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Genetic Diversity and Selection Signatures in Economically Important Traits of Ethiopian Indigenous Cattle Breed as a Base for Dairy Cattle Genetic Improvement: A Review

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ABSTRACT

The aim of this paper was to review the genetic diversities and selection signatures in economical important traits of Ethiopian indigenous cattle. This allows obtaining rapid genetic gain, predicting genomic potential and developing conservation strategies. A genetic variation among Ethiopian breeds ranging from 0.1 to 4.55% and a within variation of 95.45 to 99.9% was reported by various scholars. About 3.51% differentiation between Boran and Fogera from Begait and 2.82% differentiation of Boran from Fogera and Begait was reported. Even though the observed and expected heterozygosity values among Ethiopian cattle population was lower, research reports shown considerably higher values ranging from 0.638±0.015 in Boran and 0.714±0.022 in Raya-Azebo to 0.700± 0.014 in Ambo and 0.735±0.017 in Sheko. Genes responsible for heat tolerance, control of metabolic disease, immunity genes, high altitude and low altitude adaptation were reported in Ethiopian cattle breeds. In African indicus and European taurian cattle different genes responsible for milk production, milk fat yield and synthesis and milk composition, were reported. Genes associated with milk traits; fertility and reproduction genes were also reported in Ethiopian cattle. The presence of high within breed variation in Ethiopian cattle creates favorable conditions for further improvement through selection. Beyond identifying candidate potential genes, a detailed study targeting genomic prediction of milk yield and genomic inbreeding had better be done, which allows getting information to optimize and speed up the breeding programs and genetic improvement.

Key words: *Bos indicus*, Diversity, Genetic improvement, Selection signature.

Growth of the world population is projected to increase from 7.8 billion in 2020 to 9.7 billion by 2050 (Smith *et al*., 2020) and it is predicted that demand for animal products will increase by 50% (Singh *et al*., 2014). And according to the Food and Agriculture Organization (FAO, 2013), beyond the population increment, the global food production is experiencing challenges due to climate change, which requests doubling of the food production so as to meet the increasing demand (Eggen, 2012; Strandén *et al*., 2022). Cattle are central to the African economy (Kim *et al*., 2020; Saravanan *et al*., 2021) that plays a pivotal role in the economy through the provision of meat, dairy, leather, labor; acting as walking larder, traction power and manure and have societal importance and they are considered as a primary sources of wealth (Zerabruk *et al*., 2007; IBC, 2012; Xu *et al*., 2019; Kim *et al*., 2020). The genetic makeup of these cattle originated from the humpless *B. taurus* and the humped *B. indicus* subspecies (Taye *et al*., 2018) and they have diverse phenotypes with diverse adaptations. These breeds are classified as African Sanga (crossbred between Taurine and Zebu cattle), African Zenga (crossbred between Sanga and Zebu) and African Zebu (Edea *et al*., 2014a; Kim *et al*., 2020). These classifications (genetic differentiations) are arising due to domestication and selection pressures done naturally or artificially with human interference (Saravanan *et al*., 2021).

Several recent developments have strengthened the interest in local breeds (FAO, 2021). The reasons behind are these breeds are the source of vast environmental adaptations for diverse disease and parasite resistance, tropical climate conditions (including dry, hot, humid), excessive heat tolerance, suitable for extensive management system and are the only options for ecosystem restoration (Kim *et al*., 2017; Taye *et al*., 2018; FAO 2021; Vaidya *et al*., 2023) and even if there productivity compared

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to exotic breeds is lower, they are the only option available for millions of farmers in the African agro-pastoral systems, where exotic improved breeds under-perform in the traditional management systems (Kim *et al*., 2020).

Understanding the current genetic diversity and beneficial traits of adaptation and production in indigenous cattle breeds had an important role in order to meet the growing worldwide demands for animal source proteins and develop a breeding strategy for increased meat and milk production (Taye *et al*., 2018; Cole *et al*., 2020). Currently, to support the agricultural breeding including livestock breeding *viz*., nanotechnology (Nikita *et al*., 2023), artificial intelligence (Vinod, 2023). About 64% (estimated of 20 breeds out of 31 registered breeds) of the Ethiopian local cattle breeds had studied for their genetic diversity within and among breeds; and their ancestral origin, adaptation and introgression with Asian and European cattle breeds with varying genomic characterization approaches (Zerabruk *et al*., 2007; Hassen *et al*., 2007; Edea *et al*., 2014a; Taye *et al*., 2018; Tarekegn *et al*., 2018; Kim *et al*., 2020; Yirsaw, 2021). Genetic diversity studies showed degree of differentiation among and within the livestock breeds or populations, but the selection signature study find the actual reason for that diversification (Saravanan *et al*., 2020).

