AGRICULTURAL BIOLOGY,
2021, V. 56, Iss. 6, pp. 1123-1133
[SEL'SKOKHOZYAISTVENNAYA BIOLOGIYA]

ISSN 2412-0324 (English ed. Online)
ISSN 0131-6397 (Russian ed. Print)
ISSN 2313-4836 (Russian ed. Online)

UDC 636.2:577.21:575.174:575.2

doi: 10.15389/agrobiology.2021.6.1123eng
doi: 10.15389/agrobiology.2021.6.1123rus

THE POPULATION-GENETIC STRUCTURE OF NATIVE TAGIL CATTLE BY STR- AND SNP-MARKERS

Yu.A. **STOLPOVSKY[1] ✉, S.V. BEKETOV[1], E.V. SOLODNEVA[1], V.M. ABSALIKOV[2], A.S. ABDELMANOVA[3], E.A. GLADYR[3], N.A. ZINOVIEVA[3]**

[1]*Vavilov Institute of General Genetics RAS,* 3, ul. Gubkina, Moscow, 119333 Russia, e-mail stolpovsky@mail.ru (✉ corresponding author), svbeketov@gmail.com, eugenia.575.2012@yandex.ru;
[2]*Department of Agriculture, Oktyabrsky District of Perm Krai,* 57, ul. Lenina, Oktyabrsky District, Perm Krai, 617860 Russia, e-mail vabs1966@gmail.com;
[3]*Ernst Federal Research Center for Animal Husbandry,* 60, pos. Dubrovitsy, Podolsk District, Moscow Province, 142132 Russia, e-mail preevetic@mail.ru, elenagladyr@mail.ru, n_zinovieva@mail.ru
ORCID:
Stolpovsky Yu.A. orcid.org/0000-0003-2537-1900
Beketov S.V., orcid.org/0000-0001-7947-8688
Solodneva E.V. orcid.org/0000-0002-7178-4012
Abdelmanova A.S. orcid.org/0000-0003-4752-0727
Gladyr E.A. orcid.org/0000-0002-5210-8932
Zinovieva N.A. orcid.org/0000-0003-4017-6863
The authors declare no conflict of interests
Acknowledgements:
Supported financially by the grant 19-76-20061 of the Russian Science Foundation (http://rscf.ru)
Received September 1, 2021

Abstract

Rearing specialized cattle breeds or several intra-breed lines reduces the breed and genetic diversity and creates a real threat of extinction of native livestock. Microsatellite analysis and genome-wide SNP (single nucleotide polymorphism) genotyping are common methods to study the population genetic structure of local breeds with unique adaptive traits and diseases resistance. The history of the Tagil breed is more than 200 years old. Currently, in Russia and the world, there is the only herd of Tagil cattle of about 600 animals molecular genetic characteristics of which remain insufficiently poor studied. Here we present the first results of identification of STR and SNP genotypes of the unique local Tagil breed. The work aimed to assess genetic diversity and survey the population structure of the modern population of indigenous Tagil cattle by microsatellite analysis (STR) and genome-wide analysis of single nucleotide polymorphism (SNPs). Genotypes of the Tagil animals (TAGIL, $n = 98$; SPK Shorokhov, Perm Territory, 2021) were studied by multiplex analysis using 11 microsatellites (TGLA227, BM2113, TGLA53, ETH10, SPS115, TGLA122, INRA0623, TGL1812 ETH225, BM1824). For interbreed differentiation by STR markers in PCA, we used a set of breeds that could be potentially involved in the formation of the modern population of Tagil cattle (TAGIL) — Holstein (HLST), Kholmogory Holsteinized (Tatarstan type) (TAT), Kholmogorsk purebred (Pechora type) (PECH), black-and-white (old type) (Ch_P_OLD), Tagil (TAG) (samples from the ONIS BioTechZh database, 2020, https://www.vij.ru/2-obshchaya/226-infrastruktura-test). To cover maximum genetic diversity in genotyping of TAGIL by SNP markers, the most unrelated animals ($n = 48$) were selected based on the results of analysis of STR genotypes. Genome-wide genotyping for SNP markers was performed using a high density GGP Bovine HD 150K BeadChip DNA chip (150,000 SNPs, Illumina, Inc., USA) (10,8432 SNPs before and 62,809 SNPs after LD filtration). A database of genome-wide SNP genotypes of Tagil cattle (TAGIL) was formed to analyze the results of SNP genotyping (population genetic and phylogenetic studies). Holstein animals (HLST) ($n = 45$) were the reference group. We clearly differentiated the Tagil (TAGIL) and Holstein animals by PCA method. Cluster analysis based on genetic distances F_{ST} divided the Tagil and Holstein animals into two separate groups. Genome-wide SNP genotyping revealed genomic regions in which allelic variants are specific for the Tagil cattle (TAGIL). The hapFLK analysis showed five regions ($p < 0.01$) (chromosomes 4, 5, 8, 11, and 15, from 1.20 Mb on BTA8 to 9.61 Mb on BTA5, the number of SNPs within the regions from 24 to 92) under selection pressure in the Tagil animals (TAGIL). The STR genotyping data showed the participation of the Kholmogory cattle, Black-and-White and Holstein breeds in the Tagil breed formation with the greatest introgression of Holstein cattle which most likely was used to improve Tagil cattle in recent decades. We reveled that more than 50 % of the Tagil animals (TAGIL) have the ROH (BTA14, positions 24437778-25098364, 0.661 Mb) previously identified in the Yaroslavl and Kholmogor breeds as a region under selection pressure. This ROH region may be an element of the adaptive genetic system in indigenous Russian breeds. In 40 % Tagil animals, we additionally identified five ROH islands.

