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Genome-wide analysis of the genetic diversity of native sheep breeds and determination of potential selection signatures for climate change adaptation

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1. INTRODUCTION

1.1. Background information

Native livestock breeds represent vital domestic livestock genetic resources for long-term food security, but many breeds have suffered extensive population declines and are now at risk of being extinct (HOFFMANN, 2013; KANTANEN et al., 2000). Native breeds are currently, and are expected to remain, constrained by their poor quantitative production in the context of intensive farming. However, their inherent traits such as natural productivity, resilience, and ability to meet their nutritional needs independently make them comparatively straightforward to sustain. Consequently, incorporating local breed farming for grazing purposes can be seamlessly integrated with other economic endeavors for landowners and/or farm managers. Raising knowledge about these breeds has the potential to enable a broader range of individuals, such as both full-time and part-time farmers, to get and preserve local breeds. This, in turn, would facilitate the preservation of cultural landscapes, which are the result of the interplay between human activities and the natural environment, in a more economically efficient way. According to DAVID et al. (2011), the use of gene combinations in indigenous breeds may contribute to the advancement of sustainable intensification, which is now a significant production objective. Their potential for high resistance to disease (COLTMAN et al., 2001) also merits further investigation.

Since the Neolithic onwards, sheep (*Ovis aries*) has become an essential livestock in human production. They not only provide milk and meat for humans, but fur is an important product as well. Their tolerance to extensive management systems makes them critical in both developing and developed countries' economies (CONSORTIUM et al., 2020). Due to their global distribution and diverse array of phenotypic variations, native sheep breeds are highly suitable for research aimed at exploring genetic strategies to mitigate the adverse impacts of climate change on livestock production. In this research, the terms "native," "indigenous," and "autochthonous" will be used interchangeably to refer to sheep breeds of local origin.

1.2. Justification

Globally, indigenous sheep breeds have seen significant reductions in population size and are now facing a state of vulnerability. The understanding of native breed's genetic architecture and their genomic response to local environmental selection pressures remains limited, however, they (native breeds) offer an opportunity to potentially uncover genomic areas that are more valuable for adapting to climate change. Many studies have been conducted to explore the relationship between the genetic and phenotypic diversity of indigenous animal breeds and their ability to contribute to food security. The majority of these research works were conducted within limited geographical bounds, so limiting their ability to provide a full grasp of the subject matter on a global scale. Hence, the existing body of information pertaining to the genetic diversity, interrelationships, and adaptability of indigenous sheep breeds is fairly limited. There is a possibility that these breeds possess significant genetic variations that enable them to adapt to climate change, and these variations might potentially be incorporated into commercial breeds using genomic selection technology. Therefore, it is imperative to enhance the conservation efforts of endangered indigenous breeds and explore their adaptive characteristics via the use of contemporary genomic and bioinformatics methodologies.

The present doctoral research involves a comprehensive examination of the genomic architecture of indigenous sheep breeds that may have developed adaptations to diverse climatic zones. Furthermore, this study examines the current signatures of selection for climate change adaptability and the bio-climatic variables influencing the adaptation of sheep breeds to climatic change.

The results of this research are expected to be used by sheep breeders in order to optimize the utilization of gene-environment interaction for enhanced productivity and adaptation to the specific local environment. Moreover, the findings of this research will provide a chance to enhance the development of a breeding program aimed at maintaining genetic diversity, enhancing animal welfare and ecological management. The research will provide guidance to organizations involved in the conservation of sheep genetic resources, namely in the planning and prioritization of resources for the management and conservation of vital sheep genetic resources.

Therefore, to provide a comprehensive understanding of the genomic structure of native sheep breeds, this study aimed to achieve the following four specific objectives:

i. To perform genetic characterization to determine within and between populations genetic diversity.

ii. To detect patterns of run of homozygosity (ROH) and genomic based inbreeding coefficient (Froh) per breed.
iii. To identify signatures of selection underpinning adaptation in different climatic regions.
iv. To perform gene x environment association (GEA) to explore the complex interplay between genes and climatic variables in shaping adaptation traits.

2. LITERATURE REVIEW

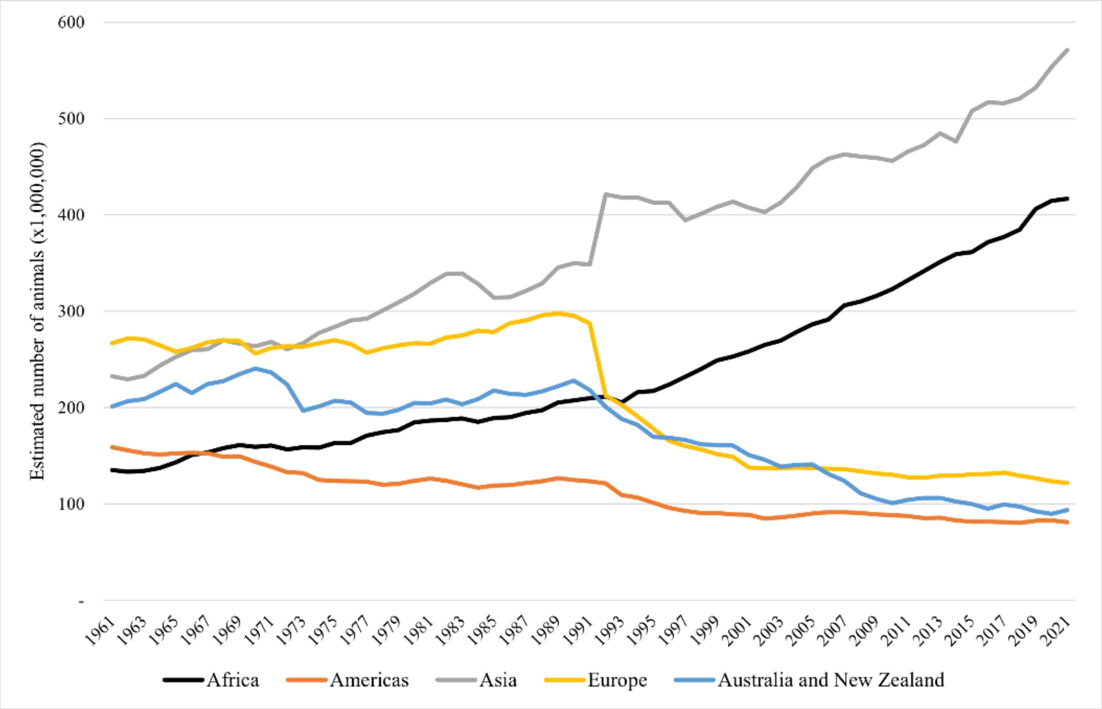
2.1. Economic importance of sheep

Sheep have been a part of domestic animals since they were first domesticated. Their contribution to global food security can be measured in terms of productivity, economic importance, and their ability to withstand the effects of climate change. The livestock sector (which includes sheep) supports the livelihoods of over 1.7 billion people, with women accounting for 70% of those employed in it (FAO, 2020). Sheep are also considered ideal livestock species because of their ability to deliver increasingly valued animal proteins to developing countries. They provide a variety of products to humanity, including meat, fur, and milk, to the local populations that raise them for subsistence or commercial purposes (DEVENDRA, 1980). Sheep productivity has not reached its potential despite playing an important role in the global economy (SKAPETAS and KALAITZIDOU, 2017). This could possibly be due to inadequate utilization of their gene x environment interaction (the expression of a trait that results from the interaction of genes and the environment). Some traits are highly impacted by genetics, while others are influenced by the environment; nonetheless, the majority of traits are regulated by one or more genes that interact with the environment in a complex manner (WAKCHAURE et al., 2016).

Sheep farming is currently regarded as the main meat sector in the future due to its efficiency and adaptability in production. More than half of the world's sheep population is said to live in arid areas, demonstrating their flexibility and future suitability to rising temperatures. Sheep grazing in ranches, wastelands, and pasturelands is thought to be one of the most important ways to prevent global warming since they increase the fertility of the grazing ground. In most regions of the world except Australia and New Zealand, native sheep breeds dominate the sheep populations. This could be due to their adaptation to the local environments; however, these autochthonous sheep genes are now endangered due to haphazard crossbreeding (GOWANE et al., 2017).

According to data from FAOSTAT (2023, https://www.fao.org/faostat, accessed on 17th August 2023) the world sheep population was estimated to reach 1.28 billion head in 2021, up from 994 million head in 1961, a 29% increase. The current highest sheep producer regions are Asia and Africa; nevertheless, it is worth mentioning that these regions are dominated by developing countries, showing that sheep are essential in these areas. The populations of sheep in the Americas, Europe, and Oceania are experiencing a decline, but in Asia and Africa, there is an observed increase in sheep numbers (see Figure 1). Table 1 displays the regional variations in the rate of change of sheep population from 2018 to 2021. During the aforementioned time frame, Asia and Africa showed population increase, whereas Europe, Australia, New Zealand, and the Americas had the most notable population drop.

Figure 1: The trend of global sheep populations by regions



Data source (FAOSTAT- https://www.fao.org/faostat/en)

Table 1*:* Global population change of sheep population between the years 2018 and 2021.

Region	Sheep population (heads)		% Change
	2021	2018	
Africa	416,965,074	383 954 675	8.5
Americas	81,199,044	82 421 347	-1.5
Asia	571,212,730	514 986 624	10.9
Australia and New Zealand	93,780,291	97 363 065	-3.7
Europe	121,651,744	130 703 609	-6.9
World	1,284,850,926	1 209 467 079	9.8

Data source (FAOSTAT- https://www.fao.org/faostat)

According to FAO-DAD-IS (2020), 8.43 percent of native sheep breeds are already extinct, 8.51 percent are highly endangered, and 11.21 percent are endangered. The reason for risk status, on the other hand, is not well understood, albeit it may be linked to climate change events that have occurred since domestication. In Africa, the risk status of 71 native sheep breeds is unknown. Many African countries may lack the capacity to assess the state of the breeds. Six breeds, however, are designated as endangered. In Asia, there are 203 breeds with an unknown risk status and 6 that are endangered. In Europe, however, 182 breeds are unknown, 115 are endangered, and 92 are extinct (FAO-DAD-IS, 2020).

2.2. The origin and domestication of sheep

Evidence from various archeological studies suggests that domestic sheep descended from the wild Asian mouflon and their domestication happened more than 11,000 before the common era (BCE) in Southwest Asia including the present Turkey, Iran, and some Arabic countries, formally referred to as fertile crescent at the Zagro Mountain of Iran (AL-ARAIMI et al., 2017; CONSORTIUM et al., 2020; EYDIVANDI et al., 2020a; LARSON and BURGER, 2013). At least two separate domestication processes are believed to have occurred, resulting in the rise of haplogroup A and B, which are the most common sheep haplogroups worldwide (PEDROSA et al., 2005; RESENDE et al., 2016). Haplogroup A populations are alleged to be descended from Asiatic mouflons (*Ovis orientalis*), and they are more common in Asian countries (MEADOWS et al., 2006; RESENDE et al., 2016). Haplogroup B haplotypes, on the other hand, are more common in Europe and descended from the European mouflon (*Ovis aries musimon*; PEDROSA et al., 2005; RESENDE et al., 2016; TAPIO et al., 2006). Is it possible that European mouflons descended from Asian mouflons before dispersing and spreading independently throughout Europe? Recent studies have averred that European mouflon are pre-domesticated (feral) forms of Asian mouflons native to Sardinia and Corsica Islands in the Mediterranean Sea (MEADOWS et al., 2006; PEDROSA et al., 2005). Other sheep haplogroups (clades), from C to E, have been discovered through further research. Clade A is said to have been discovered in China (RESENDE et al., 2016) while clades D and E in the Turkey although they seem to be rare (PEDROSA et al., 2005). The emergence of different sheep clades could be as a result of post-domestication selection pressure (natural and artificial) resulting in the phenotypic and genotypic variations, giving rise to breeds with unique quantitative traits and morphological characteristics e.g., meat production traits, wool traits, coat color, presence or absence of horns, body length , tail size etc. (MEADOWS et al., 2006).

The origin, genetic diversity, and domestication of domestic animals have been widely explored utilizing mitochondria DNA (mtDNA). Indeed, mtDNA is evolutionarily well conserved for the identification of maternal evolutionary links with wild relatives, while still being sufficiently diverse to capture genetic structure (HER et al., 2022).

2.2.1. The origin and dispersal of European sheep

Sheep from Southwest Asia dispersed to and inhabited various regions mainly following human migratory routes (PETERS et al., 1999). They dispersed to Europe via two major routes: crossing the Mediterranean Sea to large islands like Cyprus and Sardinia and through the valley of Danube across the continental Europe (TRESSET and VIGNE, 2007). Sheep were originally raised primarily for meat, but, shortly after domestication selection for other products e.g., fleece exploitation became apparent (CHESSA et al., 2009; VILA and HELMER, 2014). A further wave of migration is considered to have introduced wool-type sheep into Europe, displacing the initial hair-type sheep from which the present feral European mouflon originates (VILA and HELMER, 2014). Due to a lack of definitive archaeological evidence for the origin of specialized breeds, it is impossible to pinpoint whether sheep product specialization started in Asia or Europe (HELMER et al. 2007).

2.2.2. Origin and dispersal of African sheep

As a result of insufficient archeological and mtDNA studies on African sheep breeds, their domestication and dispersal routes remain a mystery, thus it’s a subject that must be researched more. The current evidence implies, however, that sheep were introduced from the Near East and disbursed across Africa following pastoral movements (RESENDE et al., 2016). The East African region's involvement in the expansion of sheep on the African continent is unknown, though it is assumed to have been critical in the entrance of sheep from Southern Asia or the Arabian Peninsula and/or dispersion southwards (MUIGAI and HANOTTE, 2013; RESENDE et al., 2016). Clades A and B are the most common in the region, according to studies on the matrilineal lineage of African sheep breeds, with clade B being the most common. Haplogroups C and E have been identified, however they are not as frequent as haplogroups A and B. For example, in Algeria, 87% of the Algerian individuals mtDNA belonged to haplogroup B while the rest to haplogroup C (GHERNOUTI et al., 2017). In Ethiopia three fat-ramped breeds; Afar, Blackhead Somali, and Hararghe Highland found in Eastern Ethiopia belonged to both haplogroups A and B (NIGUSSIE et al., 2019). With a frequency of 93%, the B lineage predominates among South African Zulu sheep, whereas the A lineage has a frequency of only 7% (SELEPE, 2018). Out of 67 individuals from Egyptian Barki, Ossimi and Rahmani, 62 belonged to haplogroup B while the rest belonged to A (OTHMAN et al. 2014). Only one individual from the Red Maasai, Black head Somali, East African fat tail, and Dorper sheep breeds in Kenya belonged to haplogroup A, according to RESENDE et al. (2016), whereas in Morocco, all haplogroups (A-E) were found, with B predominating once again (KANDOUSSI et al., 2020).

The few research on the matrilineal ancestry of African sheep breeds have shown how clade B arrived in Africa, however, the lack of documentation and evidence on other haplogroups is an area that needs to be investigated further in future studies. In a recent publication by WANJALA et al. (2021), the authors reported haplogroups A, B and C among the studied African sheep populations drawn from different African counties. Haplogroup B was the most dominant among them all and there was no observable phylogeographic clustering, as also observed in (HORSBURGH et al., 2010; KIJAS et al., 2009; TAREKEGN et al., 2018). However, Haplogroup A, had solely Egyptian breeds, but haplogroup C had sequences from all North African countries (Morocco, Algeria, and Egypt) suggesting that the studied populations (and from other literatures-African sheep populations) descends from European Mouflon but just differentiated into different populations separated geographically, thereby adapting to local environmental conditions. Indeed, African continent is home to a variety of sheep breeds with varied phenotypes, including tail type (fat or thin tail). The fat tail phenotype is an adaptation to hot and dry climatic conditions (AHBARA et al., 2019). It is also thought that tail type suggests the historical background as it was observed by WANJALA et al. (2020).

Between 7500 and 7000 B.P., thin-tailed sheep may have been the first sheep to reach Africa via the Suez Canal and/or the Southern Sinai Peninsula, followed by fat-tailed sheep via the Horn of Africa (MUIGAI and HANOTTE, 2013). A different angle of thought is that fat tailed phenotype developed from selection among the thin tailed sheep breeds. Small ruminants' ease of travel, usage as trade and socio-cultural exchange commodities, and their intrinsic ability to adapt to a wide range of production and ecological conditions may explain their lack of phylogeographic structure (KIJAS et al., 2012), wide dispersal, varied phenotypic and morphological characteristics as well as great genetic diversity.

2.3. Genetic diversity of global sheep populations

There have been several investigations on the genetic diversity of different domestic livestock species world-wide utilizing various genetic markers (MENEZES et al., 2020; OTHMAN et al., 2015; TAPIO et al., 2006; ZHANG et al., 2012). The majority of these research aimed to identify the origin, migratory routes, genetic diversity status within and between populations in order to categorize breeds according to their risk status and, if appropriate, recommend conservation strategies. However, the role of climate change in shaping the genome of the population, or response of the genome to prevailing climatic conditions is not well understood. Since their domestication, sheep have been exposed to both natural and artificial selection processes, which have led to many mutations and allele realignments over several generations in response to the changing climatic circumstances brought on by climate change (GAULY AND ERHARDT, 2001). Domestic animals' genomes had to respond to both natural and artificial selection to satisfy production requirements for farmers and the environment. However, in recent years, there has been an increased pressure for enhanced productivity due to the rising demand for animal products. This has led to increased selection intensity, especially in exotic sheep breeds, which is one of the main contributors to genetic diversity loss (EUSEBI et al., 2020). In earlier attempts to breed animals, heterozygosity was valued more highly than "allelic diversity". In this context, allelic diversity means the whole spectrum of potentially adaptable alleles (NOTTER, 1999). However, heterozygosity was less efficient because it did not fully address genetic heterogeneity in response to climate change.

Genetic diversity is considered a component of biodiversity, alongside ecosystems and species diversity (HOBAN et al., 2020). Genetic diversity has a vital role in the survival of species in the context of climate change since it serves as the fundamental basis for adaptation. The concept of genetic diversity may be broadly characterized as variations in the arrangement of the four base pairs (ATGC) that constitute nucleic acids and form the genetic code (REED and FRANKHAM, 2003). Diversity in genetics is crucial for a population or species to adapt to changing climatic or environmental circumstances and to increase the animals' fitness in their present and possibly changed future habitat (MCNEELY et al., 1990). Additionally, higher levels of genetic diversity encourage the coexistence of animals within an environment (CLARK, 2010). The topic of genetic diversity within and between populations (breeds) of a species has garnered significant global interest, with its inclusion in international agreements such as the Sustainable Development Goal (SDG) 2.5. This particular goal emphasizes the importance of preserving the genetic diversity of cultivated and domesticated plants and animals, as well as their wild counterparts (DUTFIELD, 2018; MOLLIER et al., 2017). Additional international agreements, such as the "European Union (EU) Biodiversity strategy for 2030 and the Green Deal" (HERMOSO et al., 2022), and the Global strategy for plant conservation (WYSE JACKSON AND KENNEDY, 2009), have acknowledged the significance of genetic diversity in safeguarding sustainable food security in the future.

Characterization of native breeds using contemporary molecular technology is required to achieve the accuracy of selection for animal welfare-related and economically significant traits (BOETTCHER et al., 2015). Multiple studies on the genetic diversity of different species/populations have proven to be highly useful, providing an opportunity for development of conservation strategies and regional-specific breeding plans to be considered (KIJAS et al., 2009; MEADOWS et al., 2006; MENDELSOHN, 2003).

2.4. Molecular markers and their application in animal genetics studies

Recent technological advancements have enabled animal geneticists and breeders to use molecular markers as a means to enhance breeding programs, expedite genetic progress, and optimize conservation techniques and decision-making processes. Several markers have been previously used for molecular investigations. Nonetheless, this section will focus on four markers that have been widely used in genetic research in domestic livestock species, especially sheep. These markers are restricted fragment length polymorphism, mitochondria DNA (mtDNA), microsatellites, and single nucleotide polymorphisms (SNPs).

2.4.1. Restricted Fragment Length Polymorphism (RFLP)

BOTSTEIN et al (1980) developed this molecular marker, which is one of the earliest. In summary, the process entails two key aspects: the production of restriction fragments from genomic DNA using a restriction enzyme treatment on an agarose gel, followed by inflating the fragments into a membrane, hybridized resulting in an auto radiogram that is evaluated. Typically, specific probes are created using genomic or c-

DNA libraries (BEN-ARI AND LAVI, 2012). In principle, all eukaryotic genomes undergo mutations which may result in either deletion or addition of nucleotides. As a result, DNA sequence gains or loses the ability to be cleaved by that restriction endonuclease. I.e., If there is no recognition site, digestion with the appropriate restriction enzyme yields a long fragment; if a recognition site exists, digestion yields two shorter fragments; and if only one of the two parental alleles has the recognition site, digestion yields two distinct electrophoretic patterns: a long fragment and two shorter fragments (BEUZEN et al., 2000). Parental identification, detection of lethal hereditary disorders, gene polymorphism studies, veterinary application, and genes responsible for quantitative traits in marker assisted selection are all examples of how this technique can be applied in animal breeding and genetics. Pcr-RFLP has been widely employed in studies of the polymorphism of the calpastine gene, which is found on ovine chromosome 5 and is thought to be involved in skeletal muscle hypertrophy in sheep and post-mortem meat softness. For example, SZKUDLAREK-KOWALCZYK et al (2011) used PCR-RFLP to identify polymorphisms in the Calpastine gene in 212 sheep from four breeds in Poland: (Black headed Mutton Sheep, Ile de France, Berrichon du Cher, and Polish Merino), and discovered that the M and N alleles were present in the CA ST/MspI locus, with 83.5 percent and 16.5 percent frequency, respectively. The frequency of M and N alleles in the CA ST/Ncol gene was 92.8 and 4.4 percent respectively. Similarly, polymorphism in the calpastine gene was found in Arabic sheep breeds, with allele A and B frequencies of 85 and 15%, respectively, and genotypes AA,AB, and BB with frequencies of 70.27, 28.82, and 0.9 percent (MOHAMMADI et al., 2008). In addition, polymorphism of the calpastine gene has also been found in Turkish sheep breeds, including Kivircik populations of Sakiz, Karacabey Merino, and Gökçeada sheep (YILMAZ et al., 2014). Furthermore, RFLP has been widely utilized in the recent past, and even in some places, it is still used in studying polymorphism of various genes as well as detection of quantitative trait loci (QTLs). However, due to its reliance on gel, the technique has certain drawbacks, including inconvenient high-throughput screening. Moreover, RFLP analysis does not detect all mutations because not all mutations result in the deletion or addition of endonuclease sites (BEUZEN et al., 2000).

2.4.2. Mitochondria DNA (mtDNA)

Since its discovery in 1980’s, mtDNA has been extensively used to study evolutionary relationship studies between species and to measure the genetic distance between populations. A full mtDNA genome has about 1600 base pairs and is inherited in a single copy through the maternal line; hence it does not undergo recombination (ZHANG et al., 2012). The rate of evolution in mitochondrial DNA (mtDNA) is higher compared to nuclear DNA. Specifically, the mtDNA control region (mtDNA cr), often referred to as the mtDNA displacement loop (mtDNA d-loop), is believed to be responsible for the observed genetic variations (BRUFORD, 2004). Moreover, the study of mitochondrial DNA (mtDNA) is considered more advantageous due to the abundance of mitochondria in cells, with hundreds to thousands of copies present. Its DNA may be extracted from minute quantities via PCR amplification, allowing DNA templates found in non-invasive biological samples like archeozoological vestiges and museum specimens to be investigated successfully (BRUFORD, 2004). Mitochondria DNA d-loop has been used to analyze historical backgrounds of several livestock species different from all parts of the world including fish (TÓTH et al., 2022), cattle (ILIE et al., 2015; LAI et al., 2006; PETRETTO et al., 2022), sheep (KANDOUSSI et al., 2020; RESENDE et al., 2016; REVELO et al., 2020; TAPIO et al., 2006), chicken (AL-JUMAILI et al., 2020), horses (CSIZMÁR et al., 2018; KUSZA et al., 2013; ZHANG et al., 2012) and many others. In sheep, the mtDNA analysis suggested that the modern sheep descends from Asiatic mouflon (HER et al., 2022; MARIOTTI et al., 2013).

2.4.3. Microsatellites

Unlike mtDNA, which is present in the mitochondrial genome, microsatellites are mostly found in the nuclear genome. Microsatellites have an entirely different inheritance pattern than mtDNA. Microsatellites are genomic regions with small repeating sequences, such as (CA)n, where n is the number of CA repetitions (BRUFORD, 2004). They are ideal markers for measuring basic genetic diversity indices, genome mapping, relatedness analysis, and population genetics due to their extensive distribution across the genome and high information richness (BEUZEN et al., 2000; BRUFORD, 2004). It is widely believed that genetically diverse populations at the species level exhibit distinct population structures due to their exposure to various non-mutual environmental influences. Using microsatellite markers, genetic diversity of multiple populations including sheep (ARORA and BHATIA, 2004; BAUMUNG et al., 2006; KUSZA et al., 2013; NIGUSSIE et al., 2019), chicken (BODZSAR et al., 2009; DE CARVALHO et al., 2020), cattle (IBEAGHA-AWEMU et al., 2004; ILIE et al., 2015; KANTANEN et al., 2000; OCAMPO et al., 2021).

