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# Comparative genomic characterization of indigenous fat-tailed Akkaraman sheep with local and transboundary sheep breeds

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## Abstract

The domestic sheep with over 1200 breeds descended from those early domesticated animals that are bred for a variety of resources such as meat, milk and wool. Akkaraman, a fat-tailed indigenous sheep breed of Türkiye, is widespread throughout Central Anatolia, with the largest indigenous sheep population. Assessing the genetic diversity and genomic structure of animal breeds is among the key contributors to deciphering adaptation to environmental extremes and constructing efficient genetic improvement strategies. Therefore, this study aimed to characterize the genome of Akkaraman breed against various world-renowned transboundary sheep and indigenous sheep with fat and thin tails. Genetic similarities and differences between those breeds have been displayed by estimating and comparing various genetic diversity indices, linkage disequilibrium (LD) estimates and fixation index ($F_{ST}$), runs of homozygosity (ROH) as well as PCA and neighbour-joining tree analysis. Akkaraman sheep were observed to form a cluster alongside Moghani, Karakas, Tibetan and Cyprus Fat Tail sheep, which are primarily the sole representatives of fat-tailed sheep in the study. This clustering was evident in both the PCA and neighbour-joining tree analysis. The Akkaraman sheep was also observed to have the lowest genomic inbreeding and one of the lowest numbers of ROHs, which might also indicate that the breed has not been exposed to historical intensive selection pressure, inbred mating or a massive population bottleneck that might leave strong marks of genomic homozygosity. The results improve our understanding of the genetic diversity in Akkaraman sheep in comparison with certain mainstream sheep breeds as well as those indigenous breeds from around the world. Additionally, findings will also provide valuable insights to perform further GWAS effectively by considering population structure, diversity and LD patterns observed among the breeds while providing practical knowledge that will contribute to designing efficient

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and successful genome-based selection programmes for worldwide sheep production systems.

**KEYWORDS**
genetic diversity, linkage disequilibrium, PCA, phylogenetic tree, runs of homozygosity

## 1 | INTRODUCTION

Historically, captivating wild Asiatic mouflon (*Ovis orientalis*) and breeding those for domestic sheep (*Ovis aries*) has been proposed to be the dawn of domestication for grazing animals in south-eastern Anatolia of Türkiye around 11,000 years ago (Cheng et al., 2023; Wei et al., 2015). Various demographic evidence has also been found around Central Anatolia as well as the southeastern part of the country, implying early attempts of domestication in the region (Vigne et al., 2005; Zeder, 2008). Since then, sheep have spread throughout the world, even those arid and extreme environments, with over 1200 breeds descended from those early domesticated animals that are bred for a variety of resources, such as meat, milk and wool (Scherf & Pilling, 2015; Taberlet et al., 2011). Many countries in the world have a variety of indigenous animal genetic resources that have evolved in the relevant ecosystems for numerous generations, which are central to sustainable production for those times of uncertainty due to their adaptive capacity and reservoir of biological diversity (Boettcher et al., 2014; Taberlet et al., 2008). Each may be an integral part of a solution against production and supply chain breaks as well as bottlenecks imposed by threats such as increased population size, climate change and recurrent pandemics. With 41 indigenous and many transboundary sheep breeds and a population size of approximately 42 million animals, Türkiye is among the top 10 largest sheep producers in the world as well as being a centre to early domestication (FAO, 2022a, 2022b). Akkaraman (i.e., White Karaman), a fat-tailed indigenous sheep breed of Türkiye, is widespread throughout Central Anatolia. The breed is characterized by its ability to endure extreme environmental conditions, including diseases and parasites, to nourish on meagre diet and to survive and reproduce under adverse conditions (Arzik et al., 2023; Kizilaslan et al., 2022; Ozmen et al., 2020). It is widely known that most of the economically important and adaptive traits are quantitative in nature, which means that the genetic architecture of the breed, especially its genetic variability plays a key role on the breed's phenotypic characteristics (Falconer & Mackay, 1996). While this is the case, one of the initial steps of managing animal genetic resources with the purpose of sustainable use and food security is to identify its current genetic architecture including genetic variability and population structure (FAO, 2007; Scherf & Pilling, 2015). Loss of genetic variability is long known to lead to a lack of fitness, poor fertility, disease susceptibility as well as low productivity (Charlesworth & Charlesworth, 2010; Falconer & Mackay, 1996; Keller & Waller, 2002). The absence of proper genomic characterization may lead to the loss of potentially valuable genetic characteristics and breed attributes due to unsupervised mating strategies, crossbreeding and extinction threats. Therefore, using genomic tools for the characterization of those indigenous breeds is quite essential to ensure the breeding of hardy and productive sheep populations as well as constructing efficient conservation programmes for future uncertainties and handicaps, with worldwide implications on sheep production systems (Boettcher et al., 2014; Yang et al., 2016).

Various molecular markers have been used to understand the genetic characteristics of certain species, breeds and economically important traits so far (Groeneveld et al., 2010; Lenstra et al., 2012; Scherf & Pilling, 2015; Unlusoy, 2023). Currently, the utilization of genome-wide SNP markers provides more robust and accurate estimations than was previously possible with low-density markers such as microsatellites (Ajmone-Marsan et al., 2023). Accordingly, various genome-wide scans were implemented with the purpose of QTL discovery (Al-Mamun et al., 2015; Kizilaslan et al., 2022; Yilmaz et al., 2022; Zhang et al., 2013) and genomic characterization in various sheep breeds (Ahbara et al., 2021; Al-Mamun et al., 2015; Kijas et al., 2012; Rekik et al., 2022). Such characterization studies have employed various analytical strategies that involve phylogenetic trees, comparison of expected ($H_E$) and observed ($H_O$) heterozygosities, various aspects of allele frequencies such as deviations from Hardy–Weinberg Equilibrium, genomic relationships and inbreeding, measures of genetic differentiation (e.g., $F_{ST}$) and population structure both within and between breeds. Moreover, pairwise estimations of linkage disequilibrium (LD) coefficient $r^2$, decay of LD with distance and runs of homozygosity (ROH) mostly undertaken within breeds (Ajmone-Marsan et al., 2023; FAO, 2011; Rekik et al., 2022; Scherf & Pilling, 2015). *F* statistics are commonly used to quantify