The findings of the research will be used to identify genes and their variants that determine adaptive and commercial traits of the Tagil breed, study the formation of its genetic structure, develop monitoring regulations to preserve the Tagil cattle breed specificity and biodiversity.

Keywords: dairy cattle, Tagil breed, microsatellites, SNP genotyping, biodiversity

The intensification of world dairy cattle breeding leads to the predominance of Holstein cows in the structure of cattle breeds. According to statistics, Holstein cattle (purebred or crossbred) in the aggregate account for 61% of the 3.47 million dairy cows in the UK [1], in the USA the proportion of cattle with Holstein breed in the pedigree is even higher and reaches 90% of the total number of dairy cows (2). In Russia, the number of Holstein cattle is still not so large (22.95%), but the black-and-white breed prevails (49.98%) [3], including partially Holsteinized. Breeding of specialized breeds or several intrabreed lines reduces the pedigree and genetic diversity of the livestock, and, as a result, a real threat of extinction of aboriginal livestock is created. In this regard, the study of the population genetic structure of local breeds, which have unique adaptive traits and resistance to a number of diseases, is attracting more and more attention [4]. Most often, such studies use microsatellite analysis or a more informative method of whole genome SNP (single nucleotide polymorphism) genotyping, which has become actively used in population genetics and breeding of cattle after deciphering its genome [5].

Using STR (short tandem repeat) markers, we studied the genetic structure of populations of local breeds of Indian zebu Ongole, Deoni, Gir, Kankrei [6], Mexican Criollo [7], as well as Red Steppe [8], Suksun, Istoben, Yaroslavl, Kholmogory, gray Ukrainian and Kholmogory (Pechora type) breeds of cattle [9]. Genome-wide SNP screening has been used to establish genetic diversity and interbreed differentiation of native South African cattle (Afrikaner, Drakensberger, Nguni) [10], five indigenous cattle breeds in Bangladesh (Chitagon Red, Pabna and Zebu Munshiganj, Northern Bengal Gray, Deshi) [11], six breeds of cattle from the Sichuan province in China (Ba Shan, Xuanhan, Pingwu, Sanjiang, Ganzi, Langshan) [12], the Irish Kerry breed [13] and Russian ancient breeds Bestuzhev, Kholmogory, Kostroma, Red Gorbatov and Yaroslavl [14, 15].

Tagil cattle is one of the oldest domestic breeds of dairy cattle in the Russian Federation. The history of the creation of this breed has more than 200 years. The formation of the main group of Tagil cattle took place in the Ural region in the Nizhny Tagil region. There is no exact information about the origin of the Tagil cattle, but the participation in its formation of the English shorthorned and Kholmogory cattle, imported from the Arkhangelsk province in 1842, was discussed [16]. There is an opinion that the Tagil breed is a product of crossing local Ural cattle with imported animals of the Kholmogory, Yaroslavl and Dutch breeds [17] and the use of Black-and-White bulls [18]. Planned selection and breeding work to improve the Tagil cattle began after the decree of the Council of People's Commissars dated July 19, 1918 "On breeding livestock" was issued. Then a strict selection of purebred Tagil sires was applied, followed by breeding "in itself", which made it possible to significantly increase the productivity of Tagil cows, and in 1930 a new Tagil breed of cattle was approved [18, 19]. Unpretentious to the conditions of feeding and keeping, Tagil cattle, when bred in the Urals, were not much inferior in terms of milk yield to black-and-white, surpassing it in fat milk content. In addition, Tagil cows, due to the specific structure of the pelvis, are distinguished by the ease of calving.

Subsequently, the massive Holsteinization of cattle led to the displacement of not only the Tagil, but also the Black-and-White breed. As a result, the only gene pool herd of Tagil cattle in Russia and the world (about 600 heads) is currently left, formed at the Shorokhov SPK in the Oktyabrsky District of the Perm

region. This gene pool, limited in number, is of undoubted interest as a source of valuable biological and economic traits; however, its molecular genetic characteristics remain insufficiently studied.

This report presents for the first time the results of identification of the STR and SNP genotypes of the unique local Tagil breed of cattle, which will allow the identification of genes and their variants that determine the biological, adaptive and productive qualities of animals of economic importance.