2.4.4. Single nucleotide polymorphism (SNP)

SNP arrays have been used in many studies on genetic diversity, adaptability, genetic admixture, and genome-wide association in sheep breeds around the world in recent years. An SNP is a single base mutation in a DNA sequence with a typical alternative of two potential nucleotides at a given site, making them biallelic co-dominants markers (VIGNAL et al., 2002). Multiple studies have been conducted on various livestock species using SNP markers e.g. (CASWELL CHOKOE et al., 2020; EYDIVANDI et al., 2020b; MONAU et al., 2020.; NOSRATI et al., 2021; PAN et al., 2018; WAGNER et al., 2021). Except for a few spots where mutation occurs, the genome of essentially every individual within the species is nearly identical. Point mutations can occur anywhere in the genome, and if their frequency in the population is more than 1%, they are utilized as SNP markers (VIGNAL et al., 2002). SNPs are more preferred than other DNA markers for four reasons: (i) They are more common than other types of polymorphism, such as microsatellites, and provide more potential markers near or in any locus of interest. (ii) Some SNPs are found in coding regions, which directly affect protein function and may be directly responsible for some of the differences between individuals in important traits. (iii) SNPs are more stable than microsatellites in terms of inheritance, making them more suitable as long-term selection markers. (iv) SNPs are more suited for high-throughput genetic study using DNA microarray technology than microsatellites (BEUZEN et al., 2000; GRIFFIN and SMITH, 2000; HEATON et al., 2002).

2.5. Environmental changes caused by climate change may alter the native sheep breed genetic diversity

The significance of climate change's influence on the performance of domestic animals cannot be overstated. The negative impacts of climate change on meat, milk, fiber, and reproductive performance are evident. According to several studies, the animal prioritizes its energy use based on its welfare, allocating more energy to environmental adaptation mechanisms at the expense of production and reproduction processes. Climate change alters the animal's natural environment, causing it to adapt or die. Thermal stress is one of the most significant limiting factors among all climate change variables. Consequently, it is important to comprehend the genetic diversity of livestock species in relation to ecological factors impacted by climate change.

Sheep productivity, reproduction, and welfare are all influenced by a complex interaction of genetics and many environmental factors, the majority of which are driven by climate change. Some of the environmental factors include high temperatures (heat stress), insufficient water, low quality and quantity of fodder, and parasite, pest and disease prevalence that varies by ecological zone. Such conditions may alter the genetic makeup of individual animals and population structure by altering the distribution of allele frequency throughout the population. The propagation and increase in frequency of beneficial alleles is expected in successive generations, since individuals with unfavorable alleles for the given environment would not live to contribute to future generations. The likelihood of advantageous alleles reaching fixation is high, leading to a reduction in genetic diversity at certain loci. This is due to the fact that almost all individuals would possess a similar allele pattern at those loci. Additionally, there would be alterations in haplotype structure and recombination patterns. Individuals that have a strong ability to thrive in such situations might be inferred to have successfully adapted to them, since they would have likely experienced selective pressures throughout the process of adaptation.

In individuals with favorable genetic makeup, certain genes that contribute to enhanced adaptability within corresponding environmental conditions come to play. The aforementioned genes would eventually propagate throughout the population, reaching fixation and so augmenting population adaptability. It has been proposed that long-term exposure to these conditions, has a significant impact on the development of adaptive qualities in indigenous sheep breeds, resulting in changes in genetic diversity at specific loci. The emerging discipline of landscape genomics facilitates the exploration of ecological factors that contribute to adaptation, with the objective of evaluating their potential impact on genetic diversity.

Hot temperatures (heat stress), insufficient or poor quality of water, low quantity and quality of feed, and the emergence, re-emergence and distribution of parasites, pests, and diseases are discussed below.

2.5.1. Hot temperatures (Heat stress)

Heat stress has been identified as one of the climate change variable constraining animal husbandry. An animal experiencing heat stress may exhibit many signs, such as an elevation in body temperature, high respiratory rate, and reduced feed intake.

According to AL-HAIDARY (2004), the animal's physiological changes serve to regulate its body temperature and provide protection against hypothermia. However, a severe physiological response to elevated environmental temperatures includes alterations in endocrine function and blood flow distribution, all of which have a detrimental effect on an animal's ability to produce, grow, and reproduce. By increasing its maintenance energy needs, the animal reduces or eliminates the effects of excessive environmental temperature stress. However, this decreases the energy available for other tasks like production, development, and reproduction, which lowers output (COLLIER et al., 2019). According to MCMANUS et al. (2020), animals experiencing acute or chronic responses to environmental stress must make modifications to their energy balance and metabolism in order to preserve homeostasis. Many previous studies have mostly examined the impact of heat stress on cattle production, whereas comparatively little attention has been given to hypothermal circumstances, perhaps attributed to the prevailing focus on future global warming forecasts.

Animals exposed to surroundings that are not thermally neutral develop coping mechanisms e.g., acclimation, acclimatization, and adaptation to help them cope with the stressors' impact on their biological systems (COLLIER et al., 2019). Acclimatization is the animal's coordinated phenotypic response to a certain environmental stressor. According to the authors, acclimation is the animal's coordinated phenotypic response to a single environmental stressor, acclimatization is the animal's coordinated response to several stressors occurring at once, and adaptation is the genetic evolution of a species over many generations as adverse environmental conditions persist. As a result, the animal experiences acclimatization rather than acclimation since environmental stressors often include a complex combination of components (COLLIER et al., 2019). However, when a population is exposed to environmental stressors over a long period of time, resulting in a genetically fixed population, long-term adaptive responses to environmental stressors happen (COLLIER et al., 2019). According to MCMANUS et al. (2020), some of the morphological traits that aid sheep breeds in adapting to challenging environmental circumstances include hair and wool, skin and coat color, and body size. These physical adaptive features may not be sufficient on their own to defend against very stressful environments. As a result, a variety of processes, such as behavioral and physiological ones, will be needed to complement an animal's physical characteristics (DWYER and LAWRENCE, 2005). Some of the acclimatization reactions include decreased feed intake, increased respiratory rate, increased sweating, and panting (MCMANUS et al., 2020). The intrinsic energy budget of the animal is significantly impacted by reduced feed intake. For instance, a heat-stressed animal may consume less food, which is exacerbated by higher energy needs for upkeep, which limits the amount of energy available for growth, production, and reproduction. An animal's energy budget and priorities were shown by HUBER (2018), who proposed that the four categories of energy use are maintenance, ontogenic growth, production, and reproduction respectively. As a result, reproductive efficiency is significantly compromised during environmental stress conditions. This includes a notable impact on a whole set of reproductive processes ranging from spermatogenesis in rams to successful conception and lambing of ewes (HANSEN, 2009).

The reproductive capacity of a sheep farm plays a crucial role in its economic performance, as various factors such as age at first mating lambing, inter-lambing interval, litter size, number of lambs weaned, and service length determine the economic efficiency of a sheep farming enterprise (RATHER et al., 2020). The importance of animal immunity is paramount in the context of the contemporary era of climate change. Environmental stress, particularly heat stress, has been seen to have a detrimental impact on the immune system of animals. Heat stress leads to an upregulation in the synthesis of heat shock proteins. These proteins play a crucial role in preventing the occurrence of non-specific protein aggregation and facilitating the restoration of cellular proteins to their native conformation. Consequently, this process initiates an intrinsic defense response at the cellular level and augments the innate immune system (SEVI and CAROPRESE, 2012; SINGH et al., 2017).

Adaptation qualities are becoming more popular and calls for them to be incorporated in breeding programs are growing, as they are predicted to improve both productivity and animal welfare. Adaptability is a multi-factorial trait driven by a complex network of genes interacting with the environment, according to multiple studies, and different genes play different roles depending on the environment and breed. In various native sheep breeds, signatures of selection for local environment adaptability have been explored and identified. For example, KIM et al. (2016) investigated selection signatures in Barki goats and sheep native to hot environments in Egypt and discovered suggestive genes for melanogenesis and thermotolerance, such as *FGF2*, *GNAI3*, and *PLCB1*; body size and development genes *MYH, TRHDE, ALDH1A3;* Nervous and autoimmune response genes *GRIA1*, *IL2*, *IL7*, *IL21*, and *IL1*. In addition, ABIED et al. (2020) performed similar study in Hetian, Karakul and Yabuyi Chinese indigenous sheep and several adaptive genes such as *HERC2* body regulation and immune response, *GJB2* and *GJA3* for body size and development, *BMPR1B* for reproduction were identified.

The long-term survival prospects of a species or population are significantly enhanced when it possesses genetic traits that facilitate adaptation to the impacts of climate change. Additionally, the ability of its members to effectively integrate various mechanisms of adaptation, particularly in response to heat stress, which is the primary constraining factor as depicted in Figure 1, further contributes to their resilience.

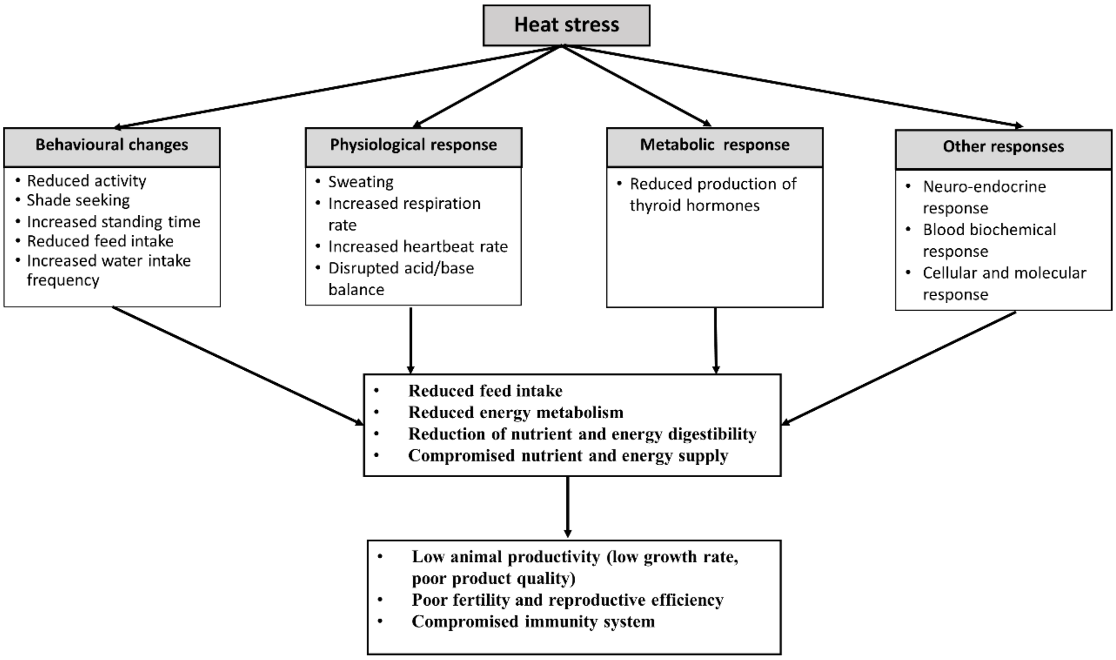


Figure 2: General sheep response mechanisms to heat stress.

2.5.2. Insufficient and/ poor quality water

Water is essential for the survival and reproduction of animals. Water's effects on animal genetic makeup, on the other hand, have not gotten the attention they deserve. Water accounts for roughly 70% of the animal's live body weight. Water quality and quantity both have an impact on sheep performance (UMAR et al., 2014).

Individual animals' ability to withstand water stress is genetically determined; therefore, indigenous sheep strains residing in arid and semi-arid environments have a more effective mechanism for water stress tolerance. Heat stress exacerbates dehydration symptoms (CHEDID et al., 2014). Dehydration is simply a loss of water from the body.

Heat stress causes elevated body temperatures, which induces physiological responses such as perspiration and vasodilation to increase heat dissipation in the environment, which increases an animal's water intake. Recent research suggests that ruminants have devised methods to manage both heat and water stress (AKERMAN et al., 2016; HUSSEIN et al., 2020), despite the deleterious effects of water stress on animal output.

The availability of herbage may also be impacted by environmental water stress, which might have a knock-on effect on animal genetic diversity. For example, ALLAHDADI and BAHREININEJAD (2019) as well as KÜCHENMEISTER et al. (2013) observed that the impact of water stress on nutritional components such as, neutral detergent fiber (NDF), acid detergent fiber (ADF) and crude proteins (CP) was more significant. The amount and quality of forage has a significant influence on an animal's overall calorie intake, thus impacting the animal's productivity, reproduction, and health outcomes.

The capacity of individuals to endure extended periods of water shortage is contingent upon their genetic lineage. Sheep breeds that have evolved to dry and semi-arid regions have notable morphological attributes, including an array of fleece colors and coats, variations in body height, differences in body size and, types and size of the tail. These features contribute to their ability to withstand heat stress and tolerate water scarcity (CHEDID et al., 2014).

2.5.3. Inadequate feed availability, digestibility, and absorption

In the current context, the phrase "feed availability" comprises the quantity and quality of feed that is accessible by the population or individual animal. A positive association has been shown between animal diet and the physiological processes of growth, reproduction, and production. The efficacy of these mechanisms is negatively affected by suboptimal and/or inadequate dietary intake. The projected increase in atmospheric carbon dioxide (CO_2) concentrations and ambient temperatures, along with changes in soil composition due to climate change, are expected to have an influence on both the quantity and quality of forage. Furthermore, it is anticipated that there would be a rise in instances of intense precipitation and extended periods of drought, leading to a wide range of year-to-year fluctuations in precipitation (GRANT et al., 2014). Based on the findings of FAY (2009), the regular variations in annual rainfall contribute to a persistent fluctuation in soil moisture levels, hence subjecting crops to the potential threat of moisture stress.

To comprehend the implication of feed availability on the genetic make-up of the indigenous sheep populations, it is essential to first understand the fundamental components of forage. The key factors that affect the quality of forage in ruminant nutrition are protein content, digestible energy levels, and the rate at which the forage passes through the digestive system. Crude proteins are synthesized by the conversion of nitrogen derived from fodder by ruminal microorganisms. The primary sources of energy are soluble carbon molecules, cellulose, and hemicellulose. Cellulose and hemicellulose exhibit digestibility, but with a constrained rate of transit, which may be impeded by the presence of lignin. The passage rate in ruminants is a multifaceted process, with a general trend indicating that better digestibility and low passage rate are with reduced lignin content (MILCHUNAS et al., 2005) hence higher absorption.

The study conducted by HABERMANN et al. (2019) demonstrates that the simultaneous occurrence of soil water stress and warming has a negative impact on fodder quality. This is mostly attributed to an increase in lignin content, as well as a reduction in the digestibility of starch and crude protein in C4 grass. C4 grasses are classified among the subfamilies Panicoideae and Eragrostoidae, which are part of the family Gramineae. These plants are mostly distributed in climates that range from cold temperate to hot-wet tropics. They are particularly abundant in semi-arid and desert areas, which are characterized by elevated levels of solar radiation, high daytime temperatures, and periods of water scarcity, either on a daily or seasonal basis (DOLINER AND JOLLIFFE, 1979).

The increase in atmospheric carbon dioxide (CO_2) levels, together with the concurrent global temperature rise, has implications for both the amount and quality of forage (BABINSZKY et al., 2011). The assessment of forage quality is predicated upon the capacity of the ingested feed to be digested and absorbed. Digestibility is a fundamental aspect of the nutritional value of feed, alongside feed consumption and energy efficiency (VAN SOEST, 2018). Digestibility may be classified into two types: apparent digestibility and true digestibility. Apparent digestibility refers to the balance of feed intake minus the amount of feces produced. On the other hand, true digestibility considers the balance between the respective feed residues that escape digestion and end up in the feces, omitting any metabolic products (SOEST, 1963). It is important to highlight that plants, specifically forage plants, have diverse reactions to the effects of climate change depending on their photosynthetic types, notably C4, C3, or CAM (BABINSZKY et al., 2011). Therefore, when climate change events become more pronounced, there is an increased probability of vegetation modification, leading to the introduction of foreign plant types that are not habituated to by the existing livestock species. As a result, animals that are genetically capable of handling toxins that come along with new plant species may survive. Also, the livestock species are driven to modify their eating practices, engage in migration, or confront the severe consequence of famine.

Moreover, the interaction of various climate change factors has the potential to modify the nutritional value of forage. This is because the present forage species may undergo adjustments in their inherent systems to cope with the changing climatic circumstances. In addition, the influence of climate change on agricultural yield will also be contingent upon the photosynthetic pathway of the crops. Nevertheless, BABINSZKY et al. (2011) observed that C3 crops are likely to have greater adverse consequences, resulting in a decrease in both the amount and quality of their herbage, because of elevated temperatures and reduced precipitation. This phenomenon has the potential to result in diminished feed consumption among animals, so reducing their calorie intake. Consequently, if the breed has an insufficient adaptation mechanism e.g., efficient metabolism, it may face the threat of extinction in the long run. The process of extinction results in the depletion of crucial animal genetic resources found within domestic animal populations.

The process known as “photosynthetic downregulation”, as described by SANZ-SÁEZ et al. (2012), occurs when there is a decrease in photosynthesis and subsequent loss in growth due to prolonged exposure to increased levels of carbon dioxide (CO2). The authors also underscored the significance of other environmental factors that interact with carbon dioxide (CO2) and surface temperature, hence influencing plant development. The factors included in this category consist of soil nitrogen levels, soil water content, atmospheric humidity, and sun radiation. Among all the factors considered, nitrogen emerges as the limiting component, exhibiting a positive correlation with forage quality. Specifically, an increase in carbon dioxide content coupled with an inadequate nitrogen supply leads to a decrease in photosynthesis, resulting in lower crop output (SANZ-SÁEZ et al., 2012). Moreover, an insufficiency of nitrogen in the soil leads to a decrease in the nitrogen content of the shoots when exposed to higher concentrations of carbon dioxide. This, in turn, results in a reduction in crude protein levels and an increase in fiber concentration, ultimately leading to a decline in the quality of forage. The determination of digestibility, ingestion, and palatability of grass forages is dependent on the quality of acid detergent fiber (ADF), neutral detergent fiber (NDF), and acid detergent lignin (ADL; REID et al., 1988; SANZ-SÁEZ et al., 2012; SOEST, 1963). The composition of NDF consists of cellulose, hemicellulose, and lignin, as stated by SANZ-SÁEZ et al. (2012). On the other hand, ADF comprises cellulose and lignin. Several studies have shown that an increased concentration of carbon dioxide (CO2) has a notable impact on the nitrogen levels in herbage. Specifically, it leads to a reduction in nitrogen concentration, while simultaneously raising the concentration of lignin. This alteration in composition results in higher carbon-to-nitrogen ratios and lignin-to-nitrogen ratios. Consequently, the overall quality of fodder is severely affected, leading to a decrease in digestibility (CHA et al. 2017).

Animal production is negatively impacted by heat stress, since it leads to a reduction in feed intake, digestibility (MAIA et al., 2020), and absorption (RÍUS, 2019). Moreover, it should be noted that heat stress has a detrimental impact on the activity of rumination, which is a crucial process in the digestive physiology of ruminant animals (MAIA et al., 2020; REITER et al., 2018). According to BEAUCHEMIN (2018), chewing and rumination are significant behavioral features that have a notable impact on feed intake and digesting efficiency. The adverse impact on these two processes results in a decrease in feed intake, thereby reducing the energy available for their noble physiological processes.

In summary, climate change has the potential to disrupt the quality, quantity, and distribution of forage. Sheep populations that possess genetic adaptations enabling them to effectively cope with toxins, as well as the ability to consume new forms of fodder to which they are not used, have a high metabolic rate and inherent capability to utilize feeds of low quality are more likely to possess advantageous traits for adapting to the challenges posed by climate change.

2.5.4. Prevalence of parasites, pests and disease vectors

The process of climate change is anticipated to facilitate the proliferation of pests, parasites, and disease vectors, hence contributing to the spread of lethal health hazards. Moreover, the pathogenicity of these pathogens may be enhanced in favorable climatic circumstances and in individuals with compromised immune systems. Consequently, it is infeasible to disregard the implications of climate change on animal well-being, alongside the conceivable internal strategies that animals may use to mitigate the health consequences.

Because the immune response is most likely genetically influenced, having a population with the genetic potential to build immunity to prevalent diseases or parasites would be good for long-term productivity. Disease/parasite tolerance refers to an animal's ability to stay productive and reproduce normally in the presence of parasites and other disease-causing agents, as well as the ability to break the pathogen's life cycle by creating internal conditions that make pathogen survival, reproduction, and growth difficult.

The anticipated increase in severe weather events, namely vectors borne diseases that exhibit seasonal and geographic patterns influenced by climate change (DE LA ROCQUE et al., 2008), is likely to result in fluctuations in the distribution, prevalence, and timing of pests and diseases (MEDLOCK and LEACH, 2015). The Intergovernmental Panel on Climate Change (IPCC, 2007) reported an anticipated expansion in the spatial dispersion of animal disease vectors that are particularly susceptible to alterations in temperature. This suggests that climate change contributes to the spreading of infectious diseases by facilitating the more efficient transmission of disease-causing agents. In addition, the occurrence of vector-borne diseases such as trypanosomiasis, Lyme disease, tick-borne encephalitis, blue tongue, and dengue fever has been shown to be associated with climate change (DE LA ROCQUE et al., 2008). Elevated temperatures have been shown to have a more pronounced influence on the life cycle of pathogenic microorganisms, resulting in a reduction in the duration of pathogen incubation, an acceleration in incubation rates, and an increased probability of vectors surviving for extended periods to facilitate the transmission of diseases (KUTZ et al., 2005). In their study, KUTZ et al. (2005) observed that a rise in temperature by 1°C had a significant impact on the larval development of the protostronglid nematode species *U. pallikuukensis*. Specifically, this temperature increase caused a shift in the nematode's life cycle from a 2-year cycle to a 1-year cycle. Consequently, the duration of transmission for the third stage of larvae was extended, leading to an increased time of larvae infection in slugs. The expansion of arthropod vectors, such as the bluetongue virus, has been found to be associated with increases in temperature. Conversely, decreases in temperature have been linked to the spread of tsetse flies in Sub-Saharan Africa. Additionally, there is evidence of a positive correlation between extreme events, both cold and hot, and disease outbreaks, such as the Rift valley fever outbreaks in East Africa (BETT et al., 2017; KUTZ et al., 2005).

Variations in immunological responses among individual animals are prevalent, and several studies have shown associations between these variations and genetic disparities among individuals. A comprehensive understanding of the interplay between genes and the environment, and its significance in the emergence of variations in immunological responses across populations, is of utmost importance in the context of long-term sheep breeding. In the light of the aforementioned health risk issues, it is advisable to investigate the indispensability of establishing an animal genetic foundation that would serve as a fundamental support for sustainable production. Consequently, sheep populations exhibiting more genetic diversity provide opportunities for improved adaptability. The implementation of selective breeding strategies aimed at enhancing disease resistance in livestock has been shown to have a positive impact on food safety. This is mostly due to the reduction in the reliance on drugs, leading to a decrease in the presence of drug residues in sheep-derived products (AGUERRE et al., 2018).

There is no doubt that genetic selection for disease resistance is conceivable (BOUIX et al., 1998; GAULY and ERHARDT, 2001), but applying pedigree selection is difficult. Fortunately, with the advent of genomic selection (VAN DER WERF, 2009), disease resistance selection has become possible, although it is still not widely used in developing countries. Mastitis is an example of a major health issue whose immunology and genetic architecture are being explored extensively. Mastitis is a condition that causes inflammation of the mammary glands and results in significant economic losses in sheep breeding (GIANNAKOPOULOS et al., 2019; LARSGARD and VAABENOE, 1993). Climate change affects environmental changes, which influence the occurrence of mastitis; hence, optimal genetic diversity in the flock would improve the breed's ability to perform even in mastitis prevalent conditions. In a study conducted by LARSGARD and VAABENOE (1993), the heritability of mastitis resistance in sheep was estimated to be 0.13 (±0.16) using the LS-method, whereas the nonlinear threshold technique yielded an estimate of 0.49. In a separate study, CONINGTON et al. (2008) conducted a comprehensive analysis and discourse on the economic ramifications associated with the breeding efforts aimed at enhancing mastitis resistance.

In recent years, there has been an increased exploration and use of marker-assisted selection for resistance. This approach aims to enhance genetic improvement while simultaneously preserving genetic diversity. This technique offers an opportunity to sustain food security in the midst of uncertainties posed by climate change. Based on the utilization of an ovine transcriptional atlas and transcriptome data obtained from milk somatic cells, BANOS et al. (2017) identified several genes, namely *SOCS2*, *CTLA4*, *C6*, *C7*, *C9*, *PTGER4*, *DAB2*, *CARD6*, *OSMR*, *PLXNC1*, *IDH1*, *ICOS*, *FYN FYB*, and *LYFR*, which were found to be subjected to selection for mastitis resistance through the application of genome-wide association studies in a population of 609 ewes belonging to the Greek Chios breed. Adaptability of sheep and their resistance to nematodes have also been investigated by several researchers, for example, Rhön sheep from Germany (GAULY AND ERHARDT, 2001) and the Polish Longwool sheep from Poland (BOUIX et al., 1998), have undergone evaluations to determine their resistance to nematodes. This assessment has facilitated the process of selecting sheep with enhanced resistance to nematode infections.

