CONNECTION BETWEEN GENE MARKERS WITH MILK PRODUCTION TRAITS OF UKRAINIAN DAIRY COWS

Yulia GRITSIENKO[1] , Michael GILL[2] , and Olena KARATIEIEVA[2]✉

[1]*Mykolaiv Research and Forensic Center of the Ministry of Internal Affairs of Ukraine, Mykolaiv, 54003, Ukraine*
[2]*Mykolaiv National Agrarian University, Mykolaiv, 54010, Ukraine*

✉Email: karateeva1207@gmail.com

Supporting Information

ABSTRACT: The purpose of this study was to obtain information on the genotyping of cows of Ukrainian dairy breeds for the presented loci capa-casein gene (CSN3), thyroglobulin (TG-5) gene, leptin (LEP), pituitary-specific transcription factor (Pit-1), and beta-lactoglobulin (BLG) by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) and to test their association with milk production. The influence of the genotype on milk yield, fat and protein content in the milk of cows of Ukrainian selection has been established. The highest levels of milk productivity traits were expected from animals with the CT genotype for the LEP gene, AA for the CSN3 gene, CC for the TG5 gene, and AA and BB for the Pit-1 gene. But at the same time, milk obtained from cows with CSN3 BB genotype were characterized by the best cheese suitability. The effect of the homo- or heterozygous state of BLG on the signs of milk production was less noticeable, and the homozygous TT genotype for the TG5 gene was not found in any of the studied breeds. The results obtained can be used in the practical work of breeding farms along with traditional methods of selection, control and preservation of the genetic diversity of specific herds at an optimal level.

Keywords: Capa-casein, Marker genes, Polymorphism, Thyroglobulin, Leptin, Pituitary transcription Factor, Beta-lactoglobulin

INTRODUCTION

In recent decades, advances in DNA-based marker technology have been able to identify regions of the genome (namely, quantitative trait loci, QTLs) underlying complex traits such as milk yield. Instead of traditional animal breeding programs based solely on phenotype and pedigree information, the application of identified QTLs to genetic evaluation provides great potential to improve selection accuracy, thereby could accelerate genetic improvement in animal productivity (Jiang et al., 2010; Kumar, 2017; Kramarenko et al., 2019).

The introduction of the molecular genetic methods in animal husbandry is associated with the development of PCR technology, made it possible to conduct a quick analysis of the connection between allelic variants of genes with productivity. With the development of DNA-based marker technology, it has become possible to identify regions of the genome (i.e., loci of quantitative traits, QTLs) that are associated with complex traits. The inclusion of the detected QTLs in the genetic evaluation allows a clear increase in selection accuracy, thereby accelerating the genetic improvement of the productive qualities of the animals. Numerous studies have been published in recent decades to identify QTLs for signs of dairy livestock dairy productivity. Advances in the detection of causal genes for complex such are slow, as association mapping results in large confidence intervals. In particular, the region in which QTL is mapped may contain a large number of possible candidate genes (Wang et al., 2014; Kusza et al., 2015). Genome-wide association studies (GWAS), based on high-throughput single nucleotide polymorphisms (SNPs) genotyping technologies, open up ample opportunities to study genes associated with signs of livestock dairy productivity, as confirmed by a number of domestic and foreign scientific studies (Arora and Bhatia, 2004; Soltani-Ghombavani et al., 2013; Zhou et al., 2019).

Breeding farm animals is an integral part of a complex breeding system. When evaluating animals of dairy breeds, not only a high level of milk productivity, but also quality indicators of milk are of great importance. Increasing yield, fat content in milk, live weight of cows is considered the classic direction of work of genetic scientists. But at the same time, there are few works, especially domestic ones, devoted to the study of marker genes associated with the protein content in milk. Although the protein content and amount in milk, its structure is of great economic importance to the processing industry. Since the consumption of raw materials, time and energy resources for the production of dairy products depend on the fat content in milk, in addition, the protein content indicator largely determines the quality of finished products (Yurnalis et al., 2013; Lu et al., 2021).

The association of polymorphism in the 3 'region of the oxidized low density lipoprotein receptor 1 (OLR1) gene with milk fat and protein in active Holstein cows of Irish selection was studied by Soltani-Ghombavani et al. (2013). Thus, scientists have found that the OLR1 is the main receptor on the cell surface for the oxidized low-density lipoprotein, actively participates in the metabolism of lipoproteins and affects the protein content in milk. According to the authors,

the OLR1 gene may be a marker gene that is associated with the production of protein content in milk. Because the genetic linkage phase can be different across breeds and populations, the use of previously identified markers to conduct marker selection is problematic, especially when marker density was low during discoveries. Consequently, high-density SNP GWASs are essential for understanding the genetic architecture of important and complex traits in cattle breeds.

A genome-wide association of milk research was carried out by Chinese scientists in Xinjiang Brown cattle of a combined direction of productivity. In their studies, the scientists evaluated five milk productivity measures: milk yield (MY), fat yield (FY), protein yield (PY), fat percentage (FP) and protein percentage (PP) in Chinese cattle breed Xinjiang Brown. The authors found two very significant SNPs associated with milk composition characteristics. One SNP is associated with a percentage of fat and is located in the cadherin-2 (CDH2) gene at 29.1 Mbp on BTA 24. The cadherin-2 is a protein coding gene and is involved in adipogenesis. Depressing the CDH2 to block the epithelial-mesenchymal reaction can weaken the production of fat content in milk. Another milk-related SNP that the authors identified was significantly associated with protein content in milk and mapped at 75.8 Mbp on Bos taurus (BTA 7), which is in a gene called the Gamma2 receptor gamma-aminobutyric acid type A subunit (GABRG2). GABRG2 primarily promotes the activity of the gamma-aminobutyric acid-controlled chloride ion channel (GABA) and is involved in the activity of the GABA-A receptor and promotes the production of the amount of protein in milk (Zhou et al., 2019; Zhang et al., 2022). Scientific research on the assessment of annual genetic progress and economic efficiency becomes the basis for the development of methods for optimizing long-term breeding programs for dairy cattle, while improving methodological approaches to solving this problem. Wang et al. (2014) established a significant association between SNPs in the histidine ammonia-lyse gene (HAL) gene and signs of cow dairy productivity of the Chinese Holstein breed, indicating the potential role of HAL variants in these signs. These identified SNPs may be genetic markers used in genomic selection schemes to accelerate the genetic growth of dairy livestock productivity traits.

Thus, domestic and foreign experience shows that the effectiveness of selection depends on many genetic, paratypical and economic factors (Ng-Kwai-Hang et al., 1984; Lund et al., 2011; Kramarenko et al., 2019; Lu et al., 2021; Pedrosa et al., 2021). The possibility of purposefully creating a highly productive animal population is significantly correlated with the presence of information about genes that control signs of productivity. In this regard, the task of identifying and using marker genes responsible for the manifestation of economically valuable signs becomes urgent.

