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## **Signatures of positive selection for local adaptation of African Native Cattle populations: a review**

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### **Abstract**

Cattle are central to the lives and diverse cultures of African people. It has played a crucial role in providing valuable protein for billions of households and sources of income and employment for producers and other actors in the livestock value chains. The long-term natural selection of African cattle typically signals signatures in the genome, contributes to high genetic differentiations across breeds. This has enabled them to develop unique adaptive traits to cope with inadequate feed supply, high temperatures, high internal and external parasites, and diseases. However, these unique cattle genetic resources are threatened by indiscriminate cross-breeding, breed replacements with exotic cosmopolitan breeds, and climate change pressures. Although there are no functional genomics studies, recent advancements in genotyping and sequencing technologies have identified and annotated limited functional genes and causal variants associated with unique adaptive and economical traits of African cattle populations. These genome-wide variants serve as candidates for breed improvement and support conservation efforts for endangered cattle breeds against future climate changes. Therefore, this review plans to collate comprehensive information on the identified selection footprints to support genomic studies in African cattle to confirm the validity of the results and provide a framework for further genetic association and QTL fine mapping studies.

**Keywords:** adaptive trait, African cattle, production traits, reproduction traits

## 1. Introduction

The tropical region covers approximately 36% of the world's land surface cover and many countries that are still developing. These areas are characterized by rainforest and savannah environments that cover a wide range of landscapes and are known for high biodiversity, including many exotic pests and diseases (Juo *et al.* 2003; Barendse, 2017). In the tropics, cattle populations provide various products and services for the people. They play a pivotal role in providing valuable protein for billions of rural and urban households, and serve as sources of income and employment for producers and other actors in the value chains (Herrero *et al.* 2013; Marshall *et al.* 2019). African cattle breeds have evolved over centuries and demonstrate a large phenotypic and genetic diversity, and this helped them to develop unique adaptive features to resist poor feed availability, high temperature, and high prevalence of internal and external parasite and disease challenges (Mirkena *et al.* 2010; Mwai *et al.* 2015). These animals are mainly kept in smallholder farms and subjected to natural and non-systematic artificial selection for economic traits. The detection of selective signatures in the genome is an essential step for guiding sustainable breed improvement to meet the current production need in various environments, particularly in light of changing environment (Fernandez *et al.* 2005), and is essential to facilitate sustainable utilization and conservation of threatened and endangered livestock breeds (McFarlane *et al.* 2006; Dalvit *et al.* 2008).

In recent decades, the demand for animal-source food has increased rapidly in developing countries due to population growth, rapid urbanization, income growth, and shifts in diet (Delgado, 2005; Thornton, 2010). To meet the ever-increasing demand for livestock products, sufficient genetic variation in livestock populations is vital for both evolution through natural selection in response to changing conditions (such as climate change, emerging diseases, and pressures on feed and water resources) and efforts to increase production through artificial selection (Biscarini *et al.* 2015). Evaluating available genetic variation is a crucial step to understand the genetic potential, which provides breeders with a tool for reliable selection decisions and conservation. To date, advances in high-throughput sequencing and SNP genotyping technologies and parallel progress in statistical techniques have allowed identifying genes and useful mutations linked with ecologically and economically important traits (Edea *et al.* 2015; Saravanan *et al.* 2021). Identifying genomic regions affected both by artificial selection and climate adaptation could help to understand how changes at the genome level modulate changes in phenotype, which holds high promises to improve animal breeding processes for production, health and welfare (Cesarani *et al.* 2018; Johnsson, 2018). Although we have begun to understand the molecular basis of African cattle genomic architectures, the molecular basis of adaptation and agro-economic traits are still poorly understood. Recent

studies of targeted and genome-wide selection signatures from African cattle population provide some insights into the mechanisms of natural and artificial selection and uncover functional genes and pathways related to adaptive and agro-economic traits. These selection footprints are suit to implement and provide a new perspective of genetic improvement in the breeding goals.

Previously, quantitative trait loci (QTL) mapping of cattle population were carried out by using low density multi-allelic markers (i.e. microsatellites) that have low detection power of genome-wide variations in complex traits (Zhang *et al.* 2012). To date, following the discovery of variants (SNPs) with immense coverage in the genome, the positive signature variants together with the phenotype and pedigree information are assisting the implementation of genome wide association study (GWAS) for the detection of genes and regulatory elements with better resolution and confidence interval for the traits of interest. Moreover, genomic selection has revolutionized genetic progress by direct analyzing causal mutation for non routinely recorded economic traits (i.e., feed efficiency, carcass and meat quality, and tick resistance) and a drastic reduction in generation intervals (Meuwissen *et al.* 2013). However, there is still a dearth of African cattle comprehensive reviews on the molecular bases of adaptive and agro-economic traits. Therefore, this review provides insights on the efforts made on detection of positive signatures in tropically adapted cattle populations which can subsequently be used to implement genomic selection for improved cattle production and productivity, and resilience in the diverse tropical environment.

## **2. Selection signatures in African cattle genome**

African cattle breeds have evolved over centuries and demonstrate a large phenotype and genetic diversities, and thus help them to adapt a wide range of environment. In the current climate change scenario, African livestock husbandry faces several challenges, such as increase in temperature and atmospheric carbon dioxide, along with variable precipitation. The interaction of these circumstances affected pasture composition, forage and water availability (Palmer *et al.* 2008; Rojas-Downing *et al.* 2018), and the expansion of livestock pests and diseases (Anyamba *et al.* 2009; Nyangiwe *et al.* 2018). Given numerous challenges including limited access to adequate nutrition and disease management, poor institutional capacities, and lack of adequate government policies and funding to develop the livestock sector, the productivity of African cattle is still less than optimal (Ibeagha-Awemu *et al.* 2019). There has been a positive attempt at balancing selection objectives and composite populations (crossbred) to combine adaptation and productivity traits suited to the available environmental resources, socio-economic, and cultural conditions (Rege *et al.* 2011; Bunning *et al.* 2019). Thus, identifying the genetic basis, disease resistance, and better production traits of local cattle breeds/stocks that are well adapted to extreme environments offers great opportunities to develop suitable breeding programs to meet the growing demand for livestock products at an unprecedented rate of climate change (Lobell *et al.* 2008; Rege *et al.* 2011).

To cope with multiple challenges and build climate-resilient livestock systems, a composite strategy involving the use of old science in different and innovative ways, and the strategic use of new technologies to understand and address problems is indispensable (Rege *et al.* 2011). The ongoing developments of high-throughput genotyping and whole genome sequencing facilities, coupled with the rapid development of statistical methods and bioinformatics pipelines, have enabled the detection of genomic variants associated with adaptive and agro-economic traits. The recent detection of genome-wide selective traits in African cattle herds has provided insights into natural and artificial selection mechanisms and identified genes and pathways associated with adaptive and agro-economic traits. Interestingly, these signatures provide a realistic procedure for defining genetic variations and assisting the selection of superior genotypes with higher breeding value for adaptive and agro-economic traits to support the livelihood of resource-poor smallholder farmers and future breeding companies.

