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GENETIC MARKERS OF GOATS
(review)

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Abstract

Goat biodiversity comprises 635 breeds from in 170 countries (https://www.fao.org/dad-is). Wide geographical distribution and positive dynamics of goat populations in recent decades are due to high adaptability to various climatic conditions and the uniqueness of goat products (I.N. Skidan et al., 2015; A.I. Erokhin et al., 2020). DNA microsatellite markers have been widely used to study genetic differentiation of goat breeds and populations in many countries (C. Wei et al., 2014; G. Mekuriaw et al., 2016). Insignificant genetic distances (F_{ST} 0.033-0.069) between goat breeds bred in Europe confirm the frequent exchange of the gene pool between them. A more significant genetic differentiation (F_{ST} 0.134-0.183) is characteristic of breeds from East and Southeast Asia due to the ecological and geographical features and the remoteness of their habitats (K. Nomura et al., 2012; G. Wang et al., 2017; P. Azhar et al., 2018). The *CSN1S1*, *CSN1S2*, *CSN2*, and *BLG* gene polymorphisms are of most interest in dairy goat breeding (N. Silanikove et al., 2010; Vorozhko I.V. et al., 2016). Eighteen allelic variants have been described in the *CSN1S1* gene, eight in *CSN2*, and 16 in *CSN3* (S. Ollier et al., 2008; T.G. Devold et al., 2010). The $CSN1S1^{AA}$ association with more protein in milk and less total lipids and medium chain fatty acids has been found (Y. Chilliard et al., 2006; D. Marletta et al., 2007). Goats with BLG^{AB} genotype have longer lactation period, produce more milk with higher fat and protein contents (A.S. Shuvarikov et al., 2019). The sequencing of the goat genome (the AdaptMap project) and the development of the 52K SNP BeadChipGoat chip has expanded the search for genome regions involved in breeding (G. Tosser-Klopp et al., 2014; A. Stella et al., 2018). There is evidence that the *RARA*, *STAT*, *PTX3*, *IL6*, *IL8*, and *DGAT1* genes are linked to dairy performance traits (P. Martin et al., 2018; D. Ilie et al., 2018). At the genomic level, the *MC1R*, *ASIP* and *KIT* are associated with wool fiber coloration, *FGF5*, *EPAS1* and *NOXA1* with wool productivity of goats and their high-altitude adaptation (X. Wang et al., 2016; S. Song et al., 2016; Guo J. et al., 2018). Thus, the evaluation of genetic relationships between breeds, the search for genes associated with economically important traits are promising for use in breeding programs and further development of goat breeding (L.F. Brito et al., 2016; S. Desire, 2016; A. Molina et al., 2018; T.E. Deniskova et al., 2020). However, despite certain achievements, until now, loci associated with economically important traits in goats, such as breeding characteristics, the level of down, wool and milk productivity, as well as determining resistance to diseases, remain largely unknown.

Keywords: goats, microsatellites, breeds, productivity, genetic differentiation, genetic markers, GWAS

Goat raising is a dynamically developing branch of animal husbandry. According to the FAO (Food and Agriculture Organization of the United Nations), in 30 years the world's goat population has almost doubled, from 589 million in

1991 to 1 billion 200 million by the beginning of 2020. Today, there are 635 goat breeds in the world, bred in 170 countries, with only 38 breeds classified as transboundary (DAD-IS, Domestic Animal Diversity Information System, http://www.fao.org/dad-is).

The purpose of our review is to summarize and analyze data on modern genetic markers for the study of biodiversity, genetic structure, determination of the degree of inbreeding, purity of breeds and populations of goats, genome-wide association studies (GWAS) in order to identify genes associated with economically important indicators of productivity.

The domestic goat (*Capra hircus*) is propagated worldwide and comprises a large variety of breeds due to their biological peculiarities, including high adaptability to various climatic conditions. Goat raising cover mountain, high-mountain, steppe and semi-desert zones with a sparse grass vegetation. Other animal species (cattle, horses, and sheep) cannot make up for the need for nutrients and energy using such limited food resources. The widespread breeding of goats and the growth of their numbers are also associated with a global trend of increasing demand for products with unique properties, which include goat down, moger, goat milk, and goat meat [1].

Since ancient times, goat down has been a row material for warm products of special lightness, softness and elasticity, which is still relevant today. Herds of fiber goats are widespread in Turkey, India, Mongolia, China, Afghanistan, Kyrgyzstan, Uzbekistan, and Russia (https://www.fao.org/faostat/en).

