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Association of two missense mutations in the *MSS51* and *KAT6B* genes with body weight at different ages in cows of the Yaroslavl breed

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Abstract. The Yaroslavl cattle is a native Russian dairy breed developed in the 19th century from the Northern Great Russian cattle, which were adapted to withstand harsh climates and poor forage conditions. Previous studies identified two breed-specific missense mutations in the *MSS51* (Ala415Glu) and *KAT6B* (Val105Met) genes that negatively impact the body weight of the animals. This study aimed to confirm the association of these missense mutations in the *MSS51* and *KAT6B* genes, along with the mutant haplotype containing both mutations, with live weight at various ages in the Yaroslavl breed using an expanded sample set. We genotyped 113 cows for these missense variants and analyzed their associations with live weight at birth, as well as at 6, 10, 12, 15, and 18 months in a combined sample of 143 animals, which includes earlier data. We employed linear regression and one-way ANOVA for statistical analysis. The results from linear regression indicated significant associations with live weight at 6, 12, and 18 months for the mutation in the *KAT6B* gene. The *MSS51* gene mutation was associated with live weight at 6, 12, 15, and 18 months. Notably, the mutant haplotype was linked to live weight across all ages from 6 to 18 months. One-way ANOVA revealed significant associations of live weight with *KAT6B* genotypes only at 6 months. For the *MSS51* gene mutation and the mutant haplotype, significant associations were found at 6, 12, 15, and 18 months. In both statistical tests, the most significant association was observed for the mutant haplotype rather than for the individual variants. These findings could be instrumental in enhancing the live weight of beef hybrids utilising the Yaroslavl cattle breed.

Key words: Yaroslavl breed; live weight; age; *KAT6B* gene; *MSS51* gene; missense mutation; haplotype; selection.

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Ассоциация двух миссенс-мутаций в генах *MSS51* и *KAT6B* с массой тела в разном возрасте у коров ярославской породы

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Аннотация. Ярославская порода крупного рогатого скота – отечественная порода молочного направления продуктивности, выведенная в XIX в. на основе северного великорусского скота, адаптированного к суровому климату и скудному рациону. Ранее у животных этой породы мы обнаружили две высокочастотные почти породоспецифичные миссенс-мутации в генах *MSS51* (Ala415Glu) и *KAT6B* (Val105Met), которые имели отрицательную связь с массой тела на выборке из 30 животных. Целью работы было подтверждение ассоциации миссенс-мутаций в генах *MSS51* и *KAT6B*, а также мутантного гаплотипа, содержащего обе мутации, с живой массой в разном возрасте у коров ярославской породы на расширенной выборке животных. Мы генотипировали 113 коров по вышеупомянутым миссенс-вариантам и на объединенной с предыдущими данными выборке в 143 животных провели анализ ассоциаций с живой массой в возрасте 0, 6, 10, 12, 15 и 18 мес. с использованием линейной регрессии и однофакторного дисперсионного анализа. С помощью линейной регрессии для мутации в гене *KAT6B* были выявлены значимые ассоциации с живой массой в возрасте 6, 12 и 18 мес. Мутация в гене *MSS51* была ассоциирована с живой массой в возрасте 6, 12, 15 и 18 мес. Гаплотип с обеими мутациями был ассоциирован с

живой массой во всех возрастах, от 6 до 18 мес. включительно. По результатам однофакторного дисперсионного анализа значимые ассоциации живой массы с генотипами по мутации в гене *KAT6B* были обнаружены только в возрасте 6 мес. Для мутации в гене *MSS51*, как и для мутантного гаплотипа, ассоциации имелись в возрасте 6, 12, 15 и 18 мес. В обоих статистических тестах наибольшей значимости достигла ассоциация не с отдельными вариантами, а с мутантным гаплотипом. Полученные данные могут быть использованы при селекции для производства говядины за счет откормочного контингента молодняка, а также помесей ярославской породы с быками мясных пород.

Ключевые слова: ярославская порода; живая масса; возраст; ген *KAT6B*; ген *MSS51*; миссенс-мутация; гаплотип; селекция.