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overall population structure, the genetic diversity and the amount of differentiation within and between populations (Crispim et al., 2013; Weir & Cockerham, 1984; Wright, 1965). Moreover, the extent of LD is critical for QTL discovery with GWAS, marker-assisted selection and genomic selection programmes conducted for the genetic improvement of various livestock species. Heterozygosity, as a measure of genetic variation within a population, is among the most widely utilized diversity parameters (Toro & Caballero, 2005). Intuitively, high levels of heterozygosity imply for higher genetic variability and vice versa. On the contrary, long runs of homozygosity (ROH) may indicate higher levels of genomic inbreeding, while extremely shorter ROH also suggests loss of genetic diversity due to a recent bottleneck. It is also useful for identifying regions of the genome that are under historical selection pressure (Peripolli et al., 2017). Comparison of these parameters among populations of different sheep breeds is expected to guide researchers and breeders through more effective conservation programmes as well as within- and between-breeds selection programmes. One of the early characterization studies conducted via SNP arrays unravelled the genomic similarities and differences among 74 global sheep breeds (Kijas et al., 2012). Accordingly, high SNP diversity and effective population size were observed for most of the breeds, suggesting no constrained and small genetic base at the early phases of domestication. Studies have also characterized the genomes and genetic diversities of various breeds, including Belclare, Beltex, Charollais, Suffolk, Texel, Vendeen, an indigenous fat-tailed sheep breed New Baisary of Kazakhistan, British and American Suffolk populations, along with Australian Poll Dorset and American Dorset populations (Kijas et al., 2009; Narzhan et al., 2022; Purfield et al., 2017; Romanov et al., 2021).

Detection of characterization parameters are crucial for designing QTL dissection studies, both traditional and genomic selection programmes and conservation studies that are aiming higher precision, faster genetic improvement and efficient management of genetic variation of the world's animal genetic resources (Kijas et al., 2009). Furthermore, assessing the genetic diversity and structure of animal breeds is among the key contributors to deciphering adaptation to environmental extremes and constructing efficient genetic improvement strategies (Boettcher et al., 2014; Groeneveld et al., 2010). Although there have been a few studies in various sheep breeds, SNP-based genome-wide studies concerning the genomic architecture of indigenous sheep breeds are still quite limited. Therefore, this study aims to define the genomic characteristics of Akkaraman sheep as well as revealing the level of differentiation and various levels and structures of genetic diversity in comparison with numerous transboundary and local sheep breeds using genome-wide single nucleotide polymorphisms (SNPs) with the aim of better understanding the nature of the breed's genome. Results of this study are strongly expected to contribute the design and analytical process of genome-wide association studies and genomic selection of the traits of economic importance in the production systems of Akkaraman sheep as well as the management and conservation of the world's animal genetic resources.

## 2 | MATERIALS AND METHODS

### 2.1 | Ethics statement

Akkaraman sheep were only sampled for blood as an experimental manipulation, which was already approved by the Local Ethics Committee of the Experimental Animals of the Ministry of Agriculture and Forestry in Türkiye with a file number of 20.November.2020/183. Genomic data for the rest of the animals were retrieved from the WIDDE database (Sempéré et al., 2015).

### 2.2 | Animal resources

The Akkaraman (AKK) population used in our study consisted of 120 randomly selected lambs from three different large-scale farms located in the outskirts of Ankara/Türkiye. Description of the overall characteristics and management practices of the study population were provided by a previous genome-wide association study (GWAS) of Akkaraman lambs (Kizilaslan et al., 2022). Briefly, the study animals were monitored as part of Türkiye's national small ruminant breeding programme, which is administered by the Ministry of Agriculture and Forestry. A phenotypic selection was applied in the herds of the study population where the selection criteria is the growth rate at weaning in each generation. The number of animals was set to 120 to avoid extreme differences between the numbers of animals among the study populations, which might eventually lead to biased estimations.

Additionally, genomic data from five mainstream transboundary breeds that are Australian Merino (AUM), Rambouillet (RMB), Suffolk (SUF), Texel (TEX), dairy Lacaune (LMI); four fat-tailed indigenous sheep breeds that are Karakas (KRS), Cyprus Fat Tail (CFT), Moghani (MOG) and Tibetan (TIB); two thin-tailed sheep breeds that are Chios (CHI) and Sakiz (SKZ); and two ancestral breeds that are Asiatic Mouflon (OOR = *Ovis orientalis*) and European Mouflon (EMU = *Ovis aries musimon*) were retrieved from the WIDDE database for the comparative genomic

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characterization of the breeds (Sempéré et al., 2015). The number of animals belonging to a total of 14 breeds were presented in Table 1.

## 2.3 | Genotyping and quality control

Blood samples of Akkaraman lambs were collected at around 6 months of age, where approximately 6 mL of blood samples were taken from *V. jugularis* into an EDTA-coated vacutainer. Samples were immediately transferred to the Genetics Laboratory of the International Center for Livestock Research and Training, Ankara/Türkiye, where the DNA extraction and genotyping were executed. DNA was extracted from those samples with the commercial Qiagen DNeasy 96 Blood & Tissue Kit and the manufacturer's protocol on the automated QIAcube HT high-throughput nucleic acid extraction instrument (Qiagen, Hilden, Germany). Following the extraction, DNA samples were exposed to a quality control (QC) step where $A_{260/280} > 1.8$; $A_{260/230} > 1.5$ and a sample amount of >20 ng/μL were sought as the minimum genotyping requirements by using a MultiSkan SkyHigh UV/VIS microplate spectrophotometer (ThermoFisher Scientific). After the DNA integrity control on gel electrophoresis, samples passing the quality control stage were proceeded to the genotyping which was carried out using the Axiom Ovine SNP Genotyping Array (50 K) via GeneTitanMulti-Channel Instrument following the manufacturer's guide (Axiom™ 2.0 Assay 96-Array Format Manual Workflow; ThermoFisher Scientific).

