Received: 28 July 2023 | Accepted: 19 August 2023

DOI: 10.1111/age.13353

REVIEW

ANIMAL GENETICS WILEY

Candidate signatures of positive selection for environmental adaptation in indigenous African cattle: A review

Sumaya Kambal[1,2,3] | **Abdulfatai Tijjani**[4,5] | **Sabah A. E. Ibrahim**[3] | **Mohamed-Khair A. Ahmed**[2] | **Joram M. Mwacharo**[6,7] | **Olivier Hanotte**[1,4,8]

[1]Livestock Genetics, International Livestock Research Institute, Addis Ababa, Ethiopia

[2]Department of Genetics and Animal Breeding, Faculty of Animal Production, University of Khartoum, Khartoum, Sudan

[3]Department of Bioinformatics and Biostatistics, National University, Khartoum, Sudan

[4]Centre for Tropical Livestock Genetics and Health, International Livestock Research Institute, Addis Ababa, Ethiopia

[5]The Jackson Laboratory, Bar Harbor, Maine, USA

[6]Scotland's Rural College and Centre for Tropical Livestock Genetics and Health, Edinburgh, UK

[7]Small Ruminant Genomics, International Centre for Agricultural Research in the Dry Areas, Addis Ababa, Ethiopia

[8]School of Life Sciences, University of Nottingham, Nottingham, UK

Correspondence
Sumaya Kambal and Olivier Hanotte, Livestock Genetics, International Livestock Research Institute, PO Box 5689, Addis Ababa, Ethiopia.
Email: somakmbal@gmail.com, olivier.hanotte@nottingham.ac.uk and o.hanotte@cgiar.org

Funding information
Bill and Melinda Gates Foundation; UK Aid FCDO; University of Nottingham (United Kingdom); ILRI Livestock CRP, CGIAR Trust Fund

Abstract
Environmental adaptation traits of indigenous African cattle are increasingly being investigated to respond to the need for sustainable livestock production in the context of unpredictable climatic changes. Several studies have highlighted genomic regions under positive selection probably associated with adaptation to environmental challenges (e.g. heat stress, trypanosomiasis, tick and tick-borne diseases). However, little attention has focused on pinpointing the candidate causative variant(s) controlling the traits. This review compiled information from 22 studies on signatures of positive selection in indigenous African cattle breeds to identify regions under positive selection. We highlight some key candidate genome regions and genes of relevance to the challenges of living in extreme environments (high temperature, high altitude, high infectious disease prevalence). They include candidate genes involved in biological pathways relating to innate and adaptive immunity (e.g. *BoLAs*, *SPAG11*, *IL1RL2* and *GFI1B*), heat stress (e.g. *HSPs*, *SOD1* and *PRLH*) and hypoxia responses (e.g. *BDNF* and *INPP4A*). Notably, the highest numbers of candidate regions are found on BTA3, BTA5 and BTA7. They overlap with genes playing roles in several biological functions and pathways. These include but are not limited to growth and feed intake, cell stability, protein stability and sweat gland development. This review may further guide targeted genome studies aiming to assess the importance of candidate causative mutations, within regulatory and protein-coding genome regions, to further understand the biological mechanisms underlying African cattle's unique adaption.

KEYWORDS
candidate genes, genome, indigenous livestock, selection sweeps

INTRODUCTION

It is widely accepted among archaeologists and animal geneticists that domestic cattle are descended from the wild aurochs (*Bos primigenius*) (Epstein, 1971; Payne, 1991). It was the commonest wild bovid species across Europe and most of Asia between the late Pleistocene and early Holocene (Felius et al., 2014; Zeuner, 1963). Moreover, cattle domestication probably occurred in two separate episodes, initially more than

10 000 years BP (~8000 BC) in the Fertile Crescent and around 3000 years later (~5000 BC) in the Indus Valley (Bruford et al., 2003; Hanotte et al., 2002; Helmer et al., 2005; Loftus et al., 1994; MacHugh et al., 1997, 2017). Today's taurine (*Bos taurus taurus*) and zebu (*Bos taurus indicus*) cattle originated from these two distinct domestication centres and two distinct wild auroch subspecies, *Bos primigenius primigenius* and *Bos primigenius nomadicus*, respectively (McTavish et al., 2013).

Following the development of agricultural societies, human migrations and trading networks, taurine and zebu cattle dispersed worldwide, as evidenced by zooarchaeological, iconographic and molecular genetic studies (Edwards et al., 2007; Kantanen et al., 2009; Pérez-Pardal et al., 2010). These global dispersals brought taurine and zebu cattle into contact with related bovid species such as yak (*Bos grunniens*), gaur (*Bos gaurus*) and banteng (*Bos javanicus*), with several episodes of hybridisation and introgression now documented (e.g. Wu et al., 2018). Also, introgressions from local aurochs probably contributed to the genetic ancestry of modern cattle, as has recently been shown for taurine cattle in the Levant (e.g. Verdugo et al., 2019) and North Africa (Ginja et al., 2023). All these evolutionary events shaped today's lineage diversity of worldwide domestic cattle.

The domestication and dispersion processes of cattle led to anthropological and natural selection pressures, which followed the development of farmers and pastoral societies worldwide (Diamond, 2002; Flint & Woolliams, 2008). These events are the roots of environmental adaptation, production variation and phenotypic diversity of modern cattle (e.g. Felius et al., 2014). Likewise, these selection events imprinted the genome's adaptive diversity and its architecture (e.g. Kim et al., 2020). The phenotypic and genetic diversity in present-day worldwide cattle breeds represents a unique genetic resource for successful and sustainable breeding improvement programmes.

With its diverse environmental conditions and its complex history of biological and agricultural introductions, the African continent is considered one of the main reservoirs of cattle diversity (Kim et al., 2020; Kim, Hanotte, et al., 2017; Mwai et al., 2015). Indigenous African cattle genomes have now been extensively studied by researchers aiming to understand the genetic basis of their unique diversity, environmental adaptation, and to a lesser extent, production traits. More particularly, several studies have sought to unravel the genomic footprints of positive selection (Bahbahani et al., 2017; Bahbahani, Afana, et al., 2018; Bovine HapMap Consortium, 2009; Kim et al., 2020; Kim, Hanotte, et al., 2017; Mekonnen et al., 2019; Taye et al., 2018; Tijjani et al., 2019, 2022).

Here, after briefly summarising the history of the genome diversity of indigenous African cattle, we review the findings on signatures of positive selection. We intend to provide a comprehensive overview of the main candidate positive signatures of selection reported in African taurine, African zebu and their crossbreds. In addition, the review aims to guide further genome studies, paving the way for the identification of candidate causative mutations (e.g. single nucleotides polymorphisms (SNPs) and structural variants (SVs)) within regulatory and coding regions to understand further the biological mechanisms underlying the unique environmental adaptation of indigenous African cattle.

The review was compiled from 22 articles, retrieved and selected from known databases (ScienceDirect and PubMed), following the Joanna Briggs Institute protocol for scoping reviews (Peters et al., 2020). These databases were accessed on 16 December 2022.

DOMESTICATION, ADMIXTURE AND INTROGRESSIONS HAVE SHAPED THE GENOMES OF AFRICAN CATTLE

The diverse ecological zones in Africa, ranging from the Sahelian arid zones to the sub-humid and humid tropical forests, and from afro-alpine altitudes to ones below sea-level, have witnessed, throughout history, cattle pastoralists' strategic mobility and settlements coupled with socio-cultural and trading activities (Figure 1, Table S1). Accompanying these early movements, the humpless taurine were the first cattle to reach and disperse within the continent, according to archaeological and molecular evidence (Blench & MacDonald, 1999; Epstein & Mason, 1984; Hanotte et al., 2002).

The first unambiguous presence of domestic cattle in the continent dates from the end of the seventh millennium BC in the South of Egypt (Gautier, 1987; Gifford-Gonzalez & Hanotte, 2011; Grigson, 1991; Lesur, 2022). Predating Asian zebu arrival, these taurine cattle dispersed across a wide geographic area that covered East, Central and West Africa, with southern movements probably following the desertification of the Sahara around the third millennium BC (Felius et al., 2014; Lesur, 2022). These taurine cattle are today mainly found in the tsetse-infested belt in the whole of the West Africa subregion, with some populations now representing the only remaining non-zebu admixed taurine cattle on the continent. Uniquely, these populations express a unique heritable tolerance to trypanosome infection, a parasitic flagellate protozoon transmitted by the tsetse fly *Glossina* sp. (Mattioli et al., 2000; Murray et al., 1984), responsible for causing trypanosomiasis. Trypanotolerance attributes have been reported in both longhorn and shorthorn African taurine cattle, including the N'Dama (longhorn taurine) and Muturu (shorthorn taurine) (Freeman et al., 2004; Hanotte et al., 2002; Tijjani et al., 2019).

The other intercontinental cattle movements in Africa stemmed from the Indian subcontinent. It was

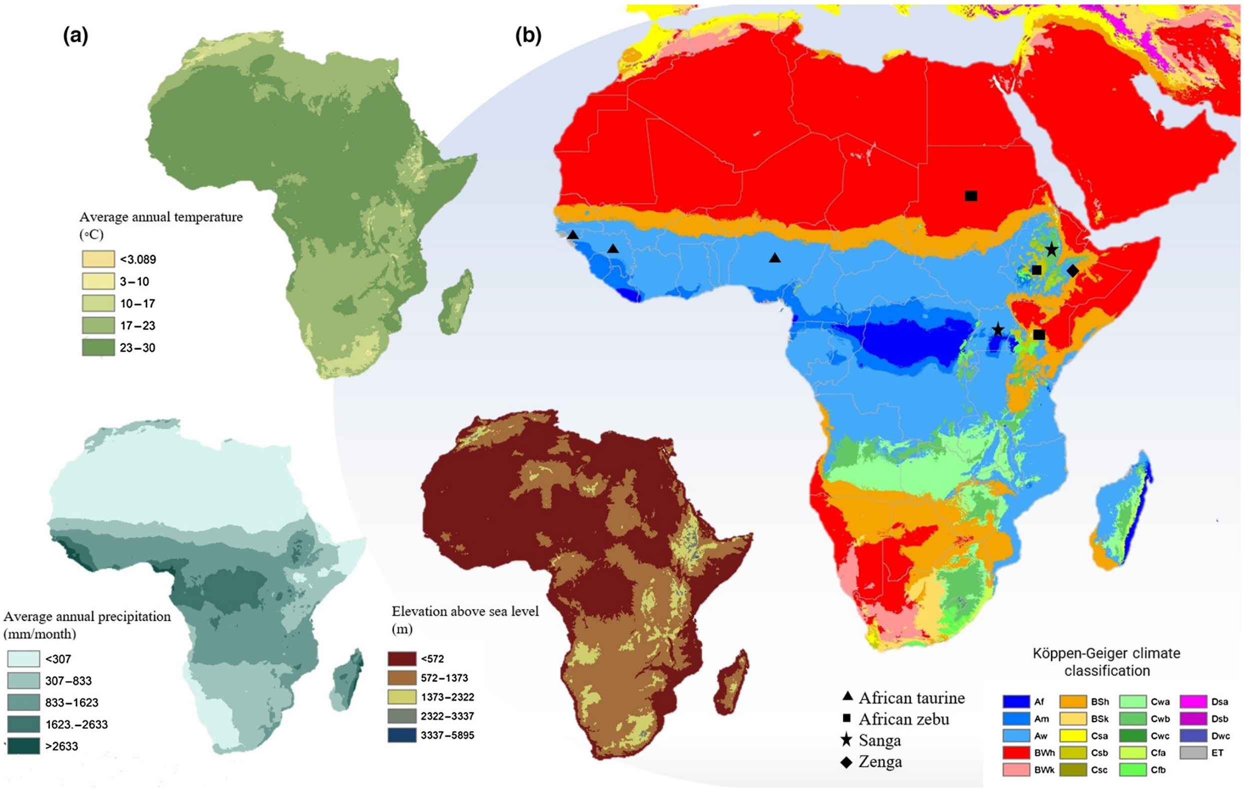

FIGURE 1 Maps of African environmental and ecological conditions faced by indigenous African cattle. (a) Annual climatic trends (mean temperature and precipitation) based on WorldClim 2.1 data (1970–2000) with a spatial resolution of 10m, and elevation in metres (Fick & Hijmans, 2017). (b) Continental location of indigenous African breed groups reported in this review (African taurine, African zebu, sanga, zenga), pinpointed on the Köppen–Geiger climate map (1980–2016) (see Table S1 for climate class abbreviations; Beck et al., 2018; Kottek et al., 2006). These maps were generated with ArcGIS v.10.7.1 (ESRI, 2019).

mainly a male-mediated introduction and dispersal of animals of Asian zebu origin. It probably involved several waves of introduction and/or migration to and within the continent. These influxes were tied to the sea-routed long-distance trading activity between the Indian subcontinent and East Africa, through the Gulf of Oman and the Strait of Bab-el-Mandeb in the Horn of Africa. The earliest evidence of humped cattle, a painting in Karnak (Egypt), dates from around 1500 BC (Epstein, 1971). The Asian zebu may have reached the African continent in large numbers in the late seventh century with the development of Swahili civilisation and societies, which were closely embedded in the Indian Ocean trading networks. It led to crossing with the already present native taurine cattle, forming the hybrid cervico-thoracic humped sanga cattle. Interestingly, a recent genetic study identified a major taurine × indicine cattle admixture event from ca. 750–1050 years ago (Kim et al., 2020). These hybrid cattle became the commonest populations in the eastern and southern regions of the African continent. Around the end of the nineteenth century, the devastating rinderpest pandemic wiped out more than two-and-a-half million heads of African cattle (Epstein, 1971). Cattle predominantly of Asian zebu background then dispersed throughout the continent. They may be the origin of today so-called African zenga cattle (zebu × sanga crosses) and African zebu (Mwai et al., 2015; Rege, 1999).

Following their complex history, indigenous African cattle breeds today represent a unique mosaic of genetic diversity. At the autosomal DNA level, genomic mosaicism has been found in most indigenous African cattle with different proportions of the two domestic subspecies (zebu and taurine) (Kim et al., 2020; Kim, Hanotte, et al., 2017). A large proportion of bulls found in East Africa and along the Sahelian belt of West Africa carry a male Y indicine chromosome (Bradley et al., 1994; Hanotte et al., 2000). A dominant zebu genome influence is now visible in nearly all indigenous African cattle populations with the exception of taurine populations living deep within the tsetse belt in West Africa. Also, all African cattle have retained their maternal mitochondrial taurine ancestry and it has recently been shown that the ancestral incompatibility between the mitochondrial DNA and the autosomal genome has contributed to the shaping of the autosomal genome of African cattle (Kwon et al., 2022; Ward et al., 2022).

It has been proposed that the African aurochs *B. primigenius africanus* might have been domesticated on the continent (Grigson, 1991). So far, no ancient or modern archaeological or genetic evidence supports such an event (Pitt et al., 2019), although it remains possible that local introgression with wild African aurochs may have shaped the genome of at least some African cattle populations. Indeed, two recent studies support local aurochs' introgression, in ancient domestic cattle from the southern Levant (Verdugo et al., 2019), a geographical area close to the taurine entry point on the African continent, and in modern Tunisia (Ginja et al., 2023).