The purpose of this work is to carry out microsatellite analysis (STR) and genome-wide analysis of single nucleotide polymorphisms (SNPs) to assess genetic diversity and establish the population structure of the modern population of aboriginal Tagil cattle.

Materials and methods. DNA was isolated from blood samples ($n = 98$) of Tagil animals (TAGIL). Samples were taken at the SPK them. Shorokhov (Perm Territory, 2021), the QIAmp® DNA Mini Kit (QIAGEN, Germany) was used for DNA extraction according to the attached protocol. The purity and concentration of the resulting DNA preparations were determined ($OD_{260/280}$, ultraviolet microspectrophotometer Implen Nano-Photometer®, Implen GmbH, Germany), the concentration of double-stranded DNA was measured using a Qubit™ (1.0) fluorimeter (Life Technologies, USA).

Animal genotypes were analyzed by multiplex analysis for 11 microsatellites (TGLA227, BM2113, TGLA53, ETH10, SPS115, TGLA122, INRA023, TGLA126, BM1818, ETH225, BM1824) using the STR panel developed at the V.I. OK. Ernst based on the recommendations of the International Society for Animal Genetics (ISAG).

Interbreed differentiation by STR-markers was carried out by the method of principal components (PCA) with the involvement of genotypes of cattle breeds that could potentially take part in the formation of the studied modern population of Tagil cattle (TAGIL): Holstein (HLST), Kholmogory Holsteinized (Tatarstan type) (TAT) , Kholmogory purebred (Pechora type) (PECH), black-and-white (old type) (Ch_P_OLD), Tagil (TAG) (samples from the ONIS BioTechJ databank, 2020, https://www.vij.ru/2-obshchaya /226-infrastruktura-test).

For genotyping by SNP markers, samples ($n = 48$) were selected based on the results of the analysis of STR genotypes. In the Structure 2.3.4 program (https://web.stanford.edu/group/pritchardlab/structure.html), the similarity coefficient Q was used to preliminarily evaluate the purebred and in the ML-Relate program (https://www.montana.edu/kalinowski/software/ml-relate/index.html) the degree of relatedness of individuals in the studied population of Tagil cattle.

Whole genome genotyping for SNP markers was performed using a GGP Bovine HD 150K BeadChip high-density DNA chip (~ 150,000 SNPs, Illumina, Inc., USA). Quality control and filtering of genotyping data for each sample and SNP was performed using the PLINK 1.9 [20] software package (https://www.co-genomics.org/plink/). The following filters were applied (corresponding commands in the PLINK program are given in parentheses): call-rate for all studied SNPs for an individual sample is not lower than 90% (--mind); call-rate for each of the studied SNPs for all genotyped samples is not less than 90% (--geno); the frequency of occurrence of minor alleles (MAF) more than 0.01 or 0.05 (--maf 0.01); deviation of SNP genotypes from the Hardy-Weinberg distribution in the totality of tested samples with a p-value $< 10^{-6}$ (--hwe). Linkage disequilibrium (LD) was also assessed using the Pearson correlation coefficient ($r^2 < 0.2$) with a step of 50 kb (--indep-pairwaise).

To analyze the results of genotyping of SNP markers (population genetic and phylogenetic studies), a database of whole genome SNP genotypes

of Tagil cattle (TAGIL) was formed. Animals of the Holstein breed (HLST) (n = 45) were introduced into the data set as a comparison group.

Observable heterozygosity (H_o), unbiased expected heterozygosity (uH_e), allelic diversity (Ar), and inbreeding coefficient F_{IS} (with 95% confidence interval) were calculated based on the obtained SNP genotypes for each data set in the R package diveRsity [21].

Principal component analysis (PCA) was performed in the PLINK 1.9 program followed by plotting in the R package ggplot2 [22]. For phylogenetic studies in the R package diveRsity [21], pairwise F_{ST} values were calculated [23]. The matrix of pairwise F_{ST} values was visualized as a Neighbor-net group genetic network in the SplitsTree 4.14.5 [24] program (https://splitstree4.software.informer.com/). The population structure and genetic homogeneity of the studied cattle breeds were determined using the Admixture 1.3 program [25] with a graphical representation using the pophelper R package [26]. The most probable number of ancestral clusters (K) was determined by calculating the cross-validation error values (CV error) for K from 1 to 5 in the Admixture 1.3 program.

To search for loci under selection pressure, selection of 0.1% SNPs with the highest F_{ST} values in pairwise comparison of breeds was used, as well as hapFLK analysis and detection of ROH islets overlapping in some individuals [15]. For islets, the minimum ROH size was taken to be 0.5 Mb with 50% of animals carrying overlapping ROHs and an ROH overlap length of at least 0.1 Mb.

Bioinformatic data processing and plotting were performed using the R Project for Statistical Computing software environment [27].

In hapFLK analysis, a threshold of significance was set $p < 0.01$. Confidence intervals (CI, 95%) are given for F_{IS} values. When determining the mean values (M), their standard errors (±SEM) were calculated.