The 50 K SNP genotypes for the rest of the breeds were recovered from the WIDDE database. Those retrieved genotypes from the database were originally obtained from the Illumina OvineSNP50v1 and AgResearch OvineHD SNP arrays and were deposited as a result of the studies conducted by (Ciani et al., 2015; Kijas et al., 2012; Rochus et al., 2018). Therefore, RS-ID's of the SNPs on different platforms were used to merge a common SNP set for the analysed breeds. Subsequently, a quality control procedure was applied where SNPs with call rate below 95%; SNPs on the X and Y chromosomes as well as mitochondrial DNA and SNPs with Minor Allele Frequency (MAF) <5% were excluded from the dataset. The dataset was also checked for individual quality control parameters for which animals with a call rate below 90% and IBS > 95% were to be omitted from the analysis, however, no animal was found to be violating these thresholds. Consequently, a total of 29,481 SNPs and 610 animals from 14 breeds were retained after QC to perform comparative genomic characterization analyses. Quality control step of the merged data set was implemented on 'GenABEL' R package (Aulchenko et al., 2007).

**TABLE 1** Genetic diversity parameters for different sheep breeds.

| Breed | *N* | $H_O$ | $H_E$ | $F_{IS}$ |
|---|---|---|---|---|
| Akkaraman (AKK) | 120 | 0.357 | 0.305 | −0.168 |
| Australian Merino (AUM) | 50 | 0.361 | 0.313 | −0.153 |
| Cyprus Fat Tail (CFT) | 30 | 0.324 | 0.274 | −0.184 |
| Chios (CHI) | 23 | 0.322 | 0.279 | −0.151 |
| European Mouflon (EMU) | 26 | 0.200 | 0.183 | −0.091 |
| Karakas (KRS) | 18 | 0.352 | 0.298 | −0.179 |
| Lacaune Milk (LMI) | 103 | 0.359 | 0.308 | −0.165 |
| Moghani (MOG) | 34 | 0.362 | 0.309 | −0.170 |
| Asiatic Mouflon (OOR) | 2 | 0.223 | 0.229 | 0.026 |
| Ramboulliet (RMB) | 102 | 0.344 | 0.299 | −0.149 |
| Sakiz(SKZ) | 22 | 0.330 | 0.274 | −0.201 |
| Suffolk (SUF) | 19 | 0.334 | 0.286 | −0.165 |
| Texel (TEX) | 24 | 0.336 | 0.289 | −0.162 |
| Tibetan (TIB) | 37 | 0.322 | 0.283 | −0.135 |
| Overall | 610 | 0.324 | 0.280 | −0.168 |

Abbreviations: $F_{IS}$, Inbreeding coefficient averaged across individuals of the population; $H_E$, Unbiased expected heterozygosity averaged across loci corrected for sample size; $H_O$, Observed heterozygosity averaged across loci; *N*, Number of observations.

## 2.4 | Genetic diversity

Assessment of the genetic diversity parameters within each population, which are the observed heterozygosity ($H_O$), unbiased expected heterozygosity (u$H_E$) and inbreeding coefficient ($F_{IS}$) were calculated by the R package 'dartR' (Gruber et al., 2018). Inbreeding coefficient was obtained as 1−(mean($H_O$)/mean(u$H_E$)). Deviations from Hardy–Weinberg equilibrium was tested based on the previously suggested calculations by computing *p*-values as half the probability of the current sample plus the probabilities of more extreme samples with the 'dartR' package (Wigginton et al., 2005). HWE cut-off for significant deviations was set to the nominal threshold of $5 \times 10^{-08}$.

## 2.5 | Genetic distance and population structure

To observe the genetic relationship and population structure within and between the breeds as well as the distance among those, Principal Components Analysis (PCA) was performed with the 'adegenet' R package

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(Jombart, 2008). Unbiased $F_{ST}$ statistics among the populations were also estimated with the 'dartR' package to obtain pairwise genetic differentiation among the sheep breeds in the dataset as described by (Weir & Cockerham, 1984). Finally, a phylogenetic tree was constructed with the Euclidian distance matrix, where the neighbour-joining (NJ) algorithm was implemented on the same R package to observe the genetic similarities and clusters among the sheep breeds (Saitou & Nei, 1987).

## 2.6 | Linkage disequilibrium analysis

Patterns of pairwise linkage disequilibrium (LD) were investigated and reported as the squared Pearson's correlation coefficient ($r^2$) between the alleles of SNPs to ease the comparison of our results with those existing reports. Pairwise average linkage disequilibrium between adjacent SNPs and the decay of linkage disequilibrium (LD decay) were estimated using the formula suggested by Hill and Robertson (1968) that was performed with the 'r2fast' function of GenABEL R package as described below:

$$r^2 = \frac{\left[f(AB) - f(A)f(B)\right]^2}{f(A)f(a)f(B)f(b)}$$

Here $(A)$, $f(a)$, $f(B)$, $f(b)$ are the allele frequencies at two different loci, where $f(AB)$ is the haplotype made of the major alleles at the loci of interest. Pairwise LD was measured only on the syntenic loci that are the loci only on the same chromosome.