### **2.1. Positive signature of selection for local adaption in indigenous cattle in African**

The adaptation of animals to different environments is typically shaped by structural and functional genomic variations (Zwane *et al.* 2021). Understanding the genetic basis of adaptive mechanisms to extreme environments is essential for conserving and improving local cattle breeds under future climate change scenarios and variable production objectives. Populations in different parts of the world show greater adaptation to their local agro-climatic conditions than exotic breeds (Rashamol and Sejian 2018). The African cattle populations have been subjected to harsh environmental pressures, including hot, dry, or humid tropical climate conditions and severe and diverse disease challenges (Kim *et al.* 2017). Long-term natural and human selection have driven different patterns of genomic variation between these cattle populations, which has helped them develop various tropical environmental adaptations (Mwai *et al.* 2015; Taye *et al.* 2018). For example, Zebu cattle are known for their superior adaptation to harsh environments, that includes resistance to various types of disease and parasites, as well as thermo tolerance (Kim *et al.* 2017; Taye *et al.* 2018; Bahbahani *et al.* 2015, 2018). Furthermore, African cattle populations are characterized by low nutrient requirements for maintenance and excellent walking ability which allows them to walk long distances in search of grazing and water to survive under poor quality feed and watering conditions (Mirkena *et al.* 2010; Taye *et al.* 2018). Exploring the characteristics of positive selection is now one of the main interests of animal geneticists, as it can be used to identify genes that regulate phenotypic changes, which hold great promise for developing breeding strategies for better production, health and welfare (Zhao *et al.* 2015; Johnsson 2018). Although there is limited availability of molecular data for African cattle, the development of statistical, bioinformatics and modeling tools allows the identification of genes linked to adaptive phenotypes of African cattle breeds (Fig. 1; Table 1).

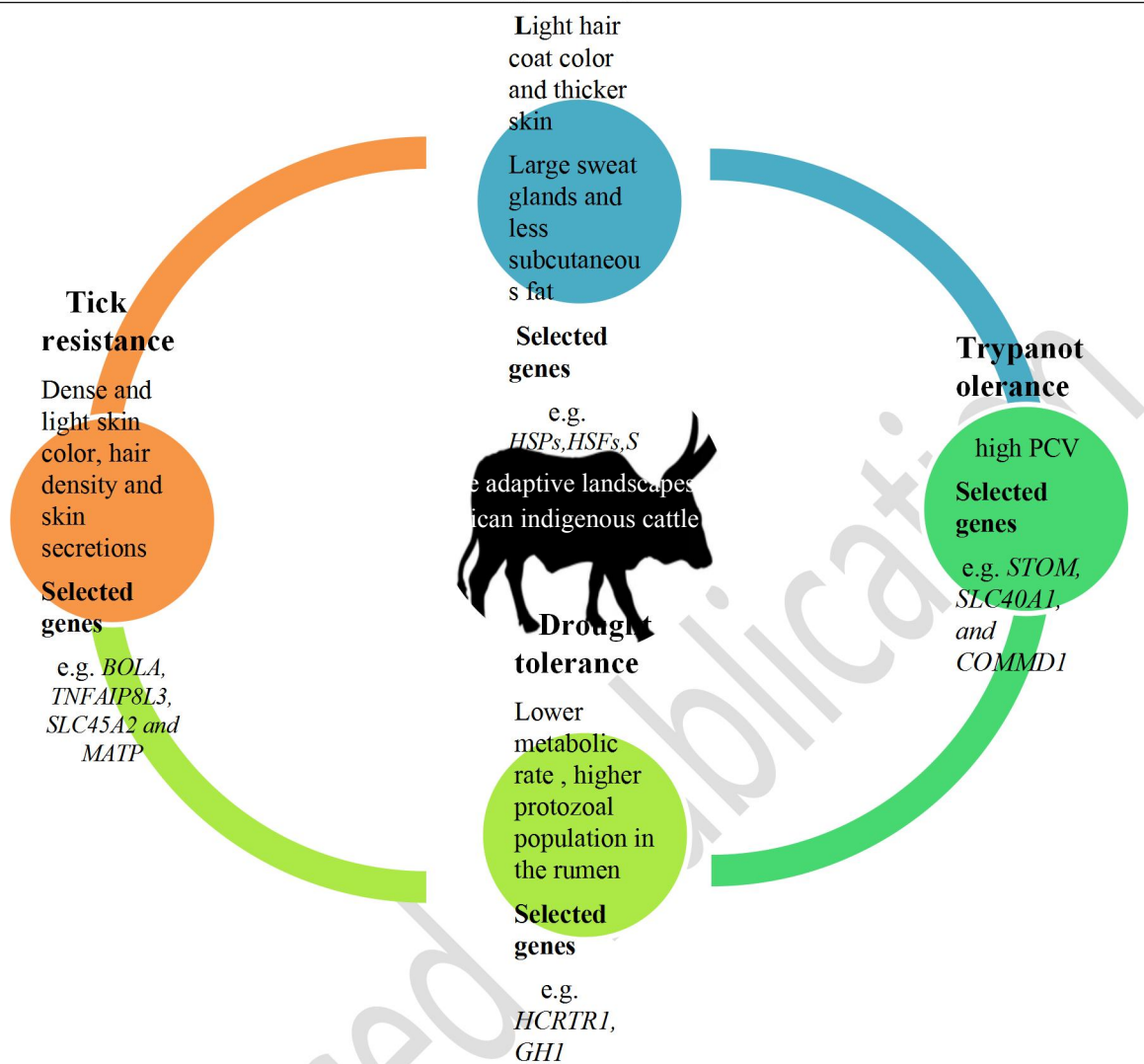


Fig. 1 Schematic representation of indigenous African cattle (*Bos indicus* and *African taurus*) adaptive attributes to tropical environmental stresses

**Heat tolerance** Heat stress is one of the major challenges that impair production and reproductive performance, metabolic and health status, and immune response of animals (Menta *et al.* 2022). Although they have poor productivity, African cattle breeds have developed heat tolerance mechanisms of lowered metabolic rates and an increased capacity to lose heat due to their experience with chronic heat stress for an extended period (Hansen 2004; Paula-Lopes *et al.* 2013; Mwai *et al.* 2015). The heat stress response is a complex adaptation that integrates many anatomical, physiological, biochemical, and molecular components (Gupta *et al.* 2013; Paula-Lopes *et al.* 2013). Morphological adaptations are physical changes in animals develop over many generations and improve their survival ability in a specific environment. Such adaptation mechanisms to heat stress are mainly affected by hair coat characteristics such as coat color, hair

length, higher density of sweat glands, slender legs, and less subcutaneous fat (Gaughan *et al.* 2019). The higher density of sweat glands and smoother and shinier hair coat in zebu cattle helps to better regulate body temperature and cellular function during heat stress (Hansen, 2004). For example, animals with light/white coats are thought to be more beneficial in hot tropical climates since they reflect 50 to 60% of direct solar radiation compared to dark-colored animals (McManus *et al.* 2009). Cattle adapted to arid environments have smooth, short, and thin hair, which helps to dissipate heat. Furthermore, animals in warmer climates have sweat glands that are larger in width, volume, perimeter, and density (Sejian *et al.* 2018). Physiological adaptability is the modification of the metabolic response to cope with extreme environmental conditions. The increase in respiration and pulse rate, rectal temperature, skin temperature, and sweating rate are some of the physiological factors which help to maintain homeostasis in animals (Indu *et al.* 2015). Moreover, decreased dry matter intake and altered water metabolism of tropical cattle are physiological responses to heat stress that adversely affect their production and reproduction.

It is widely acknowledged that the thermotolerance mechanisms of African cattle breeds have evolved genes and pathways that potentially contribute to greater tolerance attributes. For instance, complementary statistical methods (Hp, iHS, Rsb, XP-CLR and XP-EHH) identified heat shock protein gene families (*HSPB9*, *HSPA4*, *HSPA9*, *HSPA6* and *HSPH1*) that have played an important role in the response to heat stress (Bahbahani *et al.* 2015; Makina *et al.* 2015; Kim *et al.* 2017; Bahbahani *et al.* 2017; Bahbahani *et al.* 2018; Zwane *et al.* 2019; Ben-Jemaa *et al.* 2020). The differential expression of these protein families between *indicine* and *taurine* cattle signifies unique adaptive features of African Zebu in the tropics (Gautier *et al.* 2009). Moreover, heat shock factors (*HSFs*) are the transcription factors that regulate the expression of the heat shock proteins under thermal stress (Bahbahani *et al.* 2018; Taye *et al.* 2017; Paguem *et al.* 2020). It is also interesting to note that the protein phosphatases genes (*PPP3CA*, *PPP2R5E*, and *PPP4R3B*) were detected in N'Dama cattle that modulate the proteins activities in a cell, often in response to external heat stimuli (Taye *et al.* 2017). In general, these African cattle-specific selective sweeps are evidence of shared historical selection footprints and introgression, most likely due to their ancestral, geographical, and husbandry system acquaintances for resilience to the tropics. This may also reflect the pleiotropic effects of genes on other relevant adaptive and agro-economic traits.