The composition of milk is an important breeding characteristic of dairy breeds of cattle, especially in the conditions of modern animal husbandry; therefore, the task arises to analyze the influence of polymorphism of protein and lipid metabolism genes on the formation of milk productivity indicators in cows of the dairy direction of domestic breeding productivity.

MATERIALS AND METHODS

Materials
To conduct the study, experimental groups were formed from breeding cattle of the dairy direction of productivity - Ukrainian Red Dairy (URD, n = 32 heads), Ukrainian Black-speckled Dairy (UBSD, n = 32 heads), Ukrainian Red-speckled Dairy (URSD, n = 28 heads) breeds of the leading enterprise in the south of Ukraine PSP "Kolos-2011" Ochakov region.

Ethical regulation
The rules for handling animals in experiments comply with European legislation on the protection and comfort of animals kept on farms (Directive No. 95/58 EU "On the Protection of Farm Animals" of the Council of the EU of 20.07.1998, as amended by EU Regulation No. 806 / 203 of 14.04.2003, No. 91/630 EU "Minimum standards for the protection of pigs" of 19.11.1991, as amended by the EU Regulation. Pilot study protocol for blood sampling in cows approved by the local commission on bioethics of the National University of Life and Environmental Sciences Ukraine on Good Clinical Practice (GCP) for the protection and humane treatment of experimental animals.

Methods
The characterization of the polymorphism of the genes studied was determined by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) (Grodzicker et al, 1974; Alexander et al., 1988; Pedrosa et al., 2021). Genomic DNA was isolated from the peripheral blood of animals according to the method of Kostyunina et al. (2020) and using the standard commercial kit "DNA Sorb B" manufactured by Amplissens (Russia), according to the manufacturer's recommendations (Pedrosa et al., 2021). The DNA concentration was tested by electrophoresis in a 2% agarose gel. To carry out the polymerase chain reaction, a reaction mixture of 10 μL was used in operation: dH2O - 4.3 μL, PCR buffer 5 (15 mMg-1.0 mL) - 2.0 μL; Deoxynucleotide triphosphates (dNTP) mixture of 10 (2 mM each) - 0.8 μL; two primers (70 ng each) - 0.8 μl; Taq polymerase (1 ml/1000 U) - 0.1 μL; DNA 50-100 ng - 2.0 μl.

Restriction products were separated by electrophoresis in 2% agarose gel followed by staining in ethidium bromide solution. Visualization was carried out on a transciluminator in UV light, followed by electropherogram photography by a digital camera. The size differentiation of amplicons was carried out using the molecular weight marker Gene Ruler TM 50 bp DNA Ladder, SM0378 (Fermentas®, Lithuania; Oztabak et al., 2008). The temperature regime and the number of PCR amplification cycles for each gene were determined separately. For the analysis of the polymorphism of the structural loci k-Cn, βLG, TG, Pit-1, and LEP, restriction enzymes matched for each locus were used; typed immediately after PCR analysis (Grobet et al., 1998).

RESULTS AND DISCUSSION

Identification of selection signatures allows a better understanding of the evolutionary processes, functions and organization of genes in the genome. Of particular note are genes, certain allelic variants of which are associated with the quality of raw materials. In cattle, genes whose polymorphism is associated with dairy productivity are known and investigated by us (Figure 1).
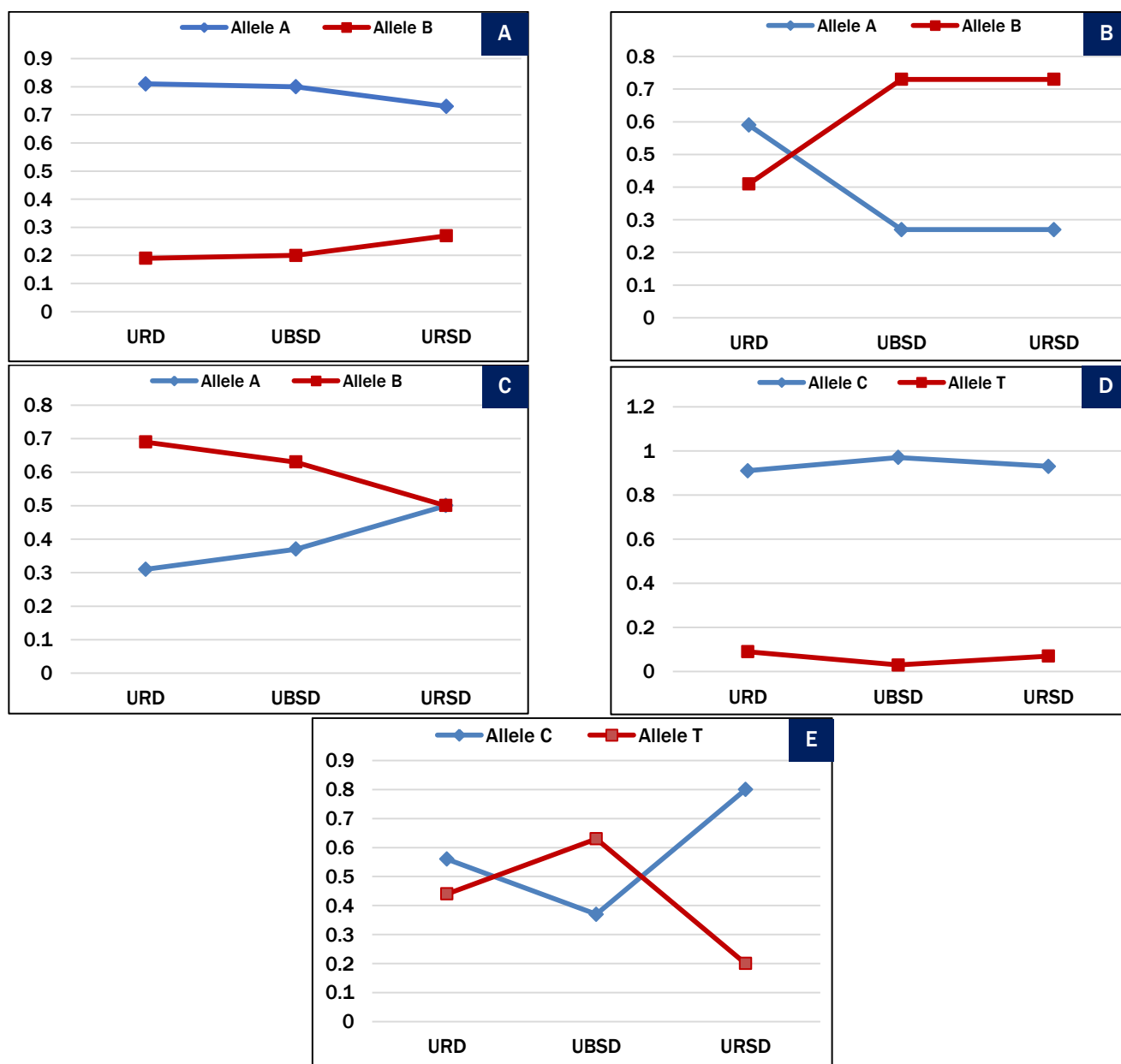

Figure 1 - Distribution of allelic variants frequencies by loci in cows. A: Capa-casein gene (CSN3); B: Beta-lactoglobulin (BLG); C: Leptin (LEP); D: pituitary-specific transcription factor (Pit-1); E: TG5 thyroglobulin (TG-5) gene. Ukrainian Red Dairy (URD): n=16, Ukrainian Black-speckled Dairy (UBSD): n=15; Ukrainian Red-speckled Dairy (URSD): n=15.