THE CONTRIBUTION OF GENOME-WIDE POLYMORPHISM STUDIES TO THE CURRENT KNOWLEDGE OF INDIGENOUS AFRICAN CATTLE DIVERSITY

Following early work using mitochondrial and microsatellite DNA markers (Bradley et al., 1996; Hanotte et al., 2002), African cattle genomes have been extensively studied using genotypic and whole genome resequencing information. These studies have included population-level assessments of genetic diversity, admixture and demography dynamics, to reveal clues on the origin and history of the populations. These studies have also paved the way for the identification of signatures of selection in the autosomal genome, to identify not only candidate genome regions but also putative genes and variants that, ultimately, might be associated with economically important, as well as environmental adaptive traits (Bahbahani et al., 2015, 2017; Bahbahani, Salim, et al., 2018; Kim et al., 2020; Tijjani et al., 2019).

Initially, genome-wide medium- and high-density SNP arrays (e.g. Illumina BovineSNP50 and BovineHD BeadChip) were used (Flori et al., 2014; Gautier et al., 2009). However, today, a growing number of studies are using high-throughput whole genome sequencing technologies and information (Table 1; Kim et al., 2020; Kim, Hanotte, et al., 2017; Taye, Lee, Caetano-Anolles, et al., 2017; Tijjani et al., 2019, 2022). Whole genome sequences of indigenous African humpless (taurine) and humped (zebu/sanga) cattle were first reported and characterised by Kim, Hanotte, et al. (2017) (Bioproject accession number PRJNA312138). In their study, they identified candidate selected genes underlying adaptive environmental traits in N'Dama, Ankole, Boran, Kenana and Ogaden breeds. By applying a comparative genome-wide analysis with European commercial breeds, they found a higher level of genetic diversity within and across the African zebu and sanga, whereas a relatively low genetic diversity was reported in a West African longhorn taurine (N'Dama) (Kim, Hanotte, et al., 2017). Similarly, Tijjani et al. (2019) reported low genetic diversity in the Muturu, a West African shorthorn taurine from Nigeria, possibly the result of population bottlenecks following adaptation to the challenges of trypanosomiasis in the humid and sub-humid West African tropical regions (d'Ieteren et al., 1998; Kim, Hanotte, et al., 2017; Tijjani et al., 2019). Following these early studies, Kim et al. (2020) (Bioproject accession no. PRJNA574857), reported the whole genome resequencing of 12 African cattle breeds (Table 1), including the Ethiopian Sheko previously analysed in Bahbahani, Afana, et al. (2018).

In all these studies, most African humped cattle were found to possess a proportion of taurine and zebu ancestries, in agreement with previous microsatellite findings (e.g. Hanotte et al., 2002). Likewise, a high proportion of zebu background was observed in the genomes of African cattle populations in the Horn of Africa, including the trypanotolerant Ethiopian Sheko. Accordingly, the latter should now be reclassified as a crossbred taurine × zebu rather than as taurine (Rege et al., 1996).

Moving to West Africa, a close relationship was found between the zebu breeds in Cameroon and Nigeria, with a higher proportion of zebu genetic background in these populations compared with the zebu introgressed West African taurine (Ibeagha-Awemu et al., 2019). Recent studies have also explored maternal and/or paternal DNA markers to trace the demography of African cattle (Bradley et al., 1994; Kambal et al., 2021; Kwon et al., 2022; Mauki et al., 2021; Pérez-Pardal et al., 2010; Ward et al., 2022). All these studies support the fact that the genetic backgrounds of different ancestral origins, admixed and selected over time in different proportions according to the geography and environment of the continent, are at the roots of the success of African cattle pastoralism.

Until now, all genome-wide re-sequencing studies of African cattle populations have relied on European taurine reference genome assemblies, making them susceptible to reference-biased variant calling. However, recently, *de novo* genome assemblies have been generated for Asian indicine (Low et al., 2020) and for two African cattle breeds (N'Dama and Ankole) (Talenti et al., 2022). These latter two were integrated with genomic data from worldwide cattle breeds, leading to the identification of 116.1 Mb of sequence not represented in the reference Hereford based genome assembly, ARS-UCD1.2 (Talenti et al., 2022). In the future, it may be expected that the availability of more *de novo* African cattle genomes and their integration into a pangenome will provide a more complete and comprehensive picture of African cattle diversity (Talenti et al., 2022).

GENOMIC FOOTPRINTS OF NATURAL SELECTION

Several studies have attempted to decipher the impact of environmental selection on the genomes of African cattle (Bahbahani et al., 2017; Hanotte et al., 2003; Kim, Hanotte, et al., 2017; Noyes et al., 2011; Orenge et al., 2011; Taye et al., 2018). Such information would be useful in designing appropriate and effective selective breeding

TABLE 1 List of publicly available whole genome sequence data of indigenous African cattle.

Breed	Breed's major class	Breed group	Breed cluster[a]	Sample size	Bioproject accession no. (GenBank)	Source
Ankole	African humped	Sanga	AAD (Uganda)	10	PRJNA312138	Kim, Hanotte, et al. (2017)
N'Dama	African humpless	Longhorn taurine	WAT (Guinea)	10		
Kenyan Boran	African Humped	Large East African zebu	EAZ (Kenya)	10		
Kenana			EAZ (Sudan)	9		
Ogaden		Small East African zebu	EAZ (Ethiopia)	9		
KEASZ[b]	African humped	Small East African zebu	EAZ (Kenya)	10	PRJNA386202	Bahbahani et al. (2017)
Muturu	African humpless	Shorthorn taurine	WAT (Nigeria)	10		
Arsi	African Humped	Small East African zebu	EAZ (Ethiopia)	10	PRJNA574857	Kim et al. (2020)
Goffa				10		
Mursi				10		
Barka		Large East African Zebu		9		
Ethiopian Boran				10		
Afar		Sanga	AAD (Ethiopia)	9		
Fogera		Zenga		9		
Horro				11		
Sheko[c]		Sanga		9		
Butana		Large East African Zebu	EAZ (Sudan)	20		
Kenana				4		
N'Dama	African Humpless	Longhorn taurine	WAT (Gambia)	3		
Bale	African humped	Small East African zebu	EAZ (Ethiopia)	10	PRJNA698721	Jang et al. (2021)
Semien				10		
Bagaria		Large East African zebu		10		
Baggara	African humped	Large East African zebu	EAZ (Sudan)	10	PRJNA858239	Tijjani et al. (2022)
Aryashi				10		
Gash				10		
Fulani				10		
Choke	African humped	Small East African zebu	EAZ (Ethiopia)	10	PRJNA841948	Terefe et al. (2022)

[a] Based on the geographical area inhabited by groups: EAZ, East African zebu; WAT, West African taurine; AAD, East African admixed which refers to both sanga and zenga groups.

[b] Kenyan East African shorthorn zebu.

[c] Sheko cattle were originally grouped as a Humpless Shorthorn Taurine.

programmes aiming to improve productivity, while preserving the environmental sustainability of cattle production systems. Natural selection events have imprinted genomic regions with distinctive variation at the genotype and phenotype levels (Oleksyk et al., 2010). Different strategies may be used to detect such environmental signatures of selection.

One of the first investigations was an on-station study at the International Livestock Research Institute, Kenya, more than two decades ago. It aimed to unravel the genetic mechanism of trypanotolerance in F2 crosses between trypanotolerant N'Dama and trypanosusceptible Kenyan Boran (Hanotte et al., 2003). It included linkage mapping analysis of microsatellite markers to identify quantitative trait loci (QTL) associated with recorded animal phenotypes. Such a study required a large number of animals with recorded phenotypes and pedigree information. Such experiments are challenging to design and expensive to implement even under controlled (on-station) conditions.

New strategies have therefore been designed, taking advantage of whole genome sequencing information on a small number of individuals with geographic coordinates of sampling as the entry-point proxies of environmental selection pressures. These strategies aim to detect the genome signature of positive selection following a selective sweep or a hitchhiking effect on a beneficial genome variant (SNPs or SVs). These will affect upstream and downstream chromosomal sites, which may rise in frequency and/or approach fixation over generations (Fay & Wu, 2000; Oleksyk et al., 2010; Saravanan et al., 2020). These alleles may arise from previously unselected background variants, *de novo* variants, or variants that may have been introduced following an admixture and/or introgression event (Peter et al., 2012; see review by Saravanan et al., 2020). Statistical models that measure allele frequency deviations, diversity loss or changes in haplotype structures enable the detection of signatures of positive selection (Qanbari & Simianer, 2014; Utsunomiya et al., 2015).

Several statistical tests may be combined to increase the detection power and reduce the likelihood of false positive results (Randhawa et al., 2016; Utsunomiya et al., 2015). The findings may also be further supported by complementary approaches such as genome-wide association studies and transcriptome analysis (e.g. Aliloo et al., 2020; Hanotte et al., 2003; Noyes et al., 2011). A significant challenge associated with the detection of positive signatures of selection is the presence of demographic factors (e.g. migration, admixture, fine-scale population structure, population expansion or bottleneck). These may result in genome variation patterns (e.g. changes in frequencies of haplotypes or SNPs) similar to those arising from positive selection (Haasl & Payseur, 2016; Nielsen et al., 2005; Weigand & Leese, 2018).

Many candidate regions under positive selection, often overlapping with genes or coding regions, have been reported in indigenous African cattle breeds. In most studies, comparisons with different cattle populations (African and non-African breeds) as well as within and between breeds were performed (Table S2). For regions with annotated genes, researchers have sought to get insights into the biological significance of the candidate genes by investigating their functions, including using functional enrichment and gene ontology analyses. The highest numbers of genomic regions under positive selection were found on BTA3, BTA5 and BTA7. These regions intersect with candidate genes having roles in several biological functions and pathways, including but not limited to growth and feed intake, cell stability, protein stability and sweat gland development (Tables 2 & S3). Table 3 summarises the information about the number of studied breeds, methods used for genome-wide variation scanning, the bovine genome of reference, statistical tests and the number of informative SNPs.

In the following sections, we highlight the genomic regions reported by these studies and the biological function of the candidate genes for three important adaptive traits in indigenous African cattle: heat tolerance, parasitic disease resistance and adaptation to high altitude (e.g. hypoxia, cold temperature, UV radiation).

Heat tolerance

Besides the deleterious impact of heat stress on cattle productivity, indirect effects stem from the impact on water availability and forage quantity and quality. The ability to dissipate excess heat, regulate body temperature and preserve water are key survival characteristics, with *B. taurus indicus* cattle being better adapted to these challenges at cellular and physiological levels than their taurine counterparts (Beatty et al., 2006; Hansen, 2004). Cattle may control their body temperatures through sensible mechanisms, including conduction, convection and radiation, and through latent mechanisms, such as sweating and panting (Dos Santos et al., 2021; Hansen, 2004). Shade seeking, drinking and reducing feed intake are behavioural strategies to maintain thermal equilibrium when an upper critical temperature is exceeded (Herbut et al., 2018), while body surface area, coat pigmentation and hair thickness and length are also of high importance (Hansen, 1990, 2004).

Several studies have reported candidate genes related to African cattle heat stress adaptation. The detection of selective sweeps overlapping heat shock proteins (HSPs) and their transcription factors (HSFs) has been linked to cattle responses to stressful environmental heat conditions. These proteins, such as HSPA4, HSPA9, HSPB9 and HSF5 may act to protect the cell and prevent protein denaturation during exposure to heat stress (Basiricò et al., 2011; Kim, Hanotte, et al., 2017). In addition, genes that encode chaperone proteins (*DNAJC8*, *DNAJC18*), which contribute to the conformational folding and unfolding of heat shock proteins (HSP70) (Kampinga & Craig, 2010), are found within a candidate genome region of low heterozygosity in African cattle (Bahbahani et al., 2017).

It is also known that heat stress induces the downregulation of expression of antioxidant enzymes, leading to oxidative stress (Chauhan et al., 2021). Comparative genomic analysis between African and commercial breeds (European and Asian) has revealed several genes involved in the control of oxidative stress, e.g. superoxide dismutase 1 (*SOD1*) and glutathione peroxidase 7 (*GPX7*) (e.g. Taye, Lee, Caetano-Anolles, et al., 2017). The SOD1 and GPX7 proteins have crucial antioxidant enzymatic activities protecting the cell from cytotoxicity and damage that may occur owing to the excessive formation of intra- and extracellular reactive oxygen species (ROS) during heat stress (Belhadj Slimen et al., 2016; Kim, Hanotte, et al., 2017).

An additional non-enzymatic antioxidant defence mechanism is suggested to be driven endogenously by glutathione and ascorbic acids (e.g. vitamins C and E). A decline in their concentration has been reported in

TABLE 2 Examples of genes intersecting candidate selective genomic regions in indigenous African cattle in relation to their environmental adaptative traits.

Trait	Candidate genes	Gene Ontology terms[a]	Associated traits and gene functions	Sources
Thermotolerance	*HSPA9*, *DNAJC18*, *DNAJC11*, *HSF5*, *PPP1R10*	GO:0051085 GO:0071218	Cell and protein stability	Bahbahani et al. (2015), Kim et al. (2020), Kooverjee et al. (2022), Taye et al. (2018)
	SOD1, *GPX7*, *SLC23A*, *PLCB1*, *SLC23A1*	GO:1901701 GO:0048015 GO:0034599	Oxidative stress response	Kim, Hanotte, et al. (2017), Taye, Lee, Caetano-Anolles, et al. (2017)
	GFTR, *ITPR2*, *SCNN1D*, *PRLH*, *GNAS*, *SLC9A4*, *SGK1*	GO:0038023 GO:0005262 GO:0005272	Sweat gland development	Kim et al. (2020), Mekonnen et al. (2019), Taye, Lee, Caetano-Anolles, et al. (2017)
	MLPH, *SLC45A2*, *HOXC12*, *ATRN*, *MC5R*, *PMEL*, *RAB37*	GO:0032438	Hair coat colour and type	Bahbahani, Salim, et al. (2018), Flori et al. (2014)
	NFATC2, *ATRN*, *IGF-1*, *PRKCZ*, *GH1*, *THEM5*, *MSTN*, *MAP3K5*, *XKR4*, *ACLY*, *PRDM16*, *NCOA2*	GO:0042531 GO:0045927 GO:0006637	Metabolism and energy hemostasis	Kooverjee et al. (2022), Taye et al. (2018), Tijjani et al. (2019, 2022)
Resistance to vector borne diseases	*CARD11*, *IL7*, *VAV1*, *PTPN6*, *BoLAs*, *GFI1B*, *TNFAIP8L3*, *SLC25A48*, *RNF152*, *RNF144B*, *POLR3A*, *TTC3*, *PPP1R14C*, *SPAG11*, *POLR3B*, *TRIM10*, *TRIM15*, *FBXO9*, *TFEC*, *IL7*, *CCR7*, *LOC512672*, *TICAM1*	GO:0006955	Immune response (innate and adaptive)	Ben-Jemaa et al. (2020), Kim et al. (2020), Mauki et al. (2022), Mekonnen et al. (2019), Taye et al. (2018)
	LTA4H, *IRAK*, *AKAP13*, *KLHL25*, *STING1*, *NLRC4*, *NLRP3*, *LTA4H*, *TNFAIP3*, *DMBT1*, *IL1RL2*	GO:0035023 GO:0030177	Inflammatory response	Bahbahani, Afana, et al. (2018), Kim, Ka, et al. (2017)
	ERN1, *CDAN1*, *MIGA1*, *PCSK6*, *SLC40A1*, *STOM*, *RPS26*	GO:0055072 GO:0045087	Anaemia	Kim, Hanotte, et al. (2017), Kim, Ka, et al. (2017), Mekonnen et al. (2019)
Adaptation to high altitude	*TFRC*, *BDNF*, *PML*, *BCL2*, *HIGD2A*, *CBFA2T3*, *ITPR2*, *RXFP2*	GO:0008630	Hypoxia response	Ben-Jemaa et al. (2020), Edea et al. (2014), Terefe et al. (2022)

[a] Based on the Gene Ontology (GO) repository.

goats (Pandey et al., 2014) during hot seasons, and a reduction in the free radical concentration is recorded in Asian buffalo supplemented with ascorbic acid (Kumar et al., 2011). It supports their attenuation effect on the consequences of oxidative stress, a result that is consistent with the positive signature of selection regions overlapping two candidate Solute Carrier Family 23 genes (*SLC23A1* and *SLC23A2*) (Taye, Lee, Caetano-Anolles, et al., 2017). These genes encode proteins that are active in bulk vitamin C transport, supporting its delivery and absorption in different tissues.