The higher density of sweat glands of African zebus is regulated by positively selected heat stress resistance genes (Table 1). *ITPR2* is a protein-coding gene that encodes *InsP3R* that helps calcium ions move into and out of cells during heat stress (Taye *et al.* 2017). It promotes the release of calcium from the extracellular interstitial fluid and the release of intracellular  $Ca^{2+}$  stores necessary for normal sweat production (Klar *et al.* 2014; Cui and Schlessinger 2015). Coat colors are easily identifiable phenotypes that play an important role in heat tolerance. The pre-melanosome (*PMEL*) is

one of the candidate genes linked to eumelanin synthesis and may therefore regulate the coat color in the small East African shorthorn zebu and Butana cattle (Bahbahani *et al.* 2015; Bahbahani *et al.* 2015). The melanogenesis genes (*SLC45A2* and *ATRN*) that regulate hair color were identified in African zebu using XP-CLR and XP-EHH statistical tests (Taye *et al.* 2017). These unique genomic regions have a role of shaping the color characteristics of African cattle population that result in enhancing conductive and convective heat loss and reduce absorption of solar radiation in tropical conditions. However, the efforts of detection of positive selection need to be supported by further transcriptome profiling and fine mapping studies to validate the signatures observed in the candidate genomic regions.

**Resistance to trypanosomosis** Trypanosomosis is one of the endemic parasitic diseases that affect cattle and other wide range of hosts in sub-Saharan Africa (Biyazen *et al.* 2014). The disease results in the loss of livestock and agricultural productivity with severe socioeconomic and public health impacts (Madalcho 2019). The significant consequences of infection include mortality, loss of body condition, abortion, and agalaxia (Troncy *et al.* 1981). Although the use of trypanocidal drugs and vector management has a positive outcome, both control methods have been shown to be not sustainable (Paling and Dwingler 1993). Furthermore, the low efficacy of the available trypanocidal drug, a faster rate of drug resistance, and the slight hope of vaccine developments necessitates the exploitation of trypanotolerance cattle breeds (d'Ieteren *et al.* 1998). Thus, using tolerant breeds in a breeding system reduces or eliminates the use of chemicals to control the trypanosomosis vector and contributes to ecosystem health (Smetko *et al.* 2015). However, most cattle in Africa are susceptible to the disease and some indigenous taurine cattle populations have evolved a tolerance to trypanosomiasis termed trypanotolerance (Murray and Dexter 1988). In Africa, 17% of cattle populations are distributed in areas with higher tsetse challenges, of which only 6% are trypanotolerant breeds (Agyemang 2005). Long-horn *taurine* (N'Dama) and short-horn *taurine* (Lagune, Baoule, Muturu, and Namchi) and a short-horn *taurine* (Sheko) from east Africa are known cattle breeds for their ability to cope with trypanosome infections (Smetko *et al.* 2015; Bahbahani *et al.* 2018; Tijjani *et al.* 2019; Paguem, *et al.* 2020). Their trypanotolerant phenotypes have been linked to their innate capacity to control the level of parasitemia and anemia (Murray *et al.* 1984). Consequently, trypanotolerant African breeds are expected to have unique genomic signatures with respect to their distinct phenotypes. However, despite the multiple burdens of diseases and parasite infections, trypanotolerant cattle populations are threatened by indiscriminate cross-breeding, which demands due attention.

Anemia is a significant clinical sign of the advancement of trypanosome infection; therefore, genes involved in regulating iron transport and homeostasis represent interesting candidates (O'Gorman *et al.* 2009). The recent study by Mekonnen *et al.* (2019) identified the candidate genes (*MIGA1*,



*CDAN1*, *HSPA9*, and *PCSK6*) associated with the evolutionary response against anemia in Sheko cattle. The mitoguardin 1 (*MIGA1*) gene is an important regulator of the development and proliferation of lymphocytes during inadequate iron uptake that plays an important role in the formation of anemia immunity (Rouault 2006). The codanin-1 (*CDAN1*) gene is another candidate gene involved in the process of erythropoiesis and play a key role in the organization of heterochromatin during the division of these developing cells. The *PCSK6* gene regulates iron homeostasis as a result of iron deficiency anemia (Guillemot and Seidah 2015). Bahbahani *et al.* (2018) also identified the genes *LTA4H*, *IL7*, *IL15*, *FCN*, *LTA4H* and *NFAM1* as potential targets of natural selection related to immunity in Sheko cattle. Another important candidate gene related to anemia is *GFI1B*. This gene modulates erythropoiesis for the expansion and differentiation of erythroid progenitors. The influence of *GFI1B* on erythropoiesis could be related to the trypanotolerance of west African *taurine* (Muturu) cattle (Tijjani *et al.* 2019). An XP-EHH test detected potential selective sweeps (*STOM*, *SLC40A1*, and *COMMD1*) that are fixed (or nearly fixed) for intensively studied trypanotolerant west African *taurine* (N'Dama) (Kim *et al.* 2017; Taye *et al.* 2017). *SLC40A1* is a cell membrane protein involved in iron export from duodenal epithelial cells. It gives instructions for making a protein called ferroportin, and this protein mediates the process of iron absorption and delivery into the bloodstream (Theurl *et al.* 2016). The Copper metabolism *MURR1* domain protein 1 (*COMMD1*) is a protein involved in multiple cellular pathways, including copper homeostasis, NF- $\kappa$ B, and hypoxia signaling (Vonk *et al.* 2014). Nuclear factor kappaB (*NF-kappaB*) signaling influences innate and adaptive immunity, inflammation, B-cell development, lymphoid organogenesis, and stress response. Malfunctioning of this gene is associated with marked accumulation of copper in hepatocytes (Smedley *et al.* 2009), adversely affecting iron absorption and transport (Da Silva *et al.* 2009). Another microsatellite study identified the *CXCR4* gene for trypanotolerance in multiple west African *taurine* (Dayo *et al.* 2009). It plays an important role in the haematopoiesis, development, and organization of immune systems. Although the value of native cattle breeds are overlooked, the use of indigenous breeds coupled with context specific breeding plans are often the best strategies for sustainable benefit from the indigenous cattle genetic resources in Africa. In fact, the positive footprint of African *taurines* for both heat and trypano challenges makes them a strong candidate for multifaceted cattle improvement in the complex conditions of the African continent. Furthermore, these unique signatures allowed us to directly target candidate genes and candidate variants that were then added to the customized chip used for routine genomic evaluation of African cattle breeds.