Introduction

There are currently more than a thousand officially recognized cattle breeds in the world (FAO, 2024). A significant part of them can be attributed to the so-called local (indigenous, native) breeds. Local breeds usually have lower productivity compared to commercial breeds with a large breeding area, but are well adapted to local climatic factors, pathogens and farming conditions (Curone et al., 2019). Local breeds are a valuable reservoir of genetic diversity that can be used to improve the adaptive and productive traits of cattle in the face of climate change around the world (Yudin, Larkin, 2019; Colombi et al., 2024).

The Yaroslavl cattle is a native Russian dairy breed developed in the 19th century on the territory of the former Yaroslavl province as the result of "folk selection", by pure breeding of the Northern Great Russian cattle, which were short and had low productivity, but were adapted to withstand harsh climates and poor forage conditions (Dmitriev, Ernst, 1989).

Animals of the Yaroslavl breed are mainly black in color. The head is white, with characteristic black markings ("glasses") around the eyes. The belly and the lower part of the limbs, as well as the tip of the tail, are white (Monoenkov, 1974). Until the beginning of the 1880s, animals of the Dutch, Tyrolean, Angeln, Simmental, Allgau, and Kholmogory breeds were imported into the Yaroslavl province in small numbers. However, it appears they did not significantly affect the Yaroslavl breed, as it retained its specific exterior (Dmitriev, Ernst, 1989). In the USSR, the Yaroslavl breed was crossed with the Friesian and Dutch cattle (since 1937), as well as with the Holstein breed (since 1978), in order to increase milk productivity (Monoenkov, 1974; Tamarova, 2009). Nevertheless, studies based on genome-wide SNP genotyping arrays (Iso-Touru et al., 2016; Yurchenko et al., 2018) and microsatellite analysis (Abdelmanova et al., 2020) have shown that the Yaroslavl breed has mostly retained its unique genetics, which differs from other Russian native and foreign breeds.

Previously, we conducted a study to search for signatures of selection in the genomes of animals of the Yaroslavl breed, in which two almost breed-specific high-frequency missense mutations were identified on chromosome 28 in the *MSS51* (Ala415Glu) and *KAT6B* (Val105Met) genes, forming a single haplotype (Ruvinskiy et al., 2022). Genotyping of these mutations and subsequent association analysis carried out on a sample of 30 cows showed a negative relationship between the mutant haplotype and the live weight of animals, as well as withers height and heart girth. We hypothesized that the mutant haplotype, being associated with lower body weight of animals, had advantages under cold climate conditions and poor food supply. Therefore, it has undergone selection in the ancestral populations of the Yaroslavl breed.

The aim of this study was to confirm the association of the missense mutations in the *MSS51* and *KAT6B* genes, as well as the mutant haplotype containing both mutations, with live weight at various ages in the Yaroslavl cows on an expanded sample set.

Materials and methods

Blood samples from 113 Yaroslavl cows from two farms of the Yaroslavl region were used in the study. Information on live weight at the age of 0, 6, 10, 12, 15 and 18 months was obtained from breeding records. DNA isolation was performed using the standard phenol-chloroform extraction method with preliminary proteolytic digestion (Sambrook, Russell, 2006). Genotyping of the missense mutations in the *MSS51* and *KAT6B* genes was carried out by restriction fragment length polymorphism (RFLP) analysis after polymerase chain reaction (PCR) (Ota et al., 2007). Primers were designed using the Vector NTI software package (Lu, Moriyama, 2004). The specificity of each primer pair was evaluated using the primer-BLAST web tool (Ye et al., 2012). The primers, PCR reaction conditions and restriction enzymes are given in Table 1. Information on 30 previously studied individuals (Ruvinskiy et al., 2022) was added to the genotyping data of 113 animals. Thus, the total sample consisted of 143 animals. The test for deviation from the Hardy–Weinberg equilibrium (--hardy option) and estimation of linkage disequilibrium between the studied SNPs (--ld option) were carried out in PLINK v1.9 (Purcell et al., 2007). Preliminarily, the genotyping data were converted to PED format recognized by the program.