An important heat adaptation biological pathway is the prolactin one. The multi-function nature of the prolactin hormone (*PRL*) was linked physiologically to homeothermic regulation with the discovery of a dominant mutation in hairy and heat-intolerant New Zealand dairy cattle (Davis et al., 2017; Littlejohn et al., 2014). Moreover, the same study found a mutation in exon 10 of the prolactin receptor (*PRLR*) gene associated with the heat-tolerant slick-coat phenotype in the taurine Senepol (Littlejohn et al., 2014).

The predicted alteration caused by SLICK variant(s) on the tertiary structure of prolactin receptor is expected to affect its interaction with the prolactin hormone, explaining the observed defect in lactation and sweat gland dysfunction (Flórez Murillo et al., 2021; Littlejohn et al., 2014; Porto-Neto et al., 2018). A recent study in the Holstein breed aimed to evaluate whether

TABLE 3 Summary of studies that used positive signature of selection approaches to identify candidate genes probably associated with environmental adaptation in indigenous African cattle.

Study	Number of breeds[a]	Genotyping method	Bovine genome reference	Number of analysed SNPs	Statistical test	Major candidate genes
Terefe et al. (2022)	6	WGS (Illumina NovaSeq 6000)	ARS-UCD1.2	~36.6 million	*iHS*, *XP-CLR*, *PBS*	*ITPR2*, *NUP133*, *SLC26A2*, *CLCA2*, *CBFA2T3*, *ABCB10*
Kooverjee et al. (2022)	2	GeneSeek Genomic Profiler 150 K	UMD3.1	117 361	*iHS*, *XP-EHH*	*SERPINH*, *DNAJC5B*, *HSPH1*, *HSPB9*, *EEF1AKMT1*
Dlamini et al. (2022)	2	Illumina BovineHD BeadChip	ARS-UCD1.2	650 430	*iHS*, *XP-EHH*	*EDNRA*, *PIK3R3*, *PCDHA4*, *SLC4A9*, *SLC25A2*
Mauki et al. (2022)	8	GBS and WGS (Illumina HiSeq 2500 platform)	UMD3.1	~3.2 million	*CLR*, *PBS*	*BOLA-DYB*, *BOLA-DOA*, *KITLG*, *SERPINE2*, *ROBO2*, *IL12A*, *DLG1*
Tijjani et al. (2022)	6	WGS (Illumina HiSeq 2000 platform)	ARS-UCD1.2	~42.9 million	*ZHp*, F_{ST}, *XP-EHH*	*PRKCZ*, *SKI*, *PLCH2*, *STAP2*, *ARHGAP26*
Ben-Jemaa et al. (2020)	8	Illumina BovineSNP50 BeadChip	ARS-UCD1.2	38 464	*iHS*, *XP-EHH*, *Rsb*	*AZU1*, *ELANE*, *GZMM*, *PRSS57*, *PRTN3*, *CFD*, *CD79B*, *MILR1*, *PECAM1*, *MAP3K3*, *TCAM1*
Kim et al. (2020)	15	WGS (Illumina HiSeq 2000 platform)	ARS-UCD1.2	~17.7 million	*iHS*, *PBS*	*HSPA9* and *DNAJC18*, *GNAS*, *MATR3*, *MZB1*, *STING1*, *NLRC4*, *FAAP24*, *WDR48*, *LRRC8A*, *IFNAR*, *CTNNA1*, *PSD2*, *NRG2*, *DNAJC18*
Mekonnen et al. (2019)	5	Illumina BovineHD BeadChip	UMD3.1	715 712	*iHS*, *Rsb*, *CLR*	*SPAG11B*, *RAET1G*, *PPP1R14C*, *TTC3*, *POLR3B*, *MIGA1*, *TTC3*, *ERN1*, *CAPG*, *GNAS*, *TTBK2*, *TTBK2*
Tijjani et al. (2019)	1	WGS (Illumina HiSeq 2000 platform)	UMD3.1	~19.9 million	*iHS*, *Rsb*	*FAM124A*, *SERPINE3*, *WDFY2*, *INTS6*, *BOLA*, *TRIM10*, *TRIM15*, *MAP3K5*, *GCM1*, *MAP7*, *CHAF1B*, *GHRHR*, *GHR*, *BOLA-DQA2*, *INTS6*
Bahbahani, Afana, et al. (2018)	1	Illumina BovineSNP50 BeadChip	UMD3.1	33 797	*iHS*, *Rsb*	*IL7*, *IL15*, *FCN2*, *ICOS*, *LTA4H* and *NFAM1*, *MEA1*, *CLGN*, *RXFP2*, *HSPA6*, *DNAJC6*, *PRLH*
Bahbahani, Salim, et al. (2018)	2	Illumina BovineHD BeadChip	UMD3.1	703 901	*iHS*, *Rsb*	*IRAK*, *IL17B*, *HSF5*, *SRD5A3*, *AFP*
Taye et al. (2018)	3	WGS (Illumina HiSeq 2000 platform)	UMD3.1	~37 million	*XP-EHH*, *XP-CLR*	*BoLA*, *TNFAIP8L3*, *SLC25A48*, *ATP2A2*, *TGM3*, *PLCB1*, *MAPK12*, *SGPL1*, *DNAJC11*, *DNAJC8*, *HSF5*, *PPP2R5E*, *GF-1*, *ESR2*, *FGFR2*
Bahbahani et al. (2017)	12	Illumina BovineHD BeadChip	UMD3.1	649 611	*meta-SS*, *Rsb*, *iHS*, *ΔAF*, *Hp*	*CCR7*, *CSF3*, *RARA*, *RXFP2*, *SPAG*, *HSPA9*, *HSPB9*, *DNAJC8*, *DNAJC18*
Kim, Hanotte, et al. (2017)	5	WGS (Illumina HiSeq 2000 platform)	UMD3.1	~37.3 million	*XP-EHH*, *XP-CLR*, F_{ST}	*HCRTR1*, *SLC40A1*, *STOM*, *SBDS*, *EPB42*, *RPS26*, *NF-kB*, *IL1RL2*, *MC1R*, *MITF*, *PDGFRA*, *BOLA*, *HSPA4*, *SOD1*, *PRLH*
Kim, Ka, et al. (2017)	2	WGS (Illumina HiSeq 2000 platform)	UMD3.1	~37.3 million	*wMI*, *XP-CLR*, *XP-EHH*	*ACCN1*, *CTNNA2*, *FHIT*, and *USH2A*, *GTF2IRD1*, *CALCR*, *FGF23*, *CDK6*, *IL1RL1*, *IL1RL2*, *SP1*, *SP7*, *CARD11*
Taye, Lee, Jeon, et al. (2017)	1	WGS (Illumina HiSeq 2000 platform)	UMD3.1	~37.3 million	*XP-EHH*, *XP-CLR*	*PLCB1*, *MAPK12*, *DNAJC11*, *DNAJC8*, *IGF-1*, *BoLA*, *TNFAIP8L3*

TABLE 3 Continued

Study	Number of breeds[a]	Genotyping method	Bovine genome reference	Number of analysed SNPs	Statistical test	Major candidate genes
Taye, Lee, Caetano-Anolles, et al. (2017)	5	WGS (Illumina HiSeq 2000 platform)	UMD3.1	~37.3 million	*XP*-CLR, XP-*EHH*	*TNFRSF10D, TNFAIP2, ALAD, CA5A, HDHD3, FTO, SOD1, GPX7, SLC23A1, PLCB1, PRLH, BHMT2, IGF-1, HSF5, GFTR, ITPR2*
Bahbahani et al. (2015)	1	Illumina BovineSNP50 BeadChip	UMD3.1	46 171	F_{ST}, *iHS, Rsb*	*IL17D, IRAK1, LOC512672, IGBP1, BCL6B, OR2AP1, ACLY, HSPB9, DNAJC7, DNAJC8, DNAJC14, DNAJC18, KRT, PMEL17*
Makina et al. (2014)	4	Illumina BovineSNP50 BeadChip	UMD3.1	21 290	F_{ST}, *FH*	*KRT222, KRT24, HSPB9, MTPN, CYM, CDC6, CDK10, KCNBI, TNS4, NDUFA12, ALOX15B, SLC25A48*
Edea et al. (2014)	5	Illumina BovineSNP50 BeadChip	UMD3.1	29 736	F_{ST}	*ATP2A3, CA2, MYO18B, SIK3, INPP4A, IREB2, ATP2A3, BDNF, PML, PRKDC, MSH2, PARP4, EPC2, CDK1, TFRC, ASAP1*
Flori et al. (2014)	1	Illumina BovineSNP50 BeadChip	UMD3.1	38 100	*iHS, Rsb*	*SILV, LRRK2, NEDD4, MAPKAPK2, B3GALTL, PDE1B, BOLA-A, TICAM1, PRDM16*
Gautier et al. (2009)	9	Illumina BovineSNP50 BeadChip	Btau4.0	36 320	*BF*, F_{ST}	*CD79A, CXCR4, DLK1, RFX3, SEMA4A, TICAM1, TRIM21, EDNRB, KRTAP8-1*

Abbreviations: GBS, genotype-by-sequencing; WGS, whole-genome sequencing.

[a] Excluding the breeds used as reference and outgroup. See Table S2 for the names of studied and reference breeds.

cattle inheriting the SLICK1 mutation in the *PRLR* gene (rs517047387; Littlejohn et al., 2014) have greater capacity for sweating (i.e. sweat gland abundance and function) than wild-type cattle (Sosa et al., 2022). It included histological, immunohistochemical and differential gene expression analyses. The mutation was not found to be associated with the proportion of sweat glands in the skin, but with an increase in the amount of the immunoreactive forkhead transcription factor A1 (FOXA1) protein. The FOXA1 protein serves to regulate the expression of a set of genes involved in the secretory function of sweat glands (Cui et al., 2012; Sosa et al., 2022).

Interestingly, we found in African indicine a signature of selection (*XP-EHH*) on BTA3 in a region intersecting with the prolactin-releasing hormone gene (*PRLH*), which harbours a highly conserved missense variant at exon 2 (Kim, Hanotte, et al., 2017; Tijjani et al., 2022). This variant might be involved in the regulation of the expression and stimulation of the prolactin hormone (PRL) and its receptor (PRLR) (Kim, Hanotte, et al., 2017). The superior heat tolerance of zebu in comparison with taurine cattle has been attributed to the large number and size of the sweat glands close to the skin surface (Collier & Gebremedhin, 2015; Hansen, 2004; Nay & Hayman, 1956; Pan, 1963). With other skin phenotypes, e.g. shorter hair and light-coloured coats, it may explain the enhanced capability of zebu cattle to dissipate heat.

Other candidate selected regions reported in African cattle include genes involved in osmoregulation (e.g. *BHMT2*, *ITPR2*, *CFTR* and *SCNN1D*) (Taye, Lee, Caetano-Anolles, et al., 2017). The *BHMT2* has a secondary beneficial effect on maintaining water balance under hyperosmotic conditions that may occur during heat stress, thus reducing the body temperature through the amount of sweat production (Del Vesco et al., 2015). Moreover, the signatures of selection at the *ITPR2* and *ITPRIP* gene regions support more effective sweating in African zebu. Both ITPR2 and ITPRIP proteins have a role in regulating the intracellular movements of calcium ions in the sweat glands (Cheruiyot et al., 2021; Klar et al., 2014; Taye, Lee, Caetano-Anolles, et al., 2017). Similarly, proteins encoded by the *GFTR* and *SCNN1D* genes are anion channels that facilitate the transport of chlorides and sodium absorption, respectively (Lee et al., 2007; McDonagh et al., 2015).

Cattle with a light coat colour will have a reduced light absorption and an excellent reflecting ability to solar radiation, contributing to body heat temperature regulation in tropical environments (Hansen, 2004). As in many mammals, the coat colour phenotype is a complex quantitative trait expressed by the interaction between several genes controlling the ratio of two major classes of melanin (eumelanin (black–brown pigment) and phaeomelanin (red–yellow pigment); Hubbard et al., 2010). It is noteworthy that signatures of selection spanning melanophilin (*MLPH*), melanocyte stimulating hormone receptor (*MC1R*), membrane-associated transporter (*SLC45A2*) and Ras oncogene family genes (*RAB17*, *RAB37*) were detected in African cattle breeds. These genes play a direct role in melanogenesis (Cieslak et al., 2011; Dlamini et al., 2022; Taye et al., 2018; Taye, Lee, Caetano-Anolles, et al., 2017; Taye, Lee, Jeon, et al., 2017). A mutation in the *MLPH* gene in dogs, cats and rabbits is thought to disrupt the transportation of melanosomes to the outer edges of melanocytes (Philipp et al., 2005); it prevents the transfer of melanosomes into the keratinocytes, thus resulting in hairs of lighter colour (Demars et al., 2018; Ishida et al., 2006).

Moreover, variants detected at *SLC45A2* have been linked to the cream colour phenotype in horse and plumage colour variation in chickens (Gunnarsson et al., 2007; Mariat et al., 2003). The *MC1R* gene, which has essential roles in skin pigmentation, is present in a signature of positive selection region on BTA18 in Nguni cattle (Makina et al., 2014). Another region putatively associated with heat tolerance is found on BTA5. It harbours the homeobox genes, *HOXC12* and *HOXC13*, which have roles in determining skin thickness and the number of hair follicles (Makina et al., 2014; Taye, Lee, Caetano-Anolles, et al., 2017; Tijjani et al., 2022). Besides environmental selection, it may also be argued that these footprints of selection involving coat colour and coat structural properties might have been directly influenced by aesthetic and social-cultural preferences.