Results. The results of principal component analysis (PCA) (Fig. 1) were obtained from the data of our microsatellite profiling of Tagil animals in comparison with the data of the previously performed STR genotyping of populations of the Holstein, Kholmogory (Holsteinized and purebred), Black-and-White and Tagil cattle breeds. It can be seen that a significant part of the Tagil cows differs from animals of other breeds, but the arrays of both populations of Tagil cattle overlap with the Holstein breed. On this basis, we further considered the Holstein breed as a comparison group.

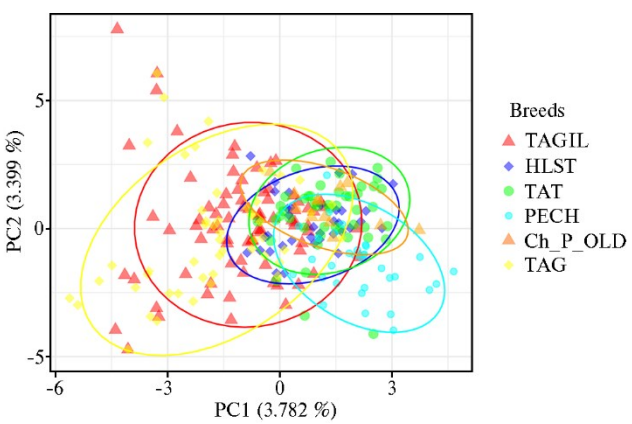

Fig. 1. Distribution of the Tagil breed animals based on genotypes by STR markers in the principal components analysis method: the modern population of Tagil cattle (TAGIL, n = 98) (Shorokhov SPK, Perm Territory, 2021), Holstein breed (HLST), Kholmogory Holsteinized breed (Tatarstan type) (TAT), Kholmogory purebred cattle (Pechora type) (PECH), Black-and-White breed (old type) (Ch_P_OLD), Tagil cattle (TAG) (samples from the ONIS BioTechJ databank, 2020).

To cover the maximum range of genetic diversity of the Tagil breed, the most unrelated animals were selected for SNP genotyping. Based on the calculation

of the similarity coefficient (Q) and the assessment of the degree of kinship (individuals with Q ≥ 0.35 were considered relatives), 51 animals (48 main and 3 spare) were selected. The selected individuals were divided into five groups: 1st with Q ≥ 90%, relatives not > 2 for each animal (although there are relatives with Q = 0.50; 37 cows); 2nd with 90% > Q ≥ 80%, no relatives > 2 for each animal (although there are relatives with Q = 0.50; 7 cows); 3rd with 80% > Q ≥ 70%, each animal has > 1 relative (none closer than with Q = 0.49; 5 cows); 4th with 70% > Q ≥ 60%, no relatives (2 cows); 5th (other) are undesirable for genotyping.

Whole genome genotyping of Tagil cattle for SNP markers was performed using the GGP Bovine HD 150K BeadChip DNA chip; the results were obtained for 48 animals (genotyping efficiency was more than 90%). The efficiency of genotyping (call rate) of the studied Tagil cows varied from 0.9900 to 0.9982. A total of 108432 SNPs were selected for analysis after quality control.

Table 1 summarizes the data of our population genetic study of the Tagil breed by SNP markers in comparison with the Holstein breed. One can see a significantly higher genetic diversity (in terms of Ar allelic diversity, observed Ho heterozygosity, and unbiased expected uHe heterozygosity) of Tagil cattle compared to Holstein. This may be the result of both less stringent selection for economically useful traits, and the participation of several breeds in the creation of Tagil cattle. The excess of heterozygotes in both populations should also be noted (see Table 1).

_1. Comparative characterization of the genetic diversity of the Tagil cattle population (Shorokhov SPK, Perm Territory, 2021) **and Holstein cattle** (ONIS BioTechJ databank, 2020) **by SNP markers** (*M*±SEM, GGP Bovine HD 150K BeadChip, Illumina, Inc., USA)

Breed	*n*	Ar	Ho	uHe	FIS [CI 95 %]
Tagil	48	1,999±0	0,408±0,001	0,398±0,000	–0,023 [–0,024; –0,022]
Holstein	45	1,989±0	0,366±0,001	0,360±0,001	–0,014 [–0,015; –0,013]

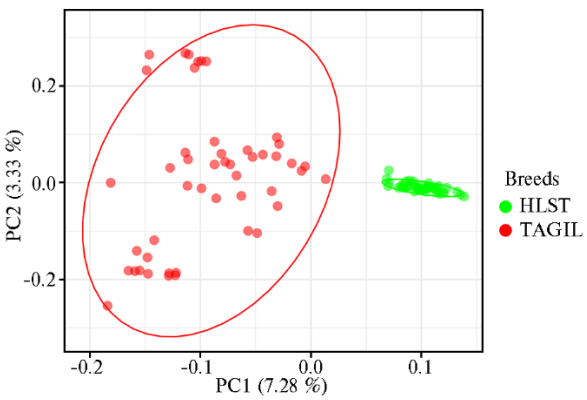

Fig. 2. Distribution of individuals of the Tagil (TAGIL, *n* = 48) (Shorokhov SPK, Perm Territory, 2021) **and Holstein breeds** (HLST, ONIS BioTechJ databank, 2020) **based on genotypes for 108432 SNPs.**

We clearly differentiated the breeds of selected animals (Tagil and Holstein) using the PCA method (Fig. 2). At the same time, unlike the Tagil Holstein breed, it turned out to be more consolidated (see Fig. 2), the first component (PC1) was responsible for 7.28% of genotypic variability and separated the Tagil cattle from the Holstein cattle.