**Resistance to tick and tick-borne diseases** Ticks are essential ectoparasites that cause significant economic and health losses in farm animals. These ectoparasites impacted about 80% of the world's cattle population, either directly by the effect of their bites or by the infectious agents they

transmit (Eskezia and Desta 2016; Hurtado and Giraldo-Ríos 2018). Babesiosis, bartonellosis, and anaplasmosis are the main parasitic diseases transmitted by ticks and have caused serious economic losses to cattle production worldwide (Eskezia and Desta 2016). Africa's hot and humid climate is a suitable habitat for tick survival (Eskezia and Desta 2016), and this causes annual losses of 160 million due to ticks and tick-borne diseases' (Olwoch *et al.* 2008). Despite multiple attempts to control tick-borne diseases, chemical control has been found to be ineffective and requires a high cost. As a result, habitat management, host genetic selection, and the development of resistance breeds are a means of preventing tick infestation (Shyma *et al.* 2015). Zebu cattle have greater tick resistance manifested by their perpetual exposure to the infected zone or by morphological differences (i.e., skin thickness, coat type, coat color, hair density, and skin secretions) (Meltzer 1996; Foster *et al.* 2007; Gasparin *et al.* 2007). Furthermore, despite the complexity of the tick-host interaction, host resistance to ticks is known to be under genetic control. To further elucidate the potential genetic mechanisms underlying tick resistance, different studies demonstrated specific genomic alterations toward tick resistance (Table 1). In this regard, the bovine lymphocyte antigen (*BOLA*) gene is the major histocompatibility complex, and plays an important role in antigen processing and presentation. It was identified as an important immune response gene that regulates tick resistance in African cattle (Kim *et al.* 2017; Taye *et al.* 2018). Furthermore, *TNF alpha* induced protein 8 like 3 (*TNFAIP8L3*) and solute carrier family 25 member 48 (*SLC25A48*) genes have also been reported in African cattle breeds in relation to tick resistance (Makina *et al.* 2015; Taye *et al.* 2018).

Skin is the largest organ of vertebrates and the target of infestation and feeding by more than 15,000 species of hematophagous arthropods (Franzin *et al.* 2017). The structure of epidermal layers and cattle skin color are the major defenses against ectoparasite invasion (e.g., tick) (Gautier *et al.* 2009; Mapholi *et al.* 2014). Interestingly, keratin genes are heteropolymeric structural proteins that form the structural framework of skin and hair cells and secrete cytokines that initiate local inflammatory responses to tick resistance (Nakamura *et al.* 2013). In epidermal transglutaminases (*TGM1* and *TGM3*) gene regions, two novels (*10:20736590* and *10:20739046*) and three known missense variants (*rs41695720*, *rs136283113* and *rs211468449*) were identified in African zebu (Taye *et al.* 2018). These  $Ca^{2+}$  dependent cross-linking enzymes regulates apoptosis and cornification of the epidermis; this provides a defense function against ectoparasites (Kongsuwan *et al.* 2010). Furthermore, Taye *et al.* (2018) have elucidated that the *SLC45A2* and *MATP* genes were found to modulate melanogenesis in a specialized cell called melanocytes. These strong signals in relation to morphological traits (e.g. skin thickness, hair cells, and color-patterning traits) are consistent with the theory of the 'domestication syndrome' in mammals, suggesting that selective pressure for ectozoan during the initial stages of domestication involved the development of dermal cell populations and led to multiple structural changes shared by various species of domesticated

animals. This could result in the shared light coat color of most African indicine cattle breeds (Marufu *et al.* 2011). Interestingly, it might support the hypothesis that ticks on light-colored cattle can be easily seen by predator birds and picked up easily, eventually contributing to their resistance to tick-born problems (Mapholi *et al.* 2014). Indeed, the continent is endowed with huge genetically diversified cattle breeds, however, genomic studies toward identifying the genomic loci related to tick resistance are limited. Therefore, further studies should be conducted on a comprehensive endemic ectoparasite resistance of indicine cattle breeds.

**Drought-tolerant** The African continent is subjected to severe recurrent droughts, resulting in scarcity of natural resources, poor quantity and quality of forages, high prevalence of livestock diseases and parasites, as well as water shortages (Masih *et al.* 2014; Dzavo *et al.* 2019). Cattle have already succumbed to several climate-driven distresses, including massive deaths, loss of body condition, and reduced productivity (Kimaro *et al.* 2018; Dzavo *et al.* 2019). Despite these severe challenges, local cattle breeds have evolved several coping mechanisms compared to exotic cattle from the northern hemisphere exposed to the same environment. Long exposure to poor nutritional quality and seasonal availability of feed exerts strong selective pressure on tropical cattle to lower their metabolic rates and increase digestive efficiency for low quality feedstuffs in the tropics (Mirkena *et al.* 2010; Taye *et al.* 2018). Hegarty (2004) indicated that the higher protozoal population in the rumen of *Bos indicus* cattle has a faster rate of digestion to ferment nitrogen-deficient poor-quality feed than *Bos taurus* cattle. This may be expected to reduce the production of methane and the ruminal long chain of fatty acid synthesis for the production of energy from low-quality diets. However, the lower metabolic rate of African cattle resulted in reduced feed intake, milk yield, thyroid hormone secretion, and growth, making them lower in performance compared to *taurine* breeds of European descent (Paguem *et al.* 2020). Recent technological and analytical advances in genomics open a new avenue for identifying genomic regions that harbor resilience in the scarcity of feed resources. Several candidate genes and gene families associated with the adaptive response to scarce and low-quality feed have been selected in African cattle (Taye *et al.* 2017; Tijjani *et al.* 2019). For example, the hypocretin receptor 1 gene (*HCRTR1*) is a G-protein coupled receptor involved in the regulation of feeding behavior identified in west African longhorn *taurine* (N'Dama) (Kim *et al.* 2017). Growth hormone 1 (*GH1*) has been identified as a positive selection for the limited food supply. Elevated *GH1* gene expression induces a physiological response to nutritional deprivation as a consequence of important seasonal fluctuations in feed availability for North African cattle (Ben-Jemaa *et al.* 2020). Furthermore, a whole genome sequence study has identified candidate genes (*MAP3K5* and *ZRANB3*) related to feed efficiency/residual feed intake of African cattle breeds (Tijjani *et al.* 2019). Mitogen-activated protein kinase kinase 5 (*MAP3K5*) is a member of a family of enzymes involved in kinase signaling cascades in the cell. It

plays an important role in cell differentiation and survival, apoptosis, and innate immune response, and is a candidate marker for residual feed intake in pig (Pu *et al.* 2016) and beef cattle (Serão *et al.* 2013). These genes selected for the scarce feed supply have led to the specialization of breeds of cattle for feeding efficiency. It might be expected that breeds with the same characteristics would show a similar picture of selection sweeps related to such specialization. Conversely, divergently specialized breeds would share few selection sweeps. However, it is an open secret that most cattle populations on the African continent are in extensive production conditions challenged by feed scarcity, which forced them to evolve many shared selection signals. These evolved footprints play a significant role directly or indirectly in response to feeding scarcity in drought-prone seasons and arid and semi-arid cattle production areas in the continent. The putative genomic regions regulating the efficient utilization of feed resources in African cattle are summarized in Table 1.