This review article is not intended to be comprehensive one covering all the diversity studies and selection signatures; because molecular based researches had alarmingly increased and new findings had published within a finger count days. Given these characters, this paper aims to review the genetic diversities and selection signatures on economically important production and fitness traits of Ethiopian indigenous cattle to be a base for dairy cattle genetic improvement programs. Selection signature analyses can help to identify numerous candidate genes associated with production and fitness traits in domesticated animals (Xu *et al*., 2019). This selection signature can be analyzed through the identification of the fingerprints of natural and artificial selection pressures in the genomes of cattle (Yirsaw, 2021). Mapping and identification of candidate genes with economic significance allows obtaining rapid genetic gain, predicting genomic potential and developing conservation strategies for indigenous cattle, irrespective of the changing climate (Terefe *et al*., 2022). Numerous genes coding for production and fitness potential of the indigenous cattle had been identified with varying demographic and adaptation histories.

Methodologies used in genetic diversity and selection signature

Genomic characterization is a precise way of characterizing breeds and helps to identify the breeds or groups of breeds that have retained their uniqueness (FAO, 2021). The genomic evolution and ancestral history can be computed with maternal lineages (mtDNA), paternal lineages (Y chromosome) and autosomal groups (Utsunomiya *et al*., 2019). Genetic diversity could be described through level of expected and observed heterozygosity, level of allelic polymorphism within and among populations / breeds (Hunde and Tadese, 2020; Yirsaw, 2021); and it can be calculated and presented with population differentiation (FST), Reynold's distance estimates (Tarekegn *et al*., 2018), principal component analysis (PCA)-based Clustering (Yirsaw, 2021) and Nei (1978) genetic distance (Hassen *et al*., 2007).

Various statistical methods and approaches have been used to detect selection signatures in African cattle breeds using DNA sequence or SNP genotype data (Edea *et al*., 2014a; Taye *et al*., 2018). The general workflow for the detection of selection signatures starts from the generation of genotype data, either using SNP microarray or high-throughput sequencing technologies (Saravanan *et al*., 2020). These methods are broadly classified into intra-population statistics (search for footprints within populations) and inter-populations statistics (the degree of differentiation due to locus-specific allele frequencies between the populations) (Saravanan *et al*., 2020). Intra population statistics includes methods based on site frequency spectrum, linkage disequilibrium and reduced local variability (Taye *et al*., 2018; Saravanan *et al*., 2020) while the inter-populations statistics had two groups, single site and haplotype-based differentiation (Tarekegn *et al*., 2018; Saravanan *et al*., 2020). Under the umbrella of the above two broad classification methods, different statistical approaches like integrated haplotype score (iHS) (Qanbari *et al*., 2011), run of homozygosity (ROH) (Ceballos *et al*., 2018), population differentiation (FST) (Wright, 1978), increased haplotype homozygosity (XP-EHH), cross population composite likelihood ratio (XP-CLR) (Kim *et al*., 2017), fixation index (F), nucleotide diversity (Pi) (Nanaei *et al*., 2020; FAO, 2023) and Tajima's D (Taye *et al*., 2017) were also used to found selection signatures footprints. The selection of the methods can depend on the data type, software and bioinformatics tools used and knowledge and interests of the researchers.

It is indicated that different methods had brought different results on genetic distance and selection sweeps (Saravanan *et al*., 2020; Nanaei *et al*., 2020); and this had an implication to use two and more complementary methods for a single study. Even though different software programs are available in SNP data quality control and analysis, many scholars had used the popular PLINK and R statistical software packages which is due to their open access, speed and reliability. Analysis of gene ontology (GO) had been also used to identify biological pathways that were targeted by selection (Edea *et al*., 2014b). Because various methods have different strengths and weaknesses and have brought different results, it is recommended to use combinations of more than two methods for the analyses of selection signatures (Saravanan *et al*., 2020; Nanaei *et al*., 2020). Use of combined methods had also contributed to reduce and avoid false selection signals that mimic signatures of selection raised due to demographic events such as population expansions, genetic bottlenecks and population subdivision (de Simoni Gouveia *et al*., 2014). Besides the presence of difference in final result between the methods and software's, the selection of the methods can also be dependent on the data type, knowledge and interests of the researchers.