## 2.7 | Genomic inbreeding and runs of homozygosity analyses

Genomic inbreeding for each animal was evaluated as the genome-wide autozygosity obtained from the genome-wide SNP data using $F_{ROH}$ statistics generated from the identified Runs of Homozygosity (ROH), which was introduced by (McQuillan et al., 2008). Correspondingly, $F_{ROH}$ was obtained as outlined below:

$$F_{ROH} = \frac{\sum L_{ROH}}{L_{AUTO}}$$

Where $\sum L_{ROH}$ is the total length of the identified ROH and $L_{AUTO}$ is the length of the autosomal genome represented by the SNPs in this study. For the identification of ROH and $F_{ROH}$ for each individual of the each breed, a sliding window approach provided by the 'detectRUNS' R package was used, where the parameters outlined below were used as the predefined criteria for defining each individual ROH (Biscarini et al., 2018). Accordingly, no LD pruning was implemented, but the minimum length for defining a ROH was set to 1 Mb for excluding those shorter ROH that possibly are the direct consequence of LD. The genome of each animal was scanned with a sliding window of 20 SNPs, where not more than one missing SNP is allowed per window and a minimum SNP density was set to one SNP per 1000 kb with a maximum gap between two consecutive SNPs to be 1000 kb distance. Finally, SNPs were included in the scanning window when the $p$-value <0.05.

# 3 | RESULTS

## 3.1 | Genetic diversity indices

In this study, three common parameters were used to evaluate the levels of genetic diversity within breeds. Observed heterozygosity ($H_O$) and unbiased expected heterozygosity ($H_E$), which are averaged across all loci, as well as inbreeding coefficients averaged across individuals of each population ($F_{IS}$) were estimated and are presented in Table 1 with the number of animals per breed observed in our study. Most of the breeds were observed to have genetic diversities between 0.322 (TIB) and 0.362 (MOG) in terms of observed heterozygosity ($H_O$) except European Mouflon (EMU) and Asiatic Mouflon (OOR) wild breeds showing the lowest heterozygosities of 0.200 and 0.223, respectively. Again, almost all breeds outperformed those unbiased expected heterozygosities ($H_E$), which are between 0.183 (EMU) and 0.313 (AUM), estimated from genome-wide SNP markers and averaged across all loci. AKK was revealed to have the fourth largest observed heterozygosity (0.357) and expected heterozygosity (0.305) among the analysed 14 breeds in terms of the genetic variability. Mainly, negative values were obtained for $F_{IS}$ except for OOR, which was observed to be 0.026. Correspondingly, regarding the absolute values of the estimations, SKZ (−0.201) displayed the largest average inbreeding coefficient within the breed, which is followed by CFT (−0.184), KRS (−0.179), MOG (−0.170) and AKK (−0.168), while the smallest absolute values for estimates were obtained for OOR (0.026) and EMU (0.091) breeds.

Finally, deviations from Hardy–Weinberg Equilibrium (HWE) were evaluated and under the nominal cut-off value of $5\times10^{-08}$, no loci were observed to violate HWE except for three from Akkaraman sheep, which might be due to the sampling process or a minor effect of population stratification.

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### 3.2 | Genetic distance and structure among the breeds

Genomic relationships between the breeds were examined with the PCA plot, which is visualized in Figure 1. The analysis resulted in the two major components, namely PC1 and PC2, explaining 2.7% and 2.1% of the variance among the breeds, respectively. Most of the breeds in our study demonstrated clear separations into visible sub-clusters with notable exceptions of European Mouflon (EMU) and Asiatic Mouflon (OOR), which are the two wild breeds that are speculated to have ancestral relationships with most of the common sheep genetic resources. The most remarkable detail provided by the PCA plot is the alignment of certain breeds into those distinct sub-clusters composed on the display. Interestingly, fat-tailed animals represented by Akkaraman (AKK), Karakas (KRS), Moghani (MOG), Cyprus Fat Tail (CFT) and Tibetan (TIB) sheep appear to form a sub-group on the PCA plot, which is quite close to that of generated by Sakiz (SKZ) and Chios (CHI) sheep. Both groups are relatively distant with the group created by Australian Merino (AUM), dairy Lacaune (LMI) and Rambouillet (RMB) as well as Texel (TEX) and Suffolk (SUF). European Mouflon (EMU) turned out to be the most genetically diverged breed among the analysed breeds with the closest relationship to those individuals of Asiatic Mouflon (OOR) as the second most distant breed to the others in our study.

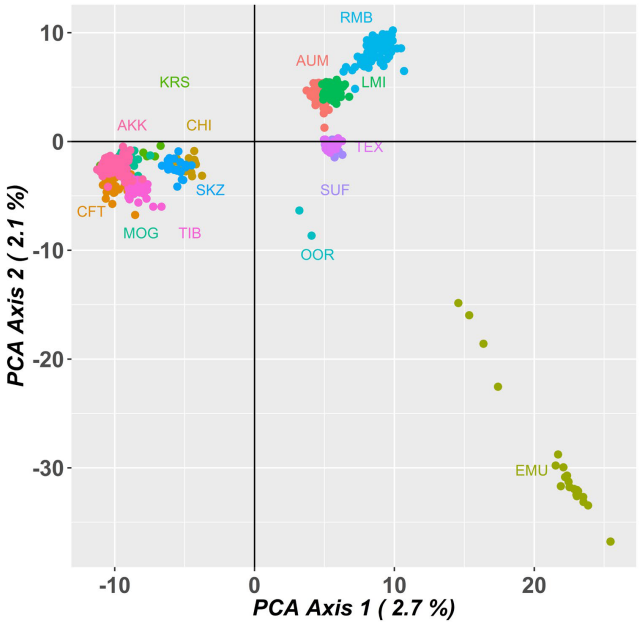


FIGURE 1 Principal components analysis (PCA) of the breeds.