The studied genes are divided into several groups: A) milk protein genes, which affect the protein content in milk, its technological properties, quality and yield of protein-containing products; B) lipid metabolism genes synthesized in adipocytes, are responsible for regulating the body weight of the animal, its consumption of feed and its fat deposits, and are also involved in the synthesis of milk fats and genes of regulatory systems, which generally affect the productive performance of the body and serve as a somatic regulator of animal growth (Khatib et al., 2007; Miluchová et al., 2018).

That's how, capa-casein (CSN3) is connected with milk protein and its coagulation characteristics, including the role of a stabilizing factor in the formation of micelles, blocking their aggregation. And when it is dissolved, milk coagulates, casein precipitate formation and clot formation and affects the mass share of fat in milk, the volume of milk yield. Beta-lactoglobulin (BLG) is associated with a higher concentration of fat and protein in milk and has a significant effect on the creation of active immunity in calves. Meanwhile, as a pituitary-specific transcription factor (Pit-1) is known for the function of increasing milk yield and fat yield. Leptin provides formation of fat deposits and increases productivity in

terms of fat content in milk during the first lactation period of livestock. Thyroglobulin (TG) affects the total percentage of fat in tissues, including milk formation (Hartati et al., 2018).

The results of analysis of allelic variants distribution of the investigated structural genes of protein and lipid metabolism in the above rocks are presented in the Tables 1 - 5. Studies of associations between productivity indicators and different genotypes of loci made it possible to establish a difference in the dependence of individual genotypes and signs of livestock breeding - yield, the content of fat and protein in milk depending on the breed belonging of cows and their individual characteristics.

Analyzing the productivity indices at the locus of the leptin gene, we found that cows of three breeds that were included in the study with the CC genotype had a significantly higher (P < 0.05) fat content in milk than cows with the CT and TT genotype (behind the higher lactation index, Table 1). At the same time, no significant difference was found between the control and experimental groups in the test animals of the above-mentioned genotypes in terms of fat content and their age no significant difference was found between the control and experimental groups.

The results of evaluation of experimental animals by the locus of the leptin gene by the parameters of utilization depending on the genotype indicated that the best were representatives with the available alleles of the breed URSD CT and exceeded the URD taken as a control group: for the first lactation by 1425 kg of milk, for the second by 3006 kg, above 825 kg (P < 0.05). In terms of protein content in milk, all animals are inferior to the control group in the range from -0.01 to -0.28% (P < 0.001) (Table 1), however, this trend is not traced in terms of protein milk content due to their milk yield. Thus, the indicators of all groups of cows at the locus of the leptin gene that were included in the study, for the first, second third and higher lactation, tend to increase their productivity, which is explained by their physiological maturity and the development of productive qualities with age. And in the context of experimental groups, heterozygous genotypes of CT turned out to be better.

Studies of the association of the leptin gene with productivity and reproducibility were carried out by Liefers et al. (2005). Thus, the authors found that the polymorphism located on intron 2 of the leptin gene explains a significant part of the variability in milk yield. An SNP associated with the first postpartum luteal activity (FPLA) was found in the propromotor region of the leptin gene. This SNP could be a potential marker of dairy cow fertility. Another SNP on the leptin promoter was associated with energy balance and dry matter intake (DMI), where high dry matter intake occurred together with higher energy balance. The scientists identified two genotype combinations of the aforementioned three associated leptin SNPs that had high hopes along with good energy balance and fecundity. Kononoff et al. (2005), observed an association between leptin genotype and carcass characteristics in beef cattle. The carcass mass of animals with CC genotype tended to increase than that of animals with TT genotype (365.5 versus 362.3 kg). No significant difference in carcass weight between TT and CT genotypes was observed.

In the course of cow productivity analysis of all three test breeds of Ukrainian selection by capa-casein locus Table 2, it was established, that individuals with AA genotype had higher yield rates, compared to the peers who were inherent in the AB genotype from 250 kg to 784 kg considering, that the yield level of the control group of the breed URD for higher lactation was 7943 ± 793.1 kg (P < 0.05). The highest level of hoot in the section of the studied breeds was characterized by cows of the Ukrainian Black-speckled Dairy breed, which had allele A in their genotype, compared to individuals who had allele B in the genome. It should be noted that only representatives of the Ukrainian Red-speckled Dairy breed are characterized by the presence of females with a homozygous BB genotype can be explained by their origin.

The revealed trends of intergenerational differentiation by fat and protein content in milk of cows with different genotypes by the capa-casein locus are multidirectional and statistically unreliable. In our opinion, this is due to the small number of groups of studied animals that are carriers of this genotype, the frequency of which is low in the populations of the breeds that were studied. Thus, we have established a relationship between economically useful signs of cow genotype by gene kapa-casein. Namely, the animal homozygous genotype AA was characterized by the inherent manifestations of milk productivity according to the signs of hoax, fat and protein content, as well as their amount in milk, compared to other genotypes, both in the context of experimental breeds and in their age dynamics. But the best raw suitability was characterized by milk obtained from cows with the BB genotype. It is also confirmed by Morkūnienė et al. (2016) which investigated the polymorphism of the kappa-casein gene of Lithuanian dairy cattle. They found that the most common genotype of AA, which had 49.2% of the studied animals. The greatest influence on the processing properties of milk was the BB genotype, found only in 2.1% of cows (Morkūnienė et al., 2016). Similar data were obtained by Machulnyi (2018), in herds of red steppe, Ukrainian Black-speckled Dairy and Ukrainian Red Dairy breeds of different body formation intensities. Representatives of homozygous AA genotypes were characterized by higher milk productivity, and the number of cows with this genotype is significantly higher in the herd, than the proportion of the capa-casein gene more technologically valuable B allele, but at the same time milk of URD and UBSD of cattle of slow formation intensity, and a rapid growth type URD will provide the highest yield of the final product within 10%, although the dairy productivity of such animals has not always been high.

When evaluating the cows of the experimental groups by the locus of the thyroglobulin gene, there was a tendency to increase the level of impact with the CC genotype, while the animals of the breed UBSD probably exceeded the control group in terms of impact (for the first lactation) by 760 kg (P<0.05). At the same time, in terms of protein content in milk, no significant difference was observed in cows with different genotypes for the thyroglobulin gene. It should be noted that in all three groups of cows there were no individuals with the TT genotype (Table 3). This indicates a low frequency of this genotype in the studied animal populations and is presumably associated with their origin.