2.6. Selection signatures for climate change adaptation

In recent times, there has been a notable increase in research endeavors aimed at elucidating the genetic mechanisms underlying the process of adaptation to climate change. Several methodologies have been developed to investigate this phenomenon, with recent advancements focusing on the identification of selection signals via the analysis of allele frequency, linkage disequilibrium, runs of homozygosity, and genetic divergence across various breeds. For instance, PAN et al. (2018) examined Chinese and Ethiopian sheep, while BAAZAOUI et al. (2021) focused on Tunisian Barbarine, Noire de Thibar, and Queue fine de l'Ouest. SARAVANAN et al. (2021) investigated the genetics of Indian Changthangi and Deccani breeds, while PAIM et al. (2022) explored the genetics of Brazilian Bariga Negra, Morada Nova, Rabo Largo, Santa Ines, and Somalis. These studies, along with others, contribute to our understanding of the genetic mechanisms underlying adaptation.

Landscape genomics (GOITOM et al., 2021) is a new field of research in the genomics era that aims to uncover the environmental factors that influence genetic variation and the genomic regions of the organism's genome that underpin local adaptation. The success of genomic investigations has been aided by the genomic revolution (MERIKANGAS and RISCH, 2003; REBBECK and SELLERS, 2018). The era of the genomic revolution is one in which massive amounts of genomic data are more easily available at a low cost. And one of the most powerful player in genomic revolution is the next generation sequencing (NGS; SHARMA et al., 2017; ZHOU et al., 2010). NGS allows for low-cost screening of the thousands to millions of SNPs in many individuals animals and populations at large (GOITOM et al., 2021). Complimentarily, access to spatial climatic data spanning several decades has also been enhanced and now such data bases e.g., WORLDCLIM data base (FICK and HIJMANS, 2017) are open source. A robust gene x environment association analysis can be performed using both data (genomic and climatic data) to identify genetic variants associated with ecological factors that could potentially influence the adaptive traits that could not be discovered physically by mare observation. Due to the dramatic environmental changes caused by climate change, individuals and populations must enhance their fitness and survival qualities like phenotypic plasticity (BOUTIN and LANE, 2014), migration, and genetic adaptation to avoid extinction.

Positive selection signatures are typically detected in population genomics by identifying regions of substantial genetic divergence among populations relative to a neutral model. Landscape genomics analysis primarily uses genomic data to find adaptive genetic variants (signatures of local selection) and potentially connect them to evolutionary processes and environmental variations (LUIKART et al., 2003). Native sheep breeds are a good model animal for investigating regionally adaptable genomic variations in various ecological conditions because they are thought to have undergone long-term selection pressure in various ecological conditions. In a recent study, researchers investigated the presence of selection pressure on adaptation and identified several genomic architectures associated with these adaptations. As mentioned earlier, the primary methodologies used in the identification of selection signatures include the examination of allele frequencies across populations to infer the presence of selective pressure within a particular population, as well as the analysis of diminished genetic diversity within a given genomic region. This approach allows for the identification of potential "selection sweeps" (STEPHAN, 2019) in genomic areas or loci where beneficial alleles have undergone an increase in frequency, resulting in reduced levels of diversity (SARAVANAN et al., 2021). Single nucleotide polymorphisms are a kind of genetic marker that is used in the process of mapping genomic variations and quantifying the reduction in diversity at a certain locus. Bioinformatics analysis methods use data derived from many SNPs distributed across the whole of the genome in order to assess their influence and identify or choose loci associated with phenotypic variation. The SNP markers are used to identify potential genes that have nucleotide variations that influence variances in traits (CARDONA TOBAR et al., 2020).

Various domestic animal species have been subject to extensive research in order to investigate a wide range of adaptive qualities through the analysis of selection signatures. For instance, SHEN et al. (2020) conducted a study on cattle, GUO et al. (2018) examined goats, MOKHBER et al. (2018) investigated buffaloes, and WIENER et al. (2021) focused on sheep. The genetic clustering of sheep populations has the potential to result in ecological and phenotypic variations. In a study conducted by KIJAS (2009), it was observed that clustering patterns in global indigenous sheep populations were influenced by both geographic origin and known breed history. Conversely, Ethiopian sheep breeds exhibited clustering patterns primarily based on morphology, specifically tail type, in addition to geographic origin. For instance, the Ethiopian sheep breeds were categorized into three distinct groups: short fat-tailed, found in cool high-altitude regions; long fat-tailed, prevalent in mid to high-altitude areas; and fat-rumped, predominantly found in arid low-altitude regions (EDEA et al., 2017). Additionally, KIJAS et al. (2012) demonstrated that comparable cohorts had substantial levels of SNP diversity. This suggests that sheep populations possess a diverse array of genetic variations, likely attributed to the influence of natural selection. In most of the studies, numerous and distinct genes were identified in sheep breeds that are thought to be responsible for indigenous sheep adaptation, implying the existence of genetic heterogeneity for adaption traits among populations. This provides an excellent opportunity to breed for adaptation that will help breeds to adapt to harsh circumstances caused by climate change. It is worth emphasizing that, even among populations exposed to comparable ecological conditions, selection fingerprints differ indicating that populations have a wide range of gene x environment interaction aiding in natural selection.

The majority of research have discovered a considerable number of different genes among sheep breeds that are believed to have a role in the adaptation of indigenous sheep. This suggests that there is genetic variation across populations when it comes to traits related to adaptation. This is a valuable opportunity to selectively breed for adaptive traits that may enhance the ability of breeds to withstand and thrive in challenging environmental conditions resulting from climate change. It is important to highlight that, even among populations exposed to similar ecological circumstances, there are variations in selection footprints, suggesting that populations exhibit a diverse array of gene-environment interactions that contribute to the process of natural selection.

3. MATERIALS AND METHODS

3.1. Ethics statement

This research did not require approval by the Scientific and Ethics Committee of the Centre for Agricultural Genomics and Biotechnology of the University of Debrecen.

3.2. Raw sample description, collection, and genotyping

This research included the analysis of 907 samples obtained from a total of 32 different native sheep breeds. Out of these samples, 620 were specifically genotyped for the purpose of this study, representing 22 breeds, hence forth referred to as raw samples/data. The other samples were obtained from publicly available databases. For instance, samples from the Magreb region were studied by BEN JEMAA et al (2019), those from Sweden were analyzed by ROCHUS et al (2020), and samples from South Africa, Iran, and China were published by KIJAS et al. (2009), whereas samples from Morocco were donated by a collaborator.

3.2.1. Breed description of the raw samples

This section describes the 22 indigenous sheep breeds whose samples were specifically collected and genotyped for this study.

3.2.1.1. Hungarian breeds

Here are described seven breeds whose samples were collected within the geographical borders of Hungary, although some of them may have originated outside Hungary. The detailed description of these breeds can be accessed from the Hungarian sheep and goat breeders' association website: https://mjksz.com.

Hungarian Merino

The breed has a high level of adaptability to the seasonal fluctuations prevailing in Hungary. The breed was developed by crossbreeding several Merion breeds, primarily with the objective of enhancing wool and milk production. Nevertheless, as a result of the considerable demand for meat with declining wool demand, the focus of breeding efforts shifted towards enhancing meat yield and reproductive efficiency. The Hungarian Merino breed is characterized by its pure white fleece and a body shape that is typical of mutton sheep. From a morphological perspective, the breed has a moderate body length, possesses a hairy abdomen and limbs, and features a head that extends beyond the height of the ears. The Hungarian Merino breed has a notable level of prolificacy, with a range of 1.3 to 1.5 lambs per lambing. The typical weight of ewes is from 54 to 58 kg, and rams may weigh up to 100 kg (Figure 3).

Figure 3: Hungarian Merino sheep

Photo by Zoltán Bagi

Hortobágy Racka

The Racka sheep of Hortobágy is renowned for its distinctive horns, which exhibit a remarkable spiral, corkscrew-like structure and are present in both males and females. The head of ewes has a distinctive V-shaped configuration (Figure 4). Conversely, the head of male of rams, possess a broader angular disposition. Rams have an average horn length of around 50 cm, while ewes have an average horn length of approximately 30 cm. The breed is characterized by its little physique, with a coat composed of densely curled, rough-textured fleece. Black and white are distinct color variants that are selectively selected in different environments (ZSOLNAI et al., 2021). The breed has a notable characteristic in which its head and legs are adorned with a dense coating of lustrous, tiny, brown, or black fur. While rams weigh between 55 and 75Kgs, ewes weigh between 35 and 45kg.

Figure 4: Hortobágy Racka sheep

Photo by Gábor Takács

Hungarian Tsigai

The Tsigai sheep breed, which has its origins in the Balkan Peninsula, was brought to the Hungarian empire in the latter half of the 18th century. The breed is medium size, with pigmentation seen in the face area and lower extremities that varies in color, ranging from black to dark brown to brown. The fleece has a mostly white coloration, with intermittent threads displaying a diverse range of hues. Some females are polled, whilst others possess curved horns in a crescent form. Similarly, males also demonstrate a coexistence of horned and non-horned individuals. Male individuals with horns have open spiral horns that are distinguished by one and a half turns. The average weight of ewes often falls within the range of 50 to 60 kg, and rams generally weigh between 75 and 90 kg (Figure 5).

Figure 5: Hungarian Tsigai sheep

Photo by Zoltán Bagi

Bábolna Tetra

The Hungarian Bábolna Tetra breed has undergone selective breeding using the Hungarian Merino, Romanov, and Finnish Landrace breeds. The individuals have a commendable physical appearance defined by a well-developed musculature and sturdy skeletal structure. Moreover, they have a lively temperament and robust physical well-being. Neither gender has horns. The breed is capable of reproduction throughout all breeding seasons throughout the year and has a reproductive potential of 1.7 lambs each lambing season. The weight of ewes typically ranges from 50 to 55 kg, while rams generally weigh between 65 and 75 kg (Figure 6).

Figure 6: Bábolna Tetra sheep

Photo from https://mjksz.com/tenyesztes/fajtak/babolna-tetra-prolific-babolna

Ile de France

The Ile de France breed is characterized by its white coat coloring and robust muscular body conformation. Historically, the breed shares genetic lineage with Merinos. This breed has positive maternal characteristics and possesses a prolificacy rate ranging from 1.4 to 1.8. The favorable trait of this particular breed is its ability to breed outside of the typical breeding season. This unique quality enables year-round breeding. The weight of mature ewes typically ranges from 70 to 90 kg, whereas rams often weigh between 100 and 140 kg (Figure 7).

Figure 7: Ile de France sheep

Photo by János Oláh

Suffolk

The breed has a physique of moderate size, characterized by a sturdy build and a notable growth rate. The primary purpose of its breeding is for mutton production, and it exhibits favorable grazing habit. The head and legs exhibit a dense array of shiny, ebony-colored hair. The breed has favorable maternal characteristics, possesses a notable capacity for milk production, and demonstrates a high level of prolificacy, with an average of 1.6 to 1.8 lambs every breeding season. The capacity to breed outside the typical breeding season facilitates the adoption of an accelerated lambing program. Suffolk has a notable degree of flexibility when subjected to intensive production methods. The breed has desirable characteristics in terms of meat shape and body structure. The mature weights of ewes may vary between 75 and 90 kg, but the mature male sheep can range from 90 to 130 kg (Figure 8).

Figure 8: Suffolk sheep

Photo from https://mjksz.com/tenyesztes/fajtak/suffolk.

Dorper

The breed was developed in South Africa through a selective breeding program that used the crossbreeding of Dorset Horn and Blackhead Persian sheep. Dorper sheep have a distinct coloration pattern, characterized by black pigmentation on their heads and upper necks, juxtaposed with white coloration on their bodies and legs (Figure 9). Dorper sheep, being a breed of hair sheep, exhibit a natural shedding of their wool, hence obviating the need for shearing. These animals engage in year-round breeding, even beyond typical breeding seasons, and exhibit a high prolificacy rate ranging from 160% to 180%. This trait renders them suitable for use in accelerated lambing programs. Dorper sheep have a calm temperament and has commendable maternal characteristics. These animals exhibit resilience in the face of drought conditions and have favourable grazing behaviours. The weight of adult rams typically ranges from 90 to 110 kg, while mature ewes often weigh between 75 and 80 kg.

Figure 9: Dorper sheep

Photo from https://mjksz.com/tenyesztes/fajtak/dorper.

White Dorper

The development of this breed also took place in South Africa via the deliberate crossbreeding of the Dorper and Afrikaner sheep breeds. The breed has a mostly white appearance, with the presence of pigmentation limited to the claws, under tail area, and udder teats (Figure 10). The White Dorper breed is categorized as a hair sheep, primarily characterized by its natural shedding of fur, hence obviating the need for shearing. This breed has the capacity for year-round breeding, making them very suitable for accelerated lambing operations. Furthermore, it is noteworthy that their degree of prolificacy is very high, falling within the range of 160 to 180%. The breed has a temperament characterized by docility and composure, along with commendable parental qualities. The positive grazing behaviour shown by this breed facilitates their ability to adapt to dry and semi-arid climatic conditions. The weight of adult rams typically ranges from 90 to 110 kg, while mature ewes often weigh between 75 and 80 kg.

Figure 10: White Dorper sheep

Photo from https://mjksz.com/tenyesztes/fajtak/white-dorper.

3.2.1.2. Romanian breeds

Two breeds were sampled from Romania. They include:

White-headed Turcana

White-headed Turcana is also known as just Turcana sheep breed. The Turcana breed is classified as a resilient mountain breed within the Zackel group, which is native to the Carpathian Mountains in Eastern Europe. Currently, there is a recorded population of 7.8 million breeding ewes for this breed. The Turcana breed is conventionally used as a triple-purpose breed, primarily raised for its meat production (with average daily weight increases ranging from 110 to 180 grams), milk production (yielding around 60 to 150 kilograms per lactation), and wool production (characterized by coarse, long staples measuring 20 to 25 centimeters in length). The Turcana breed exhibits phenotypic diversity, characterized by the presence of five recognized ecotypes and three distinct color variants (white, black, and grey). Mature ewes of this breed normally weigh between 30 and 55 kg, while rams have a weight range of 60 to 110 kg. Turcana rams have elongated, spiraled horns, whilst ewes may possess either polled or horned characteristics (Figure 11). The conception rates of ewes exhibit a range of 95% to 98%, while their prolificacy varies from 105% to 130%. These ewes demonstrate exceptional survival rates of lambs, longevity in adult animals, and adaptability to cold temperatures, low quality feeding regimes, as well as resistance to transhumance and long roads (Gavojdian, 2014; Gavojdian et al., 2016).

Figure 11: White-headed Turcana sheep

Photo by Vasile Calin Ilisiu

Rusty Tsigai

This breed is also referred to as Romanian Tsigai. The Rusty Tsigai breed is an old low-land breed that originated in Eastern Romania. Currently, there is a population of around 2.2 million Rusty Tsigai heads. The Tsigai sheep breed is widely recognized as one of the primary sheep breed groups in Eastern Europe, alongside the Zackel group. The Tsigai breed is historically known for its triple-purpose producing meat, milk, and wool. The Tsigai breed has a wide range of phenotypic diversity, with mature ewes weighing between 35 to 70 kg and rams weighing between 55 and 90 kg. The most often seen color variants in this breed are white-headed, black-headed, speckled, and rusty individuals. Tsigai sheep have two distinct horn morphologies, either pooled or spiraled horns. Figure 12 shows polled individuals. The rates of conception in ewes exhibit a range of 92% to 97%, while the prolificacy varies from 120% to 150% (Ilisiu et al., 2013; Gavojdian, 2014).

Figure 12: Rusty Tsigai sheep

Photo by Vasile Calin Ilisiu

3.2.1.3. Greek breeds

Boutsiko

The Boutsiko breed is included among the Zackel group of mountain sheep and is mostly found in the hilly areas of Epirus and West Macedonia. The estimated population of the breed is around 15,000. The breed has undergone selective breeding using the Vlahi-ko, Karakachan, and Grammoustiano indigenous Greek breeds, with the objective of improving milk and lamb yield. The Boutsiko breed has notable adaptations to vagaries of environmental circumstances, including rugged terrain, moderate rainfall, and high levels of humidity. In general, this breed has a small body structure (Figure 13), whereby the female weight between 35 and 45 kg, while the male weigh between 45 to 50 kg. The bulk of the ewes lamb in the month of November, and their reproductive capacity is quite high, exceeding 90%, although the rate of multiple births per ewe is relatively modest, ranging from 1.1 to 1.3.

Figure 13: Boutsiko sheep

Photo by Dimitrios Loukovitis

Chios

The Chios sheep breed is believed to have originated from the Greek island of Chios and is classed as a semi-fat tailed breed. The breed is said to have been developed from the crossbreeding between indigenous sheep found on Chios Island and several breeds originating from West Anatolia. The Chios sheep breed is primarily raised for its milk production under a semi-intensive production system, with a current population of 25,000 individuals.

Chios sheep are often characterized by their mostly white fleece, which is sometimes accompanied with sporadic black or brown markings. These markings are generally seen around the eyes, as well as on the ears, nose, belly, and legs of the sheep (Figure 14). The head usually exhibits a black coloration. Mature ewes weigh between 50 to 70 kg whilst mature rams weigh between 65 and 95 kg. Ewes have the ability to breed twice a year, with an average litter size ranging from 1.7 to 2.2. The breed has a notable milk production capacity, with milk yields ranging from 200 to 320 kg 210 lactation days, contingent upon the specific management and husbandry practices used. The high milk quality produced by this breed makes it ideal for cheese production.

Figure 14: Chios sheep

Photo by Dimitrios Loukovitis

3.2.1.4. Polish breeds

Heath Sheep

Heath sheep is also known as Wrzosówka in the Polish language. It is a Polish native sheep that originates from Northern Europe and belongs to the group of Northern short-tailed sheep. Heath Sheep are a breed of short, tailed sheep characterized by their grey blended woollen coat (Figure 15). The lambs of this breed are first born with a black hue, which gradually transitions to grey as they mature. The Heath Sheep is a breed known for its sheepskin, which is highly regarded for its exceptional leather quality. The observed unique traits of this breed include high fertility and seasonal breeding.

Figure 15: Heath sheep

Photo by Aldona Kawęcka

Podhale Zackel

The Podhale Zackel, also known as Cakiel podhalański in Polish, is an adaptable ancestral Polish breed that developed from sheep introduced to the Polish Carpathians many years ago by the Wallachian community. This breed is classified under the category of mountain sheep, displaying remarkable adaptations to the challenging mountainous environments. They exhibit resistance to diseases, possess longevity, and have strong maternal and herding instincts. The woolly coat exhibits characteristics such as a white coloration, a thick and dense texture, a mixed composition, a two-fraction structure, and a flock-like arrangement (Figure 16).

Figure 16: Podhale Zackel sheep

Photo by Marta Pasternak

3.2.1.5. Bosnian-Herzegovinan breeds

From Bosnia-Herzegovina, three breeds: Dubska Pramenka, Hercegovačka Pramenka and Kupreška Pramenka were studied.

Dubska Pramenka

The Bosnian Dubska Pramenka sheep is an indigenous breed renowned for its capabilities in meat, milk, and wool production. The development of this breed occurred during the mid-20th century through crossbreeding French Merinos d'Arles and German Merino-Landschaf breeds. The Dubska Pramenka sheep breed has a moderate body size, with rams and ewes weighting 120 kg and 80kg respectively. In terms of morphology, the breed has a robust and well-developed physique. The coloration of the head may vary between black and white, whereas the face mostly exhibits a black hue. In contrast to

Ewes, rams are horned and have a physique that is adorned with coarse wool. The breed is recognized for its ability to adapt to local climatic circumstances (Figure 17).

Figure 17: Dubska Pramenka sheep
Photo by Husein Ohran

Hercegovačka Pramenka

Despite its long history of being bred in Herzegovina, formal recognition of this breed did not occur until 1998. The breed is recognized for its small stature (Figure 18), since mature males may attain a weight of up to 100kg, while females can weigh up to 60kg. Additionally, the breed has a robust physique characterized by a black head, which extends symmetrically to both sides of the face. In contrast to male horned rams, the majority of females are hornless. The Hercegovačka Pramenka breed has commendable reproductive traits; ewes attain sexual maturity at 18 months and a have a prolificacy rate of 1.5 lambs per ewe. The Hercegovačka Pramenka sheep is a breed renowned for its dual-purpose capabilities, producing both milk and meat. The milk produced by this breed is used in the production of cheese.

Figure 18: Hercegovačka Pramenka sheep

Photo by Husein Ohran

Kupreška Pramenka sheep

The Kupreška Pramenka sheep is a native breed that has its origins in Bosnia and Herzegovina, specifically the Kupres plateau. It is widely thought that this breed has evolved and developed in this region. The breed was officially recognized in 1994. Kupreška Pramenka breed has a small physical stature, with rams typically attaining a weight of roughly 120 kg and females averaging around 80 kg. The coloring of the head often exhibits a range of shades, with black being the predominant hue (Figure 19). Rams are mostly horned, while ewes are polled. Ewes attain their sexual maturity at 18 months of age, with an average lambing rate of 1.8 lambs per ewe. The Kupreška Pramenka sheep breed is categorized as a dual-purpose breed, known for its ability to provide both milk and meat. According to Važić et al. (2017), the milk generated by this particular breed has exceptional quality, making it very suitable for the manufacturing of cheese.

Figure 19: Kupreška Pramenka sheep

Photo by Husein Ohran

3.2.1.6. Serbian breeds

The following two native sheep breeds originating from Serbia were among the breeds studied.

Sjenica sheep/ Sjenica Pramenka

The Sjenica sheep is a transboundary variant of the Pramenka breed, characterized as a triple product breed and classified under the long-tailed sheep group. The horns of rams exhibit a color range from yellowish to black, and include notable characteristics such as big size, a triangular form, and a distinctive spiral twist. Conversely, ewes are often polled. The profile line has a gentle convex curvature. The fleece has a white coloration. The head has distinctive pigmentation, characterized by the presence of black hair in the vicinity of the nose and lips, as well as black ears. The dark hair around the eyes has a resemblance to the appearance of sunglasses (Figure 20). The presence of dark pigmented areas manifests on the lower extremities. The fleece has a semi-permeable structure that is distinguished by its flexible interlocking mechanisms and the presence of coarse fibers. The mean weight of mature ewes is around 60 kg, while rams often weigh in excess of 70 kg. The breed is well recognized for its ability to adapt to the challenging climatic conditions found in the Sjenica-Pester plateau area, characterized by winter temperatures that may drop to -40°C and lower. The breed is well recognized as a viable choice for an extensive breeding system. The renowned Sjenica cheese, with a designation of geographical origin, is produced using milk sourced from Sjenica sheep.

Figure 20: Sjenica sheep/ Sjenica Pramenka sheep

Photo by Zsolt Becskei

Lipe sheep/Lipe Pramenka

The Lipe variety of Pramenka sheep is an autochthonous breed that traces its origins to Serbia, and it is now facing the risk of endangerment. The local inhabitants often refer to it as Gara or Garulja. This breed, known for its late maturation, serves a triple function and is being reared in semi-intensive management settings within its native environment. It has characteristic features such as a wool coat that ranges in color from white to grayish white, accompanied by a black head and legs. Ewes often exhibit a polled phenotype, but rams possess prominent and powerful horns that are triangular in form, yellowish to black in color, and exhibit a spiral twist (Figures 21). The fleece has a porous composition distinguished by elongated, pliable strands and rough filaments. The colour of lambs is often characterized by a combination of black and white. The Pramenka breed is classified under the long-tailed sheep category. Ewes averagely weigh around 55 kg, while rams weigh 65 kg. The Lipe sheep exhibits a sturdy physical appearance and possess favorable milk traits suitable for the manufacture of cheese. The breed is well-regarded for its ability to adapt to the geographically complex terrain found in the marsh regions of Pomoravlje in Serbia.

Figure 21: Lipe sheep/Lipe Pramenka sheep

Photo by Zsolt Becskei

3.2.1.7. Lithuanian breeds

Lithuanian course wool sheep

The Lithuanian course wool sheep breed is categorized as a medium-sized breed, with a mature ewe normally weighing between 30 and 40 kg, and a mature ram weighing between 40 and 50 kg. This breed is characterized by its long, coarse, and fibrous wool, which often displays a white coloration, however there are also instances of variances in color such as black, brown, or gray (Figure 22). The wool produced by this breed is used in the manufacturing of traditional Lithuanian textiles, including as carpets, blankets, and clothing. The sheep breed is characterized by its short limbs, which often reveal a naked belly covered only by coarse fleece. Additionally, this breed has robust dermis, a small nose, and a large face. Furthermore, the ears are small in size, characterized by a modest length. The breed is well recognized for its exceptional ability to withstand low temperatures and its resistance to a range of diseases and parasites. They have commendable grazing habits and a docile temperament. They are characterized as dual-purpose breed producing wool and meat. The breed has a high level of prolificacy, with ewes typically producing between 2 to 3 lambs every reproductive cycle.