Genetic diversity of Ethiopian indigenous cattle

The evolutionary history of Ethiopian cattle

Approximately 8000-10,000 years BC, the Taurine (Bos taurus taurus) and Indicine (Bos taurus indicus) cattle were domesticated from wild aurochs (Bos primigenius) in the Middle East and Indian subcontinent, respectively (Saravanan *et al*., 2021). In Africa, the earliest group of cattle known to have migrated into the continent were the *Bos taurus taurus* circa 7,000-4,000 years before present (YBP) and later the Bos taurus indicus circa 4,000-2,000 YBP from their domestication centers (Kim *et al*., 2020; Mauki *et al*., 2022). The autosomal DNA indicated that the *Bos indicus* and *Bos taurus* breeds are separated <330,000 YBP and the Bos indicus cattle of Chinese was separated <40,000 YBP from Indian and African sisters (Fig 1A) (Utsunomiya *et al*., 2019).

Ethiopia, as one of the East Africa countries, is considered the cradle of the Near-East *B. taurus* as well as the Arabian and Indian *B. indicus* cattle migration corridors (Fig 1B). According to Yirsaw (2021) and Terefe *et al*. (2022), the main reasons are the country is endowed with diverse indigenous cattle resources, diverse agro-ecology (ranging from extreme lowlands to Afro-alpine zones), located near the Horn and the East Coast and the cattle population is hybrid. With these facts Ethiopia is considered as a secondary hybridization zone for African indigenous cattle (Edea *et al*., 2014a; Yirsaw, 2021); which is evidently acknowledged with mtDNA analysis as the Ethiopian cattle had taurine ancestor (Kim *et al*., 2017; Tarekegn *et al*., 2018) on which the observed zebu influence on the country was a process of introgression. It is indicated that cattle may have penetrated to Ethiopia in the middle of the second millennium B.C (Mekuriaw and Kebede, 2015; Hagos, 2016).

The African content is rich in cattle diversity and had about 150 cattle breeds or populations which are phenotypically grouped in to taurine, zebu and the ancient stabilized taurine × zebu crossbreed known as Sanga (Kim *et al*., 2017; FAO, 2021). With similar phenotypically grouping, Ethiopia had also a range of 28 (IBC, 2012) to 31 recognized cattle breeds (DAGRIS, 2007); and this number will in near future increased due emergency of uncharacterized breeds which probably due to admixture and breed substitution and decreased due to the facing climate change and lower effective population size observed in some breeds (Edea *et al*., 2013).

Genetic diversity and distance of Ethiopian cattle

Genetic diversity is the total genomic information in a certain species, including all breeds, subpopulations and varieties that fall within that particular species (Demir *et al*., 2022). Before domestication, the major sources of genetic variation were natural selection, mutation, migration, gene flow and genetic drift; while artificial selection based on the breeders preference (Bahbahani *et al*., 2018a; Yirsaw, 2021; Demir *et al*., 2022) is the currently sources of genetic variation.

Pairwise population differentiation (FST) and Reynolds' genetic distance (Reynolds *et al*., 1983) in Ethiopian cattle estimates close relationships among breeds and higher variation within breeds (Edea *et al*., 2013; Tarekegn *et al*., 2018; Dadi *et al*., 2008). This situation coupled with the transformation of the agricultural systems leads to a rapid loss of indigenous livestock resources. A genetic variation among breeds of 4.55% (Tarekegn *et al*., 2018); 0.56% (Edea *et al*., 2013); 2% (Edea *et al*., 2014a); 0.1 -4% (Dadi *et al*., 2008) was reported between Ethiopian breeds. Even grouping of Ethiopian cattle into highland and lowland had contributed low (0.42%) group variation (Edea *et al*., 2013). Principal component analysis (Yirsaw, 2021) indicated a 3.51% differentiation between Boran and