**Table 1** Candidate genes underlying selection signatures of African cattle breeds to tropical environment stress adaptations

Candidate genes	Sequencing/ Genotyping platform	Number of observations per breeds	Statistical methods	Association	Selected cattle population/ breed	References
<i>LTA4H</i> , <i>IL7</i> , <i>IL15</i> , <i>FCN</i> , <i>LTA4H</i> , and <i>NFAM1</i>	BovineHD BeadChip	20	iHS and Rsb	Trypanotolerance	Sheko	Bahbahani <i>et al.</i> 2018
<i>STOM</i> , <i>SLC40A1</i> , <i>SBDS</i> , <i>EPB42</i> and <i>RPS26</i>	WGS	10	XP-CLR, XP-EHH	Trypanotolerance	N'Dama	Kim <i>et al.</i> 2017
<i>BOLA-DQA2</i> , <i>GFI1B</i> , <i>FAS</i> , <i>IDO2</i> and <i>PLCB1</i>	WGS	10	iHS and Rsb	Trypanotolerance	Muturu	Tijjani <i>et al.</i> 2019
<i>MON1A</i> , <i>MST1R</i> , <i>UBA7</i> , <i>FAM212</i> , <i>CAMKV</i> , <i>TRAIP</i> , <i>CDHR4</i> , <i>IP6K1</i> , <i>RNF123</i> , <i>APEH</i> and <i>MST1</i>	Microsatellites	Baoule (90), Zebu (90) Baoule-Zebu (34)	F <sub>ST</sub>	Trypanotolerance	Baoule, Zebu and Baoule- Zebu	Smetko <i>et al.</i> 2015
<i>TICAM1</i> , <i>IKBKB</i> , <i>ECSIT</i> , <i>VAV1</i> , <i>CASP8</i> and <i>ARHGAP15</i>	Affymetrix Gene Chip	25	XP-EHH	Trypanotolerance	N'Dama	Noyes <i>et al.</i> 2011
<i>MIGA1</i> , <i>CDAN1</i> , <i>HSPA9</i> , <i>PCSK6</i> , <i>SPAG11B</i> , <i>RAET1G</i> , <i>PPP1R14C</i> and <i>TTC3</i>	BovineHD BeadChip	12	CLR, iHS and Rsb	Trypanotolerance	Sheko	Mekonnen <i>et al.</i> 2019
<i>CXCR4</i>	Microsatellites	Baoule (30), Lagune (37), Somba (40) and N'Dama (30)	Ln RV and In RH	Trypanotolerance	Baoule, Lagune, Somba and N'Dama	Dayo <i>et al.</i> 2009
<i>CD79A</i> , <i>CXCR4</i> , <i>DLK1</i> , <i>RFX3</i> , <i>SEMA4A</i> , <i>TICAM1</i> and <i>TRIM21</i>	BovineSNP50 chip	N'Dama (29), Baoulé(44),	F <sub>ST</sub>	Trypanotolerance	N'Dama, Baoulé,	Gautier <i>et al.</i> 2009

		Somba(44), Nadoba(43), Lagune (45), Borgou (47)			Somba, Nadoba, Lagune, Borgou	
<i>STOM, SLC40A1 and COMMD1</i>	WGS	10	Tajima's D, XP-EHH and XP-CLR	Trypanotolerance	N'Dama	Taye <i>et al.</i> 2017
<i>HSPA4, SOD1 and PRLH</i>	WGS	10 each	XP-CLR, XP-EHH	Heat tolerance	<i>B. indicus</i>	Kim <i>et al.</i> 2017
<i>DNAJC8, DNAJC18, HSPA9 and HSPB9</i>	BovineHD BeadChip and WGS	95 for BeadChip and 10 for WGS	iHS, Rsb and Hp	Heat tolerance	Kenyan East African Zebu	Bahbahani <i>et al.</i> 2017
<i>KRT24, KRT25, KRT26, KRT27, KRT28 and HSPB9</i>	WGS	30 for each	Hp	Heat tolerance	Afrikaner, Drakensberger, and Nguni	Zwane <i>et al.</i> 2019
<i>ASIC3, HSPH1 and MVD</i>	BovineSNP50 BeadChip	Total of 221 for all breeds	F <sub>ST</sub> , iHS, Rsb and XP- EHH	Heat tolerance	Brune de l'Atlas, Guelmoise, Cheurfa, Oulmes, Tidili Baladi	Ben-Jemaa <i>et al.</i> 2020
<i>IGF-I, HSF5</i>	WGS	10 each	XP-CLR, and XPEHH	Heat tolerance	Ankole, Boran, Ogaden, N'Dama and Kenana	Taye <i>et al.</i> 2017
<i>PPP3CA, PPP2R5E and PPP4R3B</i>	WGS	10 each	Tajima's D, XP-CLR, and XPEHH	Heat tolerance	N'Dama	Taye <i>et al.</i> 2017
<i>HSF5</i>	BovineHD BeadChip	25	<i>iHS</i> and <i>Rsb</i>	Heat tolerance	Butana	Bahbahani <i>et al.</i> 2018
<i>HSPA6, DNAJC6 and PRLH</i>	BovineSNP50 BeadChip	20	iHS and Rsb	Heat tolerance	Sheko	Bahbahani <i>et al.</i> 2018
<i>HSPB9, DNAJC7, DNAJC8, DNAJC14 and DNAJC18 and PPP1R10</i>	BovineSNP50 BeadChip	425	F <sub>ST</sub> , iHS and Rsb	Heat tolerance	East African short horn Zebu	Bahbahani <i>et al.</i> 2015
<i>INTS6, OLA, ACTA1 and CTNNB1</i>	WGS	10	iHS and Rsb	Heat tolerance	Muturu	Tijjani <i>et al.</i> 2019
<i>EDNRB, TRSP1 and KRTAP8-1</i>	BovineSNP50 BeadChip	Total 252	F <sub>ST</sub>	Heat tolerance	N'Dama, Baoulé, Somba, Nadoba,	Gautier <i>et al.</i> 2009

					Lagune, Borgou, Sudanese Fulani, Kuri and Choah zebu	
<i>HSPB9</i>	BovineSNP50 BeadChip	54	$F_{ST}$	Heat tolerance	Nguni	Makina <i>et al.</i> 2015
<i>DNAJC5B</i> and <i>HSPH1</i>	Bovine 150 K	Nguni (231) and Bonsmara (252)	XP-EHH	Heat tolerance	Nguni and Bonsmara	
<i>SLC45A2</i> , <i>MLPH</i> , <i>RAB17</i> , <i>RAB37</i> and <i>ATRN</i>	WGS	10 each	XP-CLR, and XP-EHH	Coat color for het tolerance	Ankole, Boran, Ogaden, N'Dama and Kenana	Taye <i>et al.</i> 2017
<i>ITPR2</i> , <i>ITPRIP</i> , <i>CFTR</i> , <i>SCNN1D</i> and <i>SLC9A4</i>	WGS	10 each	XP-CLR, and XPEHH	Sweating and sweat gland development for het tolerance	Ankole, Boran, Ogaden, N'Dama and Kenana	Taye <i>et al.</i> 2017
<i>GPR142</i> , <i>PRKG1</i> , <i>LRBA</i> , <i>SMIM12</i> , <i>FER</i> and <i>LINGO2</i>	BovineSNP50 BeadChip	(586)	GWAS	Tick resistance	Nguni	Mapholi <i>et al.</i> 2016
<i>TNFAIP8L3</i> and <i>SLC25A48</i>	BovineSNP50 BeadChip	Afrikaner (44), Nguni (54), Drakensberger (47), Bonsmara (44)	$F_{ST}$	Tick resistance	Afrikaner, Nguni, Drakensberger and Bonsmara	Makina <i>et al.</i> 2015
<i>BOLA</i>	WGS	10 each	XP-CLR, XP-EHH	Tick resistance	<i>B. indicus</i>	Kim <i>et al.</i> 2017
<i>BoLA</i> , <i>TNFAIP8L3</i> , <i>SLC25A48</i> , <i>KRT33A</i> , <i>PRG3</i> , <i>SLC45A2</i> , <i>MLPH</i> , <i>MC5R</i> , <i>TGM1</i> and <i>TGM3</i>	WGS	10 each	XP-CLR, XP-EHH	Tick resistance	Boran, Ogaden, and Kenana	Taye <i>et al.</i> 2018
<i>ATRN</i> , <i>NFATC</i> and <i>FTO</i>	WGS	10 each	XP-CLR, XP-EHH	Feed intake and energy homeostasis	Ankole, Boran, Ogaden, N'Dama and Kenana	Taye <i>et al.</i> 2017
<i>ZRANB3</i> and <i>MAP3K5</i>	WGS	10	iHS and Rsb	Feeding efficiency	Muturu	Tijjani <i>et al.</i> 2019
<i>GH1</i>	BovineSNP50 BeadChip	Total of 221 for all breeds	FST, iHS, Rsb and XP-EHH	Adaptive response to scarce feed supply	Brune de l'Atlas, Guelmoise, Cheurfa,	Ben-Jemaa <i>et al.</i> 2020