Figure 22: Lithuanian course wool sheep

Photo by Ruta Sveistiene

3.2.1.8. Kenyan breeds

Red Maasai

The Red Maasai breed is characterized by its fat-tailed trait and is indigenous to the East African area. The primary output of this breed is meat, with occasional production of milk. The breed is held in great esteem among East African pastoral communities owing to its exceptional adaptability in arid settings and its capacity to withstand internal parasites, including *Haemonchus spp*. The Red Maasai sheep breed has a coat coloration that ranges from red to brown (Figure 23). The tail of the breed has a considerable length and girth, although its ears possess an erect and elongated morphology. The average weight of mature ewes is around 50 kg, whilst rams have an average weight of around 70 kg. The Red Maasai have a distinct trait of docility, coupled with an early onset of reproductive maturity. Ewes typically start their first lambing at around 18 months of age, and they have the capacity to undertake two reproductive cycles within a single calendar year.

Figure 23: Red Maasai sheep

Photo by George Wanjala

East African fat tail

This breed of sheep is characterized by a fat-tailed morphology. It is recognized as a dual-purpose breed, since it is primarily raised for the production of meat, with occasional milk production as well. The breed is referred to as such on account of its lengthy and fat tail, and it is presumed to have originated in the East African region. The tail is hypothesized to function as a storage site for adipose tissue, so enabling it to adapt to dry and semi-arid climates. Both rams and ewes typically lack horns, however there are few instances when males do possess horns. Ewes have commendable reproductive traits with ewes often reaching sexual maturity at 18 months of age. Furthermore, ewes have the capacity to undergo two lambing within a single year (Figure 24).

Figure 24: East African fat tail sheep

Photo by George Wanjala

3.3. Sample collection and genotyping

Table 2 provides a comprehensive overview of the sample sizes for each breed, together with their respective geographic origins and the presumed climatic conditions to which they are adapted to. Three breeds, namely HUN.IldeFr, HUN.Suff, and HUN.Tetra, were included into the study as outgroups, indicating that they are not indigenous to Hungary. In order to get well represented results, within a certain breed, samples were collected from distinct flocks. All efforts were made to include populations representing non-related adult individuals from native sheep populations.

Meanwhile, raw samples were obtained by collecting blood samples from individual animals via puncturing their jugular veins. The acquired blood samples were then stored in vacutainer tubes (THOMSON et al., 1983) and afterwards placed onto the Flinders Technology Associates (FTA) cards® (HSIAO et al., 1999; DASH et al., 2020) as shown in Figure 25. The dried FTA cards were stored at ambient temperature prior to their submission to the genotyping company. The whole procedure of DNA isolation, genotyping, and conversion of raw signals into ovine50K genotype was delegated to Neogen company limited (https://www.neogen.com), which used the Infinium® OvineSNP50 BeadChip array which features more than 50,000 evenly spaced SNP-targeting probes, providing adequate SNP density for genetic diversity and signatures of local selection. The genotype calls were determined using the ovine Oar_v3.1 assembly (CLARK et al., 2017) as a reference genome, from which the final report was derived.

Table 2: A summary of all samples (N) used in the study before quality control.

Country	**Breed name**	**Climatic zone**	**Breed code**	**N**
Hungary	Hungarian Tsigai	Continental climate	HUN.Tsig	28
	Hungarian Merino		HUN.Mer	29
	Dorper		HUN.Dor	21
	White Dorper		HUN.Dor.W	20
	Bábolna Tetra		HUN.Tetra	27
	Ile de France		HUN.IldeFr	27
	Suffolk		HUN.Suff	20
	Hortobágy Racka		HUN.Rac	28
Bosnia-Herzegovina	Kupreška Pramenka	Continental climate	BIH.KPram	31
	Hercegovačka Pramenka		BIH.HPram	27
	Dubska Pramenka		BIH.DPram	25
Greece	Boutsiko	Mediterranean	GRC.Bout	30
	Chios		GRC.Chios	32
Romania	Rusty Tsigai	Continental climate	ROU.Rtsig	30
	White head Turcana		ROU.Turc	30
Serbia	Lipe Pramenka	Continental climate	SRB.LPram	25
	Zackel Pramenka		SRB.ZPram	20
Poland	Aleksandrowice	Continental climate	POL.Alek	25
	Cakiel Podhalanski		POL.Pod	25
Sweden	Dalapäls	Nordic climate	SWE.Dal	18
	Klövsjö		SWE.Klo	19
	Gotland		SWE.Got	19
Lithuania	Coarse-wooled sheep		LTU.Bface	30
Kenya	Red Maasai	Tropical climate	KEN.RedM	50
	East African fat tail		KEN.Eaft	40
Ethiopia	Menz		ETH.Menz	34
Morocco	Morocco	North Africa’s Mediterranean	MAR	30
Magreb region	Margeb		MARG	40
South Africa	South Africa Dorper	Sub-Tropical climate	SA.Dor	21
China	Tibetan	Sub-tropical climate	CHN.Tib	37
Iran	Afshar		IR.Afs	35
	Morganii		IR.Mog	34
Total				907

N: Number of samples before QC

Figure 25. Sample processing from vacutainer tubes to FTA cards staining.
From left to right hand: blood in vacutainer tubes, blood staining on FTA card and Stained FTA cards being dried at room temperature.

3.4. Quality control and genetic diversity analyses

The raw samples acquired from Neogen were processed and transformed into plink binary files (CHANG et al., 2015) for the purpose of merging using PLINK v1.9 (PURCELL et al., 2007) them with the downloaded datasets. These merged files were then used for further analysis. The process of data filtering was conducted by using the following predetermined criteria. Individuals that were closely related (first line relatives) or duplicates, individuals with unknown sex chromosome and SNPs, individuals with missing genotypes exceeding 10%, SNPs that were genotyped in less than 90% of the samples, SNPs with a minor allele frequency below 0.05%, and SNPs that deviated from the Hardy-Weinberg equilibrium (HWE) threshold of $p < 10^{-3}$ were all excluded from the analysis. After conducting quality control measures, a total of 41,098 SNPs were omitted from the analysis due to missingness. Additionally, 115 SNPs were removed based on the HWE threshold. Furthermore, 180 SNPs were disqualified from the study based on the MAF criterion. Moreover, 40 samples were deleted from the analysis due to missing genotypes, and an additional 35 samples were removed due to their degree of relatedness. The aforementioned procedure resulted in the acquisition of a dataset including 832 samples and 42,140 SNPs, which was then used for downstream analysis. Henceforth, the dataset resulting from the implementation of quality control measures on the SNP data will be denoted as the working dataset.

3.5. Statistical analysis

3.5.1. Determination of within and between breeds genomic variation and between sheep breeds genomic relationship

Four statistical approaches were used to determine the genetic diversity levels of the studied breeds. The statistical approaches included: observed, expected heterozygosity and inbreeding coefficient, effective population size through generations, between population relationship by Principle Component Analysis (PCA) and phylogenetic tree, and ancestry analysis. To achieve these, additional QC procedures were applied to the working dataset to ensure the accurate assessment of genetic diversity within and among sheep populations. The quality control techniques included the removal of single nucleotide polymorphisms (SNPs) that showed linkage disequilibrium (LD). This measure aimed at minimizing the potential bias resulting from a small set of genomic regions as explained by YUAN (2017). The LD pruning criteria were used to exclude single nucleotide polymorphisms (SNPs) until the correlation (r^2) between any two SNPs did not exceed 0.5 within a 200 Kilobase pair range. The calculation of genetic diversity indices was performed using Arlequin software version 3.5, as described by EXCOFFIER et al. (2005). The computation of genetic diversity metrics, such as expected heterozygosity (H_e) and observed heterozygosity (H_o), was conducted using haplotype frequency. Furthermore, the assessment of inbreeding was conducted using the method known as moments F coefficient estimates, employing the following formula:

$$\frac{Observed\ Homozygosity\ count - expected\ count}{Total\ observations - expected\ count}$$

Whereby the determination of expected count is based on the minor allele frequencies (MAFs; PURCELL et al., 2007). The determination of effective population size was performed using linkage disequilibrium information (SVED, 1971). The SNeP software, developed by BARBATO et al. (2015), was used to compute the effective population size using non-LD pruned data set. Analysis of molecular variance (AMOVA; MEIRMANS, 2006) using the specially designed population genetics tool Arlequin v 3.5 (EXCOFFIER et al., 2005) was used to determine genetic variation among individuals within the population and among all the 32 studied sheep breeds. AMOVA is a strong statistical tool for describing factors impacting population structure (MENGONI and BAZZICALUPO, 2002).

To ascertain the genomic correlation/relationship between populations and, the genomic homogeneity of the animals collected, unsupervised multidimensional clustering statistical analysis (ANDERSON, 1962), commonly known as principal component analysis (MAĆKIEWICZ AND RATAJCZAK, 1993) was computed on all genotypes using plink v1.9 (Chang et al., 2015). To ascertain the evolutionary links between different sheep breeds, the computation of Wright's FST index was performed on the working dataset using R package StAMPP (PEMBLETON et al., 2013) and visualized in R studio. To determine ancestry and quantify population structure, ADMIXTURE v1.3.0 (ALEXANDER et al., 2015) was used. The investigation was conducted using pre-determined ancestry clusters (K), which were believed to include a spectrum of 2 to 36 ancestral populations. The value of K with the lowest 15-fold cross validation error was chosen as the most likely. The Q matrix that was outputted was displayed using the BITE package v2 (MILANESI et al., 2017) using membercoef.plot function which exports a circular plot.

3.5.2. Determination and detection of patterns of run of homozygosity (ROH) and genomic based inbreeding coefficient (Froh) per native sheep breed

Runs of Homozygosity are stretches of DNA within an individual's genome where all the alleles are homozygous. These patterns provide valuable insights into an individual's ancestry, evolutionary history, and the signatures of natural selection on the genome. On the other hand, genomic inbreeding, ROH-based inbreeding, or FROH (fraction of homozygosity), is a metric that quantifies the fraction of the genome occupied by extended segments of ROH.

The calculation of ROHs was performed using the detectRUN package (BISCARINI et al., 2019) in the R program, using the sliding window approach. Given the absence of widely established guidelines for calculating the ROHs, we used the criteria outlined by DZOMBA et al. (2021). To summarize, the variants were not trimmed based on linkage disequilibrium (LD), i.e. the dataset used to calculate ROH was non-LD pruned. However, the minimum length necessary for a region to be termed a run of homozygosity (ROH) was raised to 1 megabases (mb) to remove any short ROH segments that may have been influenced by LD. The calculation of the sliding window was performed using the below parameters: window size of 15 mb and applying a threshold value of 0.05 to determine the eligibility of a SNP in the run. A minimal threshold of one heterozygous genotype was established, allowing for the possibility of one missing genotype. To meet the criteria for completeness, the ROH window was required to include a minimum of 30 SNPs. Furthermore, the minimum SNP density per ROH was established as one SNP per every 100 kilobases (kb), while the maximum distance between consecutive SNPs was defined as 1 mb. The identified ROHs were classified into four distinct groups based on their length: 1–6 mb, 6–12 mb, 12–24 mb, and over 48 mb. The cumulative length of the runs of homozygosity (ROH) in each individual animal was computed and then averaged across all breeds to ascertain the breed-specific average sum of ROH length. Furthermore, the number of runs for each segment was recorded. The study included the determination of the total number of ROH, the mean number of ROH, and the average length of ROH for each breed. Additionally, the peak runs, which are the runs in which SNPs occur in more than a certain threshold of samples in a population, were determined. SNPs that occurred in runs in at least 70%, 60%, and 50% of samples in the population were used as the criteria for defining the peak runs.

3.5.3. Identification of selection signatures for climate change adaptation

Signatures of selection are patterns of genetic variation that can be used to identify instances of past or ongoing selection on specific genes or regions of the genome. To identify possible genetic selection for adaptation to climatic changes, we performed a pairwise comparison analyses of populations that were categorized depending on climate. The use of pairwise comparison was employed to mitigate the potential biases that may arise from undisclosed population structures. This investigation included the formation of four distinct groupings of populations depending on climate. (i) The population of sheep in tropical climates consisted exclusively of breeds originating from East Africa, specifically KEN.Eaft, KEN.RedM and ETH.Menz. (ii) The Mediterranean/desert climatic region included breeds from North Africa, specifically MAR and MARG. (iii) The group of sheep breeds in continental climatic regions included native breeds from Europe, with the exception of breeds from Sweden, Lithuania, HUN.Dor, HUN.Dor.W, and the outgroups. (iv) The Oceanic climate category included breeds from Lithuania and Sweden.

To compute and search for climate change adapted genomic selection sweeps, two complimentary statistical methods were used. Wright’s fixation index, often known as FST statistics (BEAUMONT, 2005*)*, was computed in plink 1.9 to ascertain genetic differentiation between two paired populations and to discover variations in allele frequencies within these populations. It is postulated that all SNPs are subject to neutral selection and are expected to exhibit little heterogeneity. Consequently, SNPs that deviate from this standard may potentially account for the observed variance between populations and are hypothesized to be subject to natural selective pressures. The second approach used in this study was Cross Population Extended Haplotype Homozygosity (XP-EHH) as described by GAUTIER and VITALIS (2012). This methodology quantifies the length of extended haplotypes and evaluates the dissimilarities between the paired populations. The XP-EHH method has been extensively used in the identification of prospective signatures of local adaptation across several domestic livestock species (CHERUIYOT et al., 2018; EDEA et al., 2019; PAIM et al., 2022). A specific genomic region, referred to as the region of interest (RoI), was considered as a potential candidate for selection sweep if it achieved a log P-value or FST value of above 0.01%. The genes were subsequently annotated within a range of 250 kilobases upstream and downstream of the probable RoI using the BioMaRt software (DURINCK et al., 2005). The ensemble database (HUBBARD et al., 2002) was used for gene hunt and annotation. Review of multiple scientific literature was also useful in determining functions of identified genes. The visualization of signatures of selection was done using a combination of R packages including tidyverse (WICKHAM AND WICKHAM, 2017) and qqman *(*TURNER, 2014*)*.

3.5.4. Genome x climatic variable analysis to determine climatic variable driving adaptation of native sheep breeds in different climatic zones

The gene x environment association or land scape genomics (MANEL et al., 2003) is a prominent approach for identifying the environmental factors that are most likely to impact breed adaptation. This methodology seems to be advantageous in comprehending the effects of climate change on the agricultural sector, with a particular emphasis on livestock species. Historically, the focus of study has mostly been on human-mediated selection signatures because of their significant economic implications. In light of the increasing apprehension about climate change and its implications for genetic diversity, there has been a recent surge in interest among academics regarding environmentally induced selection signatures, which are signatures of natural selection. Consequently, the acquisition of reliable outcomes relating to the indications of natural selection may be achieved through the use of indigenous breeds that have acclimated to diverse climatic regions. The use of global climate databases e.g., WorldClim, enables the acquisition of comprehensive global climatic information, hence facilitating an indirect methodology for investigating genetic adaptability in response to climate change. The geographical location from where the samples were obtained may serve as proxies for phenotypic adaptations to the environment. This method has been used to identify environmental variables influencing natural selection and genes likely to be under selection for adaptation (FLORI et al., 2019; GOITOM et al., 2021; WIENER et al., 2021).

In pursuit of this objective, just those samples that had GPS coordinates were subjected to analysis. Here, we conducted an analysis on a total of 626 samples, which included samples from Kenya, Ethiopia, Morocco, as well as other European samples that were genotyped for this study. Prior to analysis, rigorous quality control measures were used to ensure the reliability and accuracy of the data.

Nineteen (19) annual means of climatic variables for each sample were obtained from the WorldClim database using the corresponding GPS coordinates. The WorldClim database has historical bioclimatic variables that provide primary quantitative data on temperatures and precipitation at yearly, weekly, and seasonal intervals. These variables serve as a surrogate to characterize the climate. The data provide a concise representation of climatic conditions spanning from 1970 to 2000. These variables are in the form of raster, with a spatial resolution of 30 seconds (~1km^2).

The degree of collinearity was assessed by the use of principal component analysis (PCA), Pearson correlation, and the variance inflation factor (VIF). The correlation among all variables (Figure 26A) was assessed using base R, and then, the covariates were trimmed to ensure that the correlation between any pair of variables did not surpass 0.7. The validation process included calculating the VIF and selecting a subset of variables with VIF values below 5 (Figure 5B). Here below is the description of each climatic variable obtained from the WorldClim database.

i. bio_1 = Annual mean temperature
ii. bio_2 = Mean diurnal range (mean of monthly (max temp - min temp))
iii. bio_3 = Isothermality (bio_2/ bio_7) (×100)
iv. bio_4 = Temperature seasonality (standard deviation ×100)
v. bio_5 = Max temperature of warmest month
vi. bio_6 = Min temperature of coldest month
vii. bio_7 = Temperature annual range (bio_5- bio_6)

viii. bio_8 = Mean temperature of wettest quarter
ix. bio_9 = Mean temperature of driest quarter
x. bio_10 = Mean temperature of warmest quarter
xi. bio_11 = Mean temperature of coldest quarter
xii. bio_12 = Annual precipitation
xiii. bio_13 = Precipitation of wettest month
xiv. bio_14 = Precipitation of driest month
xv. bio_15 = Precipitation seasonality (coefficient of variation)
xvi. bio_16 = Precipitation of wettest quarter
xvii. bio_17 = Precipitation of driest quarter
xviii. bio_18 = Precipitation of warmest quarter
xix. bio_19 = Precipitation of coldest quarter

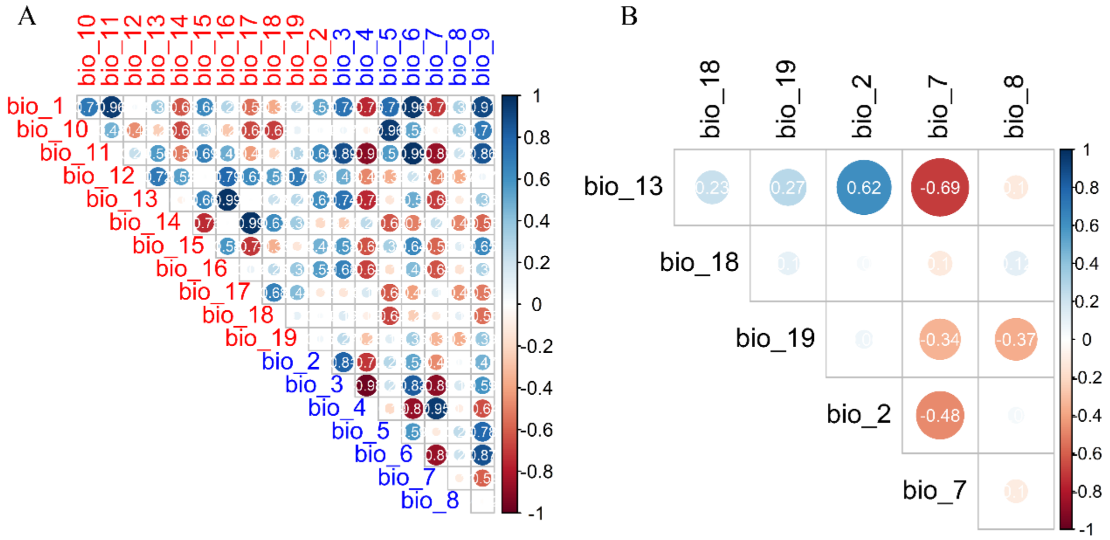


Figure 26: Correlation of all the environmental variables

A: correlation of all the variables before pruning, B: Correlation of the variables after pruning at cor < 0.7 and VIF < 5.

To determine the spatial genetic structure of populations, the K-means on principal components was used to detect the genetic clusters that minimize within cluster genetic variance, which turned to be 7 (Figure 27) . Discriminant analysis of the principal component was performed on the genotypes where 3 discriminant functions were retained (Figure 28).

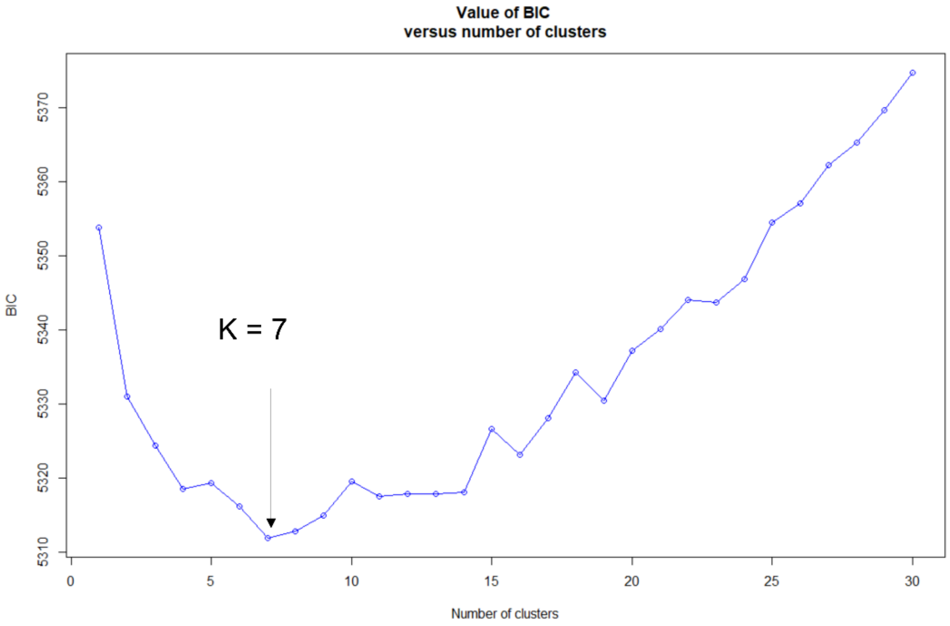


Figure 27: Number of genetic clusters (latent factors) that minimize within cluster variance.

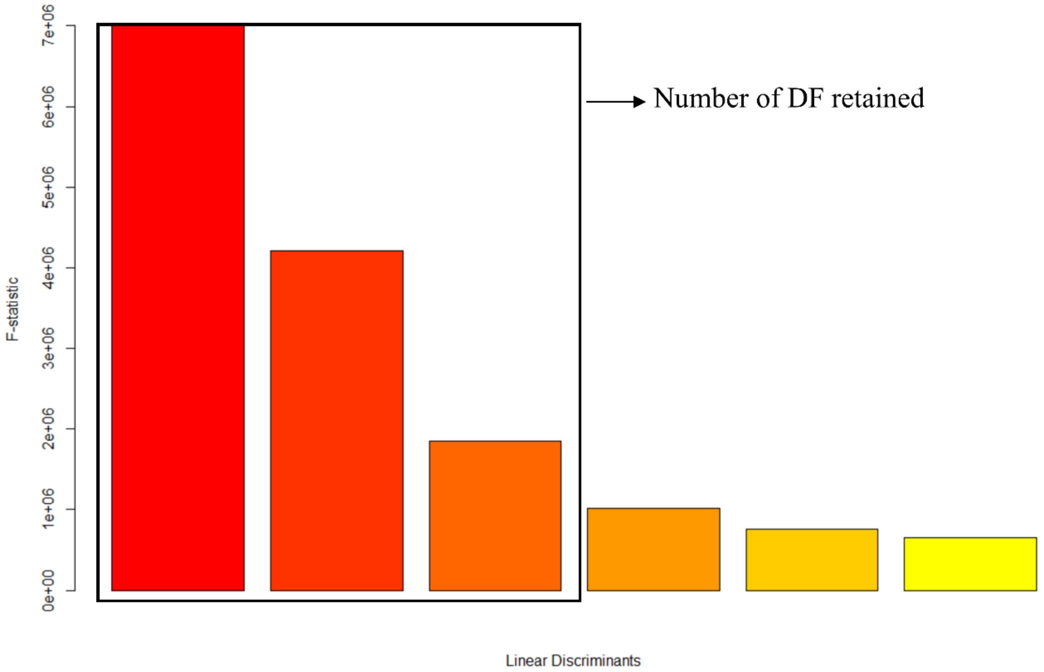


Figure 28: Discriminant analysis eigenvalues.
Inset: Discriminant functions retained.

Two statistical approaches were used in the present landscape genomics analysis: latent factor mixed models (LFMM) implemented by LFMM R package (CAYE et al., 2019) and redundancy discriminant analysis (RDA) implemented in (DIXON, 2003). Since the genome wide association studies (GWAS) encounter challenges related to confounding latent factors, LFMM package is designed to provide novel strategies for estimating parameters in LFMM. The algorithms have been specifically developed to address the issue of unobserved confounding variables (CAYE et al., 2019; SERRANITO et al., 2021).

Prior to running LFMMs, missing genotypes were imputed by relying on the best K from sNMF analysis. Then LFMM ridge regression was performed by regressing the genotypes against the five environmental variables that remained after quality control, refer to Figure 26B. In this analysis, seven latent factors were used to describe the population structure, refer to Figure 27. Signatures of selection were identified by computing the p-values for all the SNP by environment associations and then calibrated them by genomic inflation factor to reduce higher chances of obtaining false positives and negatives.