1. Abundance (heads) **of breeds and populations of goats (*Capra hircus*) bred in Russia in 2000-2019** [5-7]

Breed (population)	Year				
	2000	2005	2010	2015	2019
Altai belaya pukhovaya (down goats)					8300
Alpine goats				900	5230
Gornoaltayskaya pukhocaya (down goats)	15700	11300	27300	22200	10800
Dagestanskaya pukhocaya (down goats)	5700	16600	19500	No data	5000[a]
Dagestan sherstnaya (wool goats)	5800	16700	19600	No data	11000[a]
Donskaya (Pridonskaya) goats	2000	1600	No data	No data	No data
Saanen goats		1100	6900	19900	29770
Karachaevskaya goats	No data	No data	No data	No data	8000[a]
Murciano-Granadina goats					470
Nubian goats					330
Orenburg goats	16900	22800	20500	17200	6500
Russkaya belaya goats	No data	No data	No data	No data	170[a]
Sovetskaya sherstnaya (wool goats)	31700	88700	83300	89900	28600
Tuvinskaya grubosherstbaya (Tuvan coarse-haired goats)	No data	No data	No data	No data	7200[a]
Total	77800	158800	177100	150100	97370
Not identified	2800	28500	7100	63200	41130

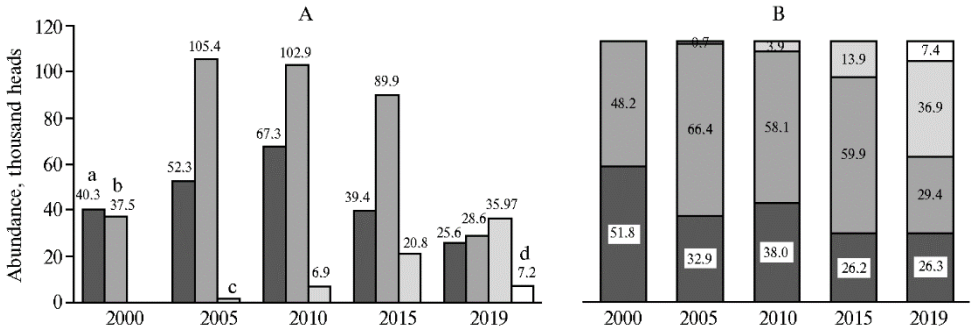
N o t e. Altai belaya pukhovaya (Altai white down goat breed) was officially approved in 2016. Saanen goats were brought to the Russian Federation in 2001, Alpine, Murciano Granadina and Nubian goats in 2015-2018. The total number of goats is calculated from official data provided by livestock breeding organizations; [a] — the number of goats based on the veterinary control records of the regional administrations of farm locations).

Over the past 10 years, goat milk production in Asia, Africa, North and South America has increased by 21.3, 18.4 and 9.5% on average. In France, Greece, Italy, Spain and the Netherlands, the share of goat milk consumption (including cheese production) is 15-20% of the total dairy production [2]. Goat milk is increasingly considered as a raw material for products with high biological and, in some cases, therapeutic value and for baby food. One of the features of goat's milk is a significantly greater dispersion of fat globules compared to cow's (average diameter of 3.19 μm and total area 21.78 cm^2/ml vs. 3.51 μm and 17.11 cm^2/ml), which provides its high digestibility due to availability for lipolytic enzymes. Goat milk contains 54.6-80.2% more unsaturated short-chain fatty acids ($C_{4:0}$-$C_{10:0}$) [3]. In addition, the high content of β-casein and a

negligible amount (virtually absent) of α_{s1}-casein, which causes allergic reactions, bring goat milk closer to human breast milk composition. Goat milk is also distinguished by the physicochemical properties of casein micelles, which contain more calcium and inorganic phosphorus, are less solvated and more resistant to heat, therefore, compared to the milk of other animal species, casein is more easily lost, which determines the high cheese suitability [4].

In Russia, 10 breeds and populations of goats for various use are currently raised. The livestock at the end of 2019 amounted to 97,370 animals (Table 1).

It should be noted that over the past 20 years there has been a significant change in the breed composition of goats in terms of productivity. Since 2015, there has been a significant decrease in the number of wool goats in terms of productivity and, accordingly, their share in the total livestock from 59.9 to 29.4%. The number of dairy goats has noticeably increased. In 2005, dairy goats were absent in the structure of Russian goat breeding, and by the end of 2019, they already accounted for 36.9% (Fig.).



Abundance of goat (*Capra hircus*) breeds for various use (A) **and their distribution** (%) (B) (the Russian Federation, 2005-2019): f — down goats, b — wool goats, c — milk goats, d — coarse-haired goats [5-7].

Currently, to accelerate goat breeding, it is not enough to use only traditional methods, and therefore there is an increasing need to integrate modern DNA technologies into the breeding process, since they can increase the efficiency of breeding through the selection of carriers of alleles associated with economically valuable traits [8, 9]. The following types of DNA markers can be distinguished, which are most widely used in the study of animal genomes, including goats: RFLP (restriction fragment length polymorphism), RAPD (randomly amplified polymorphic DNA), AFLP (amplified fragment length polymorphism), MS (microsatellites, STR, short tandem repasts), SNP (single nucleotide polymorphism), CNV (copy number variation). Microsatellites, also known as STR markers, and markers based on single nucleotide polymorphisms (SNPs) have received the greatest distribution in studies of the goat genome.