Cluster analysis based on FST genetic distances (Fig. 3) assigned animals of the Tagil and Holstein breeds into two large groups in accordance with the breed. Animals belonging to the same breed were grouped on neighboring branches of the corresponding clusters.

When performing a structural analysis, the calculation of the cross-validation error (CV) showed the minimum value of this indicator for the number of clusters K = 4. At K = 2 (Fig. 4), each of the two compared breeds (TAGIL and HLST) exhibits a specific cluster structure, while the formation of the Tagil breed shows the presence of specific Holstein ancestral genomic components. An analysis of the genetic structure at K = 3 and K = 4 indicates the participation in the

formation of the Tagil breed of three more different ancestral breeds in addition to the Holstein breed. Taking into account that specific Holstein genomic components are manifested in most of the Tagil animals, and the components of the other three ancestral breeds of Tagil cattle have only minor traces of admixture in the Holstein breed, the resulting data set can be considered suitable for searching for loci that are under selection pressure.

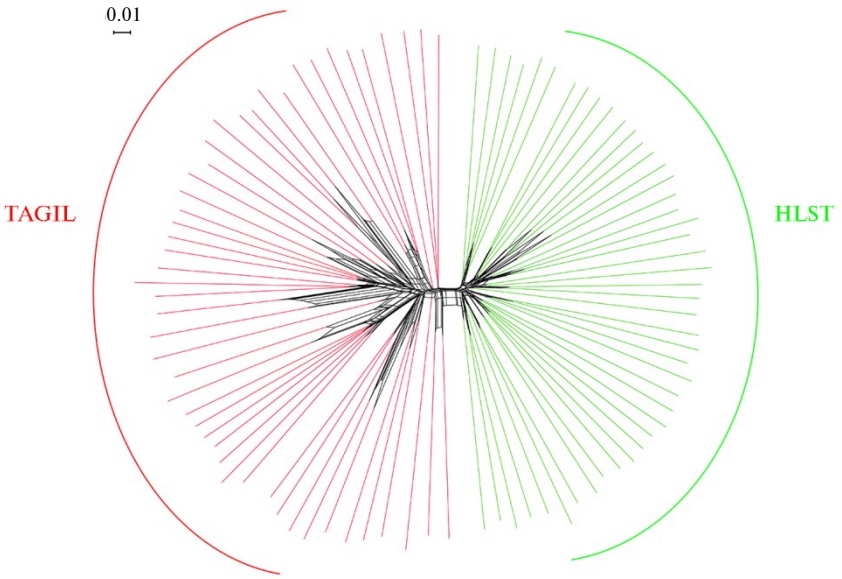

Fig. 3. Neighbor-net dendrogram based on genotypes of 108432 SNPs for selected animals of the Tagil (TAGIL, *n* = 48) (Shorokhov SPK, Perm Territory, 2021) **and Holstein breeds (**HLST, *n* = 45, ONIS BioTechJ databank, 2020) (visualization in SplitsTree 4.14.5).

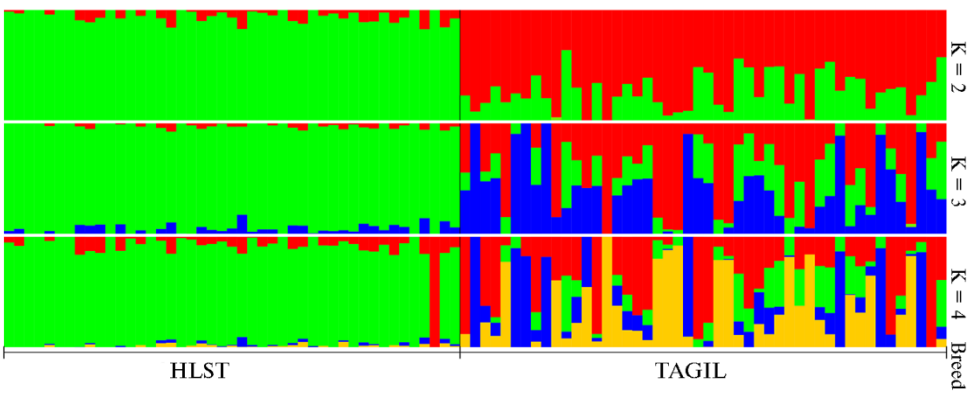

Fig. 4. Genetic structure of the Tagil breed population (TAGIL, *n* = 48, Shorokhov SPK, Perm Territory, 2021) **compared to the Holstein breed population** (HLST, *n* = 45, ONIS BioTechJ databank, 2020) **according to the Admixture analysis for 62809 SNPs** (Admixture 1.3 program, K is the number of clusters). Blue and yellow colors are genomic components of ancestral breeds identified in the Tagil breed.