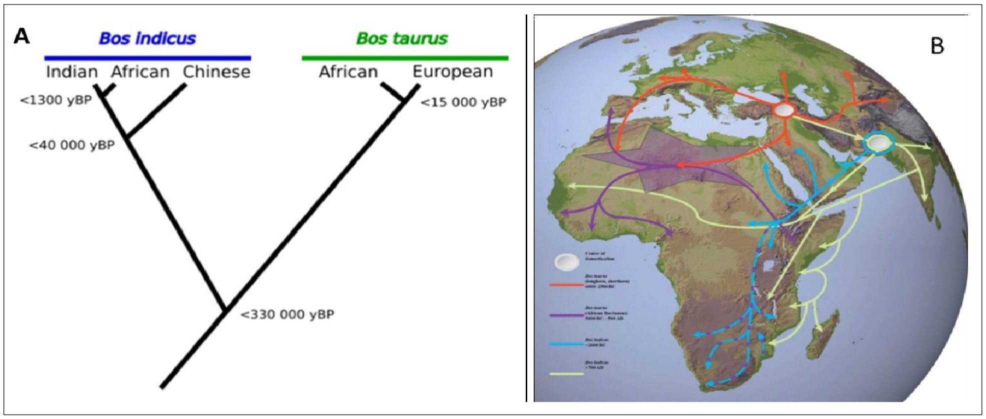


Fig 1: A) Schematic of the phylogenetic trees of autosomal genome lineages in cattle (Utsunomiya *et al*., 2019); B) Approximate migration route and the origin of Africa domestic cattle (Mwai *et al*., 2015).

Fogera from Begait and 2.82% differentiation of Boran from Fogera and Begait. However higher genetic distance between Arsi, Sheko, Horro, Guraghe Highland and Abigar cattle was reported (Hassen *et al*., 2007). The main reasons for low genetic differentiation could be a result of a recent common ancestral origin, multiple introgressions, short domestication history and admixture of the population and lack of selection pressure (Edea *et al*., 2013; Tarekegn *et al*., 2018; Hunde and Tadese, 2020). Besides, varying reports could also be a result of differences in molecular markers used, type of laboratory procedures, sample size and area coverage of each sample collected (Hunde and Tadese, 2020).

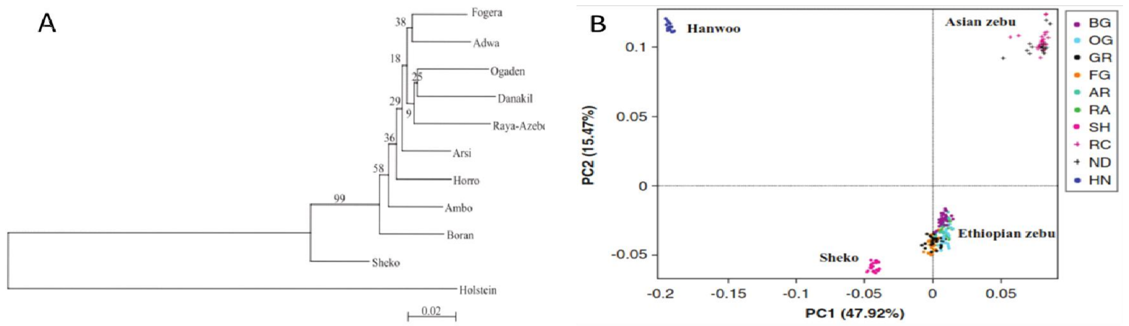
The phylogenetic analysis reported by Dadi *et al*. (2008) and PCA analysis (Edea *et al*., 2013) indicated that the Ethiopian cattle breed had two clusters (Fig 2A and B). These are Sheko in one cluster and other cattle in another cluster. Other studies also indicated that there is higher variability in Sheko breed (Hassen *et al*., 2007; Tarekegn *et al*., 2018). The authors reasoned that the breed, Sheko cattle, is originally short horn taurine cattle of East Africa; and believed that it had a different and longer evolutionary history. Edea *et al*. (2014a) also indicated that 76% (on average with exception of Sheko) of the genome of Ethiopian cattle populations shared an Asian zebu background, whereas approximately 41% and 59% of Sheko samples appeared to share taurine and indicine ancestry, respectively. But currently the breed has miniature humps due to interbreeding with zebu cattle (Dadi *et al*., 2008).

It was also reported that the observed and expected heterozygosity values among the Ethiopian cattle population was lower (Dadi *et al*., 2008; Edea *et al*., 2013). The overall mean observed and expected heterozygosity for Boran, Begayit and Fogera breeds were 0.40, 0.40, respectively (Yirsaw, 2021). Besides, a considerably higher respective observed and expected heterozygosity per population ranging from 0.638±0.015 in Boran and 0.714±0.022 in Raya-Azebo to 0.700± 0.014 in Ambo and 0.735±0.017 in Sheko was reported (Dadi *et al*., 2008); while lower observed heterozygosity of Danakil (0.363), Horro (0.387), Borana (0.374), Arsi (0.376) and Ambo (0.385) was reported (Edea *et al*., 2013).