Statistical analysis was performed using the linear regression and one-way analysis of variance (ANOVA) implemented in the "lm" and "aov" R functions, respectively. When using linear regression, the genotypes for each mutation were coded as 0, 1, and 2 according to the dose of the mutant allele. In addition to associations with genotypes, we also tested the association of live weight with the dose of the haplotype containing both mutations. Double homozygotes for mutant alleles were considered as carriers of two doses of the mutant haplotype. Animals homozygous for one gene mutation and heterozygous for the other were considered carriers of one dose. Double heterozygotes were also considered as carriers of one dose of the haplotype. We believe this assumption is justified, since, according to the genotyping results, mutations in both genes were in strong linkage disequilibrium. This means that the vast majority of double heterozygote carriers have mutant alleles in *cis* position, that is, on the same homeologous chromosome.

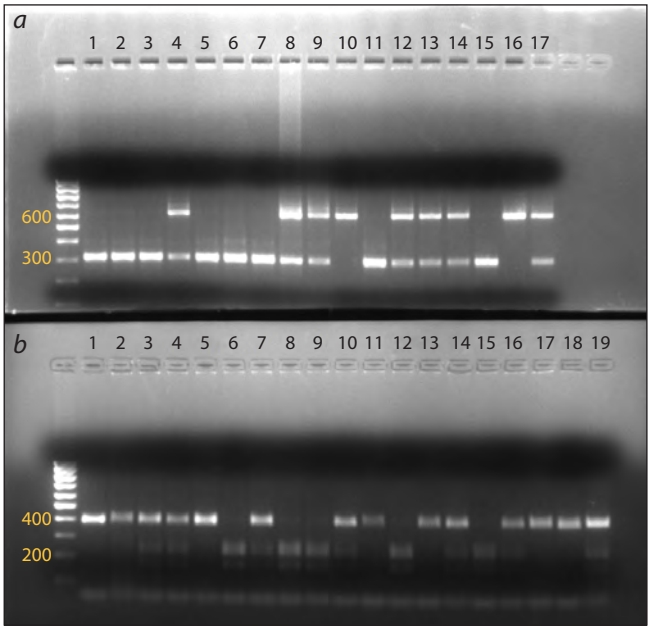
Table 1. The primers, PCR reaction conditions and restriction enzymes for genotyping of missense mutations in the *MSS51* and *KAT6B* genes

Gene, substitution	Forward, reverse primer	PCR conditions	Restriction enzyme	Fragment size
KAT6B, G>A (Val105Met)	ACTTGCAAACCCACTTTATACAGAGTGG, CTGATCTTTCTCGTGGGGTAGAAGG	1 cycle: 95 °C – 3 min 35 cycles: 95 °C – 1 min; 60 °C – 1 min; 72 °C – 55 s	HpySE526 I, cleavage at the presence of ancestral (G) allele	613 bp, upon digestion: 303 and 310 bp
MSS51, G>T (Ala415Glu)	CTTGGCTTTCTTATCCCTTCAAAGTGC, ATCCAGTCATGATCTGGCTCAGC	1 cycle: 95 °C – 3 min 35 cycles: 95 °C – 1 min; 58 °C – 1 min; 72 °C – 45 s	HinfI, cleavage at the presence of mutant (T) allele	390 bp, upon digestion: 224 and 166 bp

Results

The target fragments were amplified for both mutations and all the studied DNA samples were successfully genotyped (see the Figure). The distributions of genotype frequencies for both mutations did not deviate significantly from those expected under the Hardy–Weinberg equilibrium. The mutant allele frequencies for the *KAT6B* and *MSS51* genes were 0.455 and 0.434, respectively (Table 2). The mutant allele carrier rates were 0.72 and 0.699, respectively. The coefficient of linkage disequilibrium between the two loci was $r^2 = 0.891$.

When using linear regression, significant ($p < 0.05$) associations of the *KAT6B* gene mutation with live weight were identified at 6, 12, and 18 months (Table 3). The *MSS51* gene mutation was associated with live weight at 6, 12, 15, and 18 months. Notably, the dose of the mutant haplotype was associated with live weight across all ages from 6 to 18 months, inclusively. One-way ANOVA revealed significant associations of live weight with *KAT6B* genotypes only at 6 months. For both the *MSS51* gene mutation and the mutant haplotype, significant associations were found at 6, 12, 15, and 18 months. None of the statistical tests revealed an association with the live weight at birth.