By selecting the 0.1% SNPs with the highest FST values in a pairwise comparison of breeds, 109 SNPs located on 24 chromosomes were identified (excluding BTA8, BTA23, BTA27, BTA28, and BTA29).

Analysis of hapFLK showed the presence of five areas ($p < 0.01$) under selection pressure in the studied groups of Tagil cattle (Table 2) in comparison with Holstein. The identified regions were localized on chromosomes 4, 5, 8, 11, and 15, while a higher level of identification reliability was established for two

regions ($p < 0.001$). The length of the regions varied from 1.20 Mb (BTA8) to 9.61 Mb (BTA5), the number of SNPs localized within these regions varied from 24 to 92.

2. Characterization of chromosome (BTA) **regions under selection pressure in Tagil cattle** (TAGIL, $n = 48$, analysis by hapFLK method, Shorokhov SPK, Perm territory, 2021)

BTA	Position		Length, Mb	Most significant SNPs		Number of SNPs
	start	end		позиция	p	
4	6,842.949	10,648,384	3.81	8,495,236	7.08E-04	63
5	16,952.114	26,561,662	9.61	24,064,770	8.42E-04	92
8	50,695.489	51,899,568	1.20	51,101,318	5.14E-03	24
11	86,926.025	89,081,028	2.16	88,186,796	6.16E-03	31
15	48,905.274	54,898,376	5.99	54,218,907	5.08E-03	59

As a result of the study of the genomes of Tagil and Holstein cattle for the presence of runs of homozygosity (ROH), we identified 37 ROH islets that were found in more than 50% of animals, and 36 such regions were found in the genome of Holstein cattle, and only one is in Tagil (BTA14, positions 24437778-25098364, length 0.661 Mb). Interestingly, this region almost completely overlapped with the identical region identified in the genome of Holstein cattle (positions 24437778-25175950, length 0.750 Mb). It should be noted that the region on BTA14 in the region of 24.4-25.1 cm was previously identified as being under selection pressure in the Yaroslavl and Kholmogory breeds of cattle [15]. The structural annotation performed revealed the localization of eight genes in this region, the *XKR4*, *TMEM68*, *TGS1*, *LYN*, *RPS20*, *MOS*, *PLAG1*, and *CHCHD7*. Previously, in studies on different breeds of cattle (Holstein, Simmental, Wagyu, Hanu, etc.), it was shown that the listed genes are associated with height, exterior tallness, live weight, and feed intake [28-33].

Based on the fact that, when improving the Tagil cattle, it was crossed not only with the Holstein, but also with other black-and-white breeds of cattle (Kholmogory and Black-and-White), we lowered the threshold for the proportion of animals of the Tagil breed to 40%, whose genome contains common ROH. This made it possible to additionally identify five ROH islands in the Tagil breed (Table 3).

3. Characterization of ROH islets identified in the genome of Tagil cattle (TAGIL, $n = 48$, the threshold for the proportion of animals with total ROH is 40%, Shorokhov SPK, Perm territory, 2021)

Breed	BTA	Number of SNP	Position		Length, Mb	Proportion, %
			start	end		
TAGIL	2	15	65,513,882	65,946,493	0.433	41.7
TAGIL	14	15	33,026,716	33,348,218	0.322	41.7
TAGIL	16	4	44,372,045	44,552,678	0.181	41.7
TAGIL	20	17	71,433,871	71,720,853	0.287	41.7
TAGIL	23	18	479,600	936,645	0.457	41.7

Thus, as a result of the studies, a characterization of the population genetic characteristics of modern Tagil cattle was given and a database of full genome SNP genotypes was created that meets the established quality criteria (the number of genotyped animals with a genotyping efficiency of more than 90%). According to STR-marking, the participation of Kholmogory cattle, as well as Black-and-White and Holstein breeds in the formation of the Tagil breed was established. The greatest introgression of Holstein cattle was noted, which in the last decades, most likely, was used as an improving breed for Tagil cattle. In the analyzed population, animals of the Tagil breed are differentiated from Holstein cattle and represent a genotypically less consolidated and less structured group. In contrast to the Holstein cattle, the Tagil cattle were characterized by significantly ($p < 0.05$) higher genetic diversity and an excess of heterozygotes. Whole genome SNP genotyping revealed

genomic regions in which allelic variants are specific for the Tagil breed. When comparing the Tagil and Holstein breeds, 109 SNPs with the highest FST values were identified on 24 chromosomes in pairwise comparison. Five regions under selection pressure ($p < 0.01$) were identified in Tagil and Holstein cattle on chromosomes 4, 5, 8, 11 and 15. In more than 50% of the animals of the Tagil breed, an ROH islet (BTA14, positions 24437778-25098364, length 0.661 Mb) was found, previously identified in the Yaroslavl and Kholmogory breeds as a region under selection pressure. This ROH region may be an element of an adaptive genetic system in aboriginal breeds. In 40% of animals of the Tagil breed, five additional ROH islets are present. The data obtained by us will be used to identify genes and their variants that determine the adaptive and economically significant features of the Tagil breed, to study the history of the formation of its genetic structure, and to develop monitoring regulations to preserve the breed specificity and biodiversity of the Tagil cattle.

