association studies (GWAS)

Genome-Wide Association Studies (GWAS) investigate the statistical relationship between phenotypic traits and a wide array of genetic markers that capture significant genetic variation across the genome (McCarthy *et al.*, 2008). GWAS in various dairy cattle breeds have identified numerous quantitative trait loci (QTL) associated with important dairy traits (Bolormaa *et al.*, 2011; Pryce *et al.*, 2010; Cole *et al.*, 2011; Guo *et al.*, 2012; Bouwman *et al.*, 2018). As an assumption-free approach, GWAS evaluates associations between genomic regions such as single nucleotide polymorphisms (SNPs), genes, or QTLs—and traits of interest (Duncan and Brown 2018). The primary goal of GWAS is to detect genetic markers (often SNPs) significantly correlated with the target trait, based on statistical thresholds like p-values (Schmid and Bennewitz 2017).

Genomic data for GWAS are typically derived from SNP genotyping arrays or next-generation sequencing (NGS) technologies (Matukumalli *et al.*, 2009; Zhang *et al.*, 2019). Trait-marker associations can be analyzed using either the observed phenotypes (Bouwman *et al.*, 2011; Yodklaew *et al.*, 2017) or estimated phenotypes (pseudo-phenotypes), which provide approximations of the underlying genetic component of the trait (Garrick *et al.*, 2009; Liu *et al.*, 2014).

Statistical analysis in GWAS

Two primary approaches are employed to assess the association between SNP markers and the phenotype of interest: single-marker analysis and multi-marker analysis. In single-marker analysis, each SNP is individually tested under the null hypothesis that there

is no association between the SNP and the trait (Schmid and Bennewitz 2017). However, conducting a large number of independent tests can substantially increase the type-I error rate, leading to an excess of false positives (Zeng *et al.*, 2015). To address this, genome-wide association studies (GWAS) often implement correction methods such as the Bonferroni correction and the false discovery rate (FDR). The Bonferroni method is particularly stringent, adjusting significance thresholds to minimize false positives.

To overcome the limitations of multiple testing and the imbalance between the number of SNPs and sample size, multi-marker models were introduced. Originally developed for genomic selection (Meuwissen *et al.*, 2001), these models have become increasingly popular in GWAS (Sahana *et al.*, 2014; Goddard *et al.*, 2016). Their core principle involves fitting all SNPs simultaneously as random effects. Significant associations identified through GWAS are typically visualized using a Manhattan plot, which displays genomic coordinates on the X-axis and the negative log of the p-value on the Y-axis to highlight regions of interest (https://en.wikipedia.org/wiki/Manhattan_plot). In India, the high cost and intensive requirements of genotyping have limited the number of GWAS focused on production traits. Nevertheless, a notable study by Wara *et al.* (2019) conducted GWAS on 96 Vrindavani cattle using the genotyping-by-sequencing (GBS) method, specifically ddRADseq. The study identified three SNPs - NC_007299.6_145850854, NC_007328.5_26544467, and NC_007328.5_26544511, that showed strong associations with production-related traits.

Integrative Genomic Approach Using Selection Signatures and GWAS

This study employed a combination of selection signature analysis and genome-wide association studies (GWAS) to identify causative variants associated with key traits. This integrative approach enhances the precision of variant discovery by detecting genomic regions under selection that are also linked to phenotypic variation. The combined use of GWAS and selection signature methods is particularly effective in uncovering candidate genes related to traits that have not been heavily influenced by artificial selection over generations. This strategy can reveal chromosomal regions associated with adaptive traits such as thermoregulation in bovine.

For example, Igoshin *et al.*, (2019) applied both GWAS and selection signature analysis to identify genes involved in body temperature regulation under cold stress in Siberian cattle. Jeong *et al.* (2020) developed GMStool, a GWAS-based marker selection

tool, to improve genomic prediction. Additionally, Li *et al.* (2024) used whole-genome sequencing data to analyze runs of homozygosity (ROH), selective sweeps, and GWAS in 686 Rhode Island Red hens, providing valuable insights into trait-associated genetic markers. Collectively, these studies highlight the value of integrating genomic tools to understand genetic architecture better and support more effective breeding programs.