Microsatellites (STR markers). Due to their availability, low cost, and information content, microsatellites remain one of the most common markers in phylogenetic and taxonomic studies and are used in programs for the conservation of agricultural animal genetic resources. This is especially true for aboriginal animal husbandry in general and goat breeding in particular, since there are about 600 aboriginal goat breeds in the world [10, 11].

In the study of genetic processes in populations, Wright's F-statistics, or fixation indices, are most often used, which characterize individual (F_{IS}), subpopulation (F_{ST}) and population (F_{IT}) levels of the genetic structure of a population: $F_{IS} = (H_S - H_I)/H_S$, $F_{ST} = (H_T - H_S)/H_T$, $F_{IT} = (H_T - H_I)/H_T$, where H_I is the observed heterozygosity, H_S is the expected heterozygosity in subpopulations, H_T

is the expected heterozygosity in the entire population during panmixia. F_{IS} indicates a decrease in heterozygosity due to non-random mating, F_{IT} indicates the degree of inbreeding of individuals in the whole population. At $F_{IS, IT} > 0$, there is a deficit of heterozygous individuals, at $F_{IS, IT} < 0$, there is an excess. F_{ST} indicates a decrease in heterozygosity due to gene flow restriction and genetic drift between subpopulations. The F_{ST} for the two populations serves as the genetic distance value. At $F_{ST} < 0.05$, population differentiation is insignificant, at $F_{ST} > 0.25$ it is significant [12]. Nei expressed fixation indices through allelic frequencies, observed and expected heterozygosity for any populations, and proposed the use of genetic distances [13, 14)].

With the development of genetic methods, the number of microsatellite loci increased, which were used in the study of the biodiversity of goats with wool and down productivity. Thus, six populations of Kashmir goats from China were studied using 11 microsatellite loci, which formed three separate clusters: Tibetan goat of Plateau type and Tibetan goat of Valley type, Sichuan type (black goats, Meigu, Jianchang, Baiyu) and Xinjiang goats [15]. In another study, 14 microsatellite loci were used to study the genetic differentiation of nine Kashmiri breeds from China. The obtained F_{ST} values indicated their high genetic isolation, with the Hegu breed bred in Tibet showing the greatest remoteness [16].

Kharzinova et al. [17], in a comparative study of the Sovetskaya sherstnaya (wool goats), Tajik sherstnaya (wool goats), Orenburg pukhovaya (down goats), Alpine and Saanen dairy breeds for 10 microsatellite loci, revealed that each of these breeds has its own population genetic structure and determined the degree of genetic differentiation of breeds.

Selionova et al. (18) assessed the genetic diversity and genetic distances between wool and down breeds of goats bred in the North Caucasus (Karachaev, Dagestan pukhovaya down goats, Dagestan sherstnaya wool goats), in Siberia (Sobetskaya sherstnaya wool goats), and in the South Urals (Orenburg goats), as well as between three species of mountain goats, the Siberian ibex (*C. sibirica*), bezoar ibex (*C. aegagrus*), and tur (*C. caucasica*) using 16 microsatellite loci. Karachay goats exhibits the greatest genetic diversity, i.e., the average number of alleles per locus was 9.1 vs. 6.5-7.5 for other breeds. Subspecies of the Caucasian tur formed the first cluster, Siberian ibex formed the second cluster, and breeds of domestic goats formed the third cluster. Groups of the bezoar goat were located at the root of the third cluster, which indirectly confirms their participation as an ancestral form of domestic goats [18].

Microsatellite markers were used to study the genetic diversity of five populations of native Mongolian goats (Gurvan egch, Darhatskaya, Burakh zavkhan, Ulgiy uulan, Altay uulan), two populations of local Tuvan goats, and three breeds (Sovetskaya sherstnaya, Tajik sherstnaya wool goats and Orenburg pukhovaya down goats). Two main groups have been identified, one group includes predominantly Mongolian aboriginal populations, and the other group includes Central Asian goat breeds. Populations of the local Tuvan goat were divided between the respective groups. At the same time, Mongolian goats were characterized by high intrapopulation diversity and a low degree of genetic differences between populations [19].

A number of studies are devoted to the study of the genetic diversity of dairy goats. Wang et al. [20] used 15 microsatellite markers to study breeds bred in China, i.e., the breeds of own selection (Guanzhong, Laoshan, and Wendeng), those bred using the Saanen breed (Xinong Saanen) and imported from Europe (Nubian). The average number of alleles per locus was 4.9, F_{IS} values ranged from 0.09 to –0.08, F_{ST} was 0.08. Between breeds Wendeng and Laoshan as well as Guanzhong and Xinong there are the closest genetic links that reflected the history

of formation and geography of breeding. It has been established that all four Chinese breeds had a common ancestor, the Saanen breed, which was imported to China from Europe in the 18th century [20].

Araujo et al. [21] compared the local dairy breed Moxoto with the Alpine and Saanen goats for 11 microsatellite loci. The F_{ST} value between the Moxoto and introduced breeds was 0.08, while between the latter it was 0.03, indicating their greater genetic similarity [21].