A number of studies have assessed the impact of high temperatures on milk production in African dairy cattle (Ekine-Dzivenu et al., 2020; Moreki & Tsopito, 2013; Nesamvuni et al., 2012), with a decline in milk production correlating to the increase in the temperature–humidity index. It has been hypothesised that heat tolerant cattle breeds will better regulate their metabolism and their energy expenditure which will in turn impact milk production (Hansen, 2004). Footprints of selection in African cattle include genes involved in metabolism and feed intake pathways (e.g. *FTO*, *IGF-1*, *ATRN*, *PRKCZ*, *ACLY*, *GHR* and *NFATC2*) (Bahbahani et al., 2015; Taye, Lee, Caetano-Anolles, et al., 2017). Contributing to the regulation of metabolic heat production, these genes may represent an adaptive response of African cattle to high-temperature environments (Taye, Lee, Caetano-Anolles, et al., 2017; Tijjani et al., 2022). Of particular interest are the candidate IGF-1, ACLY and PRKCZ proteins, which are involved in insulin metabolism, carbohydrate regulation and lipid metabolic processes that are essential for the body's energy balance (Bahbahani et al., 2015; Taye, Lee, Caetano-Anolles, et al., 2017; Tijjani et al., 2022). Also, *IGF-1* and *GHR* are good examples of genes with pleiotropic effects that may influence the expression of several phenotypes. A large body of investigations has shown the association of these genes with stature, reproduction and milk production in cattle (see, Cheruiyot et al., 2021; Ge et al., 2001; Gobikrushanth et al., 2018), which may explain the variations in body size seen in zebu cattle across different environments (DAGRIS, 2007).

Vector and parasitic disease tolerance

Trypanosomiasis tolerance

Owing to its estimated economic cost, trypanosomiasis has been ranked among the top 10 global cattle diseases impacting African cattle production (Perry et al., 2002). The disease symptoms include anaemia, weight loss and a high level of blood parasitaemia. Besides its impact on productivity, it may lead to infertility and calf abortion and even be fatal if not treated. Within the geographic distribution of its biological vector, the tsetse fly *Glossina* sp., we do find a few trypanosomiasis tolerant breeds of African taurine descent (e.g. N'Dama, Muturu, Baoule and Lagune). As such, they remain healthy and productive compared with breeds of indicine or European background (Berthier et al., 2015; Chandler, 1958; Murray et al., 1984).

Several studies have now attempted to unravel the genetic control of trypanotolerance. The pioneering work of Hanotte et al. (2003) identified 10 major QTL on several chromosomes (e.g. BTA7, BTA13, BTA17 and BTA20) linked to anaemia, parasitaemia and body weight phenotypes. Interestingly, a few of the 'tolerant' alleles originated from the Kenyan Boran. Subsequent studies have identified lists of candidate genes intersecting with these QTL as well as differentially expressed genes at various time points following trypanosomiasis infection (Noyes et al., 2011; O'Gorman et al., 2009).

Recently, positive signature of selection analysis has been performed in West African taurine breeds to identify candidate genetic controls and genes linked to trypanotolerance. A strong signal with a unique haplotype pattern was found in a candidate regulatory genomic region upstream of *CARD11* gene (Kim et al., 2020; Kim, Ka, et al., 2017). The *CARD11* is involved in the activation of protein signalling complexes for T and B lymphocyte development (Pomerantz et al., 2002). This candidate regulatory region could therefore modulate the expression of *CARD11* and contribute to African taurine tolerance and defence against trypanosomiasis infection (Kim et al., 2020; Kim, Ka, et al., 2017). Other candidate adaptive selection footprints for trypanotolerance included well-known genes associated with anaemia (e.g. *STOM*) and inflammatory (e.g. *IL1RL2*) responses (Kim, Ka, et al., 2017). The *IL1RL2* could be controlling the initial parasitaemia peak by interacting with pro-inflammatory mediators and generating a cell signalling cascade that contributes to pathogen clearance.

Muturu is a trypanotolerant indigenous African taurine breed, which is found within the humid and sub-humid agro-ecologies of Nigeria. Tijjani et al. (2019)

identified strong signals of selection on BTA23 in both Muturu and N'Dama, overlapping several candidate genes of the bovine MHC Classes I and II. They also include genes linked to innate immune response (Tripartite Motif genes – TRIMs). Moreover, a possible association was hypothesised between a shared fixed non-synonymous (missense) variant at exon 3 on the *BOLA-DQA2* gene (rs208515389) and the trypanotolerance attribute of Muturu and N'Dama. Furthermore, candidate selected regions were uncovered in Muturu at BTA11 and 24 in comparison with the N'Dama. These regions intersect with the Obg-Like ATPase 1 (*NPC1*) and Growth Factor Independent 1B (*GFI1B*) genes, which both encode proteins that are essential for the development of erythrocytes and megakaryocytes (Saleque et al., 2002). Moreover, the genome-wide *iHS* score in Muturu supports a strong signature of selection on BTA23 which overlaps with several unannotated protein-coding genes and will require further functional investigations (Tijjani et al., 2019).

In South-West Ethiopia, around the Bench Maji zone, where a high prevalence of trypanosomiasis is recorded (Gebre et al., 2022), the Sheko cattle are well known for their better trypanotolerance compared with other local neighbouring breeds (e.g. Horro, Abigar) (Lemecha et al., 2006). Following *iHS*, *Rsb* and *CLR* analyses, Mekonnen et al. (2019) reported several candidate genes (e.g. *MIGA1*, *SPAG11*, *ERN1* and *CAPG*) in the Sheko which might be associated with trypanotolerance attributes, such as anaemia, immune response and neurological dysfunction. Here, the sperm-associated antigen 11 (*SPAG11*) has an important role in immune response in cattle (Avellar et al., 2007). Indeed, differential expression of the gene transcript produces isoforms encoding defensin-like peptides, which form multimeric complexes as a defence against pathogens. These isoforms were also found to have roles in recruiting T cells and dendritic cells (Yang et al., 1999).

Besides its link to anaemia, Hypoxia-Inducible Factor-1 (HIF-1) is involved in the control of the activation and functions of immune cells (Bhandari & Nizet, 2014; Palazon et al., 2014). It has a protective effect, boosted during oxygen depletion by the expression of hypoxia-inducible factors that promote immunity profiles. Indeed, low oxygen tension renders the hypoxia-inducible factor (HIF) subunits stable and able to form transcriptional complexes that, in turn, regulate an array of genes involved in innate immune cell function and pathogen clearance (Hammond et al., 2020; Schaffer & Taylor, 2015). Therefore, it is possible that two hypoxia-associated genes (*ERN1* and *CAPG*) found within footprints of selection in the Sheko are linked to the control of trypanosome infection in this breed (Mekonnen et al., 2019). Other relevant overrepresented immunity-related biological pathways in the Sheko include T-cell chemotaxis and cell–cell adhesion, interleukin-3 (IL-3) signalling and cyclin-dependent kinase (Cdk2) pathways (Bahbahani et al., 2015; Mekonnen et al., 2019).

A few shared trypanotolerance adaptive footprints of positive selection have also been found between African taurine and some African humped cattle breeds (e.g. Kenana and Borgou) (Bahbahani, Salim, et al., 2018; Gautier et al., 2009). Considering that all African humped cattle are admixed with African taurine, it is possible that the relevant ancestral taurine alleles were favoured during past admixture events.

Tick resistance

The complexity of tick-borne disease challenges in Africa includes the ability of diverse tick species to transmit a wide range of pathogenic organisms (e.g. theileriosis, anaplasmosis and babesiosis). They represent major impediments to cattle health and production, especially in the East and Southern African regions (Phiri et al., 2010). The first study aiming to understand the genetic control of tolerance to tick infestation used a protein biomarker (serum amylase) (Ashton et al., 1968). Resistance to ticks and tick-borne diseases have been reported in African cattle breeds (e.g. Boran (African zebu), Ankole and Nguni (sanga), N'Dama (African taurine) and the composite Afrikaner) (Ali & de Castro, 1993; Mapholi, 2015; Mwai et al., 2015; Wambura et al., 1998), with the cellular immune response probably playing an important role (Mattioli et al., 2000; Mwangi et al., 1998). Machado et al.'s (2010) study suggests that such adaptation may also be season specific.

Under the assumption that tick and tick-borne disease challenges were already present in the centre(s) of origin of zebu cattle on the Asian continent, the identification of footprints of positive selection in the genome may be expected (e.g. Kim et al., 2020). In a study that included four South African cattle breeds (Afrikaner, Nguni, Bonsmara and Drakensberger), several genes belonging to the keratin family (e.g. *KRT222*, *KRT24*, *KRT25*, *KRT26* and *KRT27*) were found in Nguni within a candidate selected region on BTA19 (19: 42,896,570–42,897,840) (Makina et al., 2014). The coat's skin thickness and structure may play a role here. Collagen genes, such as *COL12A1* and *COL8A1*, were also found to be under selection in some African breeds (e.g. Kenyan Boran, Kenana, and Ogaden), which were reported to be resistant to some tick-borne diseases (Taye et al., 2018). A positive linear relationship was found between the level of coat smoothness of Nguni cattle and tick count (Marufu et al., 2011). These studies support the idea that skin structural properties may represent an important physical barrier to tick infestation and their pathogenic agents. In addition, coat colour and, henceforth, melanogenesis-associated candidate genes, may also be involved (Taye, Lee, Caetano-Anolles, et al., 2017; Verissimo et al., 2002). Indeed, it is possible that breeds with lighter-coloured hair would be less susceptible to tick infestations, as ticks would be more easily seen and picked up by predators (e.g. oxpeckers) or animals self-grooming.

Another relevant epidermis-related trait in African cattle is the control of the secretion of a lubricated and acidic film of sebum on the skin, supposedly unfavourable to tick attachment (Kongsuwan et al., 2010). The *MC5R* candidate gene found at a homozygous sweep on BTA24 in African cattle is here of interest (Taye et al., 2018). This gene regulates the sebaceous glands secretion of a complex mixture of lipids, called sebum, onto the hair follicles, contributing to the skin integrity as well as the inflammatory response following the attachment of ticks (Zhang et al., 2011).

Indeed, following the biting of an ectoparasite, several inflammatory mediators are released at high concentrations, e.g. histamine, which has been shown to influence tick salivation, feeding and attachment through the enhanced recruitment of pro-inflammatory cells into biting sites (Falcone et al., 2001). Also, *PRG3* and *ATRN* are present within a candidate selected genome region in African indicine breeds (Taye et al., 2018). *PRG3* stimulates the release of histamine, one of the important determinants of tick rejection (Falcone et al., 2001). Besides, many other immune homeostasis-related genes have been reported in African humped cattle breeds that plausibly may be linked to their adaptive responses to a wide range of infectious agents transmitted by tick bites (Kim, Hanotte, et al., 2017; Makina et al., 2014; Mattioli et al., 2000; Taye et al., 2018). In a study on East African zebu breeds, Tijjani (2019) found that several shared candidate selective sweeps overlapped with tick resistance QTL. These include a region on BTA2 that overlaps a dry-season-specific tick-resistant QTL (Machado et al., 2010).

Adaptation to high altitude

In high-altitude African environments, cattle breeds face major environmental challenges such as cold temperatures, low oxygen partial pressure, high UV solar radiation and limited feed resources (Friedrich & Wiener, 2020). Despite these challenges, we do find indigenous African cattle breeds living at high altitudes, typically above 2500 m above sea level (m.a.s.l.), e.g. Bale, Simien and Choke cattle from Ethiopia (Alkorta-Aranburu et al., 2012; Rege & Tawah, 1999; Terefe et al., 2022). Uniquely adapted to the high-altitude environments, they support the livelihoods of local human communities. Edea et al. (2013, 2014) and Terefe et al. (2022) have reported candidate positively selected regions and genes enriched in functional categories (gene ontology terms and pathways) associated with high-altitude stressors, from the analysis of DNA SNP-Chip and whole-genome sequencing data, respectively.

Several studies have compared livestock populations living at high (>2500 m.a.s.l.) and low (<1500 m.a.s.l.) altitudes in Ethiopia to understand how natural selection might have shaped the genomes of cattle living at high altitudes (Edea et al., 2013, 2014; Terefe et al., 2022; Wuletaw et al., 2011). Using a genetic differentiation-based statistical test (F_{ST}), differentiated loci were found between highland- and lowland-dwelling cattle breeds. These overlap with genes involved in the responses to hypoxia (Edea et al., 2014; Terefe et al., 2022). For example, the brain-derived neurotrophic factor (*BDNF*) gene promotes changes in pulmonary artery structure and function, which may be linked to tolerance to hypoxia and ischemia (Chen et al., 2012). In the study by Edea et al. (2014) the gene ontology analysis of the candidate genes shows that the majority of these have metabolic functions (e.g. *ATP2A3*, *MYO18B*, and *INPP4A*). A reduction in body metabolic rate might be an adaptive mechanism to the high-altitude environment characterised by a lower oxygen concentration (Riek et al., 2019). In the Sheko, HIF was one of the overrepresented pathways. It is linked to the production of red blood cells (erythropoiesis) and haemoglobin, which may overcome the reduced oxygen concentration at high altitudes (Mekonnen et al., 2019). However, Wuletaw et al. (2011) failed to find any differences in haematological parameters (red blood cell counts, haemoglobin and haematocrit values) between Ethiopian Simien cattle living above 2700 m.a.s.l. and other indigenous Ethiopian breeds living at lower altitudes, including at sea level. They therefore proposed that the indigenous cattle from the Simien mountain area are adapted to high altitudes by largely eliminating the hypoxic pulmonary vasoconstrictor response (Wuletaw et al., 2011).

DISCUSSION

We provided here an overview of the candidate genomic regions under positive selection in African cattle breeds, with a focus on environmental adaptation. Studies including African crossbred cattle with exotic breeds (e.g. Cheruiyot et al., 2018; Van der Nest et al., 2021) and/or studies addressing non-environmental adaptative traits (Nanaei et al., 2020) were excluded. Henceforth, the review was compiled from 22 studies selected using three main criteria: (i) genome-wide scanning for positive selection; (ii) genome-wide analysis using genome sequences or SNP-Chip data; and (iii) inclusion of indigenous African cattle (taurine, zebu, sanga, zenga).

Several candidate regions that were either breed specific or shared between breeds were reported in each study. The challenge is therefore to identify true signals from false positive ones, e.g. following population demographic history. Here, several approaches may be envisaged. For example, replication studies may be performed with cattle populations of different evolutionary histories but living under the same environmental challenges (e.g. Bahbahani et al., 2017). The results may also be overlapped with genome-wide association studies and transcriptome analysis studies (e.g. Aliloo et al., 2020) as well as association mapping followed by targeted differential candidate gene expression analysis (e.g. Noyes et al., 2011 and O'Gorman et al., 2009 (cattle), Wragg et al., 2012, 2013 (chicken)). Equally challenging are the definition and recording of the phenotypes shaped by natural selection as well as the identification of the key environmental selection parameters at the roots of the selection pressures. Ultimately, the identification of the causative polymorphisms followed by gene editing approaches will demonstrate the relevance of the candidate selected regions and their polymorphisms. While such information is still largely missing for African indigenous cattle, it may be expected that the search for candidate causative polymorphisms will increasingly be the focus of future studies, paving the way to genome editing in African cattle.