Pairwise $F_{ST}$ values among the breeds were estimated to quantify the genetic divergence among the breeds and provided in Table 2. Correspondingly, AKK and MOG were observed to have the lowest pairwise $F_{ST}$ with 0.012, suggesting the least genetic divergence is among these breeds while EMU and OOR appear to have the greatest divergence with an $F_{ST}$ value equal to 0.190. Subsequent breeds that are suggested to be the closest to AKK by pairwise $F_{ST}$ estimations are KRS with 0.023, TIB and AUM with 0.034 and 0.033, respectively, CFT and CHI with 0.047 and 0.045, respectively. As also suggested by the PCA plot, EMU appear to be the most divergent breed compared to those in our study. On the other hand, AKK has been

TABLE 2 Pairwise $F_{ST}$ values between the sheep breeds.

| | AKK | AUM | CFT | CHI | EMU | KRS | LMI | MOG | OOR | RMB | SKZ | SUF | TEX | TIB |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| AKK | | | | | | | | | | | | | | |
| AUM | 0.033 | | | | | | | | | | | | | |
| CFT | 0.047 | 0.062 | | | | | | | | | | | | |
| CHI | 0.045 | 0.050 | 0.068 | | | | | | | | | | | |
| EMU | 0.129 | 0.122 | 0.178 | 0.168 | | | | | | | | | | |
| KRS | 0.023 | 0.043 | 0.060 | 0.057 | 0.167 | | | | | | | | | |
| LMI | 0.036 | 0.025 | 0.065 | 0.053 | 0.118 | 0.046 | | | | | | | | |
| MOG | 0.012 | 0.033 | 0.047 | 0.045 | 0.144 | 0.021 | 0.036 | | | | | | | |
| OOR | 0.059 | 0.053 | 0.103 | 0.085 | 0.190 | 0.074 | 0.059 | 0.059 | | | | | | |
| RMB | 0.041 | 0.025 | 0.071 | 0.060 | 0.123 | 0.053 | 0.034 | 0.043 | 0.064 | | | | | |
| SKZ | 0.056 | 0.063 | 0.087 | 0.059 | 0.184 | 0.070 | 0.065 | 0.057 | 0.109 | 0.072 | | | | |
| SUF | 0.062 | 0.052 | 0.096 | 0.084 | 0.159 | 0.076 | 0.053 | 0.063 | 0.091 | 0.060 | 0.097 | | | |
| TEX | 0.065 | 0.057 | 0.098 | 0.085 | 0.160 | 0.078 | 0.058 | 0.066 | 0.091 | 0.063 | 0.100 | 0.073 | | |
| TIB | 0.034 | 0.051 | 0.069 | 0.064 | 0.158 | 0.047 | 0.054 | 0.034 | 0.075 | 0.060 | 0.078 | 0.078 | 0.079 | |

Abbreviations: AKK, Akkaraman; AUM, Australian Merino; CFT, Cyprus Fat-Tailed; CHI, Chios; EMU, European Mouflon; KRS, Karakas; LMI, dairy Lacaune; MOG, Moghani; OOR, Asiatic Mouflon; RMB, Ramboulliet; SKZ, Sakiz; SUF, Suffolk; TEX, Texel; TIB, Tibetan.

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observed to have 0.059 and 0.129, with respectively, OOR and EMU, which may emphasize the closer relationships with those breeds derived from OOR and indicate the potential for the breed of origin preceding domestication to be OOR for AKK. The results were partially consistent with the PCA plot.

Finally, a phylogenetic tree was constructed using the pairwise Euclidian distances among the breeds and the neighbour-joining algorithm performed on the 'dartR' package (Figure 2). Accordingly, studied populations of the breeds exhibited a strong clustering into three major branches, where the branch is composed of CFT, TIB, KRS, MOG and AKK breeds; the second main lineage is formed by LMI, RMB, AUM, OOR, EMU, TEX and SUF breeds; and the last group by SKZ and CHI breeds. In the first branch, MOG and AKK formed a noticeable subgroup, whereas in the main branch, three strong subgroups were observed as LMI, RMB and AUM versus OOR and EMU versus TEX and SUF breeds. The furthest breeds in the tree were OOR and EMU, which is reasonable considering their ancestral role to all those others in the phylogenetic tree. Finally, it is important to note that the results between the PCA graph and the NJ tree were mostly consistent, without any conflicts regarding the misclassification of the animals during assignment into breeds.

## 3.3 | Linkage disequilibrium (LD) and LD decay

Linkage disequilibrium estimations were conducted using the *r*-squared ($r^2$) metric, specifically with the common set of 29,481 SNPs shared among the 14 analysed breeds. This dataset was created by merging information from various genotyping platforms and applying quality control criteria. The results of these estimations are detailed in Table 3. Considering the overall length of the sheep genome as ~2.61 Gb, that leaves an average of 88 kb gap between two consecutive SNPs. Accordingly, AKK was identified to have an average r-squared of 0.15 which was quite similar to those obtained for MOG, TIB, RMB, LMI and AUM. The lowest *r*-squared was obtained for OOR with 0.11, whereas LD for TEX, SUF and SKZ were demonstrated to be the highest among those analysed breeds.

On the other hand, the decay of LD with the increased physical marker distance on the genome was revealed for AKK sheep (Figure 3). Short distance LD for such as 100 kb appear to exist in AKK sheep. However, it is observable that LD in AKK quickly decays with physical distance, showing a pattern of continuous decline until just over 0.05 within a 500 kb range.

## 3.4 | Detection of runs of homozygosity (ROH)

Different parameters related to runs of homozygosity were determined for each breed, including the total count of ROH per breed (NROH), the average number of ROH per individual per breed (MNROH), the mean length of ROH per breed in kilobases (ALROH) and the ROH-based genomic inbreeding coefficient (FROH) along with its standard deviation. These findings for are presented in Table 3 for reference. The highest number of ROH per breed was found in RMB (9520 ROHs), while the lowest was in OOR (385 ROHs) which was followed by KRS (762 ROHs). On the other hand, the mean number of ROH per individual was found to be the least for AKK (41.10 ROHs), which was interestingly followed by MOG (41.47) and KRS (42.33), whereas the highest number of ROH was found for EMU (202.65 ROHs) and OOR (192.50 ROHs) wild breeds. As well as having the highest number of ROHs per animal, EMU has the largest average length of ROH with 5222 kb per run, among all studied breeds, while the shortest average ROH length was detected for MOG (2630 kb) with AKK having the second smallest ROH length, which is 3160 kb per run. The magnitude of ROH-based genomic inbreeding ($F_{ROH}$) differed significantly among the animals of the 14 analysed breeds in our study. OOR and EMU wild breeds