REFERENCES

1. *Most common of cattle in GB (NUTS 1 areas) in 01 April 2005*. London, 2005, Version 1.
2. *Holstein Association USA*. Available: http://holsteinusa.com. No date.
3. *Ezhegodnik po plemennoi rabote v molochnom skotovodstve v khozyaistvakh Rossiiskoi Federatsii (2019 g.)* [Yearbook on pedigree work in dairy cattle breeding on the farms of the Russian Federation (2019)]. Moscow, 2020 (in Russ.).
4. Mwai O., Hanotte O., Kwon Y.-J., Cho S. African indigenous cattle: unique genetic resources in a rapidly changing world. *Asian Australas. J. Anim. Sci.*, 2015, 28(7): 911-921 (doi: 10.5713/ajas.15.0002R)
5. Elsik C.G., Bovine Genome Sequencing and Analysis Consortium. The genome sequence of taurine cattle: a window to ruminant biology and evolution. *Science*, 2009, 324(5926): 522-528 (doi: 10.1126/science.1169588).
6. Kale D.S., Rank D.N., Joshi C.G., Yadav B.R., Koringa P.G., Thakkar K.M., Tolenkhomba T.C., Solanki J.V. Genetic diversity among Indian Gir, Deoni and Kankrej cattle breeds based on microsatellite markers. *Indian Journal of Biotechnology*, 2010, 9: 126-130.
7. Ulloa-Arvizu R., Gayosso-Vazquez A., Ramos-Kuri M., Estrada F.J., Montano M., Alonso R.A. Genetic analysis of Mexican Criollo cattle populations. *Journal of Animal Breeding and Genetics*, 2008, 125: 351-359 (doi: 10.1111/j.1439-0388.2008.00735.x).
8. Kramarenko A.S., Gladyr E.A., Kramarenko S.S., Pidpala T.V., Strikha L.A., Zinovieva N.A. Genetic diversity and bottleneck analysis of the Red Steppe cattle based on microsatellite markers. *Ukrainian Journal of Ecology*, 2018, 8(2): 12-17 (doi: 10.15421/2018_303).
9. Kiseleva T.Yu., Kantanen J., Vorobyov N.I., Podoba B.E., Terletsky V.P. Linkage disequilibrium analysis for microsatellite loci in six cattle breeds. *Russian Journal of Genetics*, 2014, 50(4): 406-414 (doi: 10.1134/S1022795414040048).
10. Zwane A.A., Schnabel R.D., Hoff J., Choudhury A., Makgahlela M.L., Maiwashe A., Van Marle-Koster E., Taylor J.T. Genome-Wide SNP discovery in indigenous cattle breeds of South Africa. *Front. Genet.*, 2019, 10(273): 1-16 (doi: 10.3389/fgene.2019.00273).
11. Bhuiyan M.S.A., Lee S.-H., Hossain S.M.J., Deb G.K., Afroz M.F., Lee, S.-H., Bhuiyan A.K.F.H. Unraveling the genetic diversity and population structure of Bangladeshi indigenous cattle populations using 50K SNP markers. *Animals*, 2021, 11(2381): 1-15 (doi: 10.3390/ani1108238).
12. Wang W., Gan J., Fang D., Tang H., Wang H., Yi J., Fu M. Genome-wide SNP discovery and evaluation of genetic diversity among six Chinese indigenous cattle breeds in Sichuan. *PLoS ONE*, 2018, 13(8): e0201534 (doi: 10.1371/ journal.pone.0201534).
13. Browett S., McHugo G., Richardson I.W., Magee D.A., Park S.D.E., Fahey A.G., Kearney J.F., Correia C.N., Randhawa I.A.S., MacHugh D.E. Genomic characterisation of the indigenous Irish Kerry Cattle breed. *Front. Genet.*, 2018, 9(51): 1-17 (doi: 10.3389/fgene.2018.00051).
14. Zinov'eva N.A., Dotsev A.V., Sermyagin A.A., Vimmers K., Reier Kh., Solkner I., Deniskova T.E., Brem G. Study of genetic diversity and population structure of five Russian cattle breeds using whole-genome SNP analysis. *Sel'skokhozyaistvennaya biologiya* [*Agricultural Biology*], 2016, 51(6): 788-800 (doi: 10.15389/agrobiology.2016.6.788eng).
15. Zinovieva N.A., Dotsev A.V., Sermyagin A.A., Deniskova T.E., Abdelmanova A.S., Kharzinova V.R., Sölkner J., Reyer H., Wimmers K., Brem G. Selection signatures in two oldest Russian native cattle breeds revealed using high-density single nucleotide polymorphism analysis. *PLoS ONE*, 2020, 15(11): e0242200 (doi: 10.1371/journal.pone.0242200).
16. Romanov A.I. V sbornike: *Trudy soveshchaniya veterinarnykh vrachei i predstavitelei zemstv* [In: Proceedings of the meeting of veterinarians and representatives of zemstvos]. Perm', 1913: 11-129