Examples of electropherograms of PCR-RFLP analysis for missense mutations in the studied genes.

a – genotypes for the *KAT6B* gene: GG – lanes 1, 2, 3, 5, 6, 7, 11, and 15; GA – 4, 8, 9, 12, 13, 14, and 17; AA – 10, and 16; *b* – genotypes for the *MSS51* gene: GG – lanes 1, 2, 5, 11, 13, 17, and 18; GT – 3, 4, 7, 10, 14, 16, and 19; TT – 6, 8, 9, 12, and 15.

Discussion

The results obtained in this work confirm the previously identified associations of mutations in the *MSS51* and *KAT6B* genes, as well as the mutant haplotype containing both variants, with the live weight of cows at different ages (Ruvinskiy et al., 2022). More significant association at most ages was achieved when using linear regression for both individual mutations and haplotype, compared to one-way ANOVA. This seems to indicate the additive effect of mutant alleles/haplotype. Reduced live weight in carriers of two copies of the mutant allele/haplotype compared to carriers of one copy was indeed observed in animals aged from 6 to 18 months, inclusively. At the same time, since both mutations are in

Table 2. Characteristics of genotyped missense mutations in the sample of Yaroslavl cows

Gene	Position (ARS-UCD1.2)	SNP	Genotype	Genotype frequency	Allele	Allele frequency
KAT6B	BTA28:30646253	G>A (Val105Met)	GG	0.28	G	0.545
			GA	0.531	A	0.455
			AA	0.189		
MSS51	BTA28:29414270	G>T (Ala415Glu)	GG	0.301	G	0.566
			GT	0.531	T	0.434
			TT	0.168		

Table 3. Associations of the studied mutations and the mutant haplotype with the live weight of cows at different agesте

Gene / haplotype	Genotype / dose of haplotype (number of carriers)	Live weight at the age of (kg):					
		0 months	6 months	10 months	12 months	15 months	18 months
KAT6B	GG (40)	30.5 ± 4.2	146.2 ± 22.1	214.8 ± 28.3	252.1 ± 31.7	302.1 ± 37.7	352.7 ± 34.3
	GA (76)	29.4 ± 4.4	136 ± 18.3	209.3 ± 25.8	246.3 ± 28.9	300.7 ± 36.9	344.3 ± 42.8
	AA (27)	30.2 ± 3.9	134.4 ± 13.9	205.4 ± 18.3	237 ± 29.3	284.4 ± 31.7	329.5 ± 34.9
	p-value (lm)	0.6081	**0.0074**	0.1241	**0.0457**	0.0734	**0.021**
	p-value (aov)	0.3583	**0.0113**	0.302	0.1289	0.0972	0.0627
MSS51	GG (43)	30.6 ± 4.4	146 ± 20.9	215.8 ± 28.6	252.8 ± 31.6	302.7 ± 38.1	351.7 ± 34
	GT (76)	29.3 ± 4.3	135.8 ± 18.5	208.8 ± 24.9	246.2 ± 28.4	300.9 ± 36.1	345.1 ± 42.6
	TT (24)	30.2 ± 4	134 ± 14.5	203.9 ± 18.7	234 ± 29.5	280.3 ± 31.1	325.7 ± 34.9
	p-value (lm)	0.5283	**0.0051**	0.0519	**0.0161**	**0.0322**	**0.0145**
	p-value (aov)	0.3016	**0.0084**	0.1479	**0.0482**	**0.0325**	**0.0324**
Haplotype	0 (44)	30.7 ± 4.5	146.8 ± 21.4	217.1 ± 29.5	254.3 ± 32.8	304.2 ± 38.9	352.9 ± 34.5
	1 (75)	29.2 ± 4.2	135.1 ± 17.9	208 ± 24	245.2 ± 27.3	300 ± 35.5	344.3 ± 42.4
	2 (24)	30.2 ± 4	134 ± 14.5	203.9 ± 18.7	234 ± 29.5	280.3 ± 31.1	325.7 ± 34.9
	p-value (lm)	0.4048	**0.0022**	**0.0251**	**0.007**	**0.0177**	**0.0089**
	p-value (aov)	0.1797	**0.0024**	0.0691	**0.0261**	**0.0278**	**0.0248**

Note. Data are presented as mean ± standard deviation. lm – linear regression, aov – one-way ANOVA. *p*-values that reach statistical significance are highlighted in bold.

strong linkage disequilibrium, it is difficult to determine which of them is causative, that is, directly affects the phenotype. *In silico* analysis of the effect of an amino acid substitution in the previous study predicted a significant impairment of function specifically for the mutation in *KAT6B* (Ruvinskiy et al., 2022). However, associations with live weight for the missense mutation in the *MSS51* gene were more significant than those for the *KAT6B* gene. Probably, the simultaneous presence of both mutations is important for the manifestation of their effect on live weight. This assumption is supported by the fact that associations were most significant with the dose of the mutant haplotype.