The genetic differentiation of dairy goat breeds from Thailand (Jamunapari, Alpine, Nubian, Saanen, and Toggenburg) was studied using 12 microsatellite markers. The Alpine, Saanen, and Toggenburg breeds were assigned to one phylogenetic cluster, while the Jamunapari and Nubian breeds formed two others. The average number of alleles per population per microsatellite locus was 7.4. F_{IS} values ranged from 0.18 to 0.04, F_{ST} was 0.07 [22].

Microsatellite markers were used to identify the breed of goats with maintained status in the production of dairy products. Thus, the Girgentana goats are bred on the island of Sicily, its distinctive feature is the unique quality of milk, but due to the small number of Girgentana goats are endangered, so measures are being taken to preserve the breed [23]. A panel of 20 microsatellite markers was used to genetically identify Girgentana, Maltese, and Derivata di Siria goats. Eight alleles of microsatellite markers were present in the Girgentana and Derivata di Siria breeds, but were absent in Maltese goats. Three microsatellite markers (FCB20, SRCRSP5, TGLA122), recognized as the most informative, were proposed for use in genetic monitoring of dairy products obtained from goats of the Girgentana breed and when mixed with milk from animals of other breeds [24].

In a large-scale study performed in China using 30 microsatellite loci and covering more than 2 thousand goats of 40 breeds and populations of various productivity directions, it was found that their genetic structure is mainly determined by geographical origin and periods of human migration across the country. More clearly, the genetic differentiation of goats was traced in Western China, for whose populations two clusters were established, the southwestern and northwestern. These clusters coincided with separation by natural barriers (mountain ranges, river basins) [25].

Dixit et al. [26] used 25 microsatellite markers to study genetic diversity and relationship between 20 breeds from India. Most of the loci were heterozygous, F_{IS} values ranged from 0.61 to 0.73. The Kanniadu breed showed the greatest diversity, and Osmanabadi the least. The overall F_{ST} value was 0.183, with 83.5% of the genetic variability found to be due to differences between individuals within a breed and only 16.5% between breeds. The smallest genetic distance was determined between the Ganjam and Malabari breeds (0.22), the largest between the Kanniadu and Malabari breeds (0.83) [26].

In a study of 18 native goat breeds and populations from seven East Asian countries, 26 microsatellite loci were involved. The average number of alleles per locus ranged from 2.5 to 7.6m being 5.8 on average for the studied breeds, while there was a deficit of heterozygotes and general inbreeding ($F_{IS} = 0.054$, $F_{IT} = 0.181$, $p < 0.01$). In Mongolia and Bangladesh, there was more genetic diversity in goat populations than in Japan, Korea and Indonesia. All breeds formed three clusters, the East Asian, Southeast Asian and Mongolian, which correlated with the use that the breeds are intended for, geographical origin and migration routes [27].

Cañón et al. [28] used 30 microsatellite markers to genotype 45 goat breeds from 15 European and Middle Eastern countries. In all breeds, a heterozygosity deficiency ($F_{IS} = 0.10$) and an average genetic differentiation between them was revealed. Multivariate analysis of allele frequencies revealed four clusters: the

breeds of the Eastern Mediterranean (Near East) (F_{ST} = 0.033) were the first, of the Central Mediterranean (F_{ST} = 0.040) the second, of the Western Mediterranean (F_{ST} = 0.051) the third, and of Northern and Central Europe (F_{ST} = 0.069) the fourth. The decrease in the genetic diversity of goats from the southeast to the northwest was accompanied by an increase in differentiation at the breed level. Approximately 41% of the genetic variability was associated with the geographical origin of the breeds. The data obtained were considered by the authors as confirmation of the hypothesis that livestock migrated from the Middle East to Western and Northern Europe, while the formation of breeds was more systematic in Northern and Central Europe than in the Middle East.

In a number of sources, it is proposed to consider the F_{ST} value equal to or greater than 0.25 as a significant genetic distance between breeds, from 0.05 to 0.25 as an average, less than 0.05 as insignificant [12, 13, 29, 30]. Analysis of the above data draws to the conclusion that, in general, small genetic distances (F_{ST} 0.033-0.069) have been established between breeds and populations of goats bred in Europe, which can be considered as confirmation of the frequent exchange of genes due to crossings to improve productivity. For breeds and populations of goats living in East and Southeast Asia, genetic differentiation is more significant (F_{ST} 0.134-0.183), which, apparently, is due to ecological and geographical features and remoteness of habitats.

The study of the origin of goats, the routs of their migration, genetic differentiation and features of the genetic structure as a result of adaptation to the breeding environment does not lose relevance. To obtain new data, single nucleotide polymorphisms (SNPs) are now increasingly used [31-33].

Single nucleotide polymorphisms (SNP markers). SNPs are the most common type of polymorphism in both nuclear and mitochondrial DNA. The main advantage of using SNPs as markers compared to microsatellites is their wide distribution in the genome, a clear mutational mechanism with low homoplasia and mutability.