Selection signatures in economically important traits

African indigenous cattle breeds have unique morphological features that distinguish them from other cattle that are largely the result of natural and human selection (Mwai *et al*., 2015). They have evolved to adapt to the harsh environmental conditions like livestock diseases, high solar radiation and temperature, drought and poor nutritional condition (Mbole-Kariuki *et al*., 2014; Kim *et al*., 2017). In addition, African zebu cattle are still a reliable source of draught power (Rege *et al*., 2001). Likewise, Ethiopian breeds had immense adaptation; example Sheko breed is tolerant to trypanosomosis, Barka has active disposition, Jem-Jem is well adapted to the wet and cold climate, Ogaden breed has good dairy and beef characteristics, Raya-Azebo has good draught power, Arado is a docile, good working animal, Fogera had docile temperament and good milk yield and Horro breed is known for its calm disposition with variable milk production (DAGRIS, 2007; Mwai *et al*., 2015). These environmental conditions and various adaptations of the Africa indigenous cattle provide a signal of positive selection (Kim *et al*., 2017). In the classical view, selection acts upon newly arising beneficial mutations, but under some circumstances, standing genetic variation that was previously neutral or slightly deleterious may become the source for adaptive substitutions (Burke, 2012).

The unique genetic patterns or footprints left behind in the genome of individuals under selection are called 'selection signatures'. Knowledge of selection signatures may help in understanding the basis of heat tolerance and disease resistance (adaptable traits of indigenous cattle breeds) (Saravanan *et al*., 2021); enable a better understanding of the evolutionary forces that shape the genetic constitution of populations (Edea *et al*., 2014a); acts a successful tool for the long-term improvement of livestock



BG = Begayt; OG = Ogaden; GR = Gurage; FG = Fogera; AR = Arsi; RA = Raye-Azebo; SH = Sheko; RC = Red Chittangong; ND = Non-descript and HN = Hanwoo.

Fig 2: A) Genetic relationships among Ethiopian cattle based on microsatellite loci (Dadi *et al*., 2008); B) Principal component analysis (PCA) based on autosomal SNPs of 10 cattle breeds (Edea *et al*., 2014a).

populations; allows to speed up the rate of genetic improvements (Cole *et al*., 2020; Saravanan *et al*., 2020); and used to identify genomic regions affected by natural and artificial selection that are associated with the phenotypes of specific populations (Taye *et al*., 2018).

Selection interest had varied between the production participating components like producers, processor, breeders and the scientists. Scientists, as indicated by Cole *et al*. (2020), required the selection of specific gene of interest to be expressed in the animals while, production participants, even the cost of manufacturing is higher, need to manufacture those traits with technological approaches. However, currently genomic selection provides an answer to both parties and avoids the problems of the past. Selection signatures for production (Singh *et al*., 2014; Bahbahani *et al*., 2018a; 2018b; Nanaei *et al*., 2020; Yirsaw, 2021; Saravanan *et al*., 2021), fitness (Kim *et al*., 2017; Saravanan *et al*., 2021; Yirsaw, 2021), environmental adaptation (Kim *et al*., 2017; Taye *et al*., 2018; Saravanan *et al*., 2021; Yirsaw, 2021; Demir *et al*., 2022) and adaptation to higher and lower altitudes (Terefe *et al*., 2022) was reported in Ethiopian and other *Bos indicus* cattle breeds.

Candidate genes related to immunity and tropical adaptation

Climate is the single most important ecological factor that determines the growth, development and productivity of domestic animals (Demir *et al*., 2022). The continuing steady ambient temperature increment is becoming a big challenge that lowers the productivity, even death of animals and causes a significant reduction in biodiversity (Alemayehu and Molla, 2018; Taye *et al*., 2018). Animals adapt these climatic conditions through physiological, metabolic and other inherent conditions. Presence of disease deteriorates the productivity of cattle through depressing potential traits and lower farm profitability (Cole *et al*., 2020). It was reported that more genes related to disease resistance are available in Bos indicus cattle than Bos taurus breeds (Alemayehu and Molla, 2018; Saravanan *et al*., 2021) which is due to natural selection for survival in the former and artificial selection targeting economical production traits in the later species. Advances in biotechnology allows the identification of disease causing agents though molecular markers and enables a method of reduction in pathogens or parasite abundances (Singh *et al*., 2014).