					Oulmes, Tidili Baladi	
<i>HCRT1</i>	WGS	10	XP-CLR	Circadian rhythm, feeding behavior	N'Dama	Kim <i>et al.</i> 2017
<i>TIMP2, PKM2, PRKG1, MAP3K5</i> and <i>ATP8A1</i>	WGS	10	XP-CLR and XP-EHH	Feeding efficiency	Ankole	Taye <i>et al.</i> 2017
<i>FAAP20, PRKCZ, SKI, PLCH2</i> and <i>PEX10</i>	WGS	10 each	F <sub>ST</sub> , XP- EHH and Hp	Adaptive response to scarce feed supply	Kenana, Butana, Aryashai, and Gash	Tijjani <i>et al.</i> 2022
<i>FAM110B</i> and <i>UBXN2B</i>	Bovine 150 K	Nguni (231) and Bonsmara (252)	XP-EHH	Feeding efficiency	Nguni and Bonsmara	Kooverjee <i>et al.</i> 2022

## 2.2. Selection signatures associated with milk production and compositions traits

Dairy production in Africa plays a fundamental role in the region's economic and sustainable development. It contributes to food security, combats malnutrition, and provides employment and income to millions of smallholder farm families. Milk production and composition are the most economically important traits that affect dairy cattle profitability (Nanaei *et al.* 2020). Dairy farmers in the tropics regions face many challenges, including poor performance of local breeds, disease pressure, poor feed availability, high temperatures, and generally inappropriate management conditions (Cheruiyot *et al.* 2018). Furthermore, most of the production in the tropics, particularly in Africa and Asia, takes place in smallholder systems, which are characterized by small herd sizes, lack of performance and pedigree recording, as well as the lack of standard genetic evaluation systems (Kosgey and Okeyo, 2007). Despite these constraints, genome sequencing of African cattle populations is already underway for several native and composite breeds. These genomic data will enable the development of African cattle-specific genomic tools that may be used in genome-wide selective breeding and genetic evaluation (Mwai *et al.* 2015).

Both environmental and genetic variables regulate milk production and compositional qualities. The kappa casein (*CSN3*) gene is associated with milk fat and protein percentage. It has a significant influence on milk processing properties in comparison to other casein variants. Genetic polymorphisms in the bovine *CSN3* gene have been linked to milk yield traits (milk yield, fat yield, and protein yield) (Nanaei *et al.* 2020) and composition traits (fat and protein percentages) in African cattle breeds (Ahmed *et al.* 2017). *ABCG2* and *LAP3* are another shared genes between exotic and African cattle breeds (Tijjani *et al.* 2019). Positive selection of these genes is associated with better milk production, fat, and protein yield. The beta1, 4-galactosyltransferase (*B4GAL-T1*) gene is a trans-Golgi resident enzyme that regulates the lactose biosynthesis in mammals and is a candidate

for milk production traits (Table 2). This gene modulates milk production traits, including milk, lactose, protein, and total solids production (Shahbazkia *et al.* 2012; Nanaei *et al.* 2020). Although many genes and functional pathways for milk production traits are widely identified and annotated in commercial dairy breeds, selection signals in indicine cattle breeds are limited. High within-breed genetic variations coupled with limited signal for milk production traits are a reflection of less artificial selection pressure on local cattle breeds. Over the years, African cattle dairy improvement programs have focused on crossbreeding of local cattle with exotic breeds that allow the exploitation of heterosis in economic traits. In particular, its success rate remains ineffective and most dairy farmers in the tropics faced comparatively challenging genotype and environmental interactions. However, the long-term effort on tropical cattle (e.g., Brazilian-Gir) showed exemplary genetic potential for dairy production and a relevant option for dairying in the tropics (Rewe *et al.* 2015). Therefore, the untapped potential of African cattle populations coupled with the a proper breeding plan is a promising approach to the development of tropical dairy production.

Table 2 Candidate genes underlying milk production and composition traits of indigenous African cattle breeds

Candidate genes	Sequencing/Genotyping platform	Number of observations per breeds	Statistical method	Association	Selected breed	References
<i>CSN3</i> , <i>IGFBP-2</i> , <i>RORA</i> , <i>ABCG2</i> , <i>B4GALT1</i> and <i>GHR</i>	WGS	4	FST, XP-CLR and Pi ( $\pi$ )	Milk production	Kenana	Nanaei <i>et al.</i> 2020
<i>GH1</i>	BovineSNP50 BeadChip	Total of 221	FST, iHS, Rsb and XP-EHH	Positive regulation of lactation	Brune de l'Atlas, Guelmoise, Cheurfa, Oulmes, Tidili Baladi	Ben-Jemaa <i>et al.</i> 2020
<i>BTBD17</i>	WGS	30 each	Hp	Associated with milk yield	Afrikaner, Drakensberger and Nguni	Zwane <i>et al.</i> 2019
<i>ABCG2</i> and <i>LA P3</i>	WGS	10	iHS and Rsb	Related to milk production	Muturu	Tijjani <i>et al.</i> 2019
<i>PRLH</i>	BovineHD BeadChip	20	iHS and Rsb	Milk yield	Sheko	Bahbahani <i>et al.</i> 2018

### 2.3. Selection signatures associated with meat traits

Meat and meat products are the most valuable livestock products as the main sources of high-quality protein for human consumption. Cattle are one of the most important livestock species and make up the majority of the meat consumed by humans. In sub-Saharan Africa, about 150 breeds of native cattle and recently introduced exotic and commercial mixed cattle are recognized (Rege, 1999;



Mwai *et al.* 2015). Over the years, natural selection has established a collection of breeds known to adapt to harsh conditions and has specific beef characteristics. African Sanga cattle are an intermediate type of cattle believed to be the result of interbreeding between *Bos taurus* and *Bos indicus* (Mwai *et al.* 2015; Rege and Tawah, 1999), which has better carcass and meat quality attributes than *Bos taurus* and *Bos indicus* breeds (Strydom *et al.* 2000; Strydom *et al.* 2008; Strydom *et al.* 2011). Although there are several indigenous beef cattle breeds with good beef production capability, this potential remains untapped since a strategic breeding plan for genetic improvement is rare in this region (Rewe *et al.* 2009). Furthermore, unlike the developed world, much of the African cattle improvement research and development work profoundly emphasized crossbreeding to increase milk production. Even with little success, the breeding plan consistently overlooked local cattle breeds, and this makes local cattle remain poor non-specialized breeds. However, few attempts contributed to the possibility of improving beef production in sub-Saharan Africa. For example, large-scale ranching was established in semi-arid areas of Kenya for the improvement of Kenyan Boran primarily for commercial beef production (Rewe *et al.* 2009), and pure breeding and cross-breeding of Nguni and the Afrikaner cattle with exotic counterparts in South Africa (Scholtz *et al.* 2010; Abin *et al.* 2016). A review by Rios and Van Vleck (2004) showed that most meat production and quality traits have moderate heritability; therefore, improving these traits using conventional techniques remains a challenge. To date, in addition to the estimation of genetic parameters with pedigree data, advances in molecular technology have resulted in the identification of DNA markers of farm animal species, and this has created a new avenue for identifying genes and quantitative trait loci (QTL) regions used for genomic selection (Van Marle-Köster *et al.* 2013).