In contrast, the RDA function of Vegan package allows to test the impact of specific environmental variables on the dataset. It selectively retains only those variables that have a statistically significant influence on the molecular matrix. The process of 'variable selection' may be carried out via a 'forward model building approach' (WHITLEY et al., 2000). The process of forward model selection indicated that all the 5 environmental variables were significant, hence all were included in the association analysis. The R-squared adjustment was used to account for the percentage of variance explained by the environmental predictors. Subsequently, the statistical significance of the RDA model was assessed by F-statistics, with the null hypothesis stating that there is no linear relationship between the SNP data and the environmental variables. The identification of candidate SNPs associated with local adaptation was done by assessing their loading in the ordination space. In this analysis, we calculated SNP loadings specifically from the three constrained axes although the identified were seven. Constrained axes were deliberately reduced to three since it is assumed that the first three axes have a higher impact than others. The detection of potential SNPs under divergent selection were achieved by examining the loadings that exceeded ±3 standard deviations from the average of each distribution, which corresponds to a two-tailed p-value of 0.0027 or below (FORESTER et al., 2018).

4. RESULTS

4.1. Within breed genetic diversity and inter-breed genetic relationships

4.1.1. Within breed genetic diversity

Initially, a total of 907 samples and 83,533 SNPs pre-quality control were involved in the analysis. However, due to strict quality control measures that were implemented, 832 samples and 42,140 SNPs remained for downstream analysis. Overall, the diversity indices suggest that the studied breeds exhibited comparable levels of H_o and H_e, with indications of varying degrees of inbreeding seen across the breeds. The estimates of H_o for all 32 sheep breeds ranged from 0.309 to 0.392, while the estimates of H_e ranged from 0.331 to 0.389. The F coefficients, on the other hand, varied between 0.032 and 0.362, as shown in Table 3. The examination of Ne throughout several generations, spanning up to 915 generations in the past, revealed a significant and rapid decline in the effective population size (Figure 29). Several European breeds had a Ne value below 100, with the exception of BIH.Pram, GRC.Bout, HUN.IldeFr, HUN.Mer, ROU.Turc, ROU.RTsig, and POL.Pod, which showed Ne value above 100, 13 generations ago (Table 3). The effective population size (Ne) of African and Asian breeds, with the exception of SA.Dor, exceeded 100. In contrast, the SWE.Klo breed had the lowest Ne, measuring below 50. ±0.145).

Table 3: Means (sd) of within breed genetic diversity indices.

Breed code	*N*	H_o ±sd	H_e ±sd	F	Ne_{13}
ETH.Menz	34	0.346±0.16	0.352 ±0.14	0.174 ±0.04	211
KEN.Eaft	39	0.339±0.15	0.353±0.14	0.155±0.10	224
KEN.RedM	48	0.336±0.15	0.345±0.15	0.168±0.07	162
MAR	29	0.366±0.13	0.389±0.12	0.080±0.11	176
MARG	29	0.380±0.14	0.385±0.12	0.038±0.02	245
SA.Dor	19	0.367±0.17	0.364±0.14	0.125±0.04	71
CHN.Tib	36	0.343±0.14	0.363±0.14	0.172±0.05	164
IR.Afs	33	0.373±0.15	0.366±0.14	0.089±0.03	104
IR.Mog	34	0.376±0.15	0.376±0.13	0.067±0.02	154
BIH.DPram	23	0.383±0.13	0.375±0.13	0.034±0.05	118
BIH.HPram	23	0.383±0.16	0.376 ± 0.13	0.091±0.04	88
BIH.KPram	30	0.368±0.15	0.369±0.14	0.058±0.03	92
GRC.Bout	28	0.382±0.15	0.381±0.13	0.056±0.06	108
GRC.Chios	28	0.348±0.16	0.350±0.15	0.161±0.03	96
HUN.Dor	16	0.365±0.17	0.359±0.14	0.197±0.06	45
HUN.Dor.W	16	0.372±0.17	0.367±0.14	0.178±0.06	42
HUN.IldeFr	27	0.376±0.15	0.374±0.13	0.073±0.05	102
HUN.Mer	28	0.377±0.15	0.376±0.13	0.067±0.02	132
HUN.Rac	27	0.363±0.15	0.369±0.14	0.122±0.02	95
HUN.Suff	19	0.364±0.16	0.375±0.13	0.109±0.05	70
HUN.Tetra	23	0.392±0.16	0.384±0.13	0.033±0.02	88
HUN.Tsig	25	0.359±0.16	0.371±0.14	0.115±0.08	81
POL.Alek	23	0.368±0.16	0.364±0.14	0.115±0.05	59
POL.Pod	21	0.390±0.15	0.387±0.13	0.032±0.02	101
ROU.Rtsig	25	0.392±0.15	0.388±0.12	0.022±0.03	107
ROU.Turc	28	0.385±0.15	0.384±0.12	0.039±0.02	145
SRB.LPram	24	0.350±0.15	0.369±0.13	0.138±0.07	87
SRB.ZPram	16	0.385±0.16	0.393±0.12	0.046±0.05	85
SWE.Dal	18	0.309±0.18	0.331±0.16	0.362±0.12	40
SWE.Got	19	0.351±0.17	0.362±0.15	0.193±0.02	78
SWE.Klo	19	0.342±0.17	0.362±0.15	0.327±0.07	33
LTU.Bface	25	0.378±0.16	0.365±0.13	0.253±0.05	30

Assorted: individuals came from different breeds; N: Number of samples after QC, Ne_{13}- effective population size at 13 generations ago.

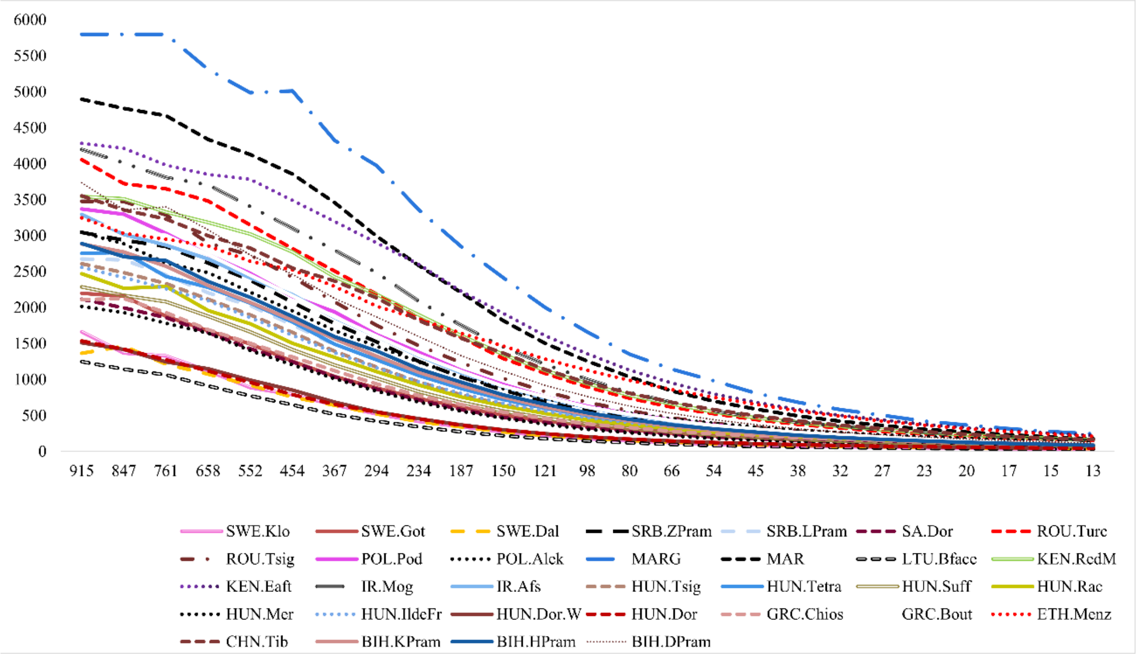


Figure 29: The trend of effective population size through generations within a population.

x-axis: number of generations; y-axis: Population size

4.1.2. Inter-breed genetic diversity and relationship

The AMOVA analysis revealed that a significant proportion of genetic variety, specifically over 91%, was found within the breed. Conversely, only a small proportion, around 8% ($p < 0.001$), was attributed to genetic variation across different breeds (Table 5).

Table 4: Genetic variation between and within the 32 sheep breeds.

Source of variation	d.f	Sum of squares	Variance components	Percentage of variation
Among populations	31	1033943.114	527.51012 Va	8.52
Within populations	1652	9357256.687	5664.19896 Vb	91.48
Total	1683	10391199.801	6191.70909	
Fixation index	0.08520, p-value < 0.001			

AMOVA was computed using distance matrix based on pairwise differences (FST)
Va- variance components among populations
Vb- Variance component between populations

The first two principal components (PCs) accounted for over 50% of the genetic variation seen in all breeds (Figure 30A), whereas the first three PCs together explained more than 64% of the variance (Figure 30B). A strong genetic proximity was seen among sheep breeds originating from the same continent, particularly those inhabiting the same climatic zone. PC’s 1 and 2 (Figure 30A) effectively differentiated breeds based on continental borders and climatological factors. The East African breeds (Tropical climate) from Kenya and Ethiopia exhibited clustering, as did the North African breeds from Morocco and other Maghreb regions. Similarly, the Asian originating breeds formed a distinct cluster. Among the European originating breeds, all except GRC.Chios exhibited correlated genomes, with HUN.Dor.W and HUN.Dor forming a separate cluster, and HUN.Dor.W and HUN.Dor clustering together with SA.Dor. With the exception of GRC.Chios, all breeds were positioned in close proximity to or along PC3, as seen in Figure 30B. Surprisingly, Asian, North African and GRC.Chios clustered together along PCA 3 Figure 30B.

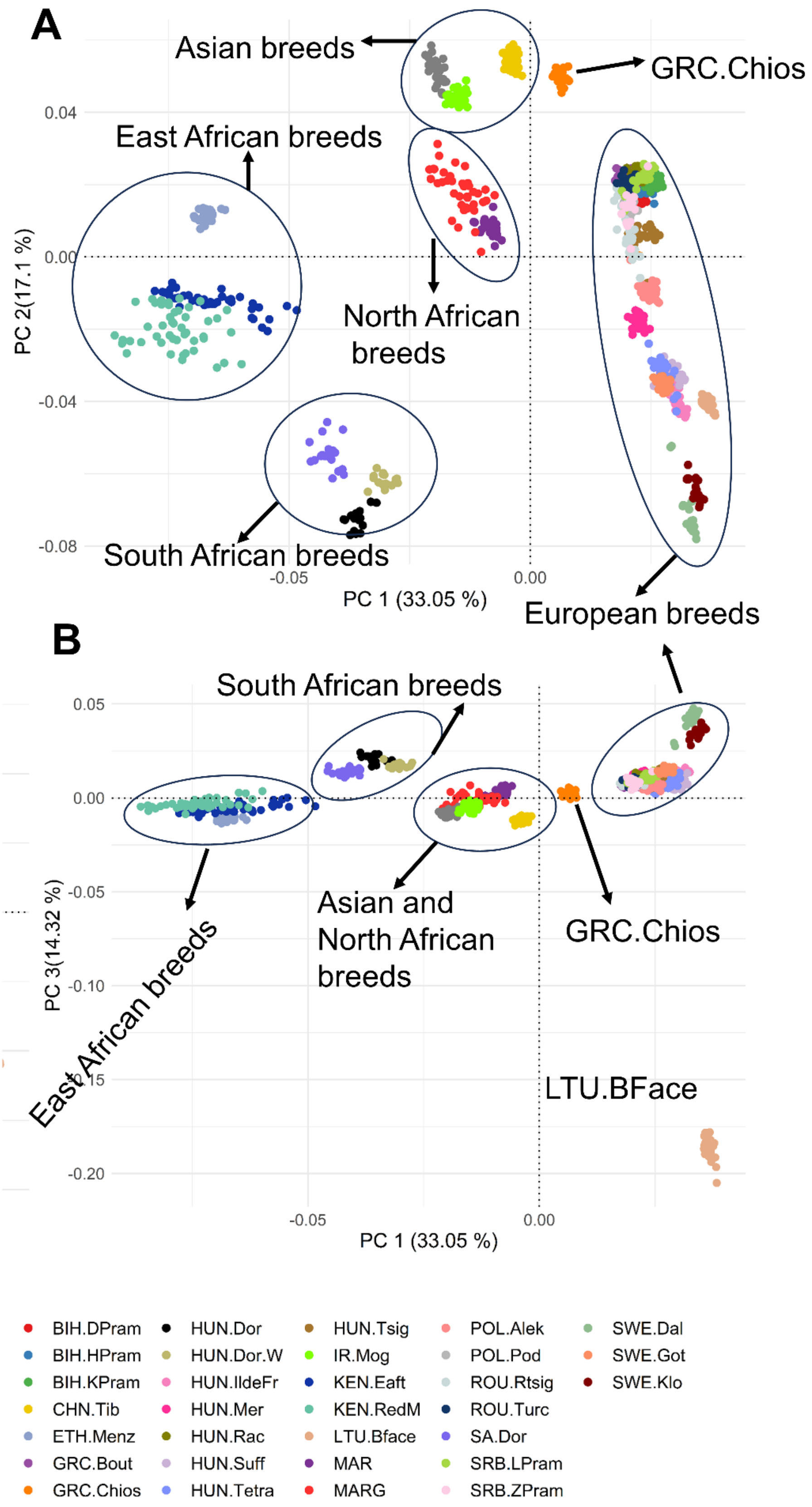


Figure 30: Principal components 1 to 3 for 32 native sheep breeds.

A: PC1 vs PC2, B: PC1 vs PC3

The phylogenetic tree (Figure 31) exhibited three primary branches, signifying three distinct patterns of breed divergence. Branch A comprises mostly African breeds together with HUN. Dor.W and HUN.Dor, as well as breeds originating from Asia and Greece. Branches B and C include all other European breeds. The sub-branches emanating from main branches linked closely related breeds that either originated from nearby geographical locations or have similar names, albeit coming from different nations. The phylogenetic tree showed a close grouping of all the outgroup breeds.

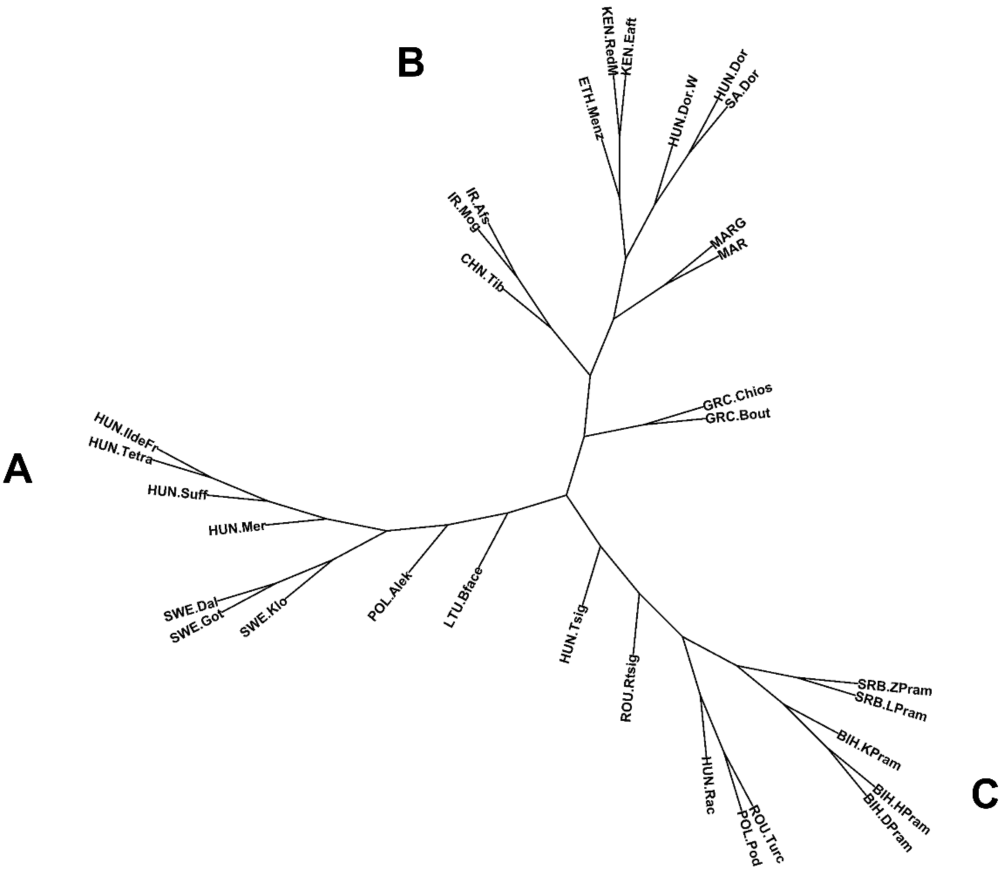


Figure 31: Phylogenetic tree showing the genetic linkages between the studied sheep breeds.

The ancestry study of the 32 breeds conducted using admixture software showed that the most probable number of clusters 25 based on the cross-validation entropy (CV; Figure 32A). It was observed that at K= 25, European breeds, which are thought to have adapted to the continental environment, had a significant level of admixture when compared to breeds from Northern Europe, Asia, and Africa (Figure 32B). Several breeds coming from Africa and Asia had discernible genetic origins at K=25, with the exception of KEN.RedM and SA. At the value of K = 32, which represents the number of breeds examined, it was seen that European breeds still had notable amounts of genetic admixture, whereas African and Asian breeds demonstrated distinct genetic ancestry.

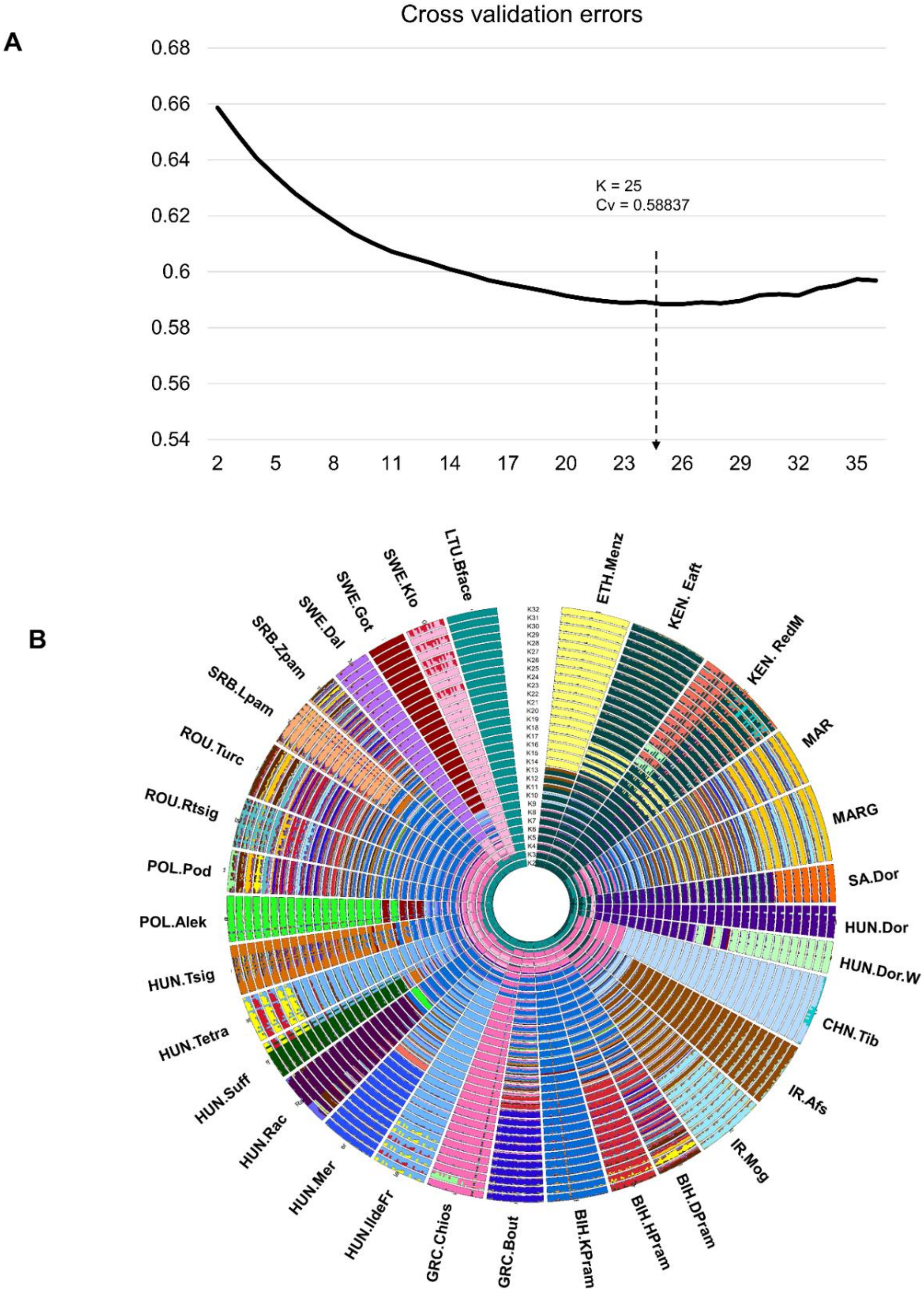


Figure 32: Ancestry member coefficient for each sheep breed samples.
A: Cross-entropy validation, B: ancestry membership from K2 to K32

4.2. Patterns of ROH and Froh genome per native sheep breed

Table 5 shows an overview of the average number of runs per class, the total counts of runs per class, and the Froh genome. In general, a discernible disparity was seen among breeds in terms of the average and count of runs in each class. The average number of runs per class within the 0-6 class varied from 1.837 for MARG to 3.448 for LTU.B face. In the class range of 12-24, the mean number of runs ranged from 7.713 for SWE.Klo to 8.9-3 for ROU.Tsig. In the class of 24-48 MB, the highest mean value was observed to be 35.540 (MAR). Conversely, in the class of >48, the highest mean value recorded was 97.417 (GRC.Bout). The latter two classes had some breeds without mean runs. Similarly, there was significant variation in the counts of runs seen among different breeds. In the counts for class 0-6 varied from 3 (MARG) to 2244 (SWE.Dal).For class 6-12, the counts ranged from 6 (SWE.Got) to 513 (LTU.Bface). The classes 12-24, 24-48, and >48 had the highest counts of 345 (LTU.Bface), 114 (LTU.Bface), and 23 (KEN.EAFT), respectively while some breeds did not register runs in these last three classes. All the breeds registered a considerable level of Froh_genome, which ranged between 0.001 (MARG) and 0.262 (LTU.Bface).

Table 5: Mean ROH, Froh (±sd) and counts of ROH per class.

Breed	Mean ROH per class					Froh_genome	Number of ROHs per class				
	0-6	6-12	12-24	24-48	> 48		0-6	6-12	12-24	24-48	> 48
BIH.DPram	2.652	8.238	16.222	34.213	51.078	0.026±0.03	265	25	20	9	1
BIH.HPram	2.672	8.199	18.163	30.060	77.469	0.036±0.03	348	38	21	12	3
BIH.KPram	3.083	8.482	16.598	31.317	58.405	0.078±0.04	522	171	103	41	2
CHN.Tib	2.767	7.479	NA	NA	NA	0.052±0.04	1460	122	NA	NA	NA
ETH.Menz	2.277	8.037	17.439	33.449	62.490	0.051±0.04	1490	30	17	10	5
GRC.Bout	2.969	8.609	16.247	32.091	97.417	0.047±0.06	369	84	49	19	3
GRC.Chios	3.004	8.179	15.584	33.868	NA	0.146±0.03	2113	324	77	18	NA
HUN.Dor	3.107	8.154	16.060	30.268	60.866	0.198±0.06	1277	274	79	18	6
HUN.Dor.W	3.113	8.294	16.180	32.912	65.658	0.186±0.06	1047	199	94	24	10
HUN.IldeFr	2.897	8.244	16.533	33.247	55.285	0.088±0.05	1153	179	50	17	1
HUN.Mer	2.811	7.950	16.196	30.454	NA	0.062±0.02	1118	115	19	7	NA
HUN.Rac	3.029	8.257	16.029	32.575	52.763	0.105±0.02	1148	246	88	16	2
HUN.Suff	3.003	8.185	16.917	31.346	50.786	0.114±0.05	755	136	76	31	2
HUN.Tetra	2.873	8.323	16.284	28.947	NA	0.044±0.02	503	66	29	7	NA
HUN.Tsig	3.214	8.465	16.607	32.352	61.885	0.117±0.08	690	247	104	37	8
IR.Afs	2.916	7.626	NA	NA	NA	0.027±0.02	653	58	NA	NA	NA
IR.Mog	2.769	7.627	NA	NA	NA	0.012±0.02	323	22	NA	NA	NA
KEN.Eaft	2.336	8.509	17.473	34.756	63.707	0.064±0.10	968	45	54	44	23
KEN.RedM	2.426	8.556	16.763	32.750	57.930	0.078±0.08	1331	194	137	60	13
LTU.Bface	3.448	8.578	16.624	32.037	59.080	0.262±0.05	789	513	346	114	14
MAR	2.758	8.634	16.991	35.540	62.400	0.064±0.11	214	55	65	45	18
MARG	1.837	NA	NA	NA	NA	0.001±0.00	3	NA	NA	NA	NA
POL.Alek	3.316	8.620	16.571	30.925	54.637	0.121±0.05	605	233	109	40	6
POL.Pod	2.666	8.381	15.578	24.712	53.070	0.023±0.02	294	36	7	2	1
ROU.Rtsig	2.816	8.903	18.276	29.609	50.988	0.025±0.03	247	45	17	5	2
ROU.Turc	2.579	8.805	16.556	29.347	53.601	0.022±0.02	309	47	16	3	1

SA.Dor	3.003	8.176	15.874	29.377	66.443	0.118±0.04	1032	187	57	9	2
SRB.LPram	3.170	8.544	16.656	30.753	56.252	0.125±0.08	550	190	133	62	8
SRB.ZPram	2.781	8.780	14.903	32.286	55.578	0.036±0.05	175	46	20	7	2
SWE.Dal	2.633	7.884	NA	NA	NA	0.130±0.05	2244	39	NA	NA	NA
SWE.Got	2.436	7.713	NA	NA	NA	0.047±0.01	958	6	NA	NA	NA
SWE.Klo	2.653	7.821	NA	NA	NA	0.118±0.03	2130	39	NA	NA	NA

NA= not available.