In addition, SNPs in goats, unlike multi-allelic microsatellites, are presented as bivalent variants. The methodological advantages of SNP analysis include the absence of special requirements for DNA quality (SNP analysis is usually carried out by obtaining short fragments less than 100 bp long), a lower degree of erroneous genotyping, the possibility of automating the process and standardizing the data obtained. The study of SNP became widespread even at the early stages of the development of DNA diagnostics of farm animals, since it is this type of variability that underlies the polymorphism of genes associated with economically valuable traits. The development of high-throughput genotyping technologies has made SNPs the dominant type of DNA markers in the study of farm animal genomes.

Currently, SNPs are considered the preferred type of marker for genomic evaluation, including genome-wide association studies, to determine the relationship between individuals, determine the degree of inbreeding and hybridization, high-resolution genetic mapping and more complete characterization of genetic resources [34].

Polymorphism of goat productivity genes. Along with phylogenetic studies, the identification of genes and their allelic variants associated with economically valuable traits is important for the selection improvement of goat productivity. For milk goats, these are primarily indicators that characterize the quantitative parameters of milk yield, namely, the milk fat and protein content [35]. The main part of milk proteins is casein, containing four fractions (α_{s1}-,

α_{s2}-, β- and κ-casein), and whey proteins (β-lactoglobulin, α-lactalbumin) [36, 37]. The influence of these proteins on the technological properties of milk and the possibility of obtaining products with specified quality parameters have been comprehensively studied, which determined the interest in studying the genes that control their synthesis [38, 39].

The gene *CSN1S1* for α_{s1}-casein whose polymorphism is determined by a set of allelic variants is the most studied. They are defined as strong for the content of α_{s1}-casein at ~ 3.5 g/l (*A*, *A'*, *B1*, *B2*, *B3*, *B4*, *C*, *H*, *L*), medium at ~ 1.1 g/l (*E*, *I*), weak at ~ 0.45 g/l (*D*, *F*, *G*), and zero-variant (*O1*, *O2*, *N*) (no α_{s1}-casein in milk) [37-39]. The so-called strong alleles are more common in breeds from Spain, Italy, France, and Greece while medium and weak alleles are widely represented in goats in New Zealand and Brazil [43, 44]. Nine allelic variants (*A*, *B*, *C*, *D*, *E*, *F*, *0*, *sub A* and *sub E*) for the *CSN1S2* gene (α_{s2}-casein), eight variants (*A*, *A1*, *O'*, *O*, *B*, *C*, *D*, *E*) for the *CSN2* gene (β-casein), and 16 (*A*, *B*, *B'*, *B''*, *C*, *C'*, *D*, *E*, *F*, *G*, *H*, *I*, *J*, *K*, *L*, *M*) for the *CSN3* gene (κ-casein) [37, 40]. The main types of caseins are encoded by genes located on the chromosome 6 and closely linked in a single cluster of 250-350 thousand bp [45].

A number of works are devoted to the influence of polymorphism of the genes of the main milk proteins on coagulation properties, nutritional value indicators, and the formation of goat productivity. It was found that in products from the milk of goats with the *AA* genotype for the *CSN1S1* gene, the protein content was 4.5% higher than from the milk of animals with the *FF* genotype, which justifies the selection of carriers of the *A* allele [40].

In goats producing milk with a low content of α_{s1}-casein, there was a significant decrease in the amount of total lipids and medium-chain fatty acids C_8-C_{12} (caprylic, capric, lauric), as well as palmitic, stearic, linoleic and conjugated linoleic acids. That is, the polymorphism of the *CSN1S1* gene affects the intensity of lipogenesis in the secretory cells of the mammary gland [46, 47].

Investigations of five Chinese goat breeds (more than 4 thousand animals), including the most common breed Shaanbei White Cashmere, sequencing of the α_{s1}-casein gene revealed only one indel mutation of 11 bp, designated as genotype *II*, which was associated with the number of kids at the first lambing. Individuals with genotype *II* had a significantly larger number of offspring compared to *ID* and *DD* genotypes, which allowed the authors to recommend this indel mutation for inclusion in breeding programs to increase multiple pregnancy [48].

A number of studies have focused on the effect of the β-lactoglobulin (*BLG*) gene on goat productivity. Shuvarikova et al. [49] found that Saanen goats with the *AB* genotype were characterized by longer lactation and produced more milk (on average by 110.2 kg, $p < 0.01$) and more milk fat and protein (by 3.7 kg and 3.5 kg, $p < 0.05$, respectively) compared to *AA* and *BB* genotypes. Similar data were obtained by Fatikhov et al. [50]. The best indicators of nutritional and biological values of yogurt and cottage cheese were noted for the milk of Nubian and Alpine goat breeds with the *BB* genotype [49].