Environmental challenges experienced by African cattle populations are complex. The definition of an agro-ecology includes many environmental parameters such as temperature, humidity, rainfall patterns and intensity, vegetation cover, etc. These environmental parameters will be influenced by the landscape topography, which may add other selection pressures (e.g. altitude). Understanding the key natural selection pressures and their interactions is an essential step in unravelling the genetic control of local adaptation. Ecological niche modelling has been applied for the identification of the main environmental selection pressures on indigenous chicken populations of Ethiopia (Kebede et al., 2021; Vallejo-Trujillo et al., 2022). A landscape genomics approach has also been used to understand environmental adaptation in indigenous Ethiopian sheep populations (Wiener et al., 2021). Applying the same approaches to identify the key environmental stressors in African cattle may help identify the most relevant candidate positively selected regions. Interestingly, in African indigenous chicken populations, some candidate positively selected regions overlap with many genes (Gheyas et al., 2021). Here, a single mutational event (SNP or SV) (Kebede et al., 2021; Vallejo-Trujillo et al., 2022) might influence several molecular pathways and phenotypes. Supergenes have been reported in butterflies (Komata et al., 2022), as well as in wild birds (Jeong et al., 2022), where they have been shown to influence morphology, plumages and behaviour. There is also now increasing evidence that SVs may be involved in ecotype differentiation of wild species (Faria et al., 2019). Still, no supergene(s) has been reported for environmental adaptation in livestock species, including cattle.

The mosaic genome of African cattle is now well established (Kim et al., 2020), with two main ancestral backgrounds (taurine, indicine) and several waves of introductions and dispersion within and across the continent. Shaped by human and natural selection, admixed taurine × indicine African cattle are now thriving on the continent. Each genome background would have brought its own set of environmental adaptations from its centres of origin. For example, there is little doubt that the successful introgression of African indicine background into African taurine populations was favoured by the indicine adaptation to the dryland environments of the Indian subcontinent (e.g. Kim et al., 2020). However, hybridisation comes at a cost and beyond F1 unselected hybrids may have reduced fitness (Adavoudi & Pilot, 2021). Of relevance here, two recent studies have reported in African hybrid cattle populations signatures of positive selection in genome regions including genes involved in nuclear-mitochondrial DNA interactions and reproduction (Kwon et al., 2022; Ward et al., 2022).

Importantly, two cattle populations with different evolutionary histories but exposed to the same environmental challenge could respond differently to the same selection pressures. So, we should not expect the same signature of positive selection to be present in these two populations. A good example is the response to heat stress, which may include, besides adaptive cellular responses, behavioural ones (Pereira et al., 2014). Even within the same molecular pathway, the mutational response may be different (e.g. prolactin pathway) (Littlejohn et al., 2014; Sosa et al., 2022). Signals of positive selection may also include genes with pleiotropic effects, such as those involved in various metabolic pathways (e.g. Bahbahani et al., 2015). Accordingly, different selection pressures may be acting on the same genomic region and associated genes, which might explain the overlapping between candidate regions in various commercial breeds (such as Holstein and Jersey), in response to artificial selection for productivity, and in indigenous African cattle in response to natural selection.

While the focus of this review was the detection of positive selection signatures, environmental selection may also involve balancing selection. In this regard, African human populations adapted to the environmental challenge of malaria (Amambua-Ngwa et al., 2012) are a relevant example. Contrastingly, the imprints of balancing selection on the genomes of African cattle are yet to be documented. However, considering the complexity of environmental challenges, with geographic areas on the African continent witnessing seasonal extreme and unpredictable weather patterns (e.g. dry and wet seasons of varied intensity) as well as several livestock parasitic diseases, balancing and/or polygenic selection might be expected. For example, it is possible that balancing selection may have favoured genes enhancing innate immunity while polygenic selection may have acted to stabilise the mosaic taurine/indicine proportions in the genomes of African cattle following the twin challenges of climate and disease adaptation.

Last but not least, the availability of a cattle pangenome will be particularly helpful to unravel the complexity of

African cattle genome diversity. This is particularly the case considering the legacy of multiple introductions and admixture on the continent of cattle populations of taurine and indicine origin. Associated with long-read sequencing (such as, Oxford Nanopore Technology and Pacific Biosciences) information, a cattle pangenome will allow complex structural variants that are difficult to call from short-read paired-end sequencing to be unravelled in fine detail. It may also offer the opportunity to discover 'African adaptation supergene(s)', for which the discovery is constrained by the limitations of short-read sequencing and today's bioinformatics tools, as well as the European taurine bias of the bovine genome of reference.

CONCLUSION

Climatic changes are impacting the pastoral and smallholder livestock production systems of the African continent. A key question is whether livestock populations across the continent possess the resilience and tolerance to deal with future environmental extremes and changing ecological conditions. This requires efforts to characterise today's breeds and to understand their current environmental adaptations and their genetic mechanisms. Domestic cattle have successfully conquered the African continent since time immemorial. However, they are now witnessing for the first time, human-driven rapid environmental changes at an unprecedented rate. There is now an urgent need to fully characterise in finer detail at genome level the uniqueness of African cattle adaptations to inform future sustainable genetic improvement programmes and new breeding strategies for African cattle populations. Furthermore, modelling and simulation-based research that takes into account several adaptive scenarios and incorporating time-series data are needed to get deeper insights into the past and future events that have shaped or may shape the genomes of modern-day African cattle. Only then will we be able to respond to the present and future needs of the African cattle industry and the consumers of livestock products and by-products.

AUTHOR CONTRIBUTIONS

Conceptualization: S.K., O.H. and A.T. Data curation: S.K. and S.A.E.I. Writing – original draft preparation: S.K. and O.H. Review & editing: O.H., J.M.M., MK. A.A., A.T. and S.K.

ACKNOWLEDGMENTS

We acknowledge the support received from the International Livestock Research Institute, Ethiopia, the Organization for Women in Science for the Developing World, the Swedish International Development Cooperation Agency and the Faculty of Animal Production at the University of Khartoum. This work is included in the framework of Sumaya Kambal's PhD project which is funded by the above-mentioned institutes.

FUNDING INFORMATION

This work was funded in part by the International Livestock Research Institute LiveGene programme, supported by the CGIAR Research Program on Livestock (Livestock CRP), which is funded by contributors to the CGIAR Trust Fund (http://www.cgiar.org/about-us/our-funders/). We acknowledge the support of the Bill & Melinda Gates Foundation, UK aid from the UK Foreign, Commonwealth, and Development Office (FCDO) under the auspices of the Centre for Tropical Livestock Genetics and Health, established jointly by the University of Edinburgh, Scotland's Rural College, and the International Livestock Research Institute (grant agreement OPP1127286). The findings and conclusions contained within this paper are those of the authors and do not necessarily reflect the positions or policies of the Bill & Melinda Gates Foundation nor the UK Government. Open-access publishing cost was supported by the University of Nottingham (United Kingdom).

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interests.

DATA AVAILABILITY STATEMENT

Output maps in ArcGIS v.10.7.1 were performed using two climate-related datasets acquired from WorldClim 2.1, which is downloadable from https://www.worldclim.org/ (Fick & Hijmans, 2017), and Köppen–Geiger climate classification downloaded from http://www.gloh2o.org/koppen/ (Beck et al., 2018; Kottek et al., 2006).

ORCID

Sumaya Kambal https://orcid.org/0000-0003-3093-7251
Abdulfatai Tijjani https://orcid.org/0000-0002-0793-9059
Sabah A. E. Ibrahim https://orcid.org/0000-0003-2908-3658
Olivier Hanotte https://orcid.org/0000-0002-2877-4767

REFERENCES

Adavoudi, R. & Pilot, M. (2021) Consequences of hybridization in mammals: a systematic review. *Genes*, 13, 50. Available from: https://doi.org/10.3390/genes13010050

Ali, M. & de Castro, J.J. (1993) Host resistance to ticks (Acari: Ixodidae) in different breeds of cattle at Bako, Ethiopia. *Tropical Animal Health and Production*, 25, 215–222. Available from: https://doi.org/10.1007/BF02250871

Aliloo, H., Mrode, R., Okeyo, A.M. & Gibson, J.P. (2020) Ancestral haplotype mapping for GWAS and detection of signatures of selection in admixed dairy cattle of Kenya. *Frontiers in Genetics*, 11, 544. Available from: https://doi.org/10.3389/fgene.2020.00544

Alkorta-Aranburu, G., Beall, C.M., Witonsky, D.B., Gebremedhin, A., Pritchard, J.K. & Di Rienzo, A. (2012) The genetic architecture of adaptations to high altitude in Ethiopia. *PLoS Genetics*, 8, e1003110. Available from: https://doi.org/10.1371/journal.pgen.1003110

Amambua-Ngwa, A., Tetteh, K.K. & Manske, M. (2012) Population genomic scan for candidate signatures of balancing selection to guide antigen characterization in malaria parasites. *PLoS Genetics*, 8, e1002992. Available from: https://doi.org/10.1371/journal.pgen.1002992

Ashton, G.C., Seifert, G.W. & Francis, J. (1968) An association between serum amylase phenotype and tick infestation in cattle. *Australian Journal of Biological Sciences*, 21, 303–308. Available from: https://doi.org/10.1071/BI9680303

Avellar, M.C.W., Honda, L., Hamil, K.G., Radhakrishnan, Y., Yenugu, S., Grossman, G. et al. (2007) Novel aspects of the sperm-associated antigen 11 (SPAG11) gene organization and expression in cattle (*Bos taurus*). *Biology of Reproduction*, 76, 1103–1116. Available from: https://doi.org/10.1095/biolreprod.106.059626

Bahbahani, H., Afana, A. & Wragg, D. (2018) Genomic signatures of adaptive introgression and environmental adaptation in the Sheko cattle of southwest Ethiopia. *PLoS One*, 13, 1–14. Available from: https://doi.org/10.1371/journal.pone.0202479

Bahbahani, H., Clifford, H., Wragg, D., Mbole-Kariuki, M.N., Van Tassell, C., Sonstegard, T. et al. (2015) Signatures of positive selection in East African shorthorn zebu: a genome-wide single nucleotide polymorphism analysis. *Scientific Reports*, 5, 11729. Available from: https://doi.org/10.1038/srep11729

Bahbahani, H., Salim, B., Almathen, F., Enezi, F.A.L., Mwacharo, J.M. & Hanotte, O. (2018) Signatures of positive selection in African Butana and Kenana dairy zebu cattle. *PLoS One*, 13, e0190446. Available from: https://doi.org/10.1371/journal.pone.0190446

Bahbahani, H., Tijjani, A., Mukasa, C., Wragg, D., Almathen, F., Nash, O. et al. (2017) Signatures of selection for environmental adaptation and zebu × taurine hybrid fitness in East African shorthorn zebu. *Frontiers in Genetics*, 8, 68. Available from: https://doi.org/10.3389/fgene.2017.00068

Basiricò, L., Morera, P., Primi, V., Lacetera, N., Nardone, A. & Bernabucci, U. (2011) Cellular thermotolerance is associated with heat shock protein 70.1 genetic polymorphisms in Holstein lactating cows. *Cell Stress & Chaperones*, 16, 441–448. Available from: https://doi.org/10.1007/s12192-011-0257-7

Beatty, D.T., Barnes, A., Taylor, E., Pethick, D., McCarthy, M. & Maloney, S.K. (2006) Physiological responses of *Bos taurus* and *Bos indicus* cattle to prolonged, continuous heat and humidity. *Journal of Animal Science*, 84, 972–985. Available from: https://doi.org/10.2527/2006.844972x

Beck, H.E., Zimmermann, N.E., McVicar, T.R., Vergopolan, N., Berg, A. & Wood, E.F. (2018) Present and future Köppen-Geiger climate classification maps at 1-km resolution. *Scientific Data*, 5, 180214. Available from: https://doi.org/10.1038/sdata.2018.214

Belhadj Slimen, I., Najar, T., Ghram, A. & Abdrrabba, M. (2016) Heat stress effects on livestock: molecular, cellular and metabolic aspects, a review. *Journal of Animal Physiology and Animal Nutrition*, 100, 401–412. Available from: https://doi.org/10.1111/jpn.12379

Ben-Jemaa, S., Mastrangelo, S., Lee, S.H., Lee, J.H. & Boussaha, M. (2020) Genome-wide scan for selection signatures reveals novel insights into the adaptive capacity in local North African cattle. *Scientific Reports*, 10, 1–14. Available from: https://doi.org/10.1038/s41598-020-76576-3

Berthier, D., Peylhard, M., Dayo, G.K., Flori, L., Sylla, S., Bolly, S. et al. (2015) A comparison of phenotypic traits related to trypanotolerance in five West African cattle breeds highlights the value of shorthorn taurine breeds. *PLoS One*, 10, e0126498. Available from: https://doi.org/10.1371/journal.pone.0126498

Bhandari, T. & Nizet, V. (2014) Hypoxia-inducible factor (HIF) as a pharmacological target for prevention and treatment of infectious diseases. *Infectious Diseases and Therapy*, 3, 159–174. Available from: https://doi.org/10.1007/s40121-014-0030-1

Blench, R. & MacDonald, K. (1999) *The origins and development of African livestock: archaeology, genetics, linguistics and ethnography*, 1st edition, London: Routledge. Available from: https://doi.org/10.4324/9780203984239

Bovine HapMap Consortium. (2009) Genome-wide survey of SNP variation uncovers the genetic structure of cattle breeds. *Science*, 324, 528–532. Available from: https://doi.org/10.1126/science.1167936

Bradley, D.G., MacHugh, D.E., Cunningham, P. & Loftus, R.T. (1996) Mitochondrial diversity and the origins of African and European cattle. *Proceedings of the National Academy of Sciences of the United States of America*, 93, 5131–5135. Available from: https://doi.org/10.1073/pnas.93.10.5131

Bradley, D.G., MacHugh, D.E., Loftus, R.T., Sow, R.S., Hoste, C.H. & Cunningham, E.P. (1994) Zebu-taurine variation in Y chromosomal DNA: a sensitive assay for genetic introgression in West African trypanotolerant cattle populations. *Animal Genetics*, 25, 7–12. Available from: https://doi.org/10.1111/j.1365-2052.1994.tb00440.x

Bruford, M.W., Bradley, D.G. & Luikart, G. (2003) DNA markers reveal the complexity of livestock domestication. *Nature Reviews Genetics*, 4, 900–910. Available from: https://doi.org/10.1038/nrg1203

Chandler, R.L. (1958) Studies on the tolerance of N'dama cattle to trypanosomiasis. *Journal of Comparative Pathology and Therapeutics*, 68, 253–260. Available from: https://doi.org/10.1016/S0368-1742(58)80025-9