4.3. Climate change adaptation selection signatures

For the purpose of this research, six pairings of population were selected based on the climatic zones they are adapted to. These pairs include tropical against Africa's Mediterranean populations, tropical against continental populations, tropical against Nordic populations, African Mediterranean against continental populations, African Mediterranean against Nordic populations, and continental versus Nordic adapted breeds. To clarify, the population group of "African Mediterranean" refers to populations in North Africa, "Nordic populations" pertains to sheep in North European region, "tropical population" refers specifically to East African populations, and "continental populations" include all other European populations except the Nordic ones.

Generally, the distribution of p-values and FST scores throughout the genome exhibited a similar pattern, with a few minor peaks seen in some pairs (Figures 33 and 34). However, it is worth noting that chromosome 3 had distinct deviations in the XP-EHH analysis (Figure 33), namely in the comparison between Tropical vs Nordic and Continental populations vs Nordic populations.

A threshold of the top 0.01% of the log p-values or FST scores yielded a substantial number of SNPs that were indicative of selection for every pair of populations. The majority of signatures were specific to each population pair. The FST-based strategy detected a greater number of signatures compared to the XP-EHH method for each population pair. Both methodologies effectively identified a limited number of shared characteristics for each pair. Appendix Tables 1-6 include a comprehensive compilation of genes that were identified for each population pair. The colored column in all the tables displays the statistical methodology that identified the gene. Occasionally, it is seen that both columns are painted, indicating that the gene/s in question were identified by both approaches.

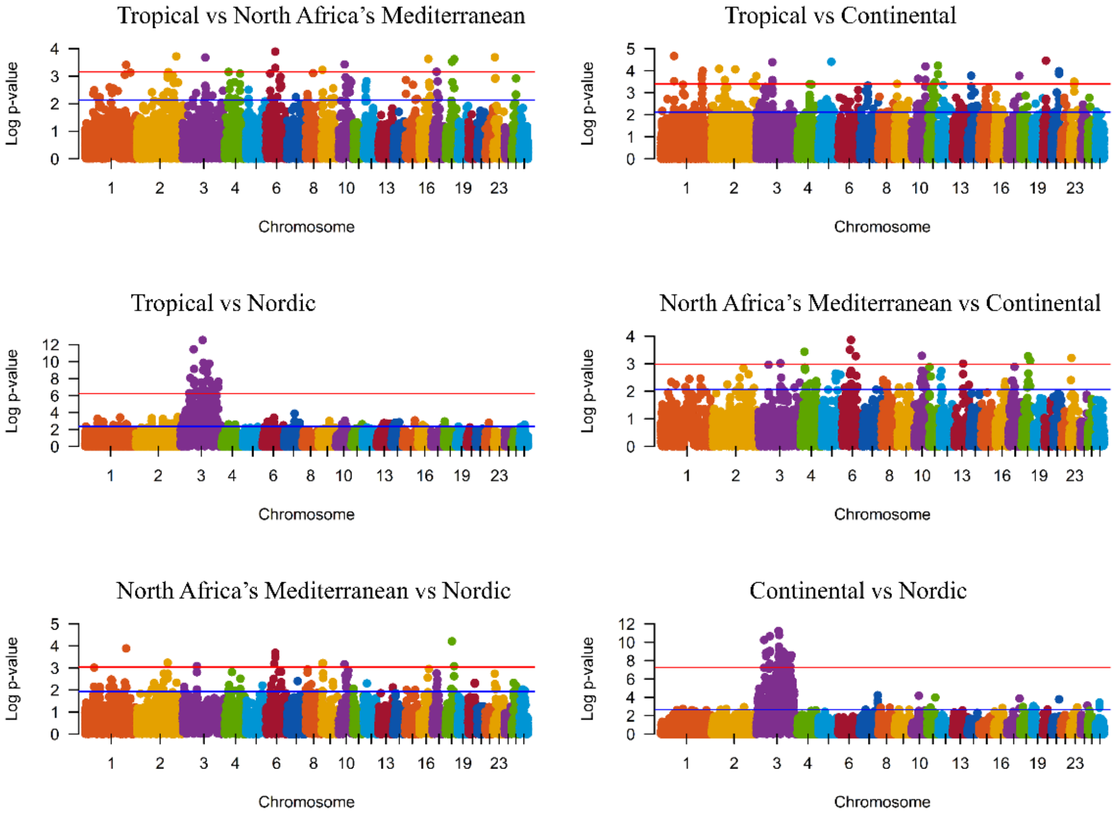


Figure 33: XP-EHH Manhattan plot showing log p-value and SNP distribution for each climate-based population pair.

Red line- suggestive threshold line at 0.01% while blue line is a genome wide line at 0.1%.

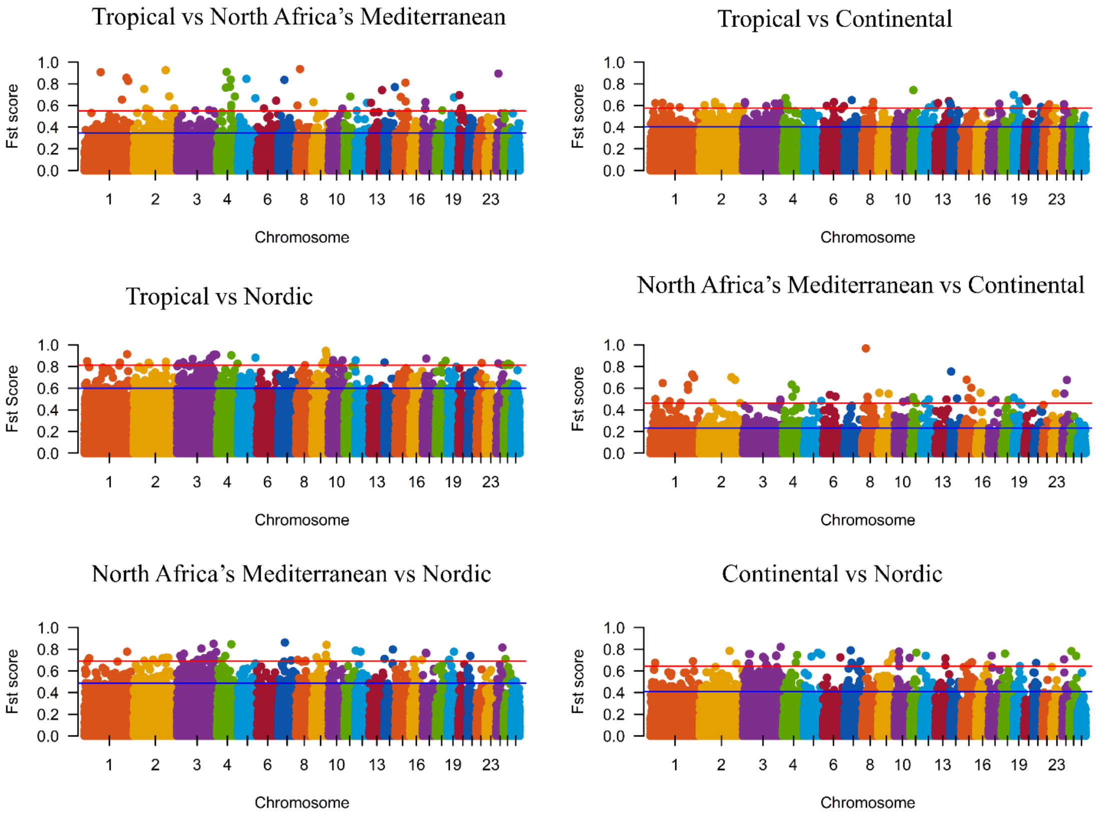


Figure 34: Manhattan plot showing FST score and SNP distribution for each climate-based population pair.

Red line- suggestive threshold line at 0.01% while blue line is a genome wide line at 0.1%.

4.4. Gene x environment association (GEA)

As a result of quality control steps of the environmental variables, only six (6) climatic variables remained for the association analysis. The six variables that were included in the analysis were bio_2, bio_7, bio_8, bio_13, bio_18, and bio_19. Hence, this part will give the post-processing outcomes of both the LFMM (ridge) and RDA statistical methodologies in relation to the five bio climatic variables. The LFMM method resulted in the identification of 133 SNPs, while the RDA approach provided a larger set of 360 SNPs. The analysis revealed a strong association between bio_2 and many SNPs using the RDA method. Conversely, the Latent Factor Mixed Model (LFMM) approach identified a greater number of SNPs in bio_8 and bio_19 compared to RDA (Table 6). Both the LFMM and RDA techniques yielded a total of 28 common outlier SNPs cutting across all climatic variables.

Table 6: Summary of number of SNPs significantly associated with each bio climatic variable.

Bio-climatic variable	LFMM	RDA
bio_2	21	127
bio_7	2	66
bio_8	18	3
bio_13	48	59
bio_18	17	102
bio_19	27	3
Total	133	360

The Gene Ontology primarily prioritized the analysis of shared SNPs identified by statistical approaches. This analysis resulted in the mapping of around 11 genes (Table 7). In general, both methods exhibited associations between SNPs and environmental variables that were largely similar, with a few exceptions. For instance, SNP DU464270_354.1 showed a discrepancy in its associations, as RDA linked it to bio_19 while LFMM associated it with bio_13. Similarly, SNP OAR3_231138606.1 also showed divergent associations, with RDA associating it with bio_7 and LFMM associating it with bio_18, similar to SNP s10898.1. A total of 11 distinct genes that are strongly believed to be responsible for driving adaptation were identified.

Table 7: Common outlier SNPs identified by both RDA and LFMM, their p values for each method, bioclimatic variables linked to the SNPs, and genes mapped near the SNPs.

SNP	Chr	BP	pRDA	pLFMM	bioRDA	bioLFMM	Gene name
s40694.1	1	285932646	0.010297	0.054294	bio_2	bio_2	-
OAR2_192491503.1	2	192491503	-0.01881	0.022217	bio_18	bio_18	STAT1
DU464270_354.1	3	132614430	-0.0125	0.042746	bio_19	bio_13	ATP5MC2
OAR3_138331159.1	3	138331159	-0.06545	-0.03431	bio_18	bio_18	TARBP2
OAR3_139371620.1	3	139371620	-0.00538	-0.02582	bio_18	bio_18	-
OAR3_231138606.1	3	231138606	-0.03065	-0.01825	bio_7	bio_18	-
OAR3_43427639.1	3	43427639	0.00301	-0.00955	bio_13	bio_13	-
s09582.1	3	85831354	0.012189	0.049759	bio_13	bio_13	-
s51845.1	3	225905945	-0.00599	0.022061	bio_13	bio_13	-
OAR6_97162589.1	6	97162589	0.014064	0.006435	bio_13	bio_13	SCD5
s21552.1	6	103818054	0.02642	0.031675	bio_13	bio_13	-
OAR7_97127242.1	7	97127242	-0.00446	0.064122	bio_13	bio_13	GSTA1
OAR7_97378846.1	7	97378846	0.060344	0.047132	bio_13	bio_13	-
s40182.1	7	88607719	0.008254	-0.00795	bio_2	bio_2	-
s52058.1	7	18561594	0.023605	0.012786	bio_13	bio_13	-
OAR11_4962381.1	11	4962381	0.005373	0.008149	bio_2	bio_2	HLF
OAR13_51727898.1	13	51727898	-0.00554	0.044412	bio_13	bio_13	-
OAR13_67246527.1	13	67246527	-0.01797	-0.03236	bio_18	bio_18,bio_2	ADIG
s66432.1	13	67952785	0.021583	0.010252	bio_18	bio_18	-
OAR16_18252778.1	16	18252778	0.005143	-0.0086	bio_18	bio_13,bio_18	-
s10898.1	18	70382783	-0.04211	-0.01173	bio_7	bio_18	-
s11142.1	18	19970738	0.024238	-0.0116	bio_13	bio_13	RHCG
s31152.1	18	19734572	-0.05197	4.98E-05	bio_18	bio_18	PLIN1
DU177621_558.1	19	56974832	0.000762	-0.02124	bio_2	bio_2	-
OAR19_15621948.1	19	15621948	-0.01489	0.013746	bio_18	bio_18	ABHD5
s08031.1	19	59803760	0.034551	-0.00581	bio_2	bio_2	-
s28575.1	21	46857187	-0.03101	-0.0279	bio_2	bio_2	-
OARX_63571789.1	27	63571789	0.069982	0.002946	bio_18	bio_18	-

5. CONCLUSIONS, RECOMMENDATIONS

Naturally and extensively bred indigenous sheep breeds primarily encounter a range of climate and environmental challenges, including increased parasitic burdens and pathogen pressure, inadequate feed quality and scarcity, extreme temperatures (both excessively high and low), and often ineffective breeding methods. In order to ensure their survival, it is necessary for these breeds to undergo genetic adaptations that enable them to thrive in specific climatic/ environmental conditions. Due to their global widespread and variability of morphological characteristics, local sheep breeds are an ideal model for studying the genetic diversity and adaptive mechanisms of domestic livestock species in the face of climate change. Hence, it is essential to determine the genetic makeup of native breeds and acquire a deeper understanding of the genetic processes behind their ability to adapt. This will serve to influence imminent genetic improvement endeavors and allow the implementation of selection programs that are conducive to climate adaptation. Researchers have the opportunity to explore the genome-wide genetic diversity, population structure, and possible genomic regions and mutations that contribute to the adaptation to climate change. To achieve success, it is essential that SNP markers possess enough genome coverage and exhibit polymorphism within each specific population. The present research included the analysis of a comprehensive set of 42,140 autosomal SNPs which are evenly distributed along the genome, hence, the present findings are believed to be reliable.

5.1. Within and between breeds genomic variation and between sheep breeds genomic relationship

5.1.1. Within breed genetic diversity

All the native breeds that were examined had reasonably high and comparable levels of heterozygosity (Table 3). The lowest values for H_o and He were 0.309 ± 0.18 and 0.331 ± 0.16, respectively, while the highest observed values for H_o and H_e were 0.392 ± 0.15 and 0.389 ± 0.12. Similar findings were seen in the Merino breeds (consisting of Merino and Merino-derived breeds) examined by CIANI (2015) and subsequently re-evaluated by ZSOLNAI (2023), as well as in global goat populations that were studied by COLLI et al. (2018), although the later study was not exclusively for indigenous breeds. While it was expected that African and Asian native sheep breeds would have higher levels of heterozygosity compared to European breeds, it was found that some European native breeds actually had higher levels of heterozygosity than the aforementioned breeds.

The F value derived from the comparison between H_o and H_e found that only seven breeds out of the 32 studied exhibited a $F < 0.055$ while the majority showed an $F > 0.055$. The seven breeds included MARG, BIH.DPram, HUN.Tetra, POL.Pod, ROU.Rtsig, ROU.Turc, and SRB.Zpram, exhibited an F value of less than 0.055. These results suggest that all the studied breeds are fairly inbred and apart from the forementioned breeds, all other breeds are highly inbred. It is not a surprise that native sheep breeds are highly inbred since the majority of them are freely grazed and they are never subjected to breeding programs as their product specialized counterparts. The persistent prevalence of inbreeding eroded the levels of heterozygosity i.e., facilitates enhancement of homozygosity which poses evolutionary disadvantages for indigenous sheep breeds, since it may lead to several detrimental consequences often associated with inbreeding depression (CHARLESWORTH & CHARLESWORTH, 1987; CHARLESWORTH & WILLIS, 2009). Historically, the management of inbreeding within populations has relied on pedigree information (GRANADO-TAJADA et al., 2020; POLAK et al., 2021). However, due to limited record-keeping practices in native sheep breeds, the utilization of molecular estimation techniques to assess inbreeding levels presents a promising avenue for enhancing breed management and mitigating the potential hazards associated with high levels of inbreeding.

The cumulative Ne for the 13 generations of all the examined breeds was estimated to be 1322. Notably, a positive correlation was seen between the number of generations and Ne from 13 to 915 generations ago, in other words, Ne of 915 generations ago was higher than Ne of 13 generations ago. Similar trend was observed in the breed-based Ne calculation (Figure). The Ne of many European sheep populations, with the exception of ROU.Turc, ROU.Rtsig, GRC.Bout, POL.Pod, and BIH.DPram., was found to be below 100, around 13 generations ago agreeing with the findings made by NOSRATI et al. (2021). With the exception of SA.Dor, all the breeds that were developed in Africa and Asia had Ne levels (Figure 29) over 100. The reason for MARG having the highest Ne is attributed to the fact that the samples were obtained from various nations and breeds. Surprisingly, the Ne of MAR was found to be lower than that of many other breeds originating from Africa and Asia, despite MAR population consisting of samples from other breeds in Morocco. TABERLET et al. (2008) assert that the International Union for

Conservation of Nature (IUCN) classifies species or breeds into categories based on their susceptibility to extinction. According to the authors, populations that are classified as critically endangered are characterized by having an Ne < 50. Similarly, populations classified as endangered have a Ne < 250, while populations classified as vulnerable have a Ne < 1000. When examining FRANKLIN'S (1980) recommendations, LYNCH and LANDE (1998) argue in favor of maintaining a minimum Ne of 500 in order to mitigate the risk of long-term population extinction. The estimated Ne of all the investigated native sheep populations was found to be less than 500. Indeed, it is noteworthy that none of the aforementioned populations had a Ne value above 250, so suggesting that all of these populations might potentially be classified as endangered. It is understood that the estimate of Ne is influenced by several aspects, such as the choice of software, the sampling methodology, and the analytical technique used. In order to get more comprehensive and dependable findings that can effectively guide future conservation strategies, we propose the use of extensive, genome-wide Ne analysis on indigenous sheep populations. Nevertheless, the results of our study provide empirical evidence that aligns with the FAO's categorization (DAD-IS, 2023; https://www.fao.org) of several indigenous European breeds as being at risk of extinction. In light of the aforementioned findings, it can be inferred that the genetic diversity in the examined breeds is undergoing a rapid decline, despite their initial richness in heterozygosity. This poses significant threats to the survival of these esteemed breeds in the face of climate change.

5.1.2. Inter-breed genetic diversity and relationship

According to the AMOVA analysis (Table 4), around 9% of the genomic variance may be attributed to inter-breed variation, whereas over 90% of the variance is attributable to intra-breed variation (FST = 0.09, $p < 0.001$). The present FST value is in concurrence with the results (FST = 0.0869) observed in global goat populations by COLLI et al. (2018). Nevertheless, the observed FST value is higher than the one computed for the overall sheep populations (FST = 0.025; KIJAS et al., 2012).

Despite the observed decline in genetic diversity among native breeds, there remains a significant degree of intra-breed variability that may be harnessed for within-breed selection. This approach holds promise for enhancing production capabilities and bolstering resilience to the impacts of climate change. The first two principal components (PCs) accounted for over 50% of the genetic variation seen across the breeds, indicating a noteworthy clustering pattern among the breeds studied. PC1, which accounted for

33.05% of the genetic variance, exhibited a distinct separation between African and Asian native breeds and their European counterparts. HUN.Dor and HUN.Dor.W were combined with SA.Dor due to their shared development in South Africa (Figure 30). The absence of overlap seen in the clustering of Asian and African native breeds indicates a distinct divergence between these two groups of populations from separate continents. The European breeds were partitioned in the center by PC2, which also segregates Asian and African native. Distinguishing partitions of European groups was challenging, with the exception of GRC.Chios, LTU.Bface, Swedish breeds, and outbreeds, which exhibited distinct clusters. The PC clustering analysis exhibited concordance with the categories seen in the phylogenetic tree (Figure 31). Based on the principles of phylogenetic clustering, it can be observed that European sheep breeds exhibit a tendency to cluster together, likely attributable to their shared evolutionary backgrounds. Within this clustering, sub-groups of breeds with similar evolutionary histories can be identified, such as the Pramenka sheep (ĆINKULOV et al., 2008; KUSZA et al., 2011) or the North European breeds (SVEISTIENE & TAPIO, 2021). Nevertheless, it is worth noting that several breeds, like HUN.Tsig, ROU.RTsig, LTU.Bface, and POL.Alek, have shown different genetic characteristics compared to their European counterparts, despite sharing similar developmental processes. As anticipated, the African and Asian breeds exhibited distinct subgroups within a larger branch, maybe as a result of their adaption to comparable climatic conditions and/or their interconnected developmental processes. The proximity observed between Greek breeds, African and Asian native sheep breeds may be attributed to either their adaptation to the Mediterranean climate, as sheep farming in Greece predominantly follows extensive production practices (BELIBASAKI et al., 2012; GELASAKIS et al., 2012; KOMINAKIS et al., 2021), or the shared developmental history. Historically, Greece is very near to the Anatolian peninsula, where agriculture was first developed, and initial domesticated sheep were also raised. Therefore, the sheep that migrated in other directions (Africa, Asia) also appeared very early in Greece, at the same time as those that migrated in the other regions. In addition, Greece's history guaranteed a continuous link between these two continents. Greece was a member of the Ottoman Empire for a very long time, which spanned North Africa, several regions of Asia, and sections of Europe. The empire's trade routes also facilitated the movement of people and animals.

Overall, the investigation has shown that African and Asian breeds exhibit significant genomic differences when compared to their European counterparts. This observation aligns with the results obtained from a global study on goats (COLLI et al., 2018), which exhibit comparable migratory and developmental patterns to sheep breeds. The authors revealed a significant molecular differentiation both within and across continents. The results of our study differ from previous research on global sheep genetics, which indicated a limited spatial structure (FARIELLO et al., 2014; KIJAS et al., 2009, 2012). It is postulated that the later research included a comprehensive range of breeds, including both transboundary and specialized breeds. Transboundary and product specialized breeds have facilitated the dissemination of genetic material across regions through the processes of crossbreeding and up-grading. These breeds are often used to engage in crossbreeding with indigenous breeds in order to enhance their productivity, whether it be for improved growth rates and carcass characteristics, or for enhanced dairy production traits and udder morphology.

The cross-entropy error from the admixture study revealed that possibly K was 25 (Figure 32A) despite having samples from 32 distinct breeds. At K = 25, several European native sheep breeds exhibited significant levels of admixture, with the exception of Nordic European breeds, HUN.Dor.W. and HUN.Dor. The MAR and MARG populations, despite samples originating from distinct breed groups, were seen to be grouped together in a same cluster agreeing with finding by BELABDI et al. (2019). Similarly, the HUN.Dor and SA.Dor populations were also identified as belonging to the same cluster despite having sampled not only from different countries but continents. However, this was expected as both populations have similar ancestry background. Remarkably, while sharing a comparable evolutionary lineage, HUN.Dor.W exhibited discernible genetic divergence from HUN.Dor. Also, at K=25, it was seen that the Asian breeds IR.Afs and IR.MOG exhibited varying degrees of admixture, indicating the presence of genetic material from several ancestral sources. In contrast, the CHN.Tib breed had a distinct cluster, indicating a lack of genetic mixing with other populations. At the value of K = 32, which represents the number of breeds examined, it was observed that some European breeds continued to show evidence of admixture, whilst their African and Asian counterparts, with the exception of KEN.RedM, displayed distinct clusters. KEN.RedM samples were collected from flocks that are subject to conservation efforts by the Kenyan Government. Occasionally, as a result of inadequate management practices, individuals from KEN.RedM flocks may intermingle with Dorper flocks that coexist on the same farm hence the need to enhance management and conservation practices. At a K = 3 (Number of continents represented by the samples), it was observed that East African breeds (KEN.Eaft, KEN.RedM and ETH.Menz) exhibited a clear separation from other breeds. Additionally, North African breeds (MAR and MARG) displayed some degree of genetic similarity with European cluster breed groups. It is worth noting that SA.Dor, HUN.Dor, and HUN.Dor.W exhibited certain genetic components associated with East African breeds, which can be attributed to the common practice of crossbreeding with the Dorper breed, widely utilized to upgrade native sheep breeds in East Africa. The findings of this study regarding the admixture level of European sheep breeds align with the conclusions drawn by KIJAS et al. (2012), who reported significant historical admixture in sheep breeds worldwide. Additionally, previous analyses of European breeds conducted by LAWSON HANDLEY et al. (2007) and PETER et al. (2007) also identified high levels of breed admixture. This study provides evidence that European Nordic sheep breeds, namely SWE.Dal, SWE.Got, SWE.Klo, and LTU.Bface, may possess distinct genomic regions that differ significantly from those found in other European native sheep breeds (DÝRMUNDSSON & NIŻNIKOWSKI, 2010; TAPIO et al., 2005; SVEISTIENE & TAPIO, 2021).