The *MSS51* gene encodes a mitochondrial translation activator predominantly expressed in muscle tissue and involved in various metabolic processes, such as fatty acid oxidation, oxidative phosphorylation, and glycolysis (Moyer, Wagner, 2015). *MSS51* knockout mice have been shown to have reduced body weight compared to normal animals. However, their weight loss was due to fat, not muscle tissue (Gonzalez et al., 2019). Other authors have shown the involvement of *MSS51* in age-related muscle loss in mice. Moreover, adding betaine, which suppresses the expression of *MSS51* mRNA, to the diet of animals slowed down the decline in muscle mass and other functional parameters of skeletal muscles with age (Chen et al., 2024).

The *KAT6B* gene encodes lysine acetyltransferase 6B involved in histone modification, particularly the acetylation of H3K9 and H3K23, which increases the accessibility of chromatin in the regions of the target genes and, accordingly, increases their expression (Bergamasco et al., 2024a). In this regard, it can be assumed that the mutation in *KAT6B* has a modifying effect on the activity of *MSS51*. Mutations in the *KAT6B* gene cause growth and developmental delay in humans (Zhang et al., 2020; Zhu et al., 2020). Of note is a study showing that mice heterozygous for a deletion in the *KAT6B* gene exhibit a significant reduction in body weight, compared to normal homozygotes. In this case, homozygotes for the deletion were not viable (Bergamasco et al., 2024b). Taken together, the biological functions of the two genes suggest that both missense variants can be causative and, probably, their effect on the live weight of animals is realized only when they are combined in a haplotype.

A limitation of this work is the fact that the study sample is represented by the animals of one sex. However, it can be assumed that the association we identified between body weight and mutations in the *MSS51* and *KAT6B* genes will be valid for bulls as well. For example, E.M.M. van der Heide et al. showed for the Aberdeen-Angus cattle that the heritability coefficients of body weight at different ages do not differ considerably between the sexes (van der Heide et al., 2016).

Also, it should be noted that the live weight of animals of the Yaroslavl breed has increased significantly over the history of its breeding. For example, in 1973, in the breeding farms of the Yaroslavl region, the average weight of heifers at the age of 0, 6, 12, and 18 months was 28, 134, 224, and 294 kg, respectively (Monoenkov, 1974). These values in our sample were 30, 139, 246, and 344 kg. Live weight was an important

selection trait of Yaroslavl cattle in the USSR, along with milk yield, since large animals capable of consuming more feed and producing more products from one stall are more efficient under industrial technology conditions (Monoenkov, 1974).

Selection to increase live weight was continued in the post-Soviet period. Thus, in most farms in the Yaroslavl region, during the period from 2000 to 2012, a significant increase in the live weight of Yaroslavl cows was recorded (Korenev et al., 2013). This can explain the fact that the frequency of mutant alleles in the populations of Yaroslavl cattle is far from fixation. It can be assumed that the selection in favor of the mutant haplotype took place in the early period of the formation of the Yaroslavl breed during "folk selection". However, later, the frequency of this haplotype in the breed began to decrease in the course of selection aimed, among other traits, at increasing the live weight of animals.

The Yaroslavl is a dairy breed. However, as mentioned above, live weight is also an important selection trait. In addition, beef production in Russia is mainly based on fattening of young stock of dairy breeds, as well as their crosses with beef breeds (Kochetkov, 2011). In particular, there is a successful experience in creating hybrids of the Yaroslavl breed with the Limousin (Kochetkov, 2011) and Galloway (Burmistrov, 2013) breeds. Our results can be used in marker-assisted and genomic selection to increase the weight of animals of the Yaroslavl breed and its hybrids.

Conclusion

In this study, we confirmed the previously identified associations of mutations in the *MSS51* and *KAT6B* genes, as well as the mutant haplotype, with live weight in Yaroslavl cows at different ages. The obtained data can be used for selection to increase the live weight of animals in cattle breeding for beef production.