In none of the studied populations of cows of Ukrainian selection, there was a significant difference between the fat content in milk among carriers of different genotypes according to the thyroglobulin gene. Although in UBSD cows carriers of the homozygous CC genotype for the TG5 gene, there was a tendency to increase milk fat content with an insignificant difference relative to the control data. But at the same time, the study and analysis of the genetic structure for the polymorphism of the TG5 gene for the leading dairy breeds of Ukraine confirmed the positive effect of the C allele on the increase in fat content in milk. Therefore, the increase in its frequency in populations of Ukrainian dairy breeds is probably due to the influence of various artificial selection factors based on the signs of inductance, the manifestation of which is associated with the polymorphism of this gene. Thus, the effect of homo- or heterozygosity of the thyroglobulin gene on most productive features of cows was established, both in the cross-section of breeds and in age dynamics. Cows that were carriers of the homozygous CC genotype are characterized by higher values of milk productivity in the section of the first, second, third and highest lactation, regardless of the breed affiliation of the cows. At the same time, another homozygous genotype of TT was not found in any of the studied breeds of UBSD, URSD and URD, which, in our opinion, is associated with the individual characteristics of these breeds and their origin, and high homozygosity according to the allele C.

There are also contradictory data of Khatib et al. (2007), who did not reveal the relationship between milk yield and milk composition with Holstein dairy cattle and the TG5 gene. A, Putra et al. (2019) found in Indonesian cattle that the TG5 gene plays an important role in the regulation of metabolism and affects the differentiation of adipocytes, growth and homeostasis of fat depots and, as a result, contributes to an increase in milk productivity of cows in such an indicator as fat content in milk. Similar data were obtained by Dubey et al. (2015) on dairy breeds of cattle Mehsana and Nili Ravi.

A study of animals with different genotypes according to the β-lactoglobulin gene showed that there was no obvious change in the increase or decrease in the milk productivity level and fat content in milk depending on the genotype in the section of research breeds of cows (Table 4). But a tendency to an increase in the protein content in milk in cows of the UBSD breed was revealed by the AB genotype by the β-lactoglobulin locus, which is statistically not reliable. Thus, the effect of the homo- or heterozygous state of BLG globulin on signs of milk productivity is less noticeable. Thus, cows of UBSD (II lactation), URSD (III lactation) with genotype AA were characterized by somewhat reduced fatigue, and the largest representatives of the first group with genotype AA were alternately during ontogenesis, with the exception of II lactation. In general, homo and heterozygous genotypes of UBSD and URD of rocks of different combinations were observed with higher productivity values.

Mixed results were also obtained by Indian scientists (Bangar et al., 2021). The results of their studies also showed that the BLG gene variants had an inauthentic association with fatigue in all genetic models. Although positive effects of BLG in some models were observed, they did not correspond to statistical significance due to high heterogeneity between studies concluding that BLG genotypes had an uncertain effect on milk yield. It was concluded that BLG markers can also be useless for increasing milk yield in Indian dairy cows. Contrasting study results were obtained by Ozdemir et al. (2018), establishing a valid relationship between BLG genotypes and daily fatigue, fat and protein content in milk, and protein quantity. Which indicates that BLG-globulin genes are useful for improving the features of selection studied and can be used as molecular markers in predicting productivity. Cardona et al. (2016), also identified additive effects at the BLG locus for all signs of milk productivity during most lactation, but there was a dominant effect only in the early stages of fat release. For this gene, allele A had a favorable genetic effect throughout lactation on milk yield and quality indicators in tropical dairy goats.

Assessment of the productivity of cows of different genotypes according to the gene of the pituitary-specific Pit-1 factor showed that cows with BB genotype probably dominated peers with AA genotype in terms of hoax level (Table 5), this trend was observed in cows with UBSD their difference between the three research groups in terms of this indicator was in the range from 1000 to 1388 kg (P>0.95). The presence of allele B in heterozygotes AB predetermined the high milkiness of cows of experimental groups, all breeds included in the study without exception. And such animals exceeded the homozygous analogues with the AA genotype. By the mass fraction of fat in milk, a probable advantage of cows with an allele A in the genotype over peers was found for which the BB genotype was characteristic (P<0.05). According to the level of protein in the milk of cows belonging to three Ukrainian dairy breeds with different genotypes by gene Pit-1 we did not establish a reliable difference in favor of this or that group. At the same time, we did not find any homozygous genotypes of the AA variant in representatives of the red dairy breed by gene Pit-1. It seems that, there is association with the individual breed features of this cattle and gene mutation during the selection process at the stage of its creation (Li et al., 2021; Seo et al., 2022). Thus, the pituitary-specific factor Pit-1 gene was associated with high-yield animals with homozygous AA and BB genotypes for all lactation among livestock UBSD and URSD, while URD cows had the best BB genotypes, which also causes milk fat content in these animals. But the amount of fat did not differ significantly between homo- and heterozygous genotypes. Mattos et al. (2004) also established in the Gyr breeding bull population associations of Pit-1 with fat percentage and fat yield, respectively, in their daughters. Edriss et al. (2009) in studies of the association of PIT-1 gene polymorphism with birth weight, milk and reproductive qualities in cows of the Isfahan Holstein breed, the Pit-1 gene was considered as a marker candidate for milk production due to the regulation of expression of the bGH and prolactin gene necessary for breast and milk development. At the same time, negative data were obtained, as Aytekin and Boztepe (2013) noted that the polymorphism of the Pit-1 gene cannot be used as a candidate gene for the selection of dairy signs in brown Swedish cattle, since the authors did not find associations between the Pit-1 gene and signs of productivity.