(in Russ.).
17. *Puti i formy sozdaniya i sokhraneniya genofonda tsennykh lokal'nykh porod* [Ways and forms of creating and preserving the gene pool of valuable local breeds]. Leningrad, 1979 (in Russ.).
18. Kremer L.A. *Tagil'skii skot* [Tagil cattle]. Moscow-Leningrad, 1931 (in Russ.).
19. Moiseeva I.G., Ukhanov S.V., Stolpovskii Yu.A. et al. *Genofondy sel'skokhozyaistvennykh zhivotnykh: geneticheskie resursy zhivotnovodstva Rossii* /Pod red. I.A. Zakharova [Gene pools of farm animals: genetic resources of animal husbandry in Russia. I.A. Zakharov (ed.)]. Moscow, 2006 (in Russ.).
20. *Plink: Whole genome association analysis toolse*t. Available: http://zzz.bwh.harvard.edu/plink/. Accessed 25.01.2017.
21. Keenan K., McGinnity P., Cross T.F., Crozier W.W., Prodöhl P.A. diveRsity: an R package for the estimation of population genetics parameters and their associated errors. *Methods in Ecology and Evolution*, 2013, 4(8): 782-788 (doi: 10.1111/2041-210X.12067).
22. Wickham H. *ggplot2: elegant graphics for data analysis.* N.-Y., 2009.
23. Weir B.S., Cockerham C.C. Estimating F-statistics for the analysis of population structure. *Evolution*, 1984, 38(6): 1358-1370 (doi: 10.2307/2408641).
24. Huson D.H., Bryant D. Application of phylogenetic networks in evolutionary studies. *Molecular Biology and Evolution*, 2006, 23(2): 254-267 (doi: 10.1093/molbev/msj030).
25. Alexander D.H., Novembre J., Lange K. Fast model-based estimation of ancestry in unrelated individuals. *Genome Research*, 2009, 19(9): 1655-1664 (doi: 10.1101/gr.094052.109).
26. Francis R.M. pophelper: An R package and web app to analyse and visualise population structure. *Molecular Ecology Resources*, 2017, 17(1): 27-32 (doi: 10.1111/1755-0998.12509).
27. R Core Team. *R: a language and environment for statistical computing. R foundation for statistical computing*, Vienna, 2018. Available: https://www.R-project.org/. No date.
28. Lindholm-Perry A.K., Kuehn L.A., Smith T.P., Ferrell C.L., Jenkins T.G., Freetly H.C., Snelling W.M. A region on BTA14 that includes the positional candidate genes LYPLA1, XKR4 AND TMEM68 is associated with feed intake and growth phenotypes in cattle. *Anim Genet.*, 2012, 43: 216-219 (doi: 10.1111/j.1365-2052.2011.02232.x).
29. Pryce J.E., Arias J., Bowman P.J., Davis S.R., Macdonald K.A., Waghorn G.C., Wales W.J., Williams Y.J., Spelman R.J., Hayes B.J. Accuracy of genomic predictions of residual feed intake and 250-day body weight in growing heifers using 625,000 single nucleotide polymorphism markers. *J. Dairy Sci.*, 2012, 95(4): 2108-2119 (doi: 10.3168/jds.2011-4628).
30. Taye M., Yoon J., Dessie T., Cho S., Oh S.J., Lee H.K., Kim H. Deciphering signature of selection affecting beef quality traits in Angus cattle. *Genes Genomics*, 2018, 40(1): 63-75 (doi: 10.1007/s13258-017-0610-z).
31. Cheruiyot E.K., Bett R.C., Amimo J.O., Zhang Y., Mrode R., Mujibi F.D.N. Signatures of selection in admixed dairy cattle in Tanzania. *Front. Genet.*, 2018, 9(607): 1-15 (doi: 10.3389/fgene.2018.00607).
32. De Las Heras-Saldana S., Clark S.A., Duijvesteijn N., Gondro C., van der Werf J.H.J., Chen Y. Combining information from genome-wide association and multi-tissue gene expression studies to elucidate factors underlying genetic variation for residual feed intake in Australian Angus cattle. *BMC Genomics*, 2019, 20(1): 939 (doi: 10.1186/s12864-019-6270-4).
33. Grigoletto L., Ferraz J.B.S., Oliveira H.R., Eler J.P., Bussiman F.O., Abreu Silva B.C., Baldi F., Brito L.F. Genetic architecture of carcass and meat quality traits in Montana tropical composite beef cattle. *Front. Genet.*, 2020, 11(123): 1-13 (doi: 10.3389/fgene.2020.00123).