A thermo tolerance in cattle was identified based on expression or activation of biological markers (Taye *et al*., 2018; Saravanan *et al*., 2021; Yirsaw, 2021). Heat shock transcription factor (HSF), heat shock proteins (HSP70, HSP90 and HSP27) (Saravanan *et al*., 2021), cellular response to heat [Gene Ontology (GO): 0034605] and regulation of pH (GO: 0006885) (Yirsaw, 2021) and genes involved in calcium signaling (ATP2A2, TGM3 and TGM1) (Taye *et al*., 2018) were reported as a contributor for thermo tolerance in different breeds of cattle. According to Terefe *et al*. (2022), a total of 144 and 20 candidate selected regions for respective high and low altitude adaptation were found in Ethiopian zebu populations. The candidate genes have different biological processes, cellular and molecular functions and pathways responsible for immune response for disease resistance and adaptation for environmental stress. For example the function of MZB1 gene is related to the endoplasmic reticulum calcium ion homeostasis, cellular signal transduction, B cell activation and T cell proliferation; and STING1 gene is responsible to the innate immune signaling response to protect the host against viral and bacterial infections (Terefe *et al*., 2023). According to reports, these genes responsible for environmental adaptation, disease resistance and immunity were continuously detected in the genome of the African livestock population due to the retained synonymous and missense mutations creating polymorphism in a single gene and gene segment's (Taye *et al*., 2017; Terefe *et al*., 2023; Getinet, 2016; Adebabay, 2018; Edea *et al*., 2018). Table 1 presents a summary of genes responsible for different tropical adaptation and immunity functions in Ethiopian and other Bos indicus cattle.

Candidate genes related to milk yield and its constituents

Since most of the indicine breeds were used for the dairy purpose, it is expected to have several genes associated with milk production traits. According to Singh *et al*. (2014), animal databases show around 344 and 71 quantitative trait loci (QTL) associated with milk yield and mastitis related traits, respectively. Table 2 summarizes those genes related to milk production in European and African cattle breeds.

In a work done on African indicus (Ankole, Kenana, N'Dama) and European taurus cattle (Hereford and Holstein) reported genes related to milk production (IGFBP2, RORA, B4GALT1, CD44, MACF1, IL15), milk fat yield and synthesis (LPIN1, ACACA, PDE3A, ABCC9), milk composition (NF2, KCNIP4, CSN3) and milk traits (GHR, NME1, ATP2B) (Nanaei *et al*., 2020). Genes associated with milk traits (prolactin, leptin, DGAT1 and ABCG2), milk protein expression [CSN1S1 (casein Q s1)], milk protein concentration [LGB $^{\beta}$-lactoglobulin)] and milk protein synthesis and fat metabolism (STAT1 (signal transducer and activator of transcription 1)) were reported (Singh *et al*., 2014). The Diacylglycerol acyl-CoA acyltransferase 1 (DGAT1) genes had reported to have high diversity, heterozygosity and polymorphic information content under Ethiopian cattle breeds (Fogera, Boran, Begait and Horro cattle) (Samuel *et al*., 2022). Besides the presence of leptin gene in Ethiopian cattle breed (Mandefro *et al*., 2021), fertility and reproduction genes (RXFP2, CLGN, MEA1) in Sheko cattle (Bahbahani *et al*., 2018b) was also reported. The distribution of different milk related genes in the autosomal chromosome were indicted (Fig 3I) and clustering and molecular phylogenetic analysis for comparison of the haplotypes of the cattle breeds with other species for SNPs of Leptin gene in Ethiopian cattle breeds (Fig 3II) was indicated.