Chauhan, S.S., Rashamol, V.P., Bagath, M., Sejian, V. & Dunshea, F.R. (2021) Impacts of heat stress on immune responses and oxidative stress in farm animals and nutritional strategies for amelioration. *International Journal of Biometeorology*, 65, 1231–1244. Available from: https://doi.org/10.1007/s00484-021-02083-3

Chen, A., Xiong, L.J., Tong, Y. & Mao, M. (2012) The neuro-protective roles of BDNF in hypoxic ischemic brain injury. *Biomedical Reports*, 1, 167–176. Available from: https://doi.org/10.3892/br.2012.48

Cheruiyot, E.K., Bett, R.C., Amimo, J.O., Zhang, Y., Mrode, R. & Mujibi, F.D.N. (2018) Signatures of selection in admixed dairy cattle in Tanzania. *Frontiers in Genetics*, 9, 607. Available from: https://doi.org/10.3389/fgene.2018.00607

Cheruiyot, E.K., Haile-Mariam, M., Cocks, B.G., MacLeod, I.M., Xiang, R. & Pryce, J.E. (2021) New loci and neuronal pathways for resilience to heat stress in cattle. *Scientific Reports*, 11, 16619. Available from: https://doi.org/10.1038/s41598-021-95816-8

Cieslak, M., Reissmann, M., Hofreiter, M. & Ludwig, A. (2011) Colours of domestication. *Biological Reviews*, 86, 885–899. Available from: https://doi.org/10.1111/j.1469-185X.2011.00177.x

Collier, R.J. & Gebremedhin, K.G. (2015) Thermal biology of domestic animals. *Annual Review of Animal Biosciences*, 3, 513–532. Available from: https://doi.org/10.1146/annurev-animal-022114-110659

Cui, C.Y., Childress, V., Piao, Y., Michel, M., Johnson, A.A., Kunisada, M. et al. (2012) Forkhead transcription factor FoxA1 regulates sweat secretion through Bestrophin 2 anion channel and Na-K-Cl cotransporter 1. *Proceedings of the National Academy of Sciences of the United States of America*, 109, 1199–1203. Available from: https://doi.org/10.1073/pnas.1117213109

DAGRIS. (2007) In: Kemp, S., Mamo, Y., Asrat, B. & Dessie, T. (Eds.) *Domestic animal genetic resources information system (DAGRIS)*. Addis Ababa: International Livestock Research Institute. Available from: http://dagris.ilri.cgiar.org/ [Accessed 17 July 2023].

Davis, S.R., Spelman, R.J. & Littlejohn, M.D. (2017) Bredding and genetics symposium: breeding heat tolerant dairy cattle: the case for introgression of the “slick” prolactin receptor variant into *Bos taurus* dairy breeds. *Journal of Animal Science*, 95, 1788–1800. Available from: https://doi.org/10.2527/jas.2016.0956

Del Vesco, A.P., Gasparino, E., de Oliveira, G.D., Zancanela, V., Soares, M.A.M. & de Oliveira Neto, A.R. (2015) Effects of methionine supplementation on the expression of oxidative stress-related genes in acute heat stress-exposed broilers. *British Journal of Nutrition*, 113, 549–559. Available from: https://doi.org/10.1017/S0007114514003535

Demars, J., Iannuccelli, N., Utzeri, V.J., Auvinet, G., Riquet, J., Fontanesi, L. et al. (2018) New insights into the melanophilin (MLPH) gene affecting coat color dilution in rabbits. *Genes*, 9, 430. Available from: https://doi.org/10.3390/genes9090430

Diamond, J. (2002) Evolution, consequences and future of plant and animal domestication. *Nature*, 418, 700–707. Available from: https://doi.org/10.1038/nature01019

d'Ieteren, G.D., Authié, E., Wissocq, N. & Murray, M. (1998) Trypanotolerance, an option for sustainable livestock production in areas at risk from trypanosomosis. *International Office of Epizootics*, 17, 154–175. Available from: https://doi.org/10.20506/rst.17.1.1088

Dlamini, N.M., Dzomba, E.F., Magawana, M., Ngcamu, S. & Muchadeyi, F.C. (2022) Linkage disequilibrium, haplotype block structures, effective population size and genome-wide signatures of selection of two conservation herds of the South African Nguni cattle. *Animals*, 12, 2133. Available from: https://doi.org/10.3390/ani12162133

Dos Santos, M.M., Souza-Junior, J.B., Dantas, M.R. & de Macedo Costa, L.L. (2021) An updated review on cattle thermoregulation: physiological responses, biophysical mechanisms, and heat stress alleviation pathways. *Environmental Science and Pollution Research*, 28, 30471–30485. Available from: https://doi.org/10.1007/s11356-021-14077-0

Edea, Z., Dadi, H., Kim, S.W., Dessie, T., Lee, T., Kim, H. et al. (2013) Genetic diversity, population structure and relationships in indigenous cattle populations of Ethiopia and Korean Hanwoo breeds using SNP markers. *Frontiers in Genetics*, 4, 35. Available from: https://doi.org/10.3389/fgene.2013.00035

Edea, Z., Dadi, H., Kim, S.W., Park, J.H., Shin, G.H., Dessie, T. et al. (2014) Linkage disequilibrium and genomic scan to detect selective loci in cattle populations adapted to different ecological conditions in Ethiopia. *Journal of Animal Breeding and Genetics*, 131, 358–366. Available from: https://doi.org/10.1111/jbg.12083

Edwards, C.J., Baird, J.F. & MacHugh, D.E. (2007) Taurine and zebu admixture in Near Eastern cattle: a comparison of mitochondrial, autosomal and Y-chromosomal data. *Animal Genetics*, 38, 520–524. Available from: https://doi.org/10.1111/j.1365-2052.2007.01638.x

Ekine-Dzivenu, C.C., Mrode, R., Oyieng, E., Komwihangilo, D., Lyatuu, E., Msuta, G. et al. (2020) Evaluating the impact of heat stress as measured by temperature-humidity index (THI) on test-day milk yield of small holder dairy cattle in a sub-Sahara African climate. *Livestock Science*, 242, 104314. Available from: https://doi.org/10.1016/j.livsci.2020.104314

Epstein, H. (1971) *The origin of the domestic animals of Africa*. New York, NY: Africana Publication Corporation.

Epstein, H. & Mason, I.L. (1984) *Evolution of domesticated animals*. London: Longman.

Esri Inc. (2019) *ArcGIS (version: 10.7.1)*. Available from: www.esri.com [Accessed 9 March 2023].

Falcone, F.H., Pritchard, D.I. & Gibbs, B.F. (2001) Do basophils play a role in immunity against parasites? *Trends in Parasitology*, 17, 126–129. Available from: https://doi.org/10.1016/S1471-4922(00)01846-8

Faria, R., Chaube, P., Morales, H.E., Larsson, T., Lemmon, A.R., Lemmon, E.M. et al. (2019) Multiple chromosomal rearrangements in a hybrid zone between Littorina saxatilis ecotypes. *Molecular Ecology*, 28, 1375–1393. Available from: https://doi.org/10.1111/mec.14972

Fay, J.C. & Wu, G.I. (2000) Hitchhiking under positive Darwinian selection. *Genetics*, 155, 1405–1413. Available from: https://doi.org/10.1093/genetics/155.3.1405

Felius, M., Beerling, M.L., Buchanan, D.S., Theunissen, B., Koolmees, P.A. & Lenstra, J.A. (2014) On the history of cattle genetic resources. *Diversity*, 6, 705–750.

Fick, S.E. & Hijmans, R.J. (2017) WorldClim 2: new 1-km spatial resolution climate surfaces for global land areas. *International Journal of Climatology*, 37, 4302–4315. Available from: https://doi.org/10.1002/joc.5086

Flint, A.P. & Woolliams, J.A. (2008) Precision animal breeding. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 363, 573–590. Available from: https://doi.org/10.1098/rstb.2007.2171

Flórez Murillo, J.M., Landaeta-Hernández, A.J., Kim, E.S., Bostrom, J.R., Larson, S.A., O'Brien, A.M. et al. (2021) Three novel nonsense mutations of prolactin receptor found in heat-tolerant *Bos taurus* breeds of the Caribbean Basin. *Animal Genetics*, 52, 132–134. Available from: https://doi.org/10.1111/age.13027

Flori, L., Thevenon, S., Dayo, G.K., Senou, M., Sylla, S., Berthier, D. et al. (2014) Adaptive admixture in the West African bovine hybrid zone: insight from the Borgou population. *Molecular Ecology*, 23, 3241–3257. Available from: https://doi.org/10.1111/mec.12816

Freeman, A.R., Meghen, C.M., MacHugh, D.E., Loftus, R.T., Achukwi, M.D., Bado, A. et al. (2004) Admixture and diversity in West African cattle populations. *Molecular Ecology*, 13, 3477–3487. Available from: https://doi.org/10.1111/j.1365-294X.2004.02311.x

Friedrich, J. & Wiener, P. (2020) Selection signatures for high-altitude adaptation in ruminants. *Animal Genetics*, 51, 157–165. Available from: https://doi.org/10.1111/age.12900

Gautier, A. (1987) Prehistoric men and cattle in North Africa: a dearth of data and a surfeit of models. In: Close, A. (Ed.) *Prehistory of arid North Africa. Essays in Honor of Fred Wendorf.* Dallas, TX: Southern Methodist University Press, pp. 163–187.

Gautier, M., Flori, L., Riebler, A., Jaffrézic, F., Laloé, D., Gut, I. et al. (2009) A whole genome Bayesian scan for adaptive genetic divergence in West African cattle. *BMC Genomics*, 10, 550. Available from: https://doi.org/10.1186/1471-2164-10-550

Ge, W., Davis, M.E., Hines, H.C., Irvin, K.M. & Simmen, R.C. (2001) Association of a genetic marker with blood serum insulin-like growth factor-I concentration and growth traits in Angus cattle. *Journal of Animal Science*, 1, 1757–1762. Available from: https://doi.org/10.2527/2001.7971757x

Gebre, T., Kapitano, B., Beyene, D., Alemu, D., Beshir, A., Worku, Z. et al. (2022) The national atlas of tsetse flies and African animal trypanosomosis in Ethiopia. *Parasites & Vectors*, 15, 491. Available from: https://doi.org/10.1186/s13071-022-05617-9

Gheyas, A.A., Vallejo-Trujillo, A., Kebede, A., Lozano-Jaramillo, M., Dessie, T., Smith, J. et al. (2021) Integrated environmental and genomic analysis reveals the drivers of local adaptation in African indigenous chickens. *Molecular Biology and Evolution*, 38, 4268–4285. Available from: https://doi.org/10.1093/molbev/msab156

Gifford-Gonzalez, D. & Hanotte, O. (2011) Domesticating animals in Africa: implications of genetic and archaeological findings. *Journal of World Prehistory*, 24, 1–23. Available from: https://doi.org/10.1007/s10963-010-9042-2

Ginja, C., Guimarães, S., da Fonseca, R.R., Rasteiro, R., Rodríguez-Varela, R., Simões, L.G. et al. (2023) Iron Age genomic data from Althiburos-Tunisia renew the debate on the origins of African taurine cattle. *iScience*, 26, 107196. Available from: https://doi.org/10.1016/j.isci.2023.107196

Gobikrushanth, M., Purfield, D.C., Colazo, M.G., Wang, Z., Butler, S.T. & Ambrose, D.J. (2018) The relationship between serum insulin-like growth factor-1 (IGF-1) concentration and reproductive performance, and genome-wide associations for serum IGF-1 in Holstein cows. *Journal of Dairy Science*, 101, 9154–9167. Available from: https://doi.org/10.3168/jds.2018-14535

Grigson, C. (1991) An African origin for African cattle? – some archaeological evidence. *African Archaeological Review*, 9, 119–144. Available from: https://doi.org/10.1007/BF01117218

Gunnarsson, U., Hellström, A.R., Tixier-Boichard, M., Minvielle, F., Bed'hom, B., Ito, S. et al. (2007) Mutations in SLC45A2 cause plumage color variation in chicken and Japanese quail. *Genetics*, 175, 867–877. Available from: https://doi.org/10.1534/genetics.106.063107

Haasl, R.J. & Payseur, B.A. (2016) Fifteen years of genomewide scans for selection: trends, lessons and unaddressed genetic sources of complication. *Molecular Ecology*, 25, 5–23. Available from: https://doi.org/10.1111/mec.13339

Hammond, F.R., Lewis, A. & Elks, P.M. (2020) If it's not one thing, HIF's another: immunoregulation by hypoxia inducible factors in disease. *The FEBS Journal*, 287, 3907–3916. Available from: https://doi.org/10.1111/febs.15476

Hanotte, O., Bradley, D.G., Ochieng, J.W., Verjee, Y., Hill, E.W. & Rege, J.E. (2002) African pastoralism: genetic imprints of origins and migrations. *Science*, 296, 336–339. Available from: https://doi.org/10.1126/science.1069878

Hanotte, O., Ronin, Y., Agaba, M., Nilsson, P., Gelhaus, A., Horstmann, R. et al. (2003) Mapping of quantitative trait loci controlling trypanotolerance in a cross of tolerant West African N'Dama and susceptible East African Boran cattle. *Proceedings of the National Academy of Sciences of the United States of America*, 100, 7443–7448. Available from: https://doi.org/10.1073/pnas.1232392100

Hanotte, O., Tawah, C.L., Bradley, D.G., Okomo, M., Verjee, Y., Ochieng, J. et al. (2000) Geographic distribution and frequency of a taurine *Bos taurus* and an indicine *Bos indicus* Y specific allele amongst sub-Saharan African cattle breeds. *Molecular Ecology*, 9, 387–396. Available from: https://doi.org/10.1046/j.1365-294x.2000.00858.x

Hansen, P.J. (1990) Effects of coat colour on physiological responses to solar radiation in Holsteins. *Veterinary Record*, 127, 333–334.

Hansen, P.J. (2004) Physiological and cellular adaptations of zebu cattle to thermal stress. *Animal Reproduction Science*, 82, 349–360. Available from: https://doi.org/10.1016/j.anireprosci.2004.04.011

Helmer, D., Gourichon, L., Monchot, H., Peters, J. & Sana, S.M. (2005) Identifying early domestic cattle from Pre-Pottery Neolithic sites on the middle Euphrates using sexual dimorphism. In: Vigne, J.-D., Peters, J. & Helmer, D. (Eds.) *The first steps of animal domestication: new archaeozoological approaches*. Oxford: Oxbow Books, pp. 86–96.