Table 1 - Association of LEP gene SNPs with signs of dairy productivity of cows									
	Locus genotype ($\bar{X} \pm S_x$) in the breed section								
Characteristic, key figure	CC			CT			TT		
	UBSD	URSD	URD	UBSD	URSD	URD	UBSD	URSD	URD
(1 lactation)	2	10	4	6	4	10	7	1	2
Milk yield, kg	6646±908	5444±1055	6356±1706	6514±489	7220±1425*ᵖ	5348±960	6166±429	5299±0	5856±660
Fat content,%	3.81±0.110	3.77±0.106*ᵖ	3.78±0.165	3.87±0.027	3.48±0.321	3.81±0.117	3.84±0.071	3.60±0	3.79±0.040
Quantity of fat, kg	252.2±27.30	205.5±42.38	243.0±74.85	256.0±17.02	270.5±56	204.3±38.78	237.2±19.23	191 ±0	222.0±27.62
Protein content,%	3.20±0.008	3.10±0.070***	3.21±0.038	3.13±0.100	3.14±0.019	3.25±0.100	3.19±0.088	3.05±0	3.33±0.025***ᵃ
Amount of protein, kg	212.7±29.07	168.7±33.15	204.5±55.69	203.7±9.92	226.3±43.74	174.1±30.49	196.2±11.42	161.6±0	194.6±20.48
(2 lactation)	2	8	4	5	2	10	6	1	2
Milk yield, kg	5123±400	6179±1697	6897±1629	6988±895	8965±581	5959±903	7232±1193	6933±0	7759±1231
Fat content,%	3.77±0.020	3.74±0.098	3.69±0.080	3.77±0.137	3.63±0.030	3.77±0.112	3.81±0.132	3.80±0	3.62±0.015
Quantity of fat, kg	193.2±16.12	236.1±62.84	253.9±55.19	262.2±24.00	325.5±23.50	223.2±28.78	275.9±46.87	264±0	280.3±43.35
Protein content,%	3.20±0	3.10±0.075**	3.20±0.025	3.14±0.128	3.10±0.050*	3.23±0.105	3.18±0.083	3±0	3.30±0.035**ᵃ
Amount of protein, kg	163.9±12.82	191.3±52.74	220.6±52.27	218.5±23.08	277.6±13.53	192.6±31.42	228.5±32.38	208±0	255.2±21
(3 lactation)	2	6	2	3	0	8	5	1	2
Milk yield, kg	9327±1719	6475±617	5173±427	5920±1408	-	7768±1090	8049±1413	5438±0	8728±772
Fat content,%	3.84±0.075	3.79±0.153	3.86±0.085	3.61±0.029	-	3.78±0.203	3.73±0.122	3.87±0	3.69±0.190
Quantity of fat, kg	359±72.94	245.4±25.80	199.8±20.88	213.9±52.85	-	296.4±50.26	299.5±53.85	210.5±0	320.6±11.92
Protein content,%	3.10±0*	3.08±0.056*	3.21±0.055	3.17±0.111	-	3.23±0.081	3.16±0.088	3.0±0	3.18±0.075
Amount of protein, kg	289.1±53.30	199.8±22.02	165.5±10.86	188.4±51.10	-	250.8±35.87	253.0±39.22	163.1±0	276.5±17.98
(lactation veins)	2	10	4	6	4	10	7	1	2
Milk yield, kg	9327±1719	7856±1186	8036±978	7847±787	8046±1539*	7221±942	7860±1474	5438±0	9245±254.5
Fat content,%	3.84±0.075	3.69±0.066	3.84±0.103*ᵇ	3.71±0.087	3.62±0.073	3.69±0.102	3.64±0.069	3.87±0	3.62±0.020
Quantity of fat, kg	359.0±72.94	289.8±46.05	307.4±31.86	290.7±22.54	292.9±59.49	265.6±33.96	285.8±51.78	210.5±0	334.7±11.06
Protein content,%	3.10±0	3.08±0.074***	3.24±0.062	3.09±0.092**ᵃ	3.11±0.038	3.23±0.070	3.16±0.069	3.00±0	3.21±0.055
Amount of protein, kg	289.1±53.30	244.4±36.79	260.2±22.00	242.2±21.67	249.9±46.70	233.2±30.31	247.8±43.12	163.1±0	296.2±3.07

Significant: *=P<0.05; **=P<0.01; ***=P<0.001 (compared to animals of the third control group); a= P<0.05; b= P<0.01. (in comparison of animals of the first experimental group with analogues of the second experimental group) Mean values with different superscripts in the column differ significantly (p<0.05). Leptin (LEP); Ukrainian Red Dairy (URD); Ukrainian Black-speckled Dairy (UBSD); Ukrainian Red-speckled Dairy (URSD).

Table 2 - Association of CSN3 gene SNPs with signs of dairy productivity of cows

Characteristic, key figure	Locus genotype ($\bar{X} \pm S_X$) in the breed section								
	AA			AB			BB		
	UBSD	URSD	URD	UBSD	URSD	URD	UBSD	URSD	URD
(1 lactation)	8	8	10	6	6	6	0	1	0
Milk yield, kg	6598±56	5999±1612**	6103±1152	6027±358***	5894±949	4932±528	-	5259±0	-
Fat content,%	3.81±0.068	3.64±0.233*	3.81±0.111	3.91±0.028**a	3.70±0.128	3.79±0.143	-	3.93±0	-
Quantity of fat, kg	251.4±22.54	225.8±63.88	233.8±50.61	239.7±19.53	218.9±41.47	186.8±20.90	-	207±0	-
Protein content,%	3.12±0.086	3.15±0.025	3.23±0.093	3.23±0.056	3.07±0.056	3.29±0.068	-	3.0±0	-
Amount of protein, kg	205.7±13.86	188.7±49.90	197.5±39.46	194.8±12.34	181.1±32.63	162.2±19.88	-	157.8±0	-
(2 lactation)	6	5	10	6	5	6	-	1	-
Milk yield, kg	7166±1317	7038±1627	6699±1187	6402±656	6136±1680	5950±1013	-	8381±0	-
Fat content,%	3.81±0.142**	3.69±0.098	3.67±0.102	3.78±0.104	3.73±0.087	3.83±0.080	-	3.83±0	-
Quantity of fat, kg	272.1±48.67	258.4±53.95	245.1±40.25	241.4±24.37	238.2±64.60	226.2±32.49	-	321.0±0	-
Protein content,%	3.11±0.102	3.15±0.060	3.21±0.094	3.23±0.058	3.05±0.060	3.26±0.060	-	3.00±0	-
Amount of protein, kg	222.1±38.32	220.2±49.16	215.6±40.89	206.0±19.68	188.1±52.91	193.8±33.09	-	251.4±0	-
(3 lactation)	4	2	6	5	4	5	-	1	-
Milk yield, kg	8638±1537*	7165±258	7854±1353	6693±1335***a	5932±777***a	6663±975	-	6228±0	-
Fat content,%	3.73±0.182	3.95±0.005	3.89±0.147	3.70±0.062	3.77±0.145	3.70±0.166	-	3.68±0	-
Quantity of fat, kg	323.3±23.22	282.7±9.84	308.4±60.98	248.2±51.88	222.1±20.72	245.9±34.86	-	229.2±0	-
Protein content,%	3.10±0.080	3.15±0.050	3.22±0.073	3.20±0.040	3.05±0.050	3.24±0.072	-	3.00±0	-
Amount of protein, kg	267.9±43.57	225,8±11.73	252.8±46.15	213.8±39.95	180.9±23.84	215.8±30.66	-	186.8±0	-
(lactation veins)	8	8	10	6	6	6	-	1	-
Milk yield, kg	8420±1358*	8193±1456	7943±793	7495±817	7650±825	7234±1017	-	6228±0	-
Fat content,%	3.68±0.099	3.68±0.094	3.75±0.116	3.71±0.068	3.68±0.058	3.66±0.122	-	3.68±0	-
Quantity of fat, kg	310.5±48.57	302.0±55.48	296.6±27.15*	278.0±30.59	281.3±30.89	264.8±36.11	-	229.2±0	-
Protein content,%	3.09±0.079	3.09±0.058	3.23±0.075	3.20±0.067	3.09±0.072	3.24±0.052	-	3.0±0	-
Amount of protein, kg	260.1±43.13	252.7±41.78	256.1±26.94	239.4±24.84	239.8±30.49	234.1±34.35	-	186.8±0	-

Significant: *=P<0.05; **=P<0.01; ***=P<0.001 (compared to animals of the third control group); a= P<0.05; b= P<0.01. (in comparison of animals of the first experimental group with analogues of the second experimental group) Mean values with different superscripts in the column differ significantly (p<0.05). Capa-casein gene (CSN3); Ukrainian Red Dairy (URD); Ukrainian Black-speckled Dairy (UBSD); Ukrainian Red-speckled Dairy (URSD).