Skeletal muscle is a major tissue providing lean tissues for meat animals. Therefore, understanding the genes and candidate genes that regulate skeletal muscle development is essential for improving animal growth and meat production efficiency. Interestingly, genes and QTL related to anatomical development were identified in the East African short-horn zebu (e.g., *LEMD3*, *LOX*, and *RXFP2*). These genes are important to maintain optimal growth and development (Bahbahani *et al.* 2017). *LEMD3* and *LOX* are associated with the development of different organs, such as the heart (*LEMD3*), lung and blood vessels (*LOX*) (Maki *et al.* 2005). A whole genome study identified *CAPZB*, *COL9A2*, *PDGFRA*, *MAP3K5*, *ZNF410*, *LIMA1* and *PKM2* genes that can affect muscle structure and development, thereby affecting meat tenderness in Ankole cattle (Taye *et al.* 2017). Indeed, meat traits are controlled by many genes and environmental factors. Measurement of these traits is difficult and expensive to measure until late in life or after the animal has been harvested. Hence, uncovering these genomic regions can be used as ideal candidates to achieve higher genetic gains through genomic selection compared to traditional pedigree-based evaluations.

Meat quality is a complex and multifactorial trait modulated by genetics and environmental factors (Listrat *et al.* 2016). The important quality traits for fresh meat are pH, color, water holding capacity,

texture, and amount of fat (intramuscular fat/marbling). At the same time, tenderness, flavor, and juiciness are the main eating quality traits of cooked meat. A genome-wide scan by Taye *et al.* (2017) identified several candidate genes that regulate the biological mechanisms of beef quality characteristics in Ankole cattle (Table 3). For example, *CAPZB*, *COL9A2*, *PDGFRA*, *MAP3K5*, *ZNF410*, and *PKM2* genes are involved in muscle structure and metabolism that affect meat tenderness. *PLA2G2A*, *PARK2*, *ZNF410*, *MAP2K3*, *PLCD3*, *PLCD1* and *ROCK1* genes are related to intramuscular fat that regulate adipose metabolism and adipogenesis (Taye *et al.* 2017). Although there are no African cattle specific candidate genes, it can be concluded that the identified pathways and genes can be used as genetic markers in the custom chip for routine genomic evaluation of African cattle breeds.

Table 3 Candidate genes underlying meat traits of African cattle breeds

Candidate genes	Sequencing/Genotyping platform	Number of observations per breeds	Statistical method	Associations	Selected breed	References
<i>CAPZB</i> , <i>COL9A2</i> , <i>PDGFRA</i> , <i>MAP3K5</i> , <i>ZNF410</i> , <i>LIMA1</i> and <i>PKM2</i>	WGS	10	XP-CLR, XP-EHH	Muscle structure and metabolism affect meat tenderness	Ankole	Taye <i>et al.</i> 2017
<i>PLA2G2A</i> , <i>PARK2</i> , <i>ZNF410</i> , <i>MAP2K3</i> , <i>PLCD3</i> , <i>PLCD1</i> and <i>ROCK1</i>	WGS	10	XP-CLR, XP-EHH	Intramuscular fat are involved in adipose metabolism and adipogenesis	Ankole	Taye <i>et al.</i> 2017
<i>MB</i> and <i>SLC48A1</i>	WGS	10		Affect meat color	Ankole	Taye <i>et al.</i> 2017
<i>MAP3K5</i> , <i>PPP2R2C</i> , <i>FGF18</i> , <i>FRS3</i> , <i>P00021</i> , <i>ACVRL1</i> , <i>CASR</i> , <i>TLX3</i> , <i>ACVR1B</i> and <i>RUNX3</i>	WGS	10	XP-CLR	Skeletal system development	Ankole	Kim <i>et al.</i> 2017
<i>LEMD3</i> , <i>LOX</i> and <i>RXFP2</i>	BovineHD BeadChip and WGS	95BeadChip and 10 WGS	iHS, Rsb and Hp	Anatomical development	East African Zebu	Bahbahani <i>et al.</i> 2017
<i>CRHR2</i>	WGS	30	Hp	Meat quality (juiciness and flavour)	Nguni	Zwane <i>et al.</i> 2021
<i>DDX19A</i> , <i>TMEM51</i> , <i>MTPN</i> , <i>IGFBP4</i> , <i>TGFB1</i> , <i>KCNB1</i> , <i>MYO6</i> , <i>KIAA11797</i> and <i>EFHD2</i>	BovineSNP50 BeadChip	Afrikaner (44), Nguni (54), Drakensberger (47), and Bonsmara (44)	$F_{ST}$	Growth and muscle development	Afrikaner, Nguni, Drakensberger and Bonsmara	Makina <i>et al.</i> 2015
<i>PRKAG3</i>	WGS	10	iHS and Rsb	Related to meat quality traits	Muturu	Tijjani <i>et al.</i> 2019
<i>GHR</i> and <i>GHRHR</i>	WGS	10	iHS and Rsb	Growth traits/ stature	Muturu	Tijjani <i>et al.</i> 2019

#### 2.4. Selection signatures associated with fertility traits

The general productivity and adaptability of cattle depend greatly on reproductive performance in a particular environment. Despite many achievements of classical animal breeding, extensive selection for milk production traits has led to a decline in female fertility in dairy cattle arising from an unfavorable correlated selection response (Kadarmideen *et al.* 2003; Jorjani, 2006). The decline in reproductive performance could affect culling rates and herd life and reduce the genetic gain from production traits. In response to such deterioration in fertility traits, genetic selection has been suggested to play a myriad role in cost-effective, cumulative, and permanent improvements of cattle fertility (Wall *et al.* 2003). Consequently, recent access to bovine whole genome sequence and high-density SNP panels has provided remarkable resources to understand the effects of domestication and artificial selection on the underlying genetic variation that contributes to phenotypic diversity (Randhawa *et al.* 2016).

Several studies shed light on candidate genes associated with cattle fertility and located in several genomic regions under the selection sweep. For instance, the recent selection in steroid 5-alpha reductase 3 gene (*SRD5A3*) was detected by iHS statistical method that regulates the development of the male reproductive system (Bahbahani *et al.* 2018). This gene converts testosterone to dihydrotestosterone to maintain differentiation of the prostate and external genitalia. Relaxin / insulin-like family peptide receptor 2 (*RXFP2*) is another candidate gene that modulates testicular descent development in zebu and native African *taurine* (Bahbahani *et al.* 2015; Bahbahani *et al.* 2017; Bahbahani *et al.* 2018). It is speculated that the candidate genes (*OR6C4* and *OR2AP1*) are involved in the guide of sperms towards oocytes during fertilization via the interaction with various chemo-attractants secreted by the oocyte-cumulus complex (Bahbahani *et al.* 2015). A positive selection on the relaxin family peptide receptor 2 (*RXFP2*) is also identified to modulate higher fertility and semen quality in zebu cattle under tropical conditions (Hansen, 2004; Bahbahani *et al.* 2018; Tijjani *et al.* 2019). In addition, the strong selection of *IGF-1* gene modulates follicular development and oocyte maturation (Taye *et al.* 2018). *ESR2* is also a protein-coding gene that controls many cellular processes, including growth, differentiation, and function of the reproductive system, and it has suggested modulating sperm quality traits (Taye *et al.* 2018). In fact, many genes essential for fertility traits are shared within the germinal organs of both sexes characterized by low heritability. Strong selection signals in these populations can be a starting point to shed light on the definite genomic selection toward high-fertility phenotypes.