References

Abdelmanova A.S., Kharzinova V.R., Volkova V.V., Mishina A.I., Dotsev A.V., Sermyagin A.A., Boronetskaya O.I., Petrikeeva L.V., Chinarov R.Y., Brem G., Zinovieva N.A. Genetic diversity of historical and modern populations of Russian cattle breeds revealed by microsatellite analysis. *Genes* (*Basel*). 2020;11(8):940. doi 10.3390/genes11080940

Bergamasco M.I., Abeysekera W., Garnham A.L., Hu Y., Li-Wai-Suen C.S.N., Sheikh B.N., Smyth G.K., Thomas T., Voss A.K. KAT6B is required for histone 3 lysine 9 acetylation and SOX gene expression in the developing brain. *Life Sci Alliance*. 2024a;8(2):e202402969. doi 10.26508/lsa.202402969

Bergamasco M.I., Vanyai H.K., Garnham A.L., Geoghegan N.D., Vogel A.P., Eccles S., Rogers K.L., Smyth G.K., Blewitt M.E., Hannan A.J., Thomas T., Voss A.K. Increasing histone acetylation improves sociability and restores learning and memory in *KAT6B*-haploinsufficient mice. *J Clin Invest*. 2024b;134(7):e167672. doi 10.1172/JCI167672

Burmistrov V.A., Pogosyan G.A., Asianin V., Golubeva A.I. Cross-breeding to thorough-bred Galloway bulls improves beef-making qualities of cattle bred in the Yaroslavl region. *Molochnoye i Myasnoye Skotovodstvo = Dairy and Meat Cattle Breed*. 2013;7:17-19 (in Russian)

Chen S., He T., Chen J., Wen D., Wang C., Huang W., Yang Z., Yang M., Li M., Huang S., Huang Z., Zhu H. Betaine delays age-related muscle loss by mitigating Mss51-induced impairment in mitochondrial respiration via Yin Yang1. *J Cachexia Sarcopenia Muscle*. 2024;15(5):2104-2117. doi 10.1002/jcsm.13558

Colombi D., Perini F., Bettini S., Mastrangelo S., Abeni F., Conte G., Marletta D., Cassandro M., Bernabucci U., Ciampolini R., Lasagna E. Genomic responses to climatic challenges in beef cattle: a review. *Anim Genet*. 2024;55(6):854-870. doi 10.1111/age.13474

Curone G., Filipe J., Cremonesi P., Piccioli-Cappelli F., Trevisi E., Amadori M. Relevance of the dairy cow biodiversity in the development of a profitable and environmentally sustainable livestock. *CABI Rev*. 2019;14:1-11. doi 10.1079/PAVSNNR201914024

Dmitriev N.G., Ernst L.K. Animal Genetics Resources of the USSR. Rome: Food and Agriculture Organization of the United Nations, 1989

FAO. Status and Trends of Animal Genetic Resources. Rome: Commission on Genetic Resources for Food and Agriculture, 2024

Gonzalez Y.I.R., Moyer A.L., LeTexier N.J., Bratti A.D., Feng S., Sun C., Liu T., Mula J., Jha P., Iyer S.R., Lovering R.M., O'Rourke B., Noh H.L., Suk S., Kim J.K., Essien Umanah G.K., Wagner K.R. *Mss51* deletion enhances muscle metabolism and glucose homeostasis in mice. *JCI Insight*. 2019;4(20):e122247. doi 10.1172/jci.insight.122247

Iso-Touru T., Tapio M., Vilkki J., Kiseleva T., Ammosov I., Ivanova Z., Popov R., Ozerov M., Kantanen J. Genetic diversity and genomic signatures of selection among cattle breeds from Siberia, eastern and northern Europe. *Anim Genet*. 2016;47(6):647-657. doi 10.1111/age.12473

Kochetkov A.A. Use of world and Russian breed resources of beef cattle to increase the production of high-quality meat in the North Caucasus and the central zone of Russia: Dr. (Agricultural Sci.) Dissertation. 2011 (in Russian)