Characteristic, key figure	Locus genotype ($X \pm S_X$) in the breed section								
	CC			CT			TT		
	UBSD	URSD	URD	UBSD	URSD	URD	UBSD	URSD	URD
(1 lactation)	14	13	13	1	2	12	0	0	0
Milk yield, kg	6436±540*	5985±1410	5676±1132	5433±0	5399±100.5	5607±1204	-	-	-
Fat content,%	3.85±0.063	3.70±0.176	3.81±0.109	3.87±0	3.55±0.050	3.76±0.149	-	-	-
Quantity of fat, kg	249.3±21.59	226.5±54.60	216.9±46.08	210.3±0	191.7±0.75	212.7±0.15	-	-	-
Protein content,%	3.16±0.086	3.12±0.056	3.25±0.092	3.30±0	3.03±0.025	3.25±0.033	-	-	-
Amount of protein, kg	202.9±13.88	186.7±45.26	184.8±36.71	179.3±0	163.3±1.69	181.8±36.96	-	-	-
(2 lactation)	12	9	13	1	2	3	-	-	-
Milk yield, kg	6851±1205	6824±1996	6502±1344	6358±0	6416±516	6051±764	-	-	-
Fat content,%	3.79±0.126	3.73±0.097	3.73±0.126	3.86±0	3.7±0.10	3.73±0.093	-	-	-
Quantity of fat, kg	259.0±43	252.9±69.94	241±44.13	245.4±0	264.0±0	224.9±22.32	-	-	-
Protein content,%	3.16±0.102	3.1±0.078	3.23±0.093	3.20±0	3.05±0.050	3.23±0.044	-	-	-
Amount of protein, kg	215.7±33.32	211.4±61.93	210.2±46.06	203.5±0	195.5±12.55	195.3±23.34	-	-	-
(3 lactation)	9	5	9	1	2	9	-	-	-
Milk yield, kg	7783±1742	6390±672	7239±1479	6601±0	6169±731	7648±137	-	-	-
Fat content,%	3.72±0.123	3.83±0.138*a	3.78±0.183	3.64±0	3.74±0.135	3.90±0.03	-	-	-
Quantity of fat, kg	290.8±67.65	244.9±30.25	275.9±60.92	240.3±0	229.4±18.97	298.2±3.05	-	-	-
Protein content,%	3.14±0.094	3.08±0.064	3.21±0.075	3.20±0	3.05±0.05	3.3±0	-	-	-
Amount of protein, kg	244.2±54.19	197.0±23.05	232.3±48.63	211.2±0	188.5±25.38	252.4±4.52	-	-	-
(lactation veins)	14	13	13	1	2	9	-	-	-
Milk yield, kg	8153±1210	7942±1380	7687±1092	6601±0	7211±2278	7637±148	-	-	-
Fat content,%	3.70±0.094	3.67±0.069	3.68±0.102	3.64±0	3.7±0.1	3.85±0.1	-	-	-
Quantity of fat, kg	301.6±43.07	292.3±52.45	282.6±38.79	240.3±0	266.5±3.09	293.9±5.72	-	-	-
Protein content,%	3.13±0.086	3.08±0.061	3.21±0.061	3.2±0	3.1±0.1	3.3±0	-	-	-
Amount of protein, kg	254.7±36.84	246.6±43.31	246.9±36.45	211.2±0	223.8±15.85	252±4.9	-	-	-

Table 3 - Association of TG5 gene SNPs with signs of dairy productivity of cows

Significant: *=P<0.05; **=P<0.01; ***=P<0.001 (compared to animals of the third control group); a= P<0.05; b= P<0.01. (in comparison of animals of the first experimental group with analogues of the second experimental group) Mean values with different superscripts in the column differ significantly (p<0.05). TG5 thyroglobulin gene (TG-5); Ukrainian Red Dairy (URD); Ukrainian Black-speckled Dairy (UBSD); Ukrainian Red-speckled Dairy (URSD).

Table 4 - Association of BLG gene SNPs with signs of cow dairy productivity

Characteristic, key figure	Locus genotype ($X \pm S_x$) in the breed section								
	AA			AB			BB		
	UBSD	URSD	URD	UBSD	URSD	URD	UBSD	URSD	URD
(1 lactation)	1	3	7	6	2	5	8	11	4
Milk yield, kg	7554±0	6681±1736	5884±1290	6663±413*b	4380±331	6014±842	6000±289	5805±123	4839±838
Fat content,%	3.7±0	3.72±0.147	3.81±0.118	3.88±0.04	3.80±0.045	3.82±0.102	3.84±0.062	3.67±0.2	3.76±0.15
Quantity of fat, kg	279.5±0	248.5±65	225.1±52.97	262.7±11.21	166±11	230.7±37.67	230.6±12.71	218.7±51.33	182.4±33.9
Protein content,%	3.20±0	3.03±0.044	3.24±0.089	3.16±0.108	3.20±0	3.3±0.058	3.17±0.081	3.12±0.053	3.21±0.106
Amount of protein, kg	241.7±0	203.6±56.21	190.2±40.03	210.1±8.13	140.2±10.61	198.5±27.69	189.8±6.66	181.1±40.17	156.2±29.40
(2 lactation)	1	2	7	5	2	5	7	8	4
Milk yield, kg	4722±0	7140±1240	6123±1373	6614±609	5475±1778	6727±880	7255±1277	7034±380	6549±1220
Fat content,%	3.75±0	3.72±0.115	3.77±0.109	3.77±0.097	3.70±0.13	3.63±0.135	3.82±0.145	3.71±0.092	3.77±0.082
Quantity of fat, kg	177.1±0	292.5±28.5	229.8±45.32	248.9±22.42	200.5±58.47	243.8±30.89	275.9±45.34	259.6±59.19	245.2±39.23
Protein content,%	3.20±0	3.05±0.05	3.21±0.088	3.17±0.136	3.23±0.075	3.29±0.05	3.16±0.078	3.08±0.063	3.19±0.095
Amount of protein, kg	151.1±0	217.2±34.27	196.5±43.6	208.8±15.56	175.2±53.23	221.2±28.57	228.0±35.77	217.1±53.92	209.3±41.9
(3 lactation)	1	2	5	4	2	3	5	4	3
Milk yield, kg	11046±0	6564±336	7304±1744	6201±1457	7424±0	6970±1483	8161±896*	5934±779**a	7671±282.4
Fat content,%	3.91±0	3.64±0.04	3.87±0.218	3.67±0.08	3.94±0	3.76±0.087	3.71±0.134	3.85±0.106	3.73±0.167
Quantity of fat, kg	431.9±0	238.8±9.6	287.4±84.58	228.2±55.94	292.5±0	261,9±55.33	302.5±35.24	228.3±26.82	285.8±10.35
Protein content,%	3.1±0	3.05±0.05	3.25±0.055	3.18±0.088	3.2±0	3.26±0.011	3.14±0.088	3.05±0.05	3.15±0.1
Amount of protein, kg	342.4±0	200.4±13.53	237.5±56.71	197.2±47.29	237.6±0	227.5±48.56	255.5±25.58	180.9±23.89	241.9±16.32
(lactation veins)	1	3	7	6	2	5	8	11	4
Milk yield, kg	11046±0	7668±1078	6947±1182**a	7376±820	8338±1085	8303±478	8181±1119	7750±1292	8174±407
Fat content,%	3.91±0	3.67±0.047	3.76±0.135	3.75±0.048	3.65±0.075	3.71±0.086	3.63±0.059	3.68±0.083	3.65±0.111
Quantity of fat, kg	431.9±0	281.7±43.09	260.4±45.36	276.6±28.39	304.7±45.82	308±19.41	296.4±38.36	285.2±48.01	297.9±14.52
Protein content,%	3.1±0	3.10±0.067	3.24±0.055	3.16±0.108	3.08±0.075	3.25±0.06	3.11±0.058	3.09±0.062	3.19±0.095
Amount of protein, kg	342.4±0	238.1±34.19	224.8±40.02	232.8±26.63	255.6±27.13	269.6±12.46	253.4±32.16	241±42.13	260.9±16.08