Case Studies on Genomic Selection Signatures Underpinning Different Traits in Cattle

Understanding the genomic basis of adaptation in cattle is paramount for sustainable livestock production under diverse and changing environmental conditions. Multiple case studies across tropical, cold, and high-altitude environments have revealed regions within cattle genomes that contribute to their adaptive resilience under positive selection. These insights integrate genetic, physiological, and functional perspectives, highlighting key candidate genes and pathways relevant for breeding programs targeting climate resilience. In indigenous African cattle, combined analyses of 22 studies identified selection signatures on chromosomes BTA3, BTA5 and BTA7, harbouring genes associated with immunity (BoLAs, SPAG11), heat stress tolerance (HSP family members, SOD1), and hypoxia response (*BDNF*, *INPP4A*). These genes orchestrate vital biological processes, including innate and adaptive immune responses, protein and cell stability, and growth and sweat gland development traits crucial for survival in extreme hot, disease-prone, and high-altitude African environments (Kambal *et al.*, 2023). Similarly, research into immune and thermo-tolerance adaptations in indigenous tropical cattle breeds underscores the role of natural selection in enriching immune-related genes such as *NCR3*, *CSF2*, the interferon gene family, and β -defensins (*DEFB4*, *DEFB7*, *DEFB10*), which confer enhanced pathogen defense and mastitis resistance. Concurrent selection on heat tolerance genes, particularly HSP70 family members (*HSPA1B*, *HSPA1L*, *HSPA12A*, *FKBP4*, and *GRXCR1*), reflects cellular mechanisms mitigating heat stress impacts, vital for survival in hot climates (Rajawat *et al.*, 2023). Genome-wide scans in Shanghai Holstein cattle, adapted to a hot, humid subtropical climate, identified over 100 selection candidate regions linked to heat stress response (e.g., *ITGA9*, *ALAD*), immunity (*IL22RA1*, *IRF8*), reproduction, and

milk production traits. Integrative analyses combining selection signatures and expression quantitative trait loci (cGTEx) reinforced the functional relevance of these genes, illustrating both natural and artificial selection shaping thermotolerance and production traits in a subtropical dairy context (Liu *et al.*, 2021). Contrasting with heat adaptation, Yanbian cattle adapted to extreme cold environments exhibit strong selective sweeps in genes central to cold stress response and phenotypic adaptations. Notably, missense mutations in the *CORT* gene (regulating hypothalamic-pituitary-adrenal axis activity) and *FGF5* (influencing hair follicle development) support physiological and morphological cold tolerance traits. Additionally, *CD36*, involved in long-chain fatty acid transport and fat metabolism, demonstrates a potential role in energy homeostasis under cold exposure (Shen *et al.*, 2020). High-altitude adaptation in cattle and related ruminants, like yak, involves polygenic selection targeting hypoxia adaptation pathways. Key genes including *EPAS1* (*HIF-2 α*), *EGLN1* and *HIF3A* regulate oxygen sensing and erythropoiesis, while others (*SOCS2*, *FGF7*) contribute to cardiovascular and morphological adjustments. Introgressive hybridization between yak and Tibetan cattle further enriches adaptive variation, emphasizing pathway-level convergent evolution as a hallmark of high-altitude resilience (Friedrich and Wiener, 2020). Finally, a comprehensive genomic study across eight Indian indigenous breeds (Gir, Harijana, Kankrej, Nelore, Ongole, Red Sindhi, Sahiwal and Tharparkar) employing multiple selection detection methods (Tajima's D, CLR, iHS, ROH) revealed signature regions enriched for heat shock proteins (*HSPB2*, *HSPB3*, *HSP20*, *HSP90AB1*, *HSF4*, *HSPA1B*) and immune function genes (*CLPB*, *GAP43*, *MITE*, *MCHR1*). These selections underscore the intertwined nature of heat tolerance and immunity as key evolutionary drivers in tropical environments and provide robust targets for marker-assisted breeding to enhance climate resilience (Nayak *et al.*, 2024).

Collectively, these case studies demonstrate the complex, multifaceted genetic architecture underlying climatic adaptation in cattle. Table 1 presents case studies highlighting the use of GWAS and selection signature analyses to investigate adaptation and production traits in various cattle populations. Such insights guide the identification of causative variants and inform targeted breeding strategies to ensure cattle health, productivity, and sustainability in the face of escalating climate challenges.

Table 1: Case Studies of Adaptation and Production Traits in Cattle Using GWAS and Selection Signature Approaches