Kravtsova et al. [51] concluded that it is desirable to include genotyping for the *weaver*, *BLG* and pituitary transcription factor (*POU1F1*) genes in breeding programs to improve milk goats. It was found that individuals carrying the complex genotypes *T2T2/S1S2/D1D2* and *T2T2/S2S2/D1D1* for the *weaver/BLG/POU1F1* genes had a higher content of fat and protein in milk (5.64 and 3.63%) than goats of other genotypes (4.08 and 3.32%). Goncharenko et al. [52] reported that the bodyweight of Belaya pukhovaya breed of down goats heterozygous for *BLG* was 0.30-0.61 kg ($p < 0.05$) higher compared to goats of other genotypes.

Study of genomes using DNA chips and sequencing. The development of genetic analysis methods based on the study of complete genomes by hundreds or thousands of single nucleotide polymorphisms distributed throughout the genome has significantly expanded the possibilities of identifying genome regions that control physiological and biochemical processes that determine the phenotypic differences of animals [53, 54].

Genome-wide association studies (GWAS) with productivity traits in goats are currently being conducted in many countries around the world [55]. The use of GWAS was preceded by the large-scale work of the International Goat Genome Consortium (IGGC; http://www.goatgenome.org) on the implementation of several research projects of the complete sequencing of the genome of these animals. The AdaptMap project has genotyped 4653 animals in 148 populations from 35 countries on five continents [56]. The developed version of the SNP panel was based on the analysis of differences in 12 million SNP variants identified in the genomes of the Saanen, Alpine, Creole, Boer, Katjang, and Savanna goat breeds. Further validation of the SNP distribution was carried out on 10 other goat breeds. As a result, 52295 SNPs were selected, which were successfully used in the 52K SNP BeadChipGoat chip (Illumina, Inc., USA) [57]. Whole genome sequencing of bird and pig genomes from different countries suggested that intense artificial selection contributed to rapid phenotypic evolution in domestic animals [58, 59]. The development of DNA chips has significantly expanded the ability to identify loci under selection pressure in pigs and cattle [60-62], as well as sheep [63, 64]. These results demonstrated how positive selection has altered the genome of domestic animals. However, it should be noted that certain restrictions on the number of individuals for SNP genotyping on chips can lead to a change in the frequency distributions of alleles, which affects the accuracy of population genetic analysis [65]. For example, almost all SNPs included in the GoatSNP50 BeadChip (Illumina, Inc., USA) were selected from six Saanen, seven Alpine, and three Creole goat populations. At the same time, it turned out that the distribution density of the detected SNPs on genomic DNA was insufficient to obtain an accurate result when assessing loci under selection pressure [57].

GWAS of British milk goats covered a set of traits, including milk yield, milk fat and protein content, somatic cell counts, exterior indicators (i.e., the udder depth, the place of its attachment, the teat shape, the angle of the teat attachment, the size and shape of the fore and hind legs, the strength of the fore and hind hooves). The total phenotypic database included 137235 records for 4563 goats examined. Association analysis revealed SNPs on chromosome 19 that were significantly associated with the amount of milk. In addition, several more SNPs were found on chromosomes 4, 8, 14 and 29, the relationship of which with milk production turned out to be less significant. Three SNPs identified on chromosome 19 were associated with attachment site and udder depth and foreleg features. SNPs with a lesser statistical relationship were found on chromosomes 4-6, 10-18, 21, 23, and 27. However, the influence level on the total variance of the trait associated with significant SNPs was low and varied from 0.4 to 7.0% for the amount of milk and from 0.1 to 13.8% for exterior indicators, which confirms their polygenic nature [66]. Wasike et al. [67] have made a similar conclusion based on the GWAS performed for milk goats in the USA.

The GWAS method was used to search for genes associated with the number of somatic cells (somatic cell count, SCC), selected as a sign of resistance to mastitis. Phenotypic data included SCC for 1941 Alpine and Saanen goats bred in France. In the Saanen breed, a significant association with SCC was shown by an SNPs identified on chromosome 19 in a region from 33 to 42 Mbp in length, which included candidate genes associated with a response to infections caused by

intramammary strains, the retinoic acid receptor α (*RARA*) gene and STAT transcription factor genes (*STAT3*, *STAT5A*, *STAT5B*). However, these associations were not found for the Alpine breed [68].

In Eastern Europe, 10 genes were identified in goats that affect resistance to mastitis and gastrointestinal infections. These were the genes for pentraxin 3 (*PTX3*), interleukin-6 (*IL6*), C-type 4 lectin domain family member 4 (*CLEC4E*), interleukin-8 (*IL8*), interleukin-1 receptor antagonist (*IL1RN*), interleukin-15alpha receptor subunit (*IL15RA*), a member of the tumor necrosis factor 13 (*TNFSF13*) superfamily, cytokine signaling suppressor 3 (*SOCS3*), tumor necrosis factor (*TNF*) and toll-like receptor 3 (*TLR3*) [69].

Another French GWAS study attempted to identify genes associated with extra lobes and udder teats in goats. The sample included 810 Saanen and 1185 Alpine goats, however, no significant associations between SNPs and these traits could be found [70].