Significant: *=P<0.05; **=P<0.01; ***=P<0.001 (compared to animals of the third control group); a= P<0.05; b= P<0.01. (in comparison of animals of the first experimental group with analogues of the second experimental group) Mean values with different superscripts in the column differ significantly (p<0.05). B: Beta-lactoglobulin (BLG); Ukrainian Red Dairy (URD); Ukrainian Black-speckled Dairy (UBSD); Ukrainian Red-speckled Dairy (URSD).

Table 5 - Association of Pit-1 gene SNPs with signs of dairy productivity of cows									

Characteristic, key figure	Locus genotype ($X \pm S_x$) in the breed section								
	AA			AB			BB		
	UBSD	URSD	URD	UBSD	URSD	URD	UBSD	URSD	URD
(1 lactation)	1	3	0	10	9	10	4	3	6
Milk yield, kg	6117±0	5690±652	-	6293±543	6202±1630	5431±1013	6622±633*[b]	5238±947	6050±1297
Fat content,%	3.83±0	3.84±0.058	-	3.86±0.057	3.63±0.211	3.77±0.134	3.83±0.065	3.69±0.127	3.85±0.085
Quantity of fat, kg	234.3±0	218.7±27.78	-	243.0±22.56	232.3±3.11	206±43.1	259.1±17.1	193.6±35.14	233.2±52.46
Protein content,%	3.20±0	3.12±0.078	-	3.15±0.11	3.11±0.051	3.22±0.098	3.20±0.025	3.1±0.067	3.30±0.077
Amount of protein, kg	195.7±0	177.1±19.15	-	197.7±12.59	192.7±51.79	175.4±32.42	211.8±18.61	162.7±29.56	199.1±41.16
(2 lactation)	1	2	-	9	6	10	3	3	6
Milk yield, kg	7732±0	4804±1107	-	7116±1176	7149±1656	6394±1002	5602±638.9	7251±1526*[b]	6458±1663
Fat content,%	4.0±0	3.81±0.025	-	3.76±0.131	3.72±0.107	3.69±0.13	3.82±0.071	3.68±0.078	3.79±0.102
Quantity of fat, kg	309.3±0	182.5±40.5	-	266.6±39.35	264.5±59.51	234.7±28	214.7±28.72	284±42.82	243.5±59.34
Protein content,%	3.2±0	3.15±0.15	-	3.14±0.11	3.06±0.061	3.20±0.094	3.23±0.044	3.12±0.022	3.28±0.069
Amount of protein, kg	247.4±0	149.7±27.66	-	222.2±31.38	219.2±52.82	205.3±35.87	181.4±23.36	226.4±49.45	211.0±52.53
(3 lactation)	1	2	-	6	3	7	3	2	4
Milk yield, kg	8489±0	6972±452	-	7556±1518	5512±477	7934±1026	7610±2290**	6903±350	6227±992
Fat content,%	4.0±0	3.79±0.15	-	3.64±0.07	3.83±0.102	3.89±0.135	3.76±0.1	3.78±0.175	3.65±0.06
Quantity of fat, kg	339.6±0	264.9±27.59	-	274.9±54.05	210.7±12.34	310.4±51.6	289.4±94.97	260.6±12.21	226.7±35.68
Protein content,%	3.1±0	3.1±0.1	-	3.17±0.111	3.03±0.044	3.20±0.095	3.13±0.044	3.1±0	3.29±0.015
Amount of protein, kg	263.2±0	216.6±20.98	-	238.9±47.43	167.0±13.23	253.9±35.04	237.3±70.08	214±0.11	204.6±32.82
(lactation veins)	1	3	-	10	9	10	4	3	6
Milk yield, kg	8489±0	7493±1287	-	7918±1300	7557±1160	7689±790	8270±1388	9061±1047	7659±1122
Fat content,%	4.0±0	3.74±0.076	-	3.65±0.067	3.66±0.069	3.73±0.136	3.82±0.044	3.68±0.069	3.69±0.089
Quantity of fat, kg	339.6±0	279.8±47.16	-	288.3±44.48	276.9±43.8	285.8±25.45	316.9±57.52	333.8±42.77	282.8±45.2
Protein content,%	3.1±0	3.05±0.067	-	3.11±0.086	3.09±0.053	3.22±0.076	3.19±0.063	3.12±0.078	3.25±0.05
Amount of protein, kg	263.2±0	228.1±36.44	-	245.1±38.07	234.8±39.83	247.3±27.02	263.7±44.87	281.6±27.94	248.8±36.6

Significant: *=P<0.05; **=P<0.01; ***=P<0.001 (compared to animals of the third control group); a= P<0.05; b= P<0.01. (in comparison of animals of the first experimental group with analogues of the second experimental group) Mean values with different superscripts in the column differ significantly (p<0.05). Pituitary-specific transcription factor (Pit-1); Ukrainian Red Dairy (URD); Ukrainian Black-speckled Dairy (UBSD); Ukrainian Red-speckled Dairy (URSD).

CONCLUSION

1. Indicators of all groups of cows by the locus of the leptin gene, which were included in the study, for the first, second third and higher lactation tended to increase their productivity, which is explained by their physiological maturity and the development of productive qualities with age. And in the context of experimental groups, heterozygous genotypes of CT turned out to be the best.

2. The relationship between the economically useful signs of cows and their genotype by the capa-casein gene has been proven. Namely, animals with homozygous genotype AA were characterized by higher manifestations of milk productivity in terms of utilization, fat and protein content, as well as their amount in milk, compared to other genotypes, both in the context of experimental breeds and in age dynamics. But the best raw suitability will be characterized by milk obtained from cows with the BB genotype.