Table 4 Candidate genes underlying reproductive traits selection signatures of African cattle

Candidate genes	Sequencing/Genotyping platform	Number of observations per breeds	Statistical method	Association	Selected breed	References
<i>GNRH1</i> , <i>MC2R</i> , <i>MC5R</i> , <i>ESR2</i> , <i>RXFP3</i> , <i>CSF1</i>	WGS	10 each	XP-CLR, XP-EHH	Reproduction function	Ankole, Boran, Ogaden, N'Dama	Taye <i>et al.</i> 2017

, <i>CIB1</i> , <i>HOXC12</i> and <i>H OXC13</i>						and Kenana	
<i>OR2AP1</i> , <i>OR6C4</i> , <i>RXFP2</i> , and <i>KLHL10</i>	BovineSNP50 BeadChip	Total 425	FST, iHS and Rsb	Superior fertility and semen quality	East African Shorthorn Zebu	Bahbahani <i>et al.</i> 2015	
<i>RXFP2</i> , <i>RARA</i> , <i>SPATA24</i> and <i>SPAG7</i>	BovineHD BeadChip and WGS	95 BeadChip and 10 WGS	iHS, Rsb and Hp	Fertility and reproduction	East African Zebu	Bahbahani <i>et al.</i> 2017	
<i>IGF-1</i> , <i>ESR2</i> and <i>FGFR2</i>	WGS	10 each	XP-CLR, XP-EHH	Follicular development oocyte maturation, and sperm quality	Boran, Ogaden, and Kenana	Taye <i>et al.</i> 2018	
<i>SRD5A3</i>	BovineHD BeadChip	25 each	iHS and Rsb	Development of male reproductive system	Butana and Kenana	Bahbahani <i>et al.</i> 2018	
<i>AFP</i>	BovineHD BeadChip	25	iHS and Rsb	Ovulation in females	Kenana	Bahbahani <i>et al.</i> 2018	
<i>RFX2</i> , <i>SRY</i> , <i>LAP3</i> and <i>GPX5</i>	WGS	10	iHS and Rsb	Reproduction and fertility traits	Muturu	Tijjani <i>et al.</i> 2019	
<i>OVOS2</i> , <i>ADIPOR2</i> , <i>WC1</i> , <i>RBBP8</i> , <i>SERPINA38</i> , <i>HOXC12</i> , <i>HOXC13</i> and <i>FBXL4</i>	BovineSNP50 BeadChip	Afrikaner (44), Nguni ( 54), Drakensberger (47), Bonsmara (44)	F <sub>ST</sub>	Spermatogenesis, ovulation rate, oestrus processes, testis and prostaglandin development	Afrikaner, Nguni, Drakensberger and Bonsmara	Makina <i>et al.</i> 2015	

### 3. Challenges and future implications

African livestock breeds are enormous and diverse and typically well adapted to the harsh environmental conditions under which they perform (Marshall *et al.* 2019). Despite their unique features, most indigenous livestock breeds are characteristically low in production and productivity. Improvements and conservation of these local breeds are a prerequisite for meeting projected human needs and resilience to an uncertain future (FAO, 2015). For more than half a century, crossbreeding has been principally applied in the tropics to exploit breed complementarities. Specifically, specialized exotic breeds have been crossed with indigenous breeds to combine the high productivity of cosmopolitan exotic breeds with the adaptive attributes of African zebu. Unfortunately, the unplanned and indiscriminate crossbreeding practices of most African countries have accelerated the threat of extinction of local cattle breeds (Rege, 1999; Rege and Gibson, 2003). The prevalence of livestock disease, adverse climatic conditions, and nutritional challenges are additional limiting factors in tropical livestock breeding. Furthermore, the conventional method used for centuries of genetic evaluations is not robust as it lacks routine recording of reliable phenotypes and analytical tools to synthesize the data, providing timely feedback to help improve farmer management and husbandry techniques (Mrode *et al.* 2019). Thus, detecting polymorphisms in genes that may influence economically important traits and adaptive attributes is crucial for the current management/improvement programs. Although indigenous African cattle are relatively less intensively studied at the genome level, the rapid developments and cost reduction of sequencing

technologies provide limited insight into African cattle genetic diversity, admixture level and signals of selection (Kim *et al.* 2017, Taye *et al.* 2017; Bahbahani *et al.* 2018; Tijjani *et al.* 2019; Zwane *et al.* 2019). However, the large majority of these signature studies were focused on genomic regions under positive selection rather than balanced selection. So, a genome scan for loci under balancing selection is essential to reveal functionally important genes that are difficult to detect using common reverse or forward genetics due to weak or indirect phenotypic effects.

Another recurring problem was the genome coverage of low-density markers imply that the alleles with low-frequencies may be undetected, in which they may be omitted from such arrays. Recently advances in high-density markers and whole genome sequence resolved the ascertainment bias associated with low-density arrays. However, all genomic tools (i.e., the reference genome and commercial SNP chips) in African cattle genomic studies were still developed with little or no information from African cattle populations (Mwai *et al.* 2015; Marshall *et al.* 2019). African cattle are more distant from the available cattle reference genome (European *Bos taurus*, i.e., *UMD3.1* and *ARS-UCD1.2*) (Mwai *et al.* 2015; Paguem *et al.* 2020). Comparison/mapping of African cattle genomic sequence with existing reference genome results in false positive signatures and eventually distort future genomic breeding decision. As a result, a *denovo* genome assembly of indigenous African cattle is essential to discover new SNPs inclusion in existing SNP assays and develop custom-made SNP chips for adjusting ascertainment bias in genome-wide selective breeding of local cattle breeds. Given genomic selection is more likely to have a profound effect on cattle improvements, a large number of phenotyped and genotyped individuals are necessary to obtain accurate genomic breeding values (Goddard and Hayes, 2009). However, phenotypic information is usually more expensive and difficult to obtain than genotypic information, particularly as the cost of genotyping declines (Biscarini *et al.* 2015). Written pedigree records are lacking in most small-holder farms in developing countries, making it almost impossible to make informed breeding decisions.

The measurement of an increasingly large array of new phenotypes (Houle *et al.* 2010), and the development of systems for automatic trait measurement and recording are a powerful tool to improve both herd management and successful breeding schemes (Berry *et al.* 2012). In addition, the sustainability of breeding programs based on traditional or genomic approaches requires a strong government attention to develop enabling policies and regulatory frameworks that encourage public-private partnerships (Mrode *et al.* 2019). Building human capacity in animal breeding, genetics, and genomics within Africa is also indispensable for designing and supporting of context specific improvements against future climate changes and conservation of local cattle breeds (Marshall *et al.* 2019). To the best of our knowledge, there is no or limited availability of functional genomic studies in African cattle. This calls for further investigation on the functional variants and key

regulatory features to validate the molecular mechanisms and pathways of previously identified African cattle-specific selection signatures.

#### **4. Conclusion**

With widespread climate change and rapid protein demand, the breeding of robust animals is crucial. African cattle breeds are distributed across the continent from the highlands of the rift valley to the Afar depression. These cattle genetic resources comprise a great variety of breeds with huge potential for studies relating to genetic diversity, productivity, and role in adaptation and disease resistance. The long history of indigenous African cattle inhabit the continent develops a mosaic of environmental adaptation that is key to their survival in multiple environmental challenges. Interestingly, unlike European *Bos taurus* and zebu cattle, African *Bos taurus* breeds possess special genomic regions that harbor trypanotolerance and heat resistance. Therefore, uncovering the genetic footprints of recent artificial and long-term natural selections of African cattle could give insight into the mechanisms of selection in general and could, moreover, help to assign chromosomal regions related to important adaptation and agro-economic traits. The limited number of candidate genes of African cattle populations is based on European breed reference assays; this dearth to understand of the complete picture of African cattle genomic architectures may have ascertainment bias or false positive results on identified candidate genes. Therefore, assembly of the African cattle reference genome is compulsory for unbiased signatures and additional SNP discoveries. Furthermore, transcriptomic studies are indispensable to validate the molecular mechanisms and pathways of African cattle-specific selection signatures and develop custom-made breeding tools.

#### **Declaration of competing interest**

The authors declare no conflict of interest.

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