Significance connotations for the ethiopian dairy development

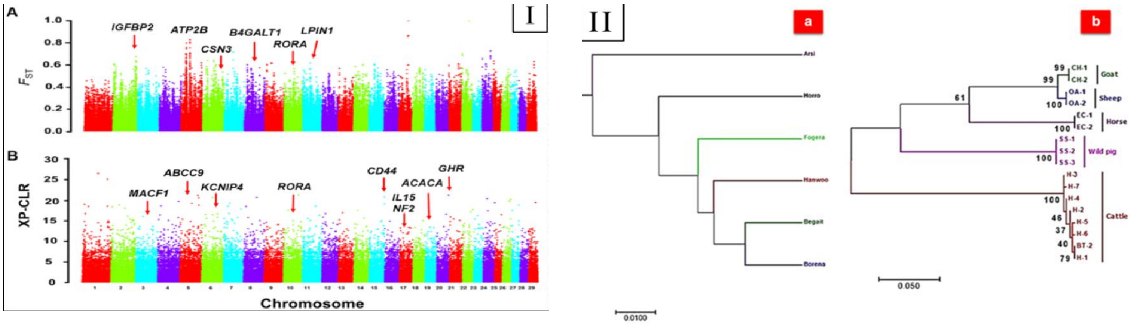
Genetic improvement provides a significant technique to improve the performance of herds through selection of superior animals to be a parent for the next generation based on their performance in target traits under the breeding program (Nwogwugwu *et al*., 2020). And the use of genomic selection in the dairy cattle is a useful tool for selecting traits with low heritability and difficult and expensive to measure, with accuracy level range of 0.8 for production traits and 0.7 for fertility (Meuwissen *et al*., 2016), increases genetic gain and reduce the generation interval (Nwogwugwu *et al*., 2020; Saravanan *et al*., 2020).

Table 1: Genes responsible for different tropical adaptation and immunity functions in *Bos indicus* cattle.

No.	Genes	Linked trait and functions	Breed name/*Bos indicus*	References
1	SOD1	Heat tolerance	Boran, Fogera, Begait	Yirsaw, 2021
2	MATR3	Fat storage		
3	IKBKE	Control of metabolic disease		
4	HSPA1B, GRXCR1	Thermo-tolerant	Tharparkar	Saravanan *et al*., 2021
5	DEFB4, DEFB7, DEFB10	Resistance to mastitis	Tharparkar	
6	FKBP4, HSPA1L, HSPA1B	Thermo-tolerant	Gir	
7	NCR3	Immunity	Gir	
8	IFNAR2	Disease resistance	Gir	
9	CSF2, IL3	Immunity	Red Sindhi	
10	HSPA12A, IL6	Thermo-tolerant	Ongole	
11	IFNT, IFNW1, IFNAC, IFNB1, IFN-a, IL6, ARID5A, ONECUT1	Immunity	Ongole	
12	HIST1H2BN	Immunity	Sahiwal	
13	GCNT3	Immunity	Kankrej	
14	HCRTR1	Circadian rhythm, feeding behavior	N'Dama	Kim *et al*., 2017
15	STOM, SLC40A1, SBDS, EPB42, RPS26	Disease resistance (Anemia)	N'Dama	
16	SOD1, PRLH	Thermoregulation	African *Bos indicus*	
17	BOLA	Tick resistance	African *Bos indicus*	Kim *et al*., 2017; Taye *et al*., 2018
18	TNFAIP8L3, SLC25A48	Tick resistance	African *Bos indicus*	Taye *et al*., 2018
19	KRT33A, KRTAP27-1, KRTAP9-1	Ectodermal invasion resistance	African *Bos indicus*	
20	SLC45A2, MLPH, RAB17, RAB37, RAB42, RAB7A, ATRN	Pigmentation of skin and hair	African Bos indicus	
21	ICOS, LTA4H, NFAM1, FCN2, IL7, IL15	Immunity genes	Sheko	Bahbahani *et al*., 2018b
22	HSPA6, DNAJC6	Heat tolerance	Sheko	
23	RARA, MED1, PRKCZ, TBX21, CCR7, IL13, IL4, EXOSC3, BAG6, OTUD4, IL18, RAP, ALPK1, CHADL, PAWR, CRKL, ELANE, TNIP3, CFD, TRIM6	GO:0050778: Positive regulation of immune response	Ethiopian indigenous cattle	Terefe *et al*., 2023
24	IL18, IL18R1, KIT, IL23A, SPHK2, STAT5B, FGR, RARA, PRKCZ, TBX21, IL13, IL4, EXOSC3, IL18, RAP, MZB1, TRIM6	GO:0002699: Positive regulation of immune effector process		
25	ITPR2, DUSP10, GIMAP4, GIMAP5, GIMAP7, VEGFC, EP300, CLCA2, SLC26A2, CBFA2T3 MSRB3, LEMD3, WIF1, HMGXB3,	High altitude adaptation	Ethiopian highland cattle breeds Ethiopian lowland cattle breeds	Terefe *et al*., 2022
26	CSF1R, RXFP2	Low altitude adaptation		
27	HSPA4, HSF1, CMPK1, NPM1, EIF2AK4	Thermo-tolerance	African zebu cattle	Edea *et al*., 2018
28	HSP70	Heat tolerance		

Table 2: Candidate genes responsible for milk production and milk related functions.