3. The influence of homo- or heterozygosity of the thyroglobulin gene on most productive features of cows, both in the section of breeds and in age dynamics, has been established. Cows carrying the homozygous CC genotype were characterized by higher values of milk productivity in the section of the first, second, third and highest lactation, regardless of the breed affiliation of the cows. At the same time, the second homozygous genotype of TT was not found in any of the studied breeds of UBSD, URSD and URD, which, in our opinion, is associated with the individual characteristics of these breeds and their origin.

4. It was determined that the effect of the homo- or heterozygous state of BLG globulin on signs of milk productivity is less noticeable. Thus, cows of UBSD (II lactation), URSD (III lactation) with genotype AA, and a slightly large representative of the first group with genotype AA alternately during ontogenesis, with the exception of II lactation, were characterized by somewhat reduced fatigue. In general, homo- and heterozygous genotypes of VHMP and UKM of rocks of different combinations were observed with higher productivity values.

5. It has been confirmed that the pituitary gene of specific Pit-1 factor was associated with high-yield animals with homozygous AA and BB genotypes for all lactation among UBSD and URSD livestock, while URD cows had the best BB genotypes, which also causes the largest amount of milk fat in these animals. But the amount of fat does not differ significantly between homo- and heterozygous genotypes.

In this way the results obtained can be used in the practical breeding work of breeding and livestock farms using traditional methods of selection, monitoring and maintaining the genetic diversity of specific herds at an optimal level. This will ultimately provide an increase in the productivity of cattle due to the introduction into reproduction of animals with more desirable genes for capacasein, thyroglobulin, leptin, pituitary transcription factor and beta-lactoglobulin.

DECLARATIONS

Corresponding author
E-mail: karateeva1207@gmail.com

Authors' contribution
G. Julia and G.Mikhail participated in the design of the study, conducted experiments and wrote the original manuscript. G. Mikhail and K. Elena helped in ordering the data and calculations. G. Julia and K. Elena critically edited the manuscript. All authors read and agreed with the published version of the manuscript.

Conflict of interests
The authors did not declare any conflict of interest.

Acknowledgements

Data availability statement
The data that support the findings of this study are available from the corresponding author upon reasonable request.

REFERENCES

Alexander G, Juvancz Z, and Szejtli J (1988). Cyclodextrins and their derivatives as stationary phases in GC capillary columns. Journal of High Resolution Chromatography, 11(1): 110-113. DOI: https://doi.org/10.1002/jhrc.1240110128

Arora R, and Bhatia S (2004). Genetic structure of Muzzafarnagri sheep based on microsatellite analysis. Small ruminant research, 54(3): 227-230. DOI: https://doi.org/10.1016/j.smallrumres.2003.11.015

Aytekin I, and Boztepe S (2013). Associations of Pit-1 gene polymorphism with milk yield and composition traits in brown swiss cattle. Journal of Animal and Plant Sciences, 23(5): 1281-1289. http://www.thejaps.org.pk/.../11.pdf

Bangar YC, Patil CS, Magotra A, and Yadav AS (2021). Meta-Analysis of Gene Polymorphism of Beta-Lactoglobulin Gene in Indian Dairy Cows. Biochemical Genetics, 1-10. DOI: https://doi.org/10.1007/s10528-021-10153-9

Cardona SJC, Cadavid HC, Corrales JD, Munilla S, Cantet RJ, and Rogberg-Muñoz A (2016). Longitudinal data analysis of polymorphisms in the κ-casein and β-lactoglobulin genes shows differential effects along the trajectory of the lactation curve in tropical dairy goats. Journal of dairy science, 99(9): 7299-7307. DOI: https://doi.org/10.3168/jds.2016-10954

Dubey PK, Goyal S, Mishra SK, Yadav AK, Kathiravan P, Arora R, and Kataria RS (2015). Association analysis of polymorphism in thyroglobulin gene promoter with milk production traits in riverine buffalo (Bubalus bubalis). Meta gene, 5: 157-161. DOI: https://doi.org/10.1016/j.mgene.2015.07.005

Edriss MA, Edriss VAHID, and Rahmani HR (2009). Association of PIT-1 gene polymorphism with birth weight, milk and reproduction traits in Isfahan Holstein cows (Brief Report). Archives Animal Breeding, 52(4): 445-447. DOI: https://doi.org/10.5194/aab-52-445-2009

Grobet L, Poncelet D, Royo LJ, Brouwers B, Pirottin D, Michaux C, and Georges M (1998). Molecular definition of an allelic series of mutations disrupting the myostatin function and causing double-muscling in cattle. Mammalian genome, 9(3): 210-213. DOI: https://doi.org/10.1038/ng0997-71

Grodzicker T, Williams J, Sharp P, and Sambrook J (1974). Physical mapping of temperature-sensitive mutations of adenoviruses. In Cold Spring Harbor symposia on quantitative biology, 39: 439-446. Cold Spring Harbor Laboratory Press. DOI: https://doi.org/10.1101/SQB.1974.039.01.056

Jiang L, Liu J, Sun D, Ma P, Ding X, Yu Y, and Zhang Q (2010). Genome wide association studies for milk production traits in Chinese Holstein population. PloS one, 5(10): e13661. DOI: https://doi.org/10.1371/journal.pone.0013661

Khatib H, Zaitoun I, Chang YM, Maltecca C, and Boettcher P (2007). Evaluation of association between polymorphism within the thyroglobulin gene and milk production traits in dairy cattle. Journal of Animal Breeding and Genetics, 124(1): 26-28. DOI: https://doi.org/10.1111/j.1439-0388.2007.00634.x

Kononoff PJ, Deobald HM, Stewart EL, Laycock AD, and Marquess FLS (2005). The effect of a leptin single nucleotide polymorphism on quality grade, yield grade, and carcass weight of beef cattle. Journal of Animal Science, 83(4): 927-932. DOI: https://doi.org/10.2527/2005.834927x

Kostyunina OV, Abdel'manova AS, Martynova EU, Zinovieva NA (2020). Search for genomic regions carrying the lethal genetic variants in the Duroc pigs. Sel'skokhozyaistvennaya biologiya [Agricultural Biology], 55(2):275-284. http://www.agrobiology.ru/articles/2-2020kostyunina-eng.pdf

Kumar V (2017). Genetic and breeding aspects of lactation. In Trends and Advances in Veterinary Genetics. Intech Open. DOI: https://doi.org/10.5772/66179

Kusza S, Sziszkosz N, Nagy K, Masala A, Kukovics S, and András J (2015). Preliminary result of a genetic polymorphism of β-lactoglobulin gene and the phylogenetic study of ten balkan and central european indigenous sheep breeds. Acta Biochimica Polonica, 62(1): 109-12. DOI: https://doi.org/10.18388/abp.2014_846

Kramarenko AS, Karatieieva OI, Lykhach AV, Lugovoy SI, Lykhach VY, Pidpala TV, and Kramarenko SS (2019). Assessing genomic taurine/zebuine admixture in the southern meat cattle based on microsatellite markers. Ukrainian