Herbut, P., Angrecka, S. & Walczak, J. (2018) Environmental parameters to assessing of heat stress in dairy cattle—a review. *International Journal of Biometeorology*, 62, 2089–2097. Available from: https://doi.org/10.1007/s00484-018-1629-9

Hubbard, J.K., Uy, J.A., Hauber, M.E., Hoekstra, H.E. & Safran, R.J. (2010) Vertebrate pigmentation: from underlying genes to adaptive function. *Trends in Genetics*, 26, 231–239. Available from: https://doi.org/10.1016/j.tig.2010.02.002

Ibeagha-Awemu, E.M., Peters, S.O., Bemji, M.N., Adeleke, M.A. & Do, D.N. (2019) Leveraging available resources and stakeholder involvement for improved productivity of African livestock in the era of genomic breeding. *Frontiers in Genetics*, 10, 357. Available from: https://doi.org/10.3389/fgene.2019.00357

Ishida, Y., David, V.A., Eizirik, E., Schäffer, A.A., Neelam, B.A., Roelke, M.E. et al. (2006) A homozygous single-base deletion in MLPH causes the dilute coat color phenotype in the domestic cat. *Genomics*, 88, 698–705. Available from: https://doi.org/10.1016/j.ygeno.2006.06.006

Jang, J., Terefe, E., Kim, K., Lee, Y.H., Belay, G., Tijjani, A. et al. (2021) Population differentiated copy number variation of *Bos taurus*, *Bos indicus* and their African hybrids. *BMC Genomics*, 22, 531. Available from: https://doi.org/10.1186/s12864-021-07808-7

Jeong, H., Baran, N.M., Sun, D., Chatterjee, P., Layman, T.S., Balakrishnan, C.N. et al. (2022) Dynamic molecular evolution of a supergene with suppressed recombination in white-throated sparrows. *eLife*, 11, e79387. Available from: https://doi.org/10.7554/eLife.79387

Kambal, S., Abdelrahim, A.E., Hanotte, O., Nakao, R., Alkhaibari, A.M. & Salim, B. (2021) Demographic expansion and high level of matrilineal diversity in two populations of East African Baggara cattle. *Journal of Animal Breeding and Genetics*, 139, 161–169. Available from: https://doi.org/10.1111/jbg.12648

Kampinga, H.H. & Craig, E.A. (2010) The HSP70 chaperone machinery: J proteins as drivers of functional specificity. *Nature Reviews Molecular Cell Biology*, 11, 579–592. Available from: https://doi.org/10.1038/nrm2941

Kantanen, J., Edwards, C.J., Bradley, D.G., Viinalass, H., Thessler, S., Ivanova, Z. et al. (2009) Maternal and paternal genealogy of Eurasian taurine cattle (*Bos taurus*). *Heredity*, 103, 404–415. Available from: https://doi.org/10.1038/hdy.2009.68

Kebede, F.G., Komen, H., Dessie, T., Alemu, S.W., Hanotte, O. & Bastiaansen, J.W. (2021) Species and phenotypic distribution models reveal population differentiation in Ethiopian indigenous chickens. *Frontiers in Genetics*, 12, 723360. Available from: https://doi.org/10.3389/fgene.2021.723360

Kim, J., Hanotte, O., Mwai, O.A., Dessie, T., Bashir, S., Diallo, B. et al. (2017) The genome landscape of indigenous African cattle. *Genome Biology*, 18, 34. Available from: https://doi.org/10.1186/s13059-017-1153-y

Kim, K., Kwon, T., Dessie, T., Yoo, D.A., Mwai, O.A., Jang, J. et al. (2020) The mosaic genome of indigenous African cattle as a unique genetic resource for African pastoralism. *Nature Genetics*, 52, 1099–1110. Available from: https://doi.org/10.1038/s41588-020-0694-2

Kim, S.J., Ka, S., Ha, J.W., Kim, J., Yoo, D.A., Kim, K. et al. (2017) Cattle genome-wide analysis reveals genetic signatures in trypanotolerant N'Dama. *BMC Genomics*, 18, 371. Available from: https://doi.org/10.1186/s12864-017-3742-2

Klar, J., Hisatsune, C., Baig, S.M., Tariq, M., Johansson, A.C.V., Rasool, M. et al. (2014) Abolished InsP$_3$ R2 function inhibits sweat secretion in both humans and mice. *The Journal of Clinical Investigation*, 124, 4773–4780. Available from: https://doi.org/10.1172/JCI70720

Komata, S., Kajitani, R., Itoh, T. & Fujiwara, H. (2022) Genomic architecture and functional unit of mimicry supergene in female limited Batesian mimic Papilio butterflies. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 377, 20210198. Available from: https://doi.org/10.1098/rstb.2021.0198

Kongsuwan, K., Josh, P., Colgrave, M.L., Bagnall, N.H., Gough, J., Burns, B. et al. (2010) Activation of several key components of the epidermal differentiation pathway in cattle following infestation with the cattle tick, Rhipicephalus (Boophilus) microplus. *International Journal for Parasitology*, 40, 499–507. Available from: https://doi.org/10.1016/j.ijpara.2009.10.013

Kooverjee, B.B., Soma, P., Van Der Nest, M.A., Scholtz, M.M. & Neser, F.W. (2022) Selection signatures in South African Nguni and Bonsmara cattle populations reveal genes relating to environmental adaptation. *Frontiers in Genetics*, 13, 909012. Available from: https://doi.org/10.3389/fgene.2022.909012

Kottek, M., Grieser, J., Beck, C., Rudolf, B. & Rubel, F. (2006) World map of the Koppen-Geiger climate classification updated. *Meteorologische Zeitschrift*, 15, 259–263. Available from: https://doi.org/10.1127/0941-2948/2006/0130

Kumar, A., Singh, G., Kumar, B.S. & Meur, S.K. (2011) Modulation of antioxidant status and lipid peroxidation in erythrocyte by dietary supplementation during heat stress in buffaloes. *Livestock Science*, 138, 299–303. Available from: https://doi.org/10.1016/j.livsci.2010.12.021

Kwon, T., Kim, K., Caetano-Anolles, K., Sung, S., Cho, S., Jeong, C. et al. (2022) Mitonuclear incompatibility as a hidden driver behind the genome ancestry of African admixed cattle. *BMC Biology*, 20, 20. Available from: https://doi.org/10.1186/s12915-021-01206-x

Lee, I.H., Campbell, C.R., Cook, D.I. & Dinudom, A. (2007) Regulation of epithelial Na channels by aldosterone: role of Sgk1. *Proceedings of the Australian Physiological Society*, 38, 95–103.

Lemecha, H., Mulatu, W., Hussein, I., Rege, E., Tekle, T., Abdicho, S. et al. (2006) Response of four indigenous cattle breeds to natural tsetse and trypanosomosis challenge in the Ghibe valley of Ethiopia. *Veterinary Parasitology*, 141, 165–176. Available from: https://doi.org/10.1016/j.vetpar.2006.04.035

Lesur, J. (2022) Origin and diffusion of cattle herding in northeastern Africa. In: Wright, E. (Ed.) *Cattle and people: interdisciplinary approaches to an ancient relationship. Archaeobiology*. Columbus, GA: Lockwood Press, p. 45. Available from: https://doi.org/10.5913/archbio04.003

Littlejohn, M.D., Henty, K.M., Tiplady, K., Johnson, T., Harland, C., Lopdell, T. et al. (2014) Functionally reciprocal mutations of the prolactin signalling pathway define hairy and slick cattle. *Nature Communications*, 5, 5861. Available from: https://doi.org/10.1038/ncomms6861

Loftus, R.T., MacHugh, D.E., Bradley, D.G., Sharp, P.M. & Cunningham, P. (1994) Evidence for two independent domestications of cattle. *Proceedings of the National Academy of Sciences of the United States of America*, 91, 2757–2761. Available from: https://doi.org/10.1073/pnas.91.7.2757

Low, W.Y., Tearle, R., Liu, R., Koren, S., Rhie, A., Bickhart, D.M. et al. (2020) Haplotype-resolved genomes provide insights into structural variation and gene content in Angus and Brahman cattle. *Nature Communications*, 11, 2071. Available from: https://doi.org/10.1038/s41467-020-15848-y

Machado, M.A., Azevedo, A.L.S., Teodoro, R.L., Pires, M.A., Peixoto, M.G.C.D., de Freitas, C. et al. (2010) Genome wide scan for quantitative trait loci affecting tick resistance in cattle (*Bos taurus* × *Bos indicus*). *BMC Genomics*, 11, 280. Available from: https://doi.org/10.1186/1471-2164-11-280

MacHugh, D.E., Larson, G. & Orlando, L. (2017) Taming the past: ancient DNA and the study of animal domestication. *Annual Review of Animal Biosciences*, 5, 329–351. Available from: https://doi.org/10.1146/annurev-animal-022516-022747

MacHugh, D.E., Shriver, M.D., Loftus, R.T., Cunningham, P. & Bradley, D.G. (1997) Microsatellite DNA variation and the evolution, domestication and phylogeography of taurine and zebu cattle (*Bos taurus* and *Bos indicus*). *Genetics*, 146, 1071–1086. Available from: https://doi.org/10.1093/genetics/146.3.1071

Makina, S.O., Muchadeyi, F.C., van Marle-Köster, E., MacNeil, M.D. & Maiwashe, A. (2014) Genetic diversity and population structure among six cattle breeds in South Africa using a whole genome SNP panel. *Frontiers in Genetics*, 5, 333. Available from: https://doi.org/10.3389/fgene.2014.00333

Mapholi, N.O. (2015) *Exploring genetic architecture of tick resistance in South African Nguni cattle*. Dissertation, Stellenbosch University.

Mariat, D., Taourit, S. & Guérin, G. (2003) A mutation in the MATP gene causes the cream coat colour in the horse. *Genetics Selection Evolution*, 35, 119–133. Available from: https://doi.org/10.1051/gse:2002039

Marufu, M.C., Qokweni, L., Chimonyo, M. & Dzama, K. (2011) Relationships between tick counts and coat characteristics in Nguni and Bonsmara cattle reared on semiarid rangelands in South Africa. *Ticks and Tick-Borne Diseases*, 2, 172–177. Available from: https://doi.org/10.1016/j.ttbdis.2011.07.001

Mattioli, R.C., Pandey, V.S., Murray, M. & Fitzpatrick, J.L. (2000) Immunogenetic influences on tick resistance in African cattle with particular reference to trypanotolerant N'Dama (*Bos taurus*) and trypanosusceptible Gobra zebu (*Bos indicus*) cattle. *Acta Tropica*, 75, 263–277. Available from: https://doi.org/10.1016/S0001-706X(00)00063-2

Mauki, D.H., Adeola, A.C., Ng'ang'a, S.I., Tijjani, A., Akanbi, I.M., Sanke, O.J. et al. (2021) Genetic variation of Nigerian cattle inferred from maternal and paternal genetic markers. *PeerJ*, 9, e10607. Available from: https://doi.org/10.7717/peerj.10607

Mauki, D.H., Tijjani, A., Ma, C., Ng'ang'a, S.I., Mark, A.I., Sanke, O.J. et al. (2022) Genome-wide investigations reveal the population structure and selection signatures of Nigerian cattle adaptation in the sub-Saharan tropics. *BMC Genomics*, 23, 1–4. Available from: https://doi.org/10.1186/s12864-022-08512-w

McDonagh, E.M., Clancy, J.P., Altman, R.B. & Klein, T.E. (2015) PharmGKB summary: very important pharmacogene information for CFTR. *Pharmacogenetics and Genomics*, 25, 149–156. Available from: https://doi.org/10.1097/FPC.0000000000000112

McTavish, E.J., Decker, J.E., Schnabel, R.D., Taylor, J.F. & Hillis, D.M. (2013) New World cattle show ancestry from multiple independent domestication events. *Proceedings of the National Academy of Sciences of the United States of America*, 110, 1398–1406. Available from: https://doi.org/10.1073/pnas.130336711

Mekonnen, Y.A., Gültas, M., Effa, K., Hanotte, O. & Schmitt, A.O. (2019) Identification of candidate signature genes and key regulators associated with trypanotolerance in the Sheko breed. *Frontiers in Genetics*, 10, 1095. Available from: https://doi.org/10.3389/fgene.2019.01095

Moreki, J.C. & Tsopito, C.M. (2013) Effect of climate change on dairy production in Botswana and its suitable mitigation strategies. *Online Journal of Animal and Feed Research*, 3, 216–221.

Murray, M., Trail, J.C., Davis, C.E. & Black, S.J. (1984) Genetic resistance to African trypanosomiasis. *The Journal of Infectious Diseases*, 149, 311–319. Available from: https://doi.org/10.1093/infdis/149.3.311

Mwai, O., Hanotte, O., Kwon, Y.J. & Cho, S. (2015) African indigenous cattle: unique genetic resources in a rapidly changing world. *Asian-Australasian Journal of Animal Sciences*, 28, 911–921. Available from: https://doi.org/10.5713/ajas.15.0002R

Mwangi, E.K., Stevenson, P., Ndung'u, J.M., Stear, M.J., Reid, S.W., Gettinby, G. et al. (1998) Studies on host resistance to tick infestations among Trypanotolerant *Bos indicus* cattle breeds in East Africa. *Annals of the New York Academy of Sciences*, 849, 195–208. Available from: https://doi.org/10.1111/j.1749-6632.1998.tb11049.x

Nanaei, H.A., Qanatqestani, M.D. & Esmailizadeh, A. (2020) Whole-genome resequencing reveals selection signatures associated with milk production traits in African Kenana dairy zebu cattle. *Genomics*, 112, 880–885. Available from: https://doi.org/10.1016/j.ygeno.2019.06.002

Nay, T. & Hayman, R.H. (1956) Sweat glands in zebu (*Bos indicus* L.) and European (*B. taurus* L.) cattle. I. Size of individual glands, the denseness of their population, and their depth below the skin surface. *Australian Journal of Agricultural Research*, 7, 482–492. Available from: https://doi.org/10.1071/AR9560482

Nesamvuni, E., Lekalakala, R., Norris, D. & Ngambi, J.W. (2012) Effects of climate change on dairy cattle, South Africa. *African Journal of Agricultural Research*, 7, 3867–3872. Available from: https://doi.org/10.5897/AJAR11.1468

Nielsen, R., Williamson, S., Kim, Y., Hubisz, M.J., Clark, A.G. & Bustamante, C. (2005) Genomic scans for selective sweeps using SNP data. *Genome Research*, 15, 1566–1575. Available from: https://doi.org/10.1101/gr.4252305

Noyes, H., Brass, A., Obara, I., Anderson, S., Archibald, A.L., Bradley, D.G. et al. (2011) Genetic and expression analysis of cattle identifies candidate genes in pathways responding to *Trypanosoma congolense* infection. *Proceedings of the National Academy of Sciences of the United States of America*, 108, 9304–9309. Available from: https://doi.org/10.1073/pnas.1013486108

O'Gorman, G.M., Park, S.D., Hill, E.W., Meade, K.G., Coussens, P.M., Agaba, M. et al. (2009) Transcriptional profiling of cattle infected with *Trypanosoma congolense* highlights gene expression signatures underlying trypanotolerance and trypanosusceptibility. *BMC Genomics*, 10, 1–21. Available from: https://doi.org/10.1186/1471-2164-10-207

Oleksyk, T.K., Smith, M.W. & O'Brien, S.J. (2010) Genome-wide scans for footprints of natural selection. *Philosophical Transactions of* *the Royal Society B: Biological Sciences*, 365, 185–205. Available from: https://doi.org/10.1098/rstb.2009.0219

Orenge, C., Munga, L., Kimwele, C., Kemp, S., Korol, A., Gibson, J. et al. (2011) Expression of trypanotolerance in N'Dama × Boran crosses under field challenge in relation to N'Dama genome content. *BMC Proceedings*, 5, 23. Available from: https://doi.org/10.1186/1753-6561-5-S4-S23

Palazon, A., Goldrath, A.W., Nizet, V. & Johnson, R.S. (2014) HIF transcription factors, inflammation, and immunity. *Immunity*, 41, 518–528. Available from: https://doi.org/10.1016/j.immuni.2014.09.008

Pan, Y.S. (1963) Quantitative and morphological variation of sweat glands, skin thickness, and skin shrinkage over various body regions of Sahiwal Zebu and Jersey cattle. *Australian Journal of Agricultural Research*, 14, 424–437. Available from: https://doi.org/10.1071/AR9630424

Pandey, N., Kataria, N., Kataria, A.K., Joshi, A., Sankhala, L.N., Asopa, S. et al. (2014) Extreme ambiences vis-à-vis endogenous antioxidants of Marwari goat from arid tracts in India. *Extreme Life, Biospeology and Astrobiology*, 4, 29–33.