Desire et al. [71] used GWAS to evaluate genomic breeding value estimator (GEBV) and identify SNPs associated with milk yield and body weight gain. Phenotypic data covered a period of one year for 320 individuals. The obtained GEBV accuracy value was low (0.28 for both indicators). Nevertheless, the authors believe that with an increase in the number of animals, the period of studies and the total number of observations, the accuracy of the genomic estimation will increase [71].

Martin et al. [72] sequenced the *DGAT1* gene and identified 29 polymorphisms, of which R251L and R396W not previously described were associated with reduced milk fat. The frequency of occurrence of the R396W mutation in Saanen and Alpine goats was 13.0% and 7.0%, respectively, the frequency of R251L for both breeds was 3.5% [72].

When using a one-step approach in combination with genomic best linear unbiased prediction (GBLUP), the accuracy of estimating the breeding value of Alpine and Saanen goats (825 individuals), which constitute the breeding core on farms in France, was increased from 22 to 37% by compared with the two-stage method and was higher than the traditional pedigree estimate [73]. Another work used several prediction estimates. The estimates were based on the best linear unbiased prediction (BLUP), single-step genomic best linear unbiased prediction (ssGBLUP), and three weighted analyses (weighted single-step genomic best linear unbiased prediction, WssGBLUP; single-step genomic best linear unbiased prediction with the maximum weight of SNPs included in the chromosomal region, $WssGBLUP_{Max}$; single-step genomic best linear unbiased prediction with the sum of the weights of the SNPs included in the chromosomal region, $WssGBLUP_{Sum}$) calculated for SNPs with regard to their effect on milk protein content. The accuracy of GEBV with ssGBLUP has improved by 5-7% compared to the traditional BLUP model. WssGBLUP more accurately identified SNPs associated with α_{s1}-casein content and proved to be more effective in predicting genomic selection values than unweighted ssGBLUP. In addition, the authors indicate that using WssGBLUP was somewhat easier to perform calculations, which speeded up genomic analysis [74].

In a Spanish study involving 50,649 records of milk production from 19,067 Florida goats, it was found that the ssGBLUP method improved the average accuracy of breeding value estimates by 1.06% compared to classical BLUP. The correlation between matrix A (pedigree) and matrix G (gene) was 0.826. The correlation between EBV (breeding value estimator) and GEBV (genomic breeding value estimator) was 0.989, but when comparing only EBV-genotyped animals, the correlation between these estimates decreased to 0.952, and the average accuracy increased by 5.86% [75].

In order to reduce the cost of genotyping in the control of origin, Talenti et al. [76], based on an analysis of 109 Alpine goats, proposed two low-density panels comprising 130 and 114 SNPs with random match probabilities of 1.51×10^{-57} and 2.94×10^{-34}, respectively. The results made it possible to determine family ties with absolute accuracy. Subsequently, an improved panel containing 195 SNPs was developed. It has been shown that at a comparable cost, the 195 SNP chip can replace microsatellite markers, but with much higher accuracy [77].

Goat wool color is a polygenic trait that is often determined by epistatic gene interactions [78]. These include genes for the melanocortin 1 receptor (*MC1R*) and its endogenous antagonist, the agouti signaling protein (*ASIP*). The *MC1R* gene plays a key role in the synthesis of melanin pigments and the control of the amount of eumelanin (black/brown) or pheomelanin (red/yellow). This has been demonstrated in several studies examining the effect of *MC1R* on color in cattle and sheep [79]. Similarly, mutations in the *MC1R* gene are associated with wool color in goats of the Girgentana, Maltese, Derivata di Siria, Murciano-Granadina, and Camosciata delle Alpi, and Saanen goats [80]. *ASIP* has an epistatic effect on the *MC1R* gene and reduces MC1R activity, which leads to increased pheomelanin synthesis. Yellow or pheomelanin pigmentation is due to the action of the dominant allele at the *ASIP* locus, while black/brown or eumelanin pigmentation is due to the action of the recessive allele [81]. In Saanen goats, the dominant allele A^{wt} (white/red) seems to be responsible for the white coat color [82]. Duplication of regions in the *ASIP* gene leads to the formation of white and black colors [83]. Another gene that affects the coat color of goats is the proto-oncogene receptor tyrosine kinase (*KIT*) gene, which is considered one of the key genes in color formation in many animal species [80, 84-86].

Wang et al. [87], based on sequencing genotyping performed on goats from eight populations, reported several genes under positive selection pressure. The *ASIP* gene was associated with coat color, the fibroblast growth factor 5 (*FGF5*) gene was associated with wool productivity, and the NADPH oxidase activator gene 1 (*NOXA1*) was associated with adaptation to altitude hypoxia [87]. Further editing of the *FGF5* gene in goat embryos led to an increase in the number of secondary hair follicles and fiber length, which confirms the positive association of the gene with cashmere productivity and the expediency of its inclusion in down goat breeding programs [88].