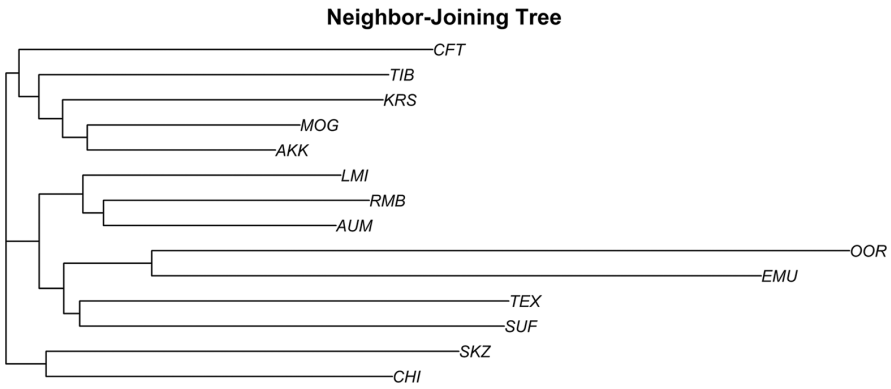


**FIGURE 2** Phylogenetic neighbour-joining (NJ) tree of the breeds.

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| Breed | $N_{ROH}$ | $MN_{ROH}$ | $AL_{ROH}$ (kb) | $F_{ROH}$ | $SD_{FROH}$ | LD ($r^2$) |
|---|---|---|---|---|---|---|
| AKK | 4932 | 41.10 | 3160 | 0.002 | 0.001 | 0.15 |
| AUM | 3245 | 63.62 | 3572 | 0.09 | 0.04 | 0.16 |
| CFT | 2260 | 75.33 | 4863 | 0.15 | 0.06 | 0.21 |
| CHI | 2761 | 120.04 | 3780 | 0.18 | 0.04 | 0.21 |
| EMU | 5269 | 202.65 | 5222 | 0.23 | 0.08 | 0.19 |
| KRS | 762 | 42.33 | 4154 | 0.07 | 0.06 | 0.19 |
| LMI | 6011 | 58.36 | 3574 | 0.08 | 0.01 | 0.16 |
| MOG | 1410 | 41.47 | 2630 | 0.04 | 0.03 | 0.15 |
| OOR | 385 | 192.5 | 3812 | 0.30 | 0.20 | 0.11 |
| RMB | 9520 | 93.33 | 3588 | 0.13 | 0.05 | 0.16 |
| SKZ | 2044 | 92.90 | 4063 | 0.15 | 0.05 | 0.22 |
| SUF | 2195 | 115.52 | 3494 | 0.16 | 0.01 | 0.22 |
| TEX | 2871 | 119.62 | 3575 | 0.17 | 0.02 | 0.22 |
| TIB | 3126 | 84.48 | 3556 | 0.12 | 0.05 | 0.15 |

**TABLE 3** Descriptive statistics of ROH and LD in different sheep breeds.

Abbreviations: $AL_{ROH}$, Average length of ROH (kb) in a breed; $F_{ROH}$, Genomic inbreeding coefficient based on ROH; $MN_{ROH}$, Mean number of ROH per individual per breed; $N_{ROH}$, Total number of ROH per breed; $SD_{FROH}$, Standard deviation of $F_{ROH}$.

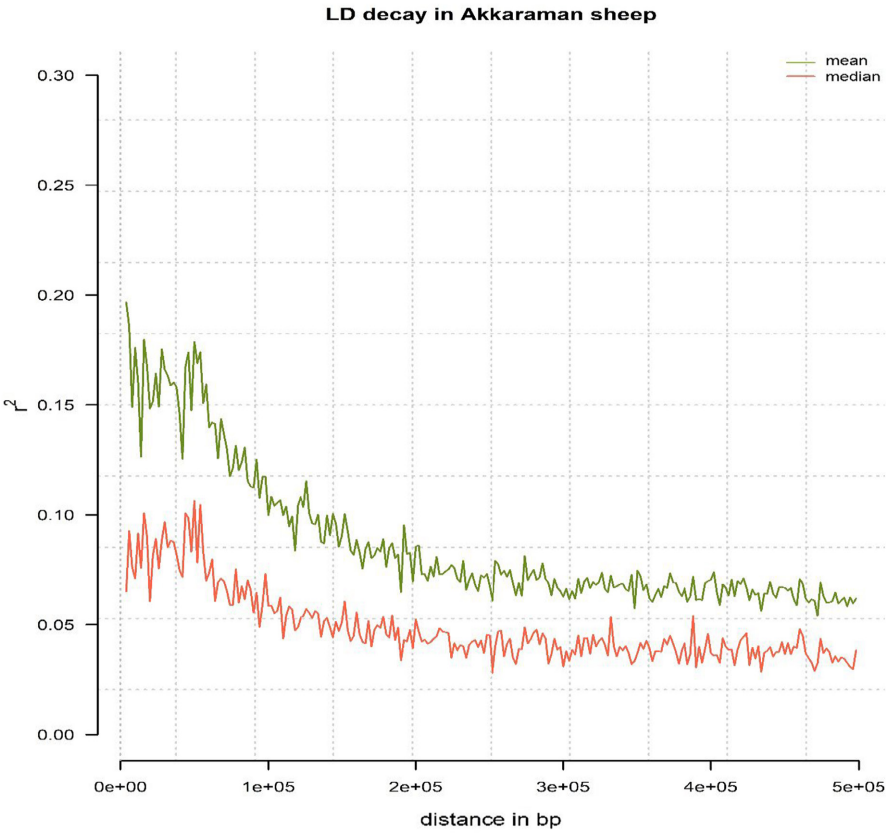


**FIGURE 3** Trends in linkage disequilibrium (LD) decay in 500 kb distance.

were identified to bear the highest genomic inbreeding evaluated by ROH with values of 0.30 and 0.23, respectively. In contrast, AKK (0.002) appear to have the lowest average genomic inbreeding, followed by MOG (0.04) among all 14 breeds. The results were partially consistent with the observed heterozygosities ($H_O$) given above in Table 1.