Payne, W.J.A. (1991) Domestication: a forward step in civilization. In: Hickman, C.G. (Ed.) *Cattle genetic resources*. Amsterdam: Elsevier, pp. 51–72.

Pereira, A.M., Titto, E.L., Infante, P., Titto, C.G., Geraldo, A.M., Alves, A. et al. (2014) Evaporative heat loss in *Bos taurus*: do different cattle breeds cope with heat stress in the same way? *Journal of Thermal Biology*, 45, 87–95. Available from: https://doi.org/10.1016/j.jtherbio.2014.08.004

Pérez-Pardal, L., Royo, L.J., Beja-Pereira, A., Curik, I., Traoré, A., Fernández, I. et al. (2010) Y-specific microsatellites reveal an African subfamily in taurine (*Bos taurus*) cattle. *Animal Genetics*, 41, 232–241. Available from: https://doi.org/10.1111/j.1365-2052.2009.01988.x

Perry, B.D., Randolph, T.F., McDermott, J.J., Sons, K.R. & Thornton, P.K. (2002) *Investing in animal health research to alleviate poverty*. Nairobi, Kenya: International Livestock Research Institute (ILRI), p. 148.

Peter, B.M., Huerta-Sanchez, E. & Nielsen, R. (2012) Distinguishing between selective sweeps from standing variation and from a de novo mutation. *PLoS Genetics*, 8, 1003011. Available from: https://doi.org/10.1371/journal.pgen.1003011

Peters, M.D.J., Godfrey, C., McInerney, P., Munn, Z., Tricco, A.C. & Khalil, H. (2020) Scoping reviews. In: Aromataris, E. & Munn, Z. (Eds.) *JBI manual for evidence sythesis*. Pennsylvania, USA: Lippincott Williams & Wilkins. Available from: https://doi.org/10.46658/JBIMES-20-01

Philipp, U., Hamann, H., Mecklenburg, L., Nishino, S., Mignot, E., Günzel-Apel, A.R. et al. (2005) Polymorphisms within the canine MLPH gene are associated with dilute coat color in dogs. *BMC Genetics*, 6, 1–5. Available from: https://doi.org/10.1186/1471-2156-6-34

Phiri, B.J., Benschop, J. & French, N.P. (2010) Systematic review of causes and factors associated with morbidity and mortality on smallholder dairy farms in Eastern and Southern Africa. *Preventive Veterinary Medicine*, 94, 1–8. Available from: https://doi.org/10.1016/j.prevetmed.2010.01.012

Pitt, D., Sevane, N., Nicolazzi, E.L., MacHugh, D.E., Park, S.D., Colli, L. et al. (2019) Domestication of cattle: two or three events? *Evolutionary Applications*, 12, 123–136. Available from: https://doi.org/10.1111/eva.12674

Pomerantz, J.L., Denny, E.M. & Baltimore, D. (2002) CARD11 mediates factor-specific activation of NF-κB by the T cell receptor complex. *The EMBO Journal*, 21, 5184–5194. Available from: https://doi.org/10.1093/emboj/cdf505

Porto-Neto, L.R., Bickhart, D.M., Landaeta-Hernandez, A.J., Utsunomiya, Y.T., Pagan, M., Jimenez, E. et al. (2018) Convergent evolution of slick coat in cattle through truncation mutations in the prolactin receptor. *Frontiers in Genetics*, 9, 57. Available from: https://doi.org/10.3389/fgene.2018.00057

Qanbari, S. & Simianer, H. (2014) Mapping signatures of positive selection in the genome of livestock. *Livestock Science*, 166, 133–143. Available from: https://doi.org/10.1016/j.livsci.2014.05.003

Randhawa, I.A., Khatkar, M.S., Thomson, P.C. & Raadsma, H.W. (2016) A meta-assembly of selection signatures in cattle. *PLoS One*, 11, e0153013. Available from: https://doi.org/10.1371/journal.pone.0153013

Rege, J.E. (1999) The state of African cattle genetic resources I. Classification framework and identification of threatened and extinct breeds. *Animal Genetic Resources*, 25, 1–25. Available from: https://doi.org/10.1017/S1014233900003448

Rege, J.E. & Tawah, C.L. (1999) The state of African cattle genetic resources II. Geographical distribution, characteristics and uses of present-day breeds and strains. *Animal Genetic Resources*, 26, 1–25. Available from: https://doi.org/10.1017/S1014233900001152

Rege, J.E.O., Yapi-Gnaoré, C.V. & Tawah, C.L. (1996) The indigenous domestic ruminant genetic resources of Africa. In: Meissner, H.H. (Ed.) *Food security in Africa. Chellenges, opportunities and target for animal production*. Proceedings 2nd Africa conference on animal agriculture. South Africa: South African Society of Animal Science, pp. 57–75.

Riek, A., Stölzl, A., Marquina Bernedo, R., Ruf, T., Arnold, W., Hambly, C. et al. (2019) Energy expenditure and body temperature variations in llamas living in the high Andes of Peru. *Scientific Reports*, 9, 4037. Available from: https://doi.org/10.1038/s41598-019-40576-9

Saleque, S., Cameron, S. & Orkin, S.H. (2002) The zinc-finger proto-oncogene Gfi-1b is essential for development of the erythroid and megakaryocytic lineages. *Genes & Development*, 16, 301–306. Available from: https://doi.org/10.1101/gad.959102

Saravanan, K.A., Panigrahi, M., Kumar, H., Bhushan, B., Dutt, T. & Mishra, B.P. (2020) Selection signatures in livestock genome: a review of concepts, approaches and applications. *Livestock Science*, 241, 104257. Available from: https://doi.org/10.1016/j.livsci.2020.104257

Schaffer, K. & Taylor, C.T. (2015) The impact of hypoxia on bacterial infection. *FEBS Journal*, 282, 2260–2266. Available from: https://doi.org/10.1111/febs.13270

Sosa, F., Carmickle, A.T., Oliveira, L.J., Sagheer, M., Saleem, M., Yu, F.H. et al. (2022) Effects of the bovine SLICK1 mutation in PRLR on sweat gland area, FOXA1 abundance, and global gene expression in skin. *Journal of Dairy Science*, 105, 9206–9215. Available from: https://doi.org/10.3168/jds.2022-22272

Talenti, A., Powell, J., Hemmink, J.D., Cook, E.A.J., Wragg, D., Jayaraman, S. et al. (2022) A cattle graph genome incorporating global breed diversity. *Nature Communications*, 13, 910. Available from: https://doi.org/10.1038/s41467-022-28605-0

Taye, M., Lee, W., Caetano-Anolles, K., Dessie, T., Cho, S., Jong Oh, S. et al. (2018) Exploring the genomes of East African Indicine cattle breeds reveals signature of selection for tropical environmental adaptation traits. *Cogent Food & Agriculture*, 4, 1552552. Available from: https://doi.org/10.1080/23311932.2018.1552552

Taye, M., Lee, W., Caetano-Anolles, K., Dessie, T., Hanotte, O., Mwai, O.A. et al. (2017) Whole genome detection of signature of positive selection in African cattle reveals selection for thermotolerance. *Animal Science Journal*, 88, 1889–1901. Available from: https://doi.org/10.1111/asj.12851

Taye, M., Lee, W., Jeon, S., Yoon, J., Dessie, T., Hanotte, O. et al. (2017) Exploring evidence of positive selection signatures in cattle breeds selected for different traits. *Mammalian Genome*, 28, 528–541. Available from: https://doi.org/10.1007/s00335-017-9715-6

Terefe, E., Belay, G., Han, J., Hanotte, O. & Tijjani, A. (2022) Genomic adaptation of Ethiopian indigenous cattle to high altitude. *Frontiers in Genetics*, 13, 960234. Available from: https://doi.org/10.3389/fgene.2022.960234

Tijjani, A. (2019) Genome diversity and adaptation of African taurine and zebu cattle. Doctoral dissertation, University of Nottingham.

Tijjani, A., Salim, B., da Silva, M.V., Eltahir, H.A., Musa, T.H., Marshall, K. et al. (2022) Genomic signatures for drylands adaptation at gene-rich regions in African zebu cattle. *Genomics*, 114, 110423. Available from: https://doi.org/10.1016/j.ygeno.2022.110423

Tijjani, A., Utsunomiya, Y.T., Ezekwe, A.G., Nashiru, O. & Hanotte, O. (2019) Genome sequence analysis reveals selection signatures in endangered trypanotolerant West African Muturu cattle. *Frontiers in Genetics*, 10, 442. Available from: https://doi.org/10.3389/fgene.2019.00442

Utsunomiya, Y.T., Pérez O'Brien, A.M., Sonstegard, T.S., Sölkner, J. & Garcia, J.F. (2015) Genomic data as the "hitchhiker's guide" to cattle adaptation: tracking the milestones of past selection in the bovine genome. *Frontiers in Genetics*, 6, 36. Available from: https://doi.org/10.3389/fgene.2015.00036

Vallejo-Trujillo, A., Kebede, A., Lozano-Jaramillo, M., Dessie, T., Smith, J., Hanotte, O. et al. (2022) Ecological niche modeling for delineating livestock ecotypes and exploring environmental genomic adaptation: the example of Ethiopian village chicken. *Frontiers in Ecology and Evolution*, 10, 866587. Available from: https://doi.org/10.3389/fevo.2022.866587

Van der Nest, M.A., Hlongwane, N., Hadebe, K., Chan, W.Y., van der Merwe, N.A., De Vos, L. et al. (2021) Breed ancestry, divergence, admixture, and selection patterns of the Simbra crossbreed. *Frontiers in Genetics*, 11, 1–13. Available from: https://doi.org/10.3389/fgene.2020.608650

Verdugo, M.P., Mullin, V.E., Scheu, A., Mattiangeli, V., Daly, K.G., Maisano Delser, P. et al. (2019) Ancient cattle genomics, origins, and rapid turnover in the Fertile Crescent. *Science*, 365, 173–176. Available from: https://doi.org/10.1126/science.aav1002

Verissimo, C.J., Nicolau, C.V., Cardoso, V.L. & Pinheiro, M.G. (2002) Haircoat characteristics and tick infestation on gyr (zebu) and crossbred (holdstein x gyr) cattle. *Archivos de Zootecnia*, 51, 389–392.

Wambura, P.N., Gwakisa, P.S., Silayo, R.S. & Rugaimukamu, E.A. (1998) Breed-associated resistance to tick infestation in *Bos indicus* and their crosses with *Bos taurus*. *Veterinary Parasitology*, 77, 63–70. Available from: https://doi.org/10.1016/S0304-4017(97)00229-X

Ward, J.A., McHugo, G.P., Dover, M.J., Hall, T.J., Ismael Ng'ang'a, S., Sonstegard, T.S. et al. (2022) Genome-wide local ancestry and evidence for mitonuclear coadaptation in African hybrid cattle populations. *iScience*, 25, 104672. Available from: https://doi.org/10.1016/j.isci.2022.104672

Weigand, H. & Leese, F. (2018) Detecting signatures of positive selection in non-model species using genomic data. *Zoological Journal of the Linnean Society*, 184, 528–583. Available from: https://doi.org/10.1093/zoolinnean/zly007

Wiener, P., Robert, C., Ahbara, A., Salavati, M., Abebe, A., Kebede, A. et al. (2021) Whole-genome sequence data suggest environmental adaptation of Ethiopian sheep populations. *Genome Biology and Evolution*, 13, evab014. Available from: https://doi.org/10.1093/gbe/evab014

Wragg, D., Mwacharo, J.M., Alcalde, J.A., Hocking, P.M. & Hanotte, O. (2012) Analysis of genome-wide structure, diversity and fine mapping of Mendelian traits in traditional and village chickens. *Heredity*, 109, 6–18. Available from: https://doi.org/10.1038/hdy.2012.9

Wragg, D., Mwacharo, J.M., Alcalde, J.A., Wang, C., Han, J.L., Gongora, J. et al. (2013) Endogenous retrovirus EAV-HP linked to blue egg phenotype in Mapuche fowl. *PLoS One*, 8, e71393. Available from: https://doi.org/10.1371/journal.pone.0071393

Wu, D.D., Ding, X.D., Wang, S., Wójcik, J.M., Zhang, Y., Tokarska, M. et al. (2018) Pervasive introgression facilitated domestication and adaptation in the *Bos* species complex. *Nature Ecology & Evolution*, 2, 1139–1145. Available from: https://doi.org/10.1038/s41559-018-0562-y

Wuletaw, Z., Wurzinger, M., Holt, T., Dessie, T. & Sölkner, J. (2011) Assessment of physiological adaptation of indigenous and crossbred cattle to hypoxic environment in Ethiopia. *Livestock Science*, 138, 96–104. Available from: https://doi.org/10.1016/j.livsci.2010.12.005

Yang, D., Chertov, O.B., Bykovskaia, S.N., Chen, Q., Buffo, M.J., Shogan, J. et al. (1999) β-Defensins: linking innate and adaptive immunity through dendritic and T cell CCR6. *Science*, 286, 525–528. Available from: https://doi.org/10.1126/science.286.5439.525

Zeuner, F.E. (1963) A history of domesticated animals. *Antiquity*, 38, 80–88. Available from: https://doi.org/10.1017/S0003598X00068952

Zhang, L., Li, W.H., Anthonavage, M., Pappas, A., Rossetti, D., Cavender, D. et al. (2011) Melanocortin-5 receptor and sebogenesis. *European Journal of Pharmacology*, 660, 202–206. Available from: https://doi.org/10.1016/j.ejphar.2010.10.100

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Kambal, S., Tijjani, A., Ibrahim, S.A.E., Ahmed, M.-K., Mwacharo, J.M. & Hanotte, O. (2023) Candidate signatures of positive selection for environmental adaptation in indigenous African cattle: A review. *Animal Genetics*, 00, 1–20. Available from: https://doi.org/10.1111/age.13353