Korenev M.M., Furaeva N.S., Khrustaleva V.I., Ursol A.Yu., Vorobyova S.S., Konovalov A.V., Kosyachenko N.M., Ilyina A.V., Muratova N.S., Gvazava D.G., Tarasenkova N.A., Malyukova M.A. Breeding Measures for the Preservation and Improvement of the Yaroslavl Cattle Breed for 2013–2020. Yaroslavl: Kantsler Publ., 2013 (in Russian)

Lu G., Moriyama E.N. Vector NTI, a balanced all-in-one sequence analysis suite. *Brief Bioinform*. 2004;5(4):378-388. doi 10.1093/bib/5.4.378

Monoenkov M.I. Yaroslavl Breed of Cattle. Yaroslavl, 1974 (in Russian)

Moyer A.L., Wagner K.R. Mammalian *Mss51* is a skeletal muscle-specific gene modulating cellular metabolism. *J Neuromuscul Dis.* 2015;2(4):371-385. doi 10.3233/JND-150119

Ota M., Fukushima H., Kulski J.K., Inoko H. Single nucleotide polymorphism detection by polymerase chain reaction-restriction fragment length polymorphism. *Nat Protoc*. 2007;2(11):2857-2864. doi 10.1038/nprot.2007.407

Purcell S., Neale B., Todd-Brown K., Thomas L., Ferreira M.A.R., Bender D., Maller J., Sklar P., de Bakker P.I.W., Daly M.J., Sham P.C. PLINK: a tool set for whole-genome association and population-based linkage analyses. *Am J Hum Genet*. 2007;81(3):559-575. doi 10.1086/519795

Ruvinskiy D., Igoshin A., Yurchenko A., Ilina A.V., Larkin D.M. Re-sequencing the Yaroslavl cattle genomes reveals signatures of selection and a rare haplotype on BTA28 likely to be related to breed phenotypes. *Anim Genet*. 2022;53(5):680-684. doi 10.1111/age.13230

Sambrook J., Russell D.W. The Condensed Protocols from Molecular Cloning: A Laboratory Manual. Cold Spring Harbor, 2006

Tamarova R.V. Will we save our Yaroslavl wet nurse? On the 140th anniversary of the creation of the Yaroslavl breed. *Vestnik APK Verkhnevolzh'ya = Agroindustrial Complex of Upper Volga Region Herald*. 2009;3(7):20-23 (in Russian)

van der Heide E.M.M., Lourenco D.A.L., Chen C.Y., Herring W.O., Sapp R.L., Moser D.W., Tsuruta S., Masuda Y., Ducro B.J., Misztal I. Sexual dimorphism in livestock species selected for economically important traits. *J Anim Sci*. 2016;94(9):3684-3692. doi 10.2527/jas.2016-0393

Ye J., Coulouris G., Zaretskaya I., Cutcutache I., Rozen S., Madden T.L. Primer-BLAST: a tool to design target-specific primers for polymerase chain reaction. *BMC Bioinformatics*. 2012;13:134. doi 10.1186/1471-2105-13-134

Yudin N.S., Larkin D.M. Whole genome studies of origin, selection and adaptation of the Russian cattle breeds. *Vavilovskii Zhurnal Genetiki i Selektsii = Vavilov J Genet Breed*. 2019;23(5):559-568. doi 10.18699/VJ19.525 (in Russian)

Yurchenko A., Yudin N., Aitnazarov R., Plyusnina A., Brukhin V., Soloshenko V., Lhasaranov B., Popov R., Paronyan I.A., Plemyashov K.V., Larkin D.M. Genome-wide genotyping uncovers genetic profiles and history of the Russian cattle breeds. *Heredity* (*Edinb*). 2018;120(2):125-137. doi 10.1038/s41437-017-0024-3

Zhang L.X., Lemire G., Gonzaga-Jauregui C., Molidperee S., Galaz-Montoya C., Liu D.S., Verloes A., … Bamshad M.J., Lee B.H., Yang X.-J., Lupski J.R., Campeau P.M. Further delineation of the clinical spectrum of *KAT6B* disorders and allelic series of pathogenic variants. *Genet Med.* 2020;22(8):1338-1347. doi 10.1038/s41436-020-0811-8

Zhu L., Lv L., Wu D., Shao J. *KAT6B* genetic variant identified in a short stature chinese infant: a report of physical growth in clinical spectrum of *KAT6B*-related disorders. *Front Pediatr*. 2020;8:124. doi 10.3389/fped.2020.00124

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