## 4 | DISCUSSION

Indigenous sheep are among the main pillars of food security. Therefore, the characterization of indigenous sheep is quite important for breeding programmes based on genomic markers such as genomic selection or traditional selection methods, QTL discovery studies for

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economically important traits and conservation programmes. Assessment of population structure and genetic diversity has been suggested to define a framework for genomic selection in sheep (Wilson et al., 2022). Recent advances in high-throughput genomic technologies and statistical information processing approaches led to genomic (i.e., genome-wide) characterization studies in those indigenous breeds with thousands of genomic markers processed altogether. Identification of genetic diversity using genome-wide DNA markers are especially useful when pedigree records of the breeds are not available (Al-Mamun et al., 2015; Deniskova et al., 2019). In a study, a genomic dataset of 74 globally divergent sheep breeds were compiled and 50 K SNP genotypes of has been made available to the researchers with relevant diversity and characterization statistics of those breeds (Kijas et al., 2012). Hence, this study aimed to unravel within-breed genetic diversity and implement comparative genomic characterisation of Akkaraman sheep against six fat- and thin-tailed indigenous breeds, five mainstream transboundary sheep and two of the main wild breeds from around the world which are collected by the studies conducted by (Ciani et al., 2015; Kijas et al., 2012; Rochus et al., 2018).

Information regarding genetic diversity is significantly important for traditional and genomic selection programmes as well as conservation programmes developed for the sustainable use of animal genetic resources (Narzhan et al., 2022; Scherf & Pilling, 2015). In terms of genetic diversity, expected heterozygosity ($H_E$), unbiased observed heterozygosity ($H_O$) and average inbreeding coefficients as Wright's $F_{IS}$ (Wright, 1951) were estimated in this study, since these are the most common parameters in use (FAO, 2011). Overall, high heterozygosities ($H_O$) were observed for the analysed 12 breeds, including Akkaraman sheep, where only the two wild breeds, namely European Mouflon (i.e., *Ovis aries musimon* = EMU) and Asiatic Mouflon (i.e., *Ovis orientalis* = OOR), turned out to have quite low genetic diversities. Except for actually having low diversity, one of the main reasons for that could be that these two breeds were not used to develop the genome-wide SNP arrays, which leads to ascertainment bias in the concluded arrays (Kijas et al., 2012). The study found slightly higher expected heterozygosities ($H_E$) for AUM (0.37), TIB (0.34), CFT (0.31), KRS (0.34), MOG (0.36), SKZ (0.31), CHI (0.32), LMI (0.36), RMB (0.38) breeds. Besides, various other expected heterozygosity measurements were revealed for Australian Suffolk (0.37), Irish Suffolk (0.33), Scottish Texel (0.33), New Zealand Texel (0.34) and German Texel (0.35) by the same study, which was also considerably higher than the estimates in our study. Since the studies share mainly a common sample set excluding Akkaraman sheep as well as Suffolk and Texel populations, the differences could be attributed to the SNP marker sizes with 49,034 SNPs used by the researchers versus 29,481 SNPs in our study. As might be expected, increase in the number of polymorphic loci analysed might lead to change in the expected heterozygosities. Additionally, the consistent and mostly 4–6% lower estimations than those studies with the same dataset for those overlapping breeds is also supportive of this explanation. For the $F_{IS}$, excess of negative values indicates the abundance of heterozygotes in the analysed 13 breeds, which is confirmed by the observed heterozygosities exceeding expected heterozygosities for individual breed evaluations. One of the reasons that OOR showed a positive value for the $F_{IS}$ estimations could be due to the deficit of sample size. On the other hand, obtained heterozygosities and inbreeding coefficients ($F_{IS}$) indicate an excess of heterozygotes in most of the breeds including Akkaraman sheep, which is advantageous in terms of population bottlenecks, future threats of extinction and eventual contribution to the sustainability of sheep production systems (Nielsen & Slatkin, 2013; Simm, 1998).

According to the PCA plot, analysis of the 14 breeds showed clear stratification into four separate groups, whereas EMU and OOR remained distinct from all other breeds, of which EMU was the furthest diverged breed and OOR was the second that was located away from those groups, though with a closer position on the plot. Fat-tailed breeds such as Karakas, Cyprus Fat Tail, Moghani and Tibetan sheep, which are breeds that are classified to be Asiatic by Kijas et al. (2012) formed a strong sub-cluster in the PCA plot by overlapping also Akkaraman sheep. Previously, strong evidence suggested that Karakas is a variety of Akkaraman sheep which is also supported by the results of our study (Ozmen et al., 2020; Yalcin, 1986). Furthermore, Sakiz and Chios breeds, which are closest to the sub-group created by those fat-tailed Asian breeds, are known to share the same breed origin (i.e., Chios) with recent geographic isolation on the Chios Island and Türkiye as it is also supported by our findings as well as other studies (Kijas et al., 2012; Sönmez, 1962). Interestingly, Cyprus Fat Tail was previously found to be closer to the sub-group formed by Chios and Sakiz rather than the Moghani sheep (Kijas et al., 2012). In our study, $F_{ST}$ values and phylogenetic tree were also supportive of the arguments proposed above, while Akkaraman has the lowest differentiation from those other fat-tailed sheep in comparison with the remaining breeds. Furthermore, Suffolk and Texel, as Northern European breeds, were also grouped previously by a phylogenetic tree created by (Rochus et al., 2018). At a global scale, PCA graph, Fst values and phylogenetic tree display strong genetic divisions for fat-tailed sheep (i.e., Akkaraman, Karakas, Moghani, Tibetan and Cyprus Fat Tail) and sheep with

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Merino background (i.e., Australian Merino, Milk Lacaune and Rambouillet) as well as those with Eastern Europe origin (Suffolk and Texel) and other thin-tailed sheep (i.e., Chios and Sakiz). Hence based on the findings suggested by those analytical tools it is possible to speculate that those clustered breeds share the same ancestral origin when considered within groups. On the other hand, the wide differentiation of Akkaraman from those groups formed by Milk Lacaune, Rambouillet, Australian Merino, Suffolk, Texel as well as *Ovis orientalis* and *Ovis aries musimon* might lead us to suggest that the breed could be originated from some other ancestral breed than those, which is a hypothesis remain to be validated.