5.2. Patterns of ROH and Froh genome per breed

The length of the ROH is a vital genetic tool used to ascertain the historical patterns of population growth. ROHs are haplotypes derived from shared genetic material inherited from common ancestors in previous generations (CEBALLOS et al., 2018). The presence of runs of ROHs spanning 1-6 mb indicates the presence of haplotypes derived from ancestors who are somewhat distant in the past. Conversely, ROHs exceeding 48 mb suggest the presence of haplotypes derived from more recent ancestors (CEBALLOS et al., 2018). In the present study, different classes of runs were observed in several breeds suggesting different stages of development. It also shows that previous ancestors also had some levels of genomic inbreeding. Some breeds like Marg, SWE.Got, SWE.Dal, SWE.Klo, IR.Afs, IR.Mog, HUN.Mer and GRC.Chios did not have long runs, particularly runs of class 12-24 and above, possibly suggesting proper molecular management especially breeds from European countries and they are being bred for diversity. The absence of long runs in IR.Afs and IR.Mog might perhaps be attributed to the substantial size of the population. Conversely, in the case of Mog, this could be ascribed to significant individual variability, given the samples were collected from diverse flocks located in various countries. Furthermore, when the length ROH classes increased along the genome, there was a corresponding drop in the mean and counts of ROHs. In essence, it can be noted that the frequency of ROH for genomic regions spanning 1-6 mb exhibited a progressive decline as the ROH classes increased, reaching its lowest point for class > 48 mb across all populations. This implies that the ancient populations had a higher degree of consanguinity compared to contemporary groups (GRANERO et al., 2022). Moreover, the presence of runs may serve as a potential signal of selection, since previous research has shown that genomic areas undergoing selection tend to coincide with regions characterized by an abundance of ROH, sometimes referred to as "ROH islands" (ZHANG et al., 2015). ROH islands are described by BOSSE et al. (2012) as genomic areas exhibiting the most concentrated distribution of runs of homozygosity (ROHs).

Although some breeds didn’t have long runs, all the studied breeds showed some levels of genomic inbreeding (Froh_genome, Table 5). It is important to highlight the significance of inbreeding in relation to the decline in fitness and production. The practice of consanguineous mating may lead to the transmission of haplotypes that are identical by descent (IBD), resulting in the occurrence of extended homozygous regions in the offspring, i.e runs of >48 mbs in length. These locations have the ability to enhance the risks of co-appearance of lethal recessive alleles, hence decreasing the fitness traits of the population.

5.3. Signatures of climate change adaptation

The agricultural industry is profoundly impacted by climate change, resulting in a simultaneous decrease in indicators of biodiversity, including genetic diversity among species. Multiple scenarios and forecasts pertaining to climate change indicate that livestock species need to exhibit the inherent ability to adapt and withstand diverse environmental factors. These variables include, but are not limited to, heat stress, prolonged drought, and the occurrence and recurrence of infectious diseases. The genetic adaptability of animals has a vital role in influencing their survival, longevity, and sustained output. This research examines the adaptation of local sheep breeds to four distinct climatic zones, namely African tropical, African Mediterranean (Desert), European continental, and European Nordic (Cold conditions). In order to exploit the cumulative changes in allele frequency and haplotype length across climate-based populations, a comparative analysis was conducted on pairs of populations utilizing both FST and XP-EHH methodologies. A considerable number of genes per population pair was identified, and it is hypothesized that these genes are differentially associated with the process of adaptation to climate change. Some of these genes identified in each population pair are discussed below.

5.3.1. Tropical and Africa's Mediterranean climatic zones

Tropical sheep have adaptations that enable them to thrive in regions characterized by consistently high temperatures, ample precipitation, and elevated humidity-temperature index throughout the year. In contrast, Mediterranean sheep have evolved to withstand the challenges posed by hot and arid summers, as well as mild and moist winters. Notably, several flocks of Mediterranean sheep have even adapted to survive in desert environments within the Mediterranean region. Both suggestive and genome-wide lines (Figures 33 and 34 - Tropical vs Africa's Mediterranean) show that the whole genome plays a crucial role in the adaptation to these climatic zones. However, the presence of a greater number of genes on chromosomes 1 and 2 (Appendix Table 1) suggests that, while the whole genome plays a crucial role in facilitating differential adaptation in these two climatic regions, chromosomes 1 and 2 may have a more significant influence on the adaptive process. The gene *ARF5*, responsible for ADP ribosylation factor 5, was identified to be located on chromosome 4 in sheep. The genes *ARF1*, *ARF2*, and *ARF6*, which are implicated in intracellular localization, belong to a family of *ARFs* (LEE et al., 1997). However, it has been shown that in some species, particularly sheep, the gene *ARF5* exhibits supplementary functions such as triggering immune responses and controlling programmed cell death, also known as apoptosis. This is particularly relevant in the case of sheep raised in desert environments, where they are subjected to elevated temperatures that may lead to substantial cell apoptosis. Additional genes that have been implicated in the regulation of immune response include the *CDID* gene (HOPKINS et al., 2000; RHIND et al., 1999) and the *IL12RB2* gene, both of which have shown significant associations with immune response to *Haemonchus* nematodes (ESTRADA-REYES et al., 2019a). Although there is little available information on the impact of the gene *DDX21* in sheep, its role in pigs has been investigated and shown to have a favorable regulatory effect on the swine reproductive and respiratory syndrome virus (LI et al., 2022). In the context of sheep, it is hypothesized that this particular gene may play a role in the regulation of reproductive processes, alongside *GLUD1* (BROWN et al., 2017; SÁNCHEZ-RAMOS et al., 2023) and *BMPR1A* (KOMINAKIS et al., 2017; YULIANG et al., 2020), specifically on chromosome 25.

5.3.2. Tropical vs Continental climatic populations

The continental climate adapted sheep, in contrast to their tropical counterparts, have developed adaptations to cope with the fluctuations in temperature and precipitation that occur between the seasons. Based on the findings of this study, both suggestive and genome-wide lines (Figures 33 and 34 - Tropical vs Continental climatic) imperatively assert that the whole genome plays a significant role in determining the differential adaptation of native sheep between tropical and continental climates. Furthermore, the genes retrieved from the ensemble database were found to be distributed across many chromosomes across the genome (Appendix Table 2). The *SLC30A7* gene is primarily implicated in the facilitation of mineral transport, namely zinc, throughout the physiological systems of animals. Zinc is required by a multitude of enzymes involved in processes including immunity, growth, and reproduction (HUANG et al., 2023). The maintenance of cellular zinc homeostasis is of utmost importance, as its deficiency may lead to inhibited development, compromised immune function, and decreased reproductive capabilities. ZHANG et al. (2021) have also shown that *SLC30A7* may possess antioxidant properties in mice. The gene *EGRI* is a multifunctional zinc-finger factor which belongs to the early response gene family. The gene exhibits rapid activation in response to several biological agents including hormones, growth factors and neurotransmitters (THIEL & CIBELLI, 2002). It is regarded as multifunctional gene due to its regulation of several biological processes, including cell differentiation, death, and migration (XU et al., 2022). In this study, we propose that the identified gene has a dual role in regulating both the immunological response and growth in sheep. On the other hand, the *ANXA2* gene has been found to have an impact on the composition of milk proteins and fatty acids (CALVO et al., 2006; MARTÍNEZ-ROYO et al., 2010; PECKA-KIEŁB et al., 2018). Additionally, a separate study has indicated that the *ANXA2* gene plays a role in the immune response during acute inflammation (GASTARDELO et al., 2009) in mice.

5.3.3. Tropical vs Nordic climatic populations

The Lithuanian and Sweden sheep breeds were categorized into the climatic area of Nord Europe, characterized by relatively mild summers and somewhat colder winters compared to continental regions. It is worth noting that while Nordic breeds may possess varying degrees of adaptation to distinct climatic conditions, they were grouped together based on their geographical location in Europe. The presence of a prominent peak on chromosome 3 (Figure 33: Tropical vs Nordic) indicates a potential significance in the differential adaptation seen between the two distinct environmental zones. Figure 34 (Tropical vs Nordic) illustrates the distribution of SNPs above the threshold line across all chromosomes in the whole genome. This distribution suggests that the entire genome plays a role in determining adaptation traits. In Appendix Table 3, some of the genes found included gene *GDI2* which has been implicated in various biological processes, such as the generation of antibodies against diverse human tumor cells (WU et al., 2022; ZHANG et al., 2021) and the regulation of embryonic development (WU et al., 2022). Similarly, the *POMC* gene is recognized as a versatile gene that is involved in feed intake, skin pigmentation, and growth and development (MILLINGTON, 2007; QUARTA et al., 2021). In sheep, it is hypothesized that this gene may play a pivotal role in heat tolerance, since pigmentation has been strongly linked to the processes of heat absorption and dissipation. In contrast, previous studies have shown associations between *RAB1A*, *IL1b*, and *IL1A* and various immunological responses across several species (BONNEFONT et al., 2012; JIANG et al., 2011; LU et al., 2022; YARO et al., 2019).

5.3.4. North Africa’s Mediterranean vs Continental climatic populations

Under this pair, XP-EHH method produced a Manhattan plot that had one major peak on chromosome 6 and some multiple minor peaks (Figure 33 - Africa’s Mediterranean vs Continental) showing that under this method, chromosome 6 could be majorly harboring genomic regions determining adaptation in these climatic regions. However, FST method several minor peaks cross the genome (Figure 34- Africa’s Mediterranean vs Continental) suggesting significant allele distribution differences between both populations. Some of the genes that were identified in this pair (Appendix Table 4) have been proposed to underpin several types of immune response. These genes, such as *CBx, CXCL8, CXCL1*, and *CXCL10* (BONNEFONT et al., 2012; RUDDOCK-D’CRUZ et al., 2008), have been separately identified using different techniques. Additionally, *IL12RB2* has been identified as a gene related to resistance/susceptibility to *Haemonchus contortus* (ESTRADA-REYES et al., 2019b) nematodes. Other genes associated with the immune response include *TLR9*, which has been suggested as a potential factor in heat stress tolerance (SAADATABADI et al., 2023) and immune response (SARAFIDOU et al., 2013), as well as *CR2* and *IL15* (RUTEMARK et al., 2012; SANAD et al., 2014). The stimulation of growth, skeletal, and muscular development is attributed to the presence of a growth hormone receptor (*GHR*) gene (AKHATAYEVA et al., 2022). These developmental processes have equal importance in the context of climate change adaptation, as they determine an animal's body size, which in turn has direct implications for feed intake, metabolism, and tolerance to heat stress. The significance of reproductive efficiency in climate change adaptation is of comparable importance since it represents a fundamental survival traits of the breed. In the present investigation, we successfully identified and mapped a number of genes associated with the enhancement of reproductive efficiency. Notably, the gene *BMRP2*, which is involved in multiple ovulation (FABRE et al., 2006) and gene *INHA* (Bao et al., 2023; Tian et al., 2010).

5.3.5. North Africa's Mediterranean vs Nordic climatic populations

This population pair resulted in the identification of a total of 59 genes. Among these genes, 52 were successfully mapped using the FST methodology, while the remaining 7 were mapped using the XP-EHH method (Appendix Table 5). Both methodologies discovered a single gene, namely *RELN*. In contrast to the presence of discernible peaks on chromosome 3 in other pairings featuring Nordic population (Figures 33 and 34), this pair did not yield a prominent peak, however, it was observed that Chromosome 3 exhibited a comparatively larger number of genes when compared to the other chromosomes (Appendix Table 5). Consequently, we posit that chromosome 3 may play a pivotal role in facilitating differential adaptation between these climatic zones. The gene *RELN* has been identified as a protein coding gene that plays a crucial role in brain development and neural migration across several animal species, including humans (SUÁREZ-VEGA et al., 2013). The gene may play a crucial role in facilitating climate change adaptation, since adaptive features are influenced by several factors and need efficient coordination among physiological systems. Moreover, as previously highlighted, many other genes were detected in this comparative analysis that may be implicated in the immune response. These genes include *IL1B, IL1A, IL13, IL5, CXLs, CXCL8, CXCL1, CD9, TLR9,* and *DDX21*. Previous studies have shown a correlation between genes such as *MTNR1B* and the ability for seasonal reproduction (HE et al., 2020; MIGAUD et al., 2005). Conversely, the impact of genes like *MSTN* on growth and muscle development has been documented (CHEN et al., 2023). *MSTN* gene serves as a suppressor of muscle growth, and its occurrence in desert sheep may be rationalized due to the significance of their reduced body size in facilitating adaptation to heat stress and limited feed supplies.

5.3.6. Continental vs Nordic populations

In comparison to the preceding population pairs, this pair exhibits a reduced degree of climatic divergence between the respective climatic areas. Here, both the FST and XP-EHH methodologies identified a total of 75 unique genes. Specifically, the FST methodology detected 55 genes, while the XP-EHH approach detected 20 genes (Appendix Table 6). Both approaches successfully identified eight genes: *RPL23A, AVR1A*, *GAPDH, CD9, CBx, ATP5MC2, KRT2.11,* and *TNFRSF1A.* The gene *RPL23A* has been documented to play a role in various biological processes across different species. For instance, in rice, it has been linked to the ability to tolerate dehydration stress (MOIN et al., 2017). In dairy cattle, this gene has been proposed to influence milk traits (LI et al., 2019), immune response (GAO et al., 2007), and male reproductive efficiency (HE et al., 2021), indicating its multifaceted functionality, whereas the impact of *AVR1A* on reproductive social behavior in humans has been documented by MAHER et al. (2011). Additionally, a study conducted by ZAMORANO-ALG et al. (2017) showed a strong correlation between *AVR1A* and milk production in Holstein Friesian cattle under heat stress conditions. This finding implies that *AVR1A* plays a significant role in the genetic regulation of heat stress tolerance. To the best of our current understanding, there is a lack of scientific research that elucidates the specific role and functionality of this particular gene in the ovine species necessitating pathway analysis in future studies. Additional genes that play a vital role in adaptation in this pair include *GAPDH* and *ATP5MC2*, which govern energy metabolism, *KRT2.11*, which has been seen to facilitate the progression of wool growth (POWELL and BELTRAME, 1994), and *TNFRSF1A*, which has been demonstrated to impact the response to photoperiodism (KRÓL et al., 2016). It is vital to point out that these geographical areas have freezing winters, and the use of woolen coverings aids in the thermoregulation of the animals. Moreover, it should be noted that these breed groups exhibit seasonal breeding patterns, which are influenced by the ratio of daytime to night-time. Consequently, the genes responsible for out-of-season breeding in sheep are subject to selective pressures.

5.3.7. Common genes in all population pairs

In the present study, it was shown that all combinations of climatic conditions and populations yielded a total of over 400 unique genes, which are suspected to be facilitating the unique adaptive capacity of indigenous sheep breeds in response to climate change. While there were no common identified genes for all pairs, there were shared genes in more than two climate based pairwise combinations. For instance, genes *CFTR* and *CTTNBP2* were seen in all possible combinations, except for the pair consisting of the Tropical and North Africa's Mediterranean populations. On the other hand, the gene *CBX5* was present in all combinations, except for the pair comprising North Africa's Mediterranean and Nordic populations. Although there is less documentation on the function of the ovine *CFTR* gene, substantial research has been conducted on the association between the human *CFTR* gene and cystic fibrosis (FAN et al., 2018). The gene *CBX5* has been linked to immunological response, whilst the gene *CTNBP2* has been related with neural functioning. The coordination of physiological responses to environmental stress is facilitated by the proper functioning of neurons.

5.4. Gene x environment association

Gene x environment association studies provide researchers the chance to identify selection signatures caused by climate change as opposed to recent selection, which is identified by more traditional techniques like the ones mentioned above, namely the FST and XP-EHH approaches. In the present study, six bio_climate variables were used in the association study. Although the six variables were used, it is crucial to remember that they were only kept because of a collinearity problem. As a result, it is crucial to emphasize that these variables only serve as a sample of the 20 environmental factors that were previously extracted from the WorldClim database. Cumulatively, over 450 distinct SNPs were shown to be strongly correlated with the six bioclimatic factors, demonstrating the importance of climate change in influencing a population's genomic architecture. Only 28 of these SNPs were common in both statistical methods used, hence for the sake of this research, gene ontology was only conducted for these 28 SNPs.

The gene *STAT1* has recently been identified as a thermotolerance gene that is possibly responsible for the physiological and reproductive sheep adapted in arid and semi-arid climatic conditions (CASTILLO-SALAS et al., 2023; LUNA-RAMIREZ et al., 2023). The gene was found to be located in close proximity to the SNP

OAR2_192491503.1 on chromosome 2. Furthermore, there is a strong correlation between this gene and the variable bio_18, which represents the precipitation levels during the hottest month. The reproductive trait is significantly impacted by environmental factors, particularly precipitation and maximum temperature. These factors determine the levels of the temperature humidity index, which in turn affects the occurrence of heat stress. The *ATP5MC2* gene, as described by BRADY et al. (2023), has a role in metabolic processes. Furthermore, it exhibits a substantial correlation with bio_19 (precipitation of the coldest quarter; RDA) and bio_13 (precipitation of the wettest month; LFMM). Precipitation has a crucial role in shaping the distribution of herbage, which subsequently influences energy intake and metabolism on a broader scale. The gene *TARBP2* has been identified as playing a crucial role in the immune response to parasites (ZAMANI et al., 2018). Given that climatic change has a significant impact on the occurrence, reappearance, and spread of pests, it is probable that this gene plays a vital role in modulating adaptive immunity. The gene *SCD5* was identified as having a significant association with the trait bio_13 using both methods. This gene has been previously reported to play a role in determining the body size of sheep (XU et al., 2021). On the other hand, *PLIN1* has been found to be responsible for muscle development and the composition of intramuscular fatty acids (ZHANG et al., 2022). Additionally, *ABHD5* has been identified as a gene involved in milk yield and the development of subcutaneous adipose tissue (ABOUSOLIMAN et al., 2021; WANG et al., 2023; YANG et al., 2020). Body size has a substantial influence in the context of climate change. Smaller-bodied individuals exhibit several advantageous traits, like reduced energy demands and improved capacity for heat dissipation. Therefore, the small body size may be regarded as a significant physical characteristic that confers adaptability in response to changes in climatic conditions. Several other genes have been identified and found to be strongly associated with the climatic variables that were used in the association study. For instance, *GSTA1* is a well-regarded gene known for its role in detoxification (REN et al., 2019). Another gene, *HLF*, is involved in non-specific immunity and the absorption of iron (RAZA et al., 2022). *ADIG* is associated with fat metabolism (Zhang et al., 2021), while *RHCG* is involved in ammonium uptake and enhances the utilization of ingested feed (XIANG et al., 2016).

The present comprehensive investigation has shown that indigenous sheep breeds have a high degree of genetic diversity, but with a rapid decline in diversity levels. The observed decline in effective population size across all analyzed breeds is a cause for concern. Notably, none of the breeds exhibited an Ne above 250, indicating that all breeds are possibly at risk of extinction in the face of climate change. The first two principal components explained more than 50% of the genomic variance seen across all the breeds, indicating the presence of unique genomic structures in indigenous sheep breeds. This differentiation might be attributed to factors such as geographical isolation or the influence of climatic zones on the genomes. The ancestral clustering indicated that despite being genetically diverse, European originating native breeds showed high levels of admixture at both K=25 and K=32. Consistent admixture erodes the uniqueness and integrity of specific native breeds. The categorization of local breeds based on climate resulted in the identification of over 400 distinct genes, which are mostly exclusive to each climate-based pair of populations. This finding suggests that each breed group has a unique capability for adaptability, hence can't replace each other. The majority of genes exhibit immune-related activities, so emphasizing the need to selectively breed animals that possess disease resistance traits in response to the current climate change circumstances. In addition, the distinctive pattern and distribution of ROHs further underscored the distinctiveness of the genome of each breed. Furthermore, studies on gene x environment associations have shown that precipitation and temperature are significant climatic factors that play a crucial role in shaping the genetic makeup of a breed, leading to adaptive changes. All the genes identified under GEA are either responsible for immunity, metabolism, or productivity. This study supports the assertion that indigenous sheep breeds continue to possess significant genetic diversity, but with a rapid decline which may be attributed to inadequate genetic management practices or haphazard crossbreeding. The study findings also indicate that indigenous sheep breeds possess a distinctive capacity to adapt to climatic climate change, making them valuable for the purpose of selectively breeding for climate change adaptation. This, in turn, would enhance the resilience and durability of sheep breeds. In addition, results of this study can be used to enhance breed conservation programs for mitigation of climate change effects.

6. NEW SCIENTIFIC RESULTS

Genetic characterization of indigenous sheep breeds to determine within- and between populations genetic diversity.

i. Despite high levels of within-breed genetic diversity, the 32 native sheep breeds are at risk of extinction due to a decline in effective population size. Furthermore, genetic clustering patterns suggest continental demarcations refined by climatic zones whereas European breeds are highly admixed.

Detection of patterns of run of homozygosity (ROH) and genomic based inbreeding coefficient (Froh).

i. The distribution of ROH segments across all breeds revealed a predominance of short segments (0-6 and 6-24 Mb) accompanied by a scarcity of long segments (>24 Mb). This pattern is indicative of genomic inbreeding primarily originating from inbreeding events that transpired several generations ago.

Identification of signatures of selection underpinning adaptation in different climatic regions.

i. A comprehensive analysis of climate-based pairwise groups revealed over 400 distinct signatures of climate change adaptation, with only three genes (*CFTR*, *CTTNBP2*, and *CBX5*) consistently appearing across multiple pairings.

Gene x environment association (GEA) to explore the complex interplay between genes and climatic variables in shaping adaptation traits.

i. A gene-environment association study revealed that temperature and rainfall are crucial climatic factors driving native sheep adaptation, with ten specific genes (*STAT1, ATP5MC2, TARBP2, SCD5, GSTA1, HLF, ADIG, RHCG, PLIN1*, and *ABHD5*) exhibiting significant associations with these climatic factors.

7. PRACTICAL RESULTS

The findings of this study provide valuable insights that can be utilized to enhance conservation efforts for endangered breeds and inform decisions regarding conservation priorities for certain breeds. According to the current findings, it may be inferred that African and Asian breeds, whose risk status is currently unclear, may now be classified as endangered due to the fact that all of them exhibited a Ne value below 250.

Other more specific practical usability of these results are as follows:

i. High within breed genetic diversity can be exploited to enhance within breed selection.

ii. The findings that demonstrate a rapid decrease in Ne, as well as the persistently low Ne numbers, have valuable implications for the development of a conservation program aimed at preserving sheep genetic resources.

iii. The results indicating a significant degree of breed admixture may be used by breeding and/or conservation farms to intentionally facilitate the restoration of pure breeds. This can be achieved via the rigorous selection of individuals that are either purebred or exhibit characteristics consistent with the breed's original traits, for the purpose of breeding future generations.

iv. Information on ROH pattern may be used to improve breed molecular-based management to enhance genetic diversity, adaptation to specific climatic zones as well as reduce Froh_genome.

v. The unique capacity for adaptability shown by paired population groupings in different climatic zones suggests that each breed has distinct adaptive characteristics, making them irreplaceable. Consequently, it is imperative to undertake conservation measures for endangered breeds. Nevertheless, these indigenous breeds may be used to enhance the adaptability of specialized breeds by introducing genes associated with adaptation into them.

vi. Understanding the climatic variables driving sheep adaptability offers an opportunity to develop proper breeding programs to genetically counter the effects of climate change to sheep industry.

vii. The research has identified many genes, including *STAT1, ATP5MC2, TARBP2, SCD5, GSTA1, HLF, ADIG, RHCG, PLIN1, ABHD5*, and others, which have the potential to be included in marker assisted selection which holds a promise for improving breeding strategies aimed at enhancing the resilience of sheep breeds to climate change.

8. SUMMARY

The utilization of indigenous sheep breeds has the potential to contribute to the mitigation of climate change's impact on the global availability of animal protein. The examination of the genomic architecture of indigenous sheep in relation to climate change facilitates the identification of genetic diversity and adaptability hotspots, which can contribute to the enhancement of conservation efforts for animal genetic resources. Using ovine50K SNP chips of 832 samples from 32 breeds from various climatic zones, the genomic insight of native sheep breeds sampled from different climatic zones is presented, a finding that can be utilized in the development of climate specific adapted sheep breeds.