No.	Genes	Breeds	Reference
1	CACNA2D1, ADARB2, WDR37, LARP4B	Ayrshire	Saravanan *et al.*, 2021
2	KCNIP4, SLIT2, ADAP2, LTF	Brown swiss	
3	SYN3, TIMP3, RFK, ACACA, HNF1B, SCAP	Guernsey	
4	ADARB2, WDR37, LARP4B, ZMYND11, PRNP, CDH4	Holstein friesian	
5	LPHN2, ADARB2, WDR37, LARP4B	Jersey	
6	NCR3, ATF6B, MSH5	Gir	
7	VIT, TRHR	Hariana	
8	PTK2, TRAPPC9, DCHS1, ILK, APBB1, TRIM3	Kankrej	
9	ARL4, CA8, WDR7, NODAL	Ongole	
10	DIS3L, SLC8A1	Red Sindhi	
11	DCHS1, ILK, APBB1, TRIM3	Sahiwal	
12	DGAT1, GHR, ABCG2	Kenyan and Buttana	Bahbahani *et al.*, 2018a
13	DGAT1	Fogera, Boran, Begait and Horro	Samuel *et al.*, 2022
14	Leptin SNPs (LEP-73, LEP-143, LEP-399, LEP-411, LEP-495)	Fogera, Boran, Begait, Arsi and Horro cattle	Mandefro *et al.*, 2021
15	PRLH	Sheko cattle	Bahbahani *et al.*, 2018b



(H = Haplotype, BT = *Bos taurus*, SS = *Sus scrofa*, EC = *Equus caballus*, OA = *Ovis aries* and CH = *Capra hircus*)

Fig 3: I) Genomic landscape of positive selection signatures for milk associated traits using the FST (A) and XP-CLR (B) values (Nanaei *et al.*, 2020). II) UPGMA tree of the six cattle breeds based on SNP data with linked software, MEGA X (a) and Molecular phylogenetic analysis for comparison of the haplotypes of the cattle breeds with other species (b) for Leptin gene SNPs (Mandefro *et al.*, 2021).

Economically important traits in farm animals largely consist of complex and continuously distributed phenotypes and understanding of their structure and function in the genome had bought international interest in the use animal genetic resources (Alemayehu and Molla, 2018). The presence of genes responsible for climatic resistance with a varying diversity in the Ethiopian cattle benefits the country in potential use of them for future generation under the continuously changed climatic condition. Demir *et al*. (2022) indicated that the conservation of genomic variants in adaptation will allow animals to adapt to future challenges, benefit farms for sustainable use of local breeds and these animals will be the only answers in the ongoing global warming.

The continuous admixture between different Ethiopian breeds due to in search of feed and water (Boran cattle), escaping of flood of Lake Tana (Fogera cattle), indiscriminate crossbreeding (Sheko cattle) and increased urbanization and crop intensification (lowering grazing lands), will create a gene flow and population bottleneck and become a big factor in threatening unique cattle breeds. Even though these cases had lowered the genetic diversity among breeds, still there is a wider within breed diversity that allows selection and preservation of unique genetic variants in these breeds. Understanding the presence of genetic diversity and selection signatures in milk production, disease resistance and other productivity traits in Ethiopian cattle benefits the actors in dairy sector; allows designing effective improvement and conservation strategies that targets the production and management conditions of producers and farmers; and will provide a basis for future genome-wide association studies and investigations into genomic targets of selection in dairy cattle. But, realization of these genetic potentials will require placing those animals in the right environment and management conditions.

CONCLUSIONS AND FUTURE APPLICATION

The genetic diversity and population structure studies indicated that the Ethiopian cattle breeds are closely related and are at risk of becoming genetically homozygous. However, the presence of high within breed variation creates favorable conditions for further improvement through selection. The molecular studies in the Ethiopian cattle breeds had been limited to the well-known breeds thus even though the cost of genomic study is expensive, unaddressed breeds with wider adaptations and production performances had better be considered to print out the full picture of breed diversity and differentiation among Ethiopian cattle's. Besides, genomic prediction of milk yield, prediction of inbreeding and other production traits need to be considered to get information to optimize and speed up the breeding performances and genetic improvement.

Conflict of interest

All authors declared that there is no conflict of interest.

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