The existence of linkage disequilibrium (LD) between any two markers reflects non-random segregation of alleles at those two loci. Estimates of LD lays foundations for genome-wide association studies (GWAS) as well as those marker-assisted selection decisions and genomic selection (i.e. Genome-wide Selection, Genomic Prediction) practices (Al-Mamun et al., 2015). Effective population size and evolutionary forces such as selection, mutation and admixture as well as recombination events affects the speed of LD decay and the extent of LD (Wang, 2005). Therefore, comparison of LD among the breeds of a species allows to speculate about the overall diversity levels as well as to understand the nature of previous selection decisions applied to those breeds. In our study, LD estimations were both implemented for two adjacent SNPs, which on average have 88 kb pairwise distance, as well as LD decay until 500 kb distance between pairs of markers. Akkaraman sheep came out to have one of the lowest LD among the analysed breeds right after Asiatic mouflon, which is also an indicator of lower selection pressure, higher effective population size ($N_E$) and recombination rate in Akkaraman sheep (Qanbari, 2020). Sheep have low LD estimates compared to the other species. Although for a smaller physical distance such as 50–60 kb, previously lower LD estimates than that obtained by our study for Akkaraman sheep were observed in Merino, Chinese Merino, Texel, Romney, Valle del Belice, Pinzirita, Comisana and various crossbreds with faster LD decay patterns (Abdullah Al-Mamun et al., 2015; Liu et al., 2017; Mastrangelo et al., 2014; Prieur et al., 2017).

Sheep populations that are exposed to inbred mating for a long period have a genomic structure indicating a rise of autozygosity, which also give rise to the uninterrupted runs of homozygosity (ROH). Various other forces also lead to the ROHs in the genome, which mainly are intensive selection pressure, founder effect and genetic drift (Peripolli et al., 2017). Akkaraman sheep have been observed to hold the least average number of ROHs (41.10) per individual among the 14 breeds of the study, while still higher than those obtained for Merino and Poll Dorset as well as Tunisian sheep (Abdullah Al-Mamun et al., 2015; Ahbara et al., 2021). The average length of ROH observed in Akkaraman was also the second lowest (3160 kb) and estimated genomic inbreeding $F_{ROH}$ (0.002) was the lowest compared to the other breeds in the study, which is also supportive of its relatively high diversity observed. The $F_{ROH}$ estimation for Akkaraman sheep was significantly lower than the estimates of many breeds from around the world such as indigenous breeds from Kyrgyzstan and many South African and global sheep populations (Deniskova et al., 2019; Dzomba et al., 2021). Regarding the Akkaraman sheep breed, the information provided by our study on the genetic diversity, population structure and extent of LD and ROH in the genome of the breed will help further GWA studies, conservation programmes and genomic selection programmes to be designed most efficiently. In genomic selection, especially the GEBV accuracies mostly depend on the traits's heritability, genetic architecture and the effective population size of the targeted genome. Our study observed low levels of LD and quite high levels of diversity, which may lead to suggest that the accuracies of GEBVs in this sheep breed could be lower than populations with higher LD exposed under similar scenarios. Therefore, for those studies and further characterization studies, larger samples and denser marker sets are suggested for efficient implementation and increased accuracy in Akkaraman sheep.

## 5 | CONCLUSIONS

The current study is the first study characterizing the genetic architecture of Akkaraman sheep breed in comparison with the mainstream transboundary breeds and other indigenous and wild sheep populations with high-density genome-wide distributed SNPs. Indigenous sheep breeds comprehend a great share of the world's animal genetic resources and constitute the main pillars of sustainable production and food security. We have displayed genetic similarities and differences between those breeds by estimating and comparing various genetic diversity indices, linkage disequilibrium (LD) estimates and fixation index ($F_{ST}$), runs of homozygosity (ROH) as well as PCA and neighbour-joining tree analysis. Akkaraman sheep were found to be clustered with Moghani, Karakas, Tibetan and Cyprus Fat Tail sheep, which are the fat-tailed sheep in the study, both as a result of PCA and neighbour-joining tree analysis. These are also supported by $F_{ST}$ estimations. From an evolutionary perspective, those breeds are also expected to behave genetically similar regarding the traits of economic

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importance and adaptive superiority, which is a hypothesis that remained to be validated by further studies. On the other hand, the cluster of Akkaraman sheep has been observed to be considerably diverged from those *Ovis orientalis* and *Ovis aries musimon*, which might lead us to hypothesize that the breed could be originated from another ancestral breed than those. That remains to be validated with a larger diversified sample set. In any case, the large genetic diversity of Akkaraman sheep validates the existence of a large genetic variance to implement a comprehensive selection on the breed, without a great danger of imposing an inbreeding depression in the near future. The fact that Akkaraman sheep has the lowest genomic inbreeding and one of the lowest numbers of ROHs also reveals that the breed has not been exposed to any historical intensive selection pressure, inbred mating or a massive population bottleneck for a long period to leave strong marks of genomic homozygosity. The results of the current study improve our understanding of the genetic diversity in Akkaraman sheep in comparison with certain mainstream sheep breeds as well as those indigenous breeds from around the world. Additionally, our findings will be useful to perform further GWA studies effectively both considering population structure, diversity and LD patterns observed among the breeds. Finally, the results of our study also provide valuable insights into the influence of long-term selection applied to these breeds and provide practical knowledge that will contribute to designing efficient and successful genome-based selection programmes for worldwide sheep production systems.

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## CONFLICT OF INTEREST STATEMENT

The authors of the study declare no conflict of interest.

## DATA AVAILABILITY STATEMENT

The data of the study are available from the corresponding author upon request.

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