Results of this study underscore that, although the breeds under study exhibit significant genetic diversity, there is an alarming decline in this diversity, as evidenced by the effective population size. African breeds distinctly positioned themselves on one facet of PCA 1, without any overlap, signifying their unique genomic structures. Conversely, European indigenous sheep breeds display a rich genetic variation; however, a pronounced admixture was noted in several breeds, compromising their genetic distinctiveness. While the studied breeds exhibited some levels of inbreeding, analysis runs of homozygosity (ROH) patterns suggest that these breeds past ancestral inbreeding events may be more influential than recent ones. This was shown by deficiency of long ROHs (24-48 and > 48 mb). Also, the ROH patterns showed that these breeds underwent different historical development stages.

Over 400 genes were potentially linked to climate change adaptation. Intriguingly, the majority of these genes are exclusive to specific climate-based populations, underscoring the unique adaptive capacities inherent to each studied group. Notably, a significant proportion of these genes are associated with immune responses, emphasizing the imperative of breeding disease-resistant livestock in the current context of climate change. Analysis of landscape genomics revealed that rainfall and temperature are likely drivers of adaptation in these population. Interestingly, nine genes (*HLF, ATP5MC2, SCD5, GSTA1, STAT1, TARBP2, ADIG, PLIN1, ABHD5)* with diverse functions related to immunity, growth, and development were found to be located near SNPs that were significantly associated with these climatic variables.

This study reinforces the notion that while indigenous sheep breeds retain substantial genetic diversity, it is diminishing, potentially due to suboptimal genetic management or admixture events. Furthermore, our findings highlight the innate capability of native sheep breeds to adapt to climatic change, positioning them as invaluable resources for breeding traits associated with climate resilience, thereby enhancing the overall robustness of sheep populations.

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10. LIST OF PUBLICATION

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List of publications related to the dissertation

Foreign language scientific articles in Hungarian journals (1)

1. **Wanjala, G.**, Astuti, P. K., Bagi, Z., Strausz, P., Kusza, S.: Livestock breeding for welfare, adaptation and sustainability: an overview of the novel traits and breeding concerns in sheep, dairy, beef and poultry.
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2. **Wanjala, G.**, Kichamu, N., Cziszter, L. T., Astuti, P. K., Kusza, S.: An on-station analysis of factors affecting growth traits of Pure Red Maasai and Dorper sheep breeds under an extensive production system.
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In: Book of abstract : Multidisciplinary Conference on Sustainable Development : 25-26 May 2023 : Section : Animal Resources Bioengineering, Faculty of Bioengineering of Animal Resources, Tinmisoara, 17, 2023, (ISSN 2821-4293)

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01 February, 2024

11. STATEMENTS

STATEMENT

I wrote this thesis in the framework of the University of Debrecen Doctoral School of Animal Science for the purpose of obtaining a doctoral degree (Ph.D.) at the University of Debrecen.

Debrecen, 20.........................

....

PhD candidate

STATEMENT

I hereby certify that the doctoral candidate .... has carried out his/her work under my/our supervision within the framework of the above-mentioned Doctoral School between 20......-20....... The candidate has made a decisive contribution to the results of the thesis through his/her independent creative work, and the thesis is the candidate's independent work. I/we recommend that the thesis be accepted.

Debrecen, 20...............................

....

supervisor

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13. ANNEXES

Appendix Table 1: Genes possibly under selection that may be influencing adaptation to Tropical and North Africa's Mediterranean climatic zones.

Gene name	Chr	start position	end position	XP-EHH	FST
CP	1	237003297	237050085		🟦
CD1D	1	107108011	107111215		🟦
IL12RB2	1	42584598	42656778		🟦
GJA8	1	97977457	97978779		🟦
IFNAR1	1	120422988	120448951		🟦
IFNAR2	1	120551218	120571823		🟦
SLC30A7	1	77384118	77477030		🟦
SPP2	1	6767995	6787884		🟦
UGT1A1	1	7058779	7192169		🟦
FABP3	2	235135457	235145925	🟪	
CD28	2	204611103	204645238	🟪	
CTLA4	2	204777523	204784522	🟪	
IDH1	2	209236699	209259307	🟪	
UBQLN1	2	35845653	35897664		🟦
CXCR4	2	173602065	173605247		🟦
DARS1	2	173737054	173799138		🟦
PRKAG3	2	219781028	219787070		🟦
CBX5	3	132139439	132149313	🟪	
KRT2.11	3	133897662	133903960	🟪	
GGTA2P	3	14290904	14322530		🟦
ARF5	4	91893378	91895222	🟪	🟦
PRR15	4	66566695	66567075	🟪	
TRA2A	4	32094068	32111994	🟪	
PRDX2	5	10811752	10813968		🟦
IGFBP7	6	72423581	72437525	🟪	
CSN1S1	6	85089487	85102981	🟪	
CSN2	6	85116827	85122776	🟪	
CSN1S2	6	85184160	85195356	🟪	
CSN3	6	85309552	85316834	🟪	
CXCL8	6	88474889	88477180	🟪	
CXCL1	6	88610487	88611559	🟪	
SIX6	7	69617164	69619027		🟦
SIX1	7	69737971	69741086		🟦
ESR2	7	73323879	73369246		🟦
CGA	8	49919904	49921988		🟦
LYN	9	36031532	36077272		🟦
SDR16C5	9	36264636	36276508		🟦
YWHAZ	9	76021905	76053607		🟦
RPL23A	11	19771126	19774188		🟦
B4GALNT2	11	36929322	36992982		🟦
PYGB	13	41883741	41916422		🟦

GDI2	13	42036764	42067988		🟦
EIF6	13	64112500	64115629		🟦
HAMP	14	45097469	45098753		🟦
RABAC1	14	50323373	50326352		🟦
BSP5	14	50624978	50632184		🟦
BSP1	14	50660967	50664808		🟦
HSD17B2	14	8023136	8121295		🟦
ARNTL	15	38890197	38925292		🟦
FGF10	16	30468674	30562188		🟦
IL15	17	15757663	15773243		🟦
CRYBB3	17	64996177	65001296		🟦
MCP-3	18	33632415	33635335		🟦
MYD88	19	11552444	11553764		🟦
HYAL2	19	49974113	49976684		🟦
GNAI2	19	50053939	50072431		🟦
DYA	20	7198200	7208505		🟦
PSMB8	20	7273093	7280060		🟦
SLC39A7	20	7489214	7493043		🟦
TFAP2A	20	44602287	44618637		🟦
STX1B	24	27112495	27119563		🟦
ITGAM	24	27341076	27384550		🟦
DDX21	25	25041120	25063768	🟪	
BMPR1A	25	40997429	41138024		🟦
GLUD1	25	41211513	41249952		🟦

Appendix Table 2: Genes possibly under selection that could be influencing adaptation to Tropical and Continental climatic zones.

Gene name	Chr	start position	end position	XP-EHH	FST
IL12A	1	225475115	225481557	🟪	
FCER1A	1	108571005	108576852	🟪	
SLC30A7	1	77384118	77477030	🟪	🟦
RTP4	1	198138027	198223956	🟪	
ST6GAL1	1	198413998	198470076	🟪	
ADIPOQ	1	198618705	198631249	🟪	
FCGR3A	1	111039478	111049403		🟦
ATP5PO	1	119867566	119874405		🟦
GUCA2A	1	16472798	16474553		🟦
ID3	2	242185986	242190773	🟪	
GSN	2	2156199	2187147		🟦
RRAGA	2	87042040	87042984		🟦
PLIN2	2	87100232	87108066		🟦
TUBA4A	2	220175495	220179114		🟦
INHA	2	220476722	220479658		🟦
COPS7B	2	232572509	232589655		🟦
TSPO	3	217975199	217979418	🟪	
QPCT	3	86615354	86644936		🟦
GGTA2P	3	14290904	14322530		🟦
CBX5	3	132139439	132149313		🟦
HOXC6	3	132338094	132340389		🟦
BTG1	3	128382099	128382467		🟦
CTTNBP2	4	50432535	50603933		🟦
SRI	4	72313120	72325811		🟦
CFTR	4	50695189	50881696		🟦
ASZ1	4	50928081	50995999		🟦
TXNDC15	5	43710058	43724747	🟪	
EGR1	5	47225278	47227722	🟪	🟦
RAB8A	5	6621954	6641188		🟦
CYP4F21	5	7130482	7140600		🟦
SCGB3A2	5	56573739	56577006		🟦
SCD5	6	97078068	97147726		🟦
UGT2B7	6	84148570	84165137		🟦
MYOZ2	6	6265305	6302669		🟦
ANXA2	7	46840046	46885147	🟪	🟦
SFXN1	7	5392697	5431839		🟦
SIX6	7	69617164	69619027		🟦
DGAT1	9	13566142	13575279	🟪	
YWHAZ	9	76021905	76053607		🟦
NOG	11	6946976	6947674	🟪	
RPL23A	11	19771126	19774188		🟦
CR2	12	4724266	4770968		🟦

CAPN2	12	25191495	25241603		🟦
DEGS1	12	25467996	25473652		🟦
OXT	13	51437893	51438654	🟪	
PYGB	13	41883741	41916422	🟪	
GDI2	13	42036764	42067988	🟪	
IZUMO1	14	54408615	54411844	🟪	
LHB	14	54608835	54609803	🟪	
FTO	14	21524991	21953995	🟪	
HSD11B2	14	34383881	34389053		🟦
LCAT	14	34760896	34764094		🟦
SLC12A4	14	34764805	34781054		🟦
BSP5	14	50624978	50632184		🟦
BSP1	14	50660967	50664808		🟦
ARNTL	15	38890197	38925292	🟪	
AK6	16	10361305	10375165	🟪	
PUS1	17	44746977	44758079	🟪	
TLR2	17	3837859	3840213		🟦
CRYBB3	17	64996177	65001296		🟦
CYP11A1	18	33216420	33230614	🟪	
TLR9	19	48643163	48646651		🟦
HYAL2	19	49974113	49976684		🟦
GNAI2	19	50053939	50072431		🟦
DYA	20	7198200	7208505		🟦
PSMB8	20	7273093	7280060		🟦
SLC39A7	20	7489214	7493043		🟦
CDKN1A	20	10678753	10680684		🟦
PIM1	20	11149857	11153603		🟦
BRMS1	21	43692683	43696794	🟪	
NPAS4	21	43768738	43776312	🟪	
CFL1	21	43277409	43278376	🟪	
CPT1A	21	45444763	45488917		🟦
ARL3	22	22438505	22468540	🟪	
CYP17A1	22	22557939	22564240	🟪	
LIPA	22	10697729	10736804		🟦
AIMP2	24	37907715	37915133		🟦
RAC1	24	38166137	38175158		🟦
ACTB	24	38675524	38677778		🟦
ITGAM	24	27341076	27384550		🟦
SLC25A4	26	14223802	14227499		🟦

Appendix Table 3: Genes possibly under selection that could be influencing adaptation to Tropical and Nordic climatic zones.

Gene name	Chr	start position	end position	XP-EHH	FST
IL12A	1	225475115	225481557	🟪	
CYP2J	1	34675227	34712820		🟦
FCGR3A	1	111039478	111049403		🟦
FCGR2B	1	111115681	111132021		🟦
GJA8	1	97977457	97978779		🟦
LPAR1	2	12325968	12488187		🟦
ARL5A	2	156582026	156602931		🟦
UBQLN1	2	35845653	35897664		🟦
IL22	3	151427327	151432602	🟪	
AVPR1A	3	156234256	156237118	🟪	
CDK4	3	161617799	161623974	🟪	
CD4	3	207583194	207608610	🟪	
IL23A	3	162937547	162939092	🟪	
CDK2	3	163272423	163276634	🟪	
TSPAN9	3	210551090	210559530	🟪	
HPCAL1	3	19461213	19466847	🟪	
C3H12orf29	3	124227630	124238082	🟪	
DCN	3	127427409	127458485	🟪	
CBX5	3	132139439	132149313	🟪	
ATP5MC2	3	132715794	132719269	🟪	
KRT2.11	3	133897662	133903960	🟪	
POMC	3	32466656	32469942	🟪	🟦
RAB10	3	33194136	33253935	🟪	
MB	3	178866680	178877963	🟪	
LALBA	3	137390403	137392415	🟪	
RPS26	3	36864246	36864593	🟪	
RAB1A	3	43095625	43108334	🟪	🟦
IL1B	3	60023514	60034494	🟪	🟦
IL1A	3	60078287	60088697	🟪	🟦
QPCT	3	86615354	86644936		🟦
ARL1	3	170323044	170331040		🟦
PDGFB	3	214647932	214666037		🟦
IGFBP6	3	133213326	133216912		🟦
ATF4	3	214930338	214931586		🟦
AQP5	3	136155831	136159185		🟦
TEF	3	216504368	216525599		🟦
IFT27	3	179967963	179990650		🟦
CPT1B	3	224090383	224102291		🟦
LYZ	3	150434369	150439510		🟦
TOB2	3	216550007	216551006		🟦
RELN	4	44668137	45205142		🟦

RHEB	4	113405934	113425611		🟦
GHRHR	4	65350354	65364813		🟦
AQP1	4	65387133	65430981		🟦
CTTNBP2	4	50432535	50603933		🟦
CFTR	4	50695189	50881696		🟦
ASZ1	4	50928081	50995999		🟦
SCGB3A2	5	56573739	56577006		🟦
SPARC	5	60405206	60427607		🟦
ATOX1	5	60474740	60479122		🟦
SLC39A3	5	18496941	18503765		🟦
CSF2	5	19956144	19958155		🟦
IL3	5	19971457	19973243		🟦
MEF2C	5	85606652	85706150		🟦
H2AZ1	6	24826878	24828144		🟦
ARF6	7	39947130	39947657		🟦
IL25	7	21163579	21166254		🟦
PYGL	7	40814121	40860779		🟦
CGA	8	49919904	49921988		🟦
SNAI2	9	32778177	32780624		🟦
UBB	11	32806436	32807122		🟦
AVPR1B	12	3157314	3162821		🟦
PYGB	13	41883741	41916422	🟪	
GDI2	13	42036764	42067988	🟪	🟦
HAMP	14	45097469	45098753	🟪	
MMP7	15	5709290	5717067		🟦
CD3E	15	28501024	28510846		🟦
CD3D	15	28516680	28519879		🟦
ERP29	17	61783505	61790600		🟦
CRYBB3	17	64996177	65001296		🟦
SLC25A38	19	12564363	12579674		🟦
RPSA	19	12610248	12622050		🟦
LTF	19	52870333	52903163		🟦
DYA	20	7198200	7208505		🟦
PSMB8	20	7273093	7280060		🟦
SLC39A7	20	7489214	7493043		🟦
MTNR1B	21	1373657	1392132		🟦

Appendix Table 4: Genes possibly under selection that could be influencing adaptation to North Africa's Mediterranean and Continental climatic zones.

Gene name	chr	start position	end position	XP-EHH	FST
KAP7	1	122988317	1.23E+08		🟦
NUDT16	1	256658861	2.57E+08		🟦
FCGR3A	1	111039478	1.11E+08		🟦
IL12RB2	1	42584598	42656778		🟦
GJA8	1	97977457	97978779		🟦
YBX1	1	16961480	16979580		🟦
ST6GAL1	1	198413998	1.98E+08		🟦
ADIPOQ	1	198618705	1.99E+08		🟦
AHSG	1	198806196	1.99E+08		🟦
PRD-SPRRII	1	102078660	1.02E+08		🟦
FABP3	2	235135457	2.35E+08	🟪	
NDUFB6	2	100489026	1.01E+08		🟦
BMPR2	2	203653532	2.04E+08		🟦
INHA	2	220476722	2.2E+08		🟦
COPS7B	2	232572509	2.33E+08		🟦
C3H12orf29	3	124227630	1.24E+08	🟪	
CBX5	3	132139439	1.32E+08	🟪	
CHCHD3	4	96481673	96764597	🟪	
MET	4	51540365	51625496		🟦
CDK5	4	113025302	1.13E+08		🟦
CTTNBP2	4	50432535	50603933		🟦
NPVF	4	70625131	70628520		🟦
CFTR	4	50695189	50881696		🟦
ASZ1	4	50928081	50995999		🟦
ST7	4	51108667	51268178		🟦
NR3C1	5	51733916	51850972		🟦
SCGB3A2	5	56573739	56577006		🟦
CXCL8	6	88474889	88477180	🟪	
CXCL1	6	88610487	88611559	🟪	
CXCL10	6	90551375	90552865	🟪	
IGFBP7	6	72423581	72437525		🟦
MYOZ2	6	6265305	6302669		🟦
ANXA2	7	46840046	46885147		🟦
FABP5	9	57354087	57359292		🟦
FABP4	9	57536525	57541042		🟦
SNAI2	9	32778177	32780624		🟦
FBXL3	10	52599500	52614788	🟪	
ATP7B	10	21656704	21730091		🟦
RPL23A	11	19771126	19774188		🟦

B4GALNT2	11	36929322	36992982		🟦
SLC25A19	11	55213585	55223216		🟦
V15	11	41105175	41108801		🟦
KRT35	11	41168178	41172256		🟦
ACLY	11	41537705	41574994		🟦
CR2	12	4724266	4770968	🟪	
PANK2	13	50616964	50645766	🟪	
OXT	13	51437893	51438654	🟪	
EIF6	13	64112500	64115629		🟦
HAMP	14	45097469	45098753		🟦
HSD17B2	14	8023136	8121295		🟦
DBP	14	54318156	54323546		🟦
CA11	14	54323408	54330118		🟦
IZUMO1	14	54408615	54411844		🟦
LHB	14	54608835	54609803		🟦
ILK	15	45862134	45869041		🟦
ARFIP2	15	45974282	45977812		🟦
SMPD1	15	46057287	46061343		🟦
GHR	16	31832933	32000445		🟦
IL15	17	15757663	15773243		🟦
CYP1A1	18	32844396	32846884		🟦
RHCG	18	20048798	20073060		🟦
PLIN1	18	20192837	20204324		🟦
LYZL4	19	14551207	14554680		🟦
SS18L2	19	14656138	14659569		🟦
TLR9	19	48643163	48646651		🟦
CCND3	20	15789513	15889722		🟦
CPT1A	21	45444763	45488917		🟦
ACTB	24	38675524	38677778		🟦
STX1B	24	27112495	27119563		🟦
ITGAM	24	27341076	27384550		🟦

Appendix Table 5: Genes possibly under selection that could be influencing adaptation to North Africa’s Mediterranean and Nordic climatic zones.

Gene name	Chr	start position	end position	XP-EHH	FST
RABGGTB	1	51396950	51403534	🟪	
AGTR1	1	237523905	237524984	🟪	
FCGR3A	1	111039478	111049403		🟦
FCGR2B	1	111115681	111132021		🟦
SPP2	1	6767995	6787884		🟦
LPAR1	2	12325968	12488187		🟦
ALDOB	2	21476904	21623190		🟦
MSTN	2	118144443	118149433		🟦
AVPR1A	3	156234256	156237118		🟦
GAPDH	3	207818504	207822814		🟦
CD9	3	208069062	208082480		🟦
ARL1	3	170323044	170331040		🟦
HPCAL1	3	19461213	19466847		🟦
NDUFA12	3	131047599	131075182		🟦
ATP5MC2	3	132715794	132719269		🟦
PDGFB	3	214647932	214666037		🟦
ATF4	3	214930338	214931586		🟦
TEF	3	216504368	216525599		🟦
POMC	3	32466656	32469942		🟦
IFT27	3	179967963	179990650		🟦
RHOB	3	28196686	28197309		🟦
RAB1A	3	43095625	43108334		🟦
LYZ	3	150434369	150439510		🟦
IL1B	3	60023514	60034494		🟦
IL1A	3	60078287	60088697		🟦
TOB2	3	216550007	216551006		🟦
TNFRSF1A	3	207980687	207984844		🟦
RELN	4	44668137	45205142	🟪	🟦
ARF5	4	91893378	91895222	🟪	
CTTNBP2	4	50432535	50603933		🟦
CFTR	4	50695189	50881696		🟦
RETN	5	14185287	14186266		🟦
SCGB3A2	5	56573739	56577006		🟦
IL13	5	19262767	19264701		🟦
IL5	5	19436398	19438650		🟦
CXCL8	6	88474889	88477180	🟪	
CXCL1	6	88610487	88611559	🟪	
H2AZ1	6	24826878	24828144		🟦
MYOZ2	6	6265305	6302669		🟦
ARF6	7	39947130	39947657		🟦
PYGL	7	40814121	40860779		🟦

CCN2	8	57077576	57079077		🟦
SQLE	9	28005936	28027215		🟦
SNAI2	9	32778177	32780624		🟦
TTPA	9	40878359	40916472		🟦
FBXL3	10	52599500	52614788	🟪	
AVPR1B	12	3157314	3162821		🟦
CYTH2	14	54190465	54198809		🟦
DBP	14	54318156	54323546		🟦
CA11	14	54323408	54330118		🟦
IZUMO1	14	54408615	54411844		🟦
CIB1	18	20723490	20727112		🟦
FURIN	18	20886453	20896498		🟦
LYZL4	19	14551207	14554680		🟦
SS18L2	19	14656138	14659569		🟦
TLR9	19	48643163	48646651		🟦
CCND3	20	15789513	15889722		🟦
MTNR1B	21	1373657	1392132		🟦
DDX21	25	25041120	25063768	🟪	

Appendix Table 6: Genes possibly under selection that could be influencing adaptation to Continental and Nordic climatic zones.

Gene name	Chr	start position	end position	XP-EHH	FST
RABGGTB	1	51396950	51403534		🟦
ATP5PO	1	119867566	119874405		🟦
CD80	1	182614039	182637278		🟦
GSK3B	1	182940427	183155532		🟦
ST6GAL1	1	198413998	198470076		🟦
ADIPOQ	1	198618705	198631249		🟦
AHSG	1	198806196	198813239		🟦
LPAR1	2	12325968	12488187		🟦
NDUFB6	2	100489026	100504967		🟦
IL22	3	151427327	151432602	🟪	🟦
AVPR1A	3	156234256	156237118	🟪	
CD4	3	207583194	207608610	🟪	
GAPDH	3	207818504	207822814	🟪	🟦
CD9	3	208069062	208082480	🟪	🟦
IL23A	3	162937547	162939092	🟪	
CCND2	3	209738382	209761224	🟪	
CDK2	3	163272423	163276634	🟪	
MAPKAP1	3	10350236	10567880	🟪	
C3H12orf29	3	124227630	124238082	🟪	
DCN	3	127427409	127458485	🟪	
CBX5	3	132139439	132149313	🟪	🟦
ATP5MC2	3	132715794	132719269	🟪	🟦
KRT2.11	3	133897662	133903960	🟪	🟦
POMC	3	32466656	32469942	🟪	
RAB10	3	33194136	33253935	🟪	
MB	3	178866680	178877963	🟪	
TSPO	3	217975199	217979418	🟪	
LALBA	3	137390403	137392415	🟪	
YEATS4	3	150127699	150154299	🟪	
IL1B	3	60023514	60034494	🟪	
IL1A	3	60078287	60088697	🟪	
TNFRSF1A	3	207980687	207984844	🟪	🟦
SLC2A3	3	206193144	206206504		🟦
AVPR1A	3	156234256	156237118	🟪	🟦
CDK4	3	161617799	161623974		🟦
ARL1	3	170323044	170331040		🟦
HPCAL1	3	19461213	19466847		🟦
NDUFA12	3	131047599	131075182		🟦
HOXC6	3	132338094	132340389		🟦
PDGFB	3	214647932	214666037		🟦
IGFBP6	3	133213326	133216912		🟦
ATF4	3	214930338	214931586		🟦

AQP5	3	136155831	136159185		🟦
TEF	3	216504368	216525599		🟦
RHOB	3	28196686	28197309		🟦
RPS26	3	36864246	36864593		🟦
RAB1A	3	43095625	43108334		🟦
LYZ	3	150434369	150439510		🟦
TOB2	3	216550007	216551006		🟦
CTTNBP2	4	50432535	50603933		🟦
CFTR	4	50695189	50881696		🟦
RAB8A	5	6621954	6641188		🟦
SLC39A3	5	18496941	18503765		🟦
H2AZ1	6	24826878	24828144		🟦
ARF6	7	39947130	39947657		🟦
PYGL	7	40814121	40860779		🟦
SNAI2	9	32778177	32780624		🟦
GH	11	47540169	47541799	🟪	
AVPR1B	12	3157314	3162821		🟦
SLC25A33	12	42049646	42075896		🟦
HAMP	14	45097469	45098753		🟦
CYTH2	14	54190465	54198809		🟦
DBP	14	54318156	54323546		🟦
CA11	14	54323408	54330118		🟦
IZUMO1	14	54408615	54411844		🟦
MMP13	15	5258462	5270880		🟦
FSHB	15	59188092	59190048		🟦
IL15	17	15757663	15773243		🟦
CIB1	18	20723490	20727112		🟦
FURIN	18	20886453	20896498		🟦
MYD88	19	11552444	11553764		🟦
BRMS1	21	43692683	43696794	🟪	
NPAS4	21	43768738	43776312	🟪	
MTNR1B	21	1373657	1392132		🟦