S. No.	Trait Studied	Cattle Breed / Population	Method Used	Key Findings / Candidate Genes	Reference
1	Heat tolerance, Immunity, Hypoxia	Indigenous African cattle (multiple breeds)	Selection Signature (Review of 22 studies)	<i>BoLAs, PAG11, HSP</i> family, <i>SOD1, BDNF, INPP4A</i> on BTA3, BTA5, BTA7; immunity, heat tolerance, hypoxia response	Kambal <i>et al.</i> , 2023
2	Immune response & thermo-tolerance	Indigenous tropical breeds (Gir, Red Sindhi, Tharparkar, Ongole)	Selection Signature	<i>NCR3, CSF2, IFN</i> genes, β -defensins (<i>DEFB4, 7, 10</i>); <i>HSPA1B, HSPA1L, HSPA12A, FKBP4, GRXCR1</i> for thermotolerance	Nayak <i>et al.</i> , 2023; Nayak <i>et al.</i> , 2025
3	Thermal adaptation, disease resistance	Shanghai Holstein cattle	iHS and ROH with cGTE _{ex} QTL integration	<i>ITGA9, ALAD</i> (heat stress); <i>IL22RA1, IRF8</i> (immunity); <i>SNRPA1, SLC39A11</i> (reproduction), milk production genes	Liu <i>et al.</i> , 2021
4	Cold climate adaptation	Yanbian cattle vs. N'Dama (control)	Whole-genome resequencing, CLR, Fst, XP-CLR, $\theta\pi$	<i>CORT</i> (HPA axis, cold stress), <i>FGF5</i> (hair follicle development), <i>CD36</i> (fat digestion and fatty acid transport)	Shen <i>et al.</i> , 2020
5	High-altitude adaptation	Tibetan cattle, yak, other ruminants	Comparative genomics, introgression analysis	<i>EPAS1 (HIF-2α), EGLN1, HIF3A</i> (hypoxia response); <i>SOCS2, FGF7</i> (cardiovascular; morphology)	Friedrich and Wiener, 2020
6	Heat tolerance & immunity	Indian indigenous breeds (Gir, Hariana, Kankrej, Nelore, Ongole, Red Sindhi, Sahiwal, Tharparkar)	50K SNP chip; Tajima's D, CLR, iHS, ROH	<i>HSPB</i> family, <i>HSF4, CLPB, GAP43, MTF, MCHR1</i> ; co-selection of thermotolerance and immunity genes	Nayak <i>et al.</i> , 2024
7	Milk yield & fat %	Holstein	GWAS	<i>DGAT1, GHR, PRLR</i>	Olsen <i>et al.</i> , 2002
8	Milk production	Jersey, Holstein	Selection Signature (iHS, FST)	Selection around <i>DGAT1, ABCG2</i>	Flori <i>et al.</i> , 2009
9	Body weight & stature	Sahiwal (Indian)	GWAS	<i>HMG2, NCAPG-LCORL, PLAG1</i>	Mishra <i>et al.</i> , 2020
10	Milk yield	Vrindavani	Selection Signature (FST, iHS)	<i>LRP1B, TNNI3K, APOB, CACNA2D1, FAM110B, SPATA17</i>	Singh <i>et al.</i> , 2020
11	Growth traits	Brahman and Tropical Composite	GWAS	<i>PLAG1, LCORL</i>	Fortes <i>et al.</i> , 2013
12	Milk fat %, protein %, SNF	Tharparkar (Indian)	GWAS	<i>DGAT1, SCD, LALBA, CSN3</i> variants	Patel <i>et al.</i> , 2022
13	Feed efficiency	Nellore (Brazilian Zebu)	GWAS	<i>GHRHR, IGF1R, LEPR</i>	Utsunomiya <i>et al.</i> , 2013
14	Reproductive traits	Holstein-Friesian	GWAS	Loci near <i>GNRHR, LHCGR</i>	Cole <i>et al.</i> , 2011
15	Carcass & Meat Quality	Angus, Hereford	Selection Signature (XP-EHH)	<i>MSTN, CAPN1</i>	Randhawa <i>et al.</i> , 2014

FUTURE PROSPECTS AND CONCLUSION

Integrating selection signatures with genome-wide association studies (GWAS) offers a powerful approach to uncovering the genetic architecture of adaptation and production traits in cattle. This synergy connects evolutionary processes with practical breeding objectives, paving the way for precision livestock management. As bioinformatics tools and high-throughput sequencing technologies continue to evolve, the resolution and accuracy of selection signature detection will improve, enhancing our understanding of traits such as disease resistance, climate adaptation, and productivity. By combining methods like F_{ST} , XP-EHH, and iHS with GWAS, researchers can pinpoint candidate genes subjected to positive selection. This approach can also be particularly valuable in addressing the challenges posed by climate change to cattle populations. Integrative analyses can identify genetic variants linked to heat tolerance, drought resistance, and immune responses. This precision breeding strategy can accelerate genetic improvements while preserving genetic diversity. Incorporating machine learning techniques with genomic data further refines the identification of complex trait-associated regions, enhancing the accuracy of genetic predictions. Future research may extend these approaches by incorporating epigenomics, transcriptomics, and metabolomics, providing a more comprehensive understanding of gene-trait interactions and enabling more holistic selection strategies. As these technologies advance, ethical considerations surrounding biodiversity conservation and animal welfare will become increasingly important. Integrative studies must balance production goals with sustainability to ensure the long-term viability of cattle breeds.

The future of cattle genomics lies in leveraging these integrative strategies to develop resilient, productive, and sustainable livestock systems. With ongoing innovation, this field will be crucial in addressing global food security and advancing agricultural sustainability. Ultimately, leveraging these integrative genomic tools can empower sustainable breeding strategies, bolster conservation programs, and ensure cattle populations' continued resilience and productivity in India and beyond.

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