Guo et al. [89] performed genome-wide sequencing of 38 goats of three Chinese breeds, the Nanjiang Yellow, Jintang Black, and Tibetan cashmere and compared them with the genomes of 30 goats of five other breeds, as well as with the genomes of 21 bezoar goats from AdaptMap databases. As a result, a new SNP (c.-253G>A) associated with down productivity and adaptation to low temperatures in Tibetan cashmere goats was identified in the 5′-UTR region of the *FGF5* gene. A high frequency of occurrence of the *AGG* allele in the exon 12 of the desmoglein 3 gene (*DSG3*), which determines cell adhesion and is expressed mainly in the skin, has also been established [89]. Genome comparison of cashmere goats of different breeds have shown that loci under selection pressure are associated with color (*IRF4*, *EXOC2*, *RALY*, *EIF2S2*, *KITLG*), reproduction (*KHDRBS2*) and adaptation to altitude (*EPAS1*) [90]. The selection pressure for the endothelial PAS domain-containing protein 1 (*EPAS1*) gene was established by Song et al. [90] in exome sequencing of 330 Tibetan cashmere goats well adapted to mountainous environments [90].

We examined selective loci in a population of native Karachay goats ($n = 37$) by analyzing runs of homozygosity (ROH). In total, 17 ROH regions larger than 0.1 Mb were identified, which were found in the genome in more than 50% of

Karachay goats (including 6 ROH regions identified in more than 60% of animals) (Table 2). To confirm these data and select positional candidate genes, it is necessary to study a larger population of goats of the Karachay breed.

2. Runs of homozygosity (ROHs) in the genomes of more than 50% of Karachay goats (*Capra hircus*)

Chromosome	SNP number	Position		Length, Mb	Candidate genes
		start	end		
1	6	123,995,551	124,276,659	0.281	
3	7	91,992,725	92,358,697	0.366	
7	5	47,720,691	47,985,489	0.265	
7	10	50,213,129	50,678,375	0.465	
	4[a]	50,385,448	50,599,960	0.215	*HTR4*, *FBXO38*
11	13	14,570,133	15,147,019	0.577	
	7[a]	14,850,176	15,108,357	0.258	*BIRC6*, *TTC27*
11	12	37,444,185	37,989,059	0.545	
	10[a]	37,518,114	37,955,681	0.438	*CLHC1*, *RPS27A*, *MTIF2*, *CCDC88A*[b], *CFAP36*[b], *PPP4R3B*[b], *PNPT1*[b]
11	3	95,963,081	96,081,413	0.118	
12	7	24,713,474	25,070,617	0.357	
12	13	34,478,328	35,027,103	0.549	
	7[a]	34,509,187	34,826,053	0.317	
13	8	60,716,743	61,161,390	0.445	
	5[a]	60,913,235	61,123,452	0.210	*HCK*, *TM9SF4*, *PLAGL2*, *POFUT1*, *KIF3B*, *ASXL1*
14	11	74,881,431	75,466,670	0.585	
	7[a]	74,881,431	75,240,511	0.359	*MMP16*
21	8	54,788,196	55,179,468	0.391	
23	5	27,849,491	28,042,905	0.193	
25	5	3,491,087	3,753,620	0.263	
27	3	32,676,747	32,783,591	0.107	
27	3	32,905,720	33,015588	0.110	
28	7	15,314,246	15 639,373	0.325	

N o t e. [a] — ROH in the genomes of more than 60% animals; [b] — genes present in more than 70% animals ("Studies of the genomic diversity of goats of different breeds, searching for selection marks in the population of Karachay goats based on full genome SNP genotyping, biochemical blood analysis and phenotype". Moscow, 2020).

Thus, in the world's goat raising, there are many breeds and populations of goats intended for various us, the vast majority of which are aboriginal. Goat biodiversity has been fairly well studied using microsatellite DNA loci. To obtain new fundamental knowledge about the origin of goats, genetic drift, and genetic relationships between domestic goats and their wild ancestors, genome-wide analysis and genome scanning using DNA chips have been widely used recently. Data were obtained on the relationship of the goat genes *CSN1S1*, *CSN1S2*, *CSN2*, *BLG*, *RARA*, *STAT*, *PTX3*, *IL6*, *IL8*, *DGAT1* with milk productivity and milk quality. The association has been demonstrated of *MC1R*, *ASIP*, and *KIT* genes with the color of wool and down, *FGF5*, *EPAS1*, and *NOXA1* genes with wool productivity and adaptation to high-altitude hypoxia. At present, certain progress has been made in understanding the formation of goat biodiversity, the prospects of the genomic approach in the selection of wool and milk breeds. However, the loci associated with economically important traits (reproduction, down and wool productivity, wool color, the amount of milk and the content of milk protein and fat, somatic cell counts, etc.) and those associated with adaptiveness and resistance to diseases are still little studied. Therefore, efforts should be focused on these issues and searching for candidate genes based on genomic and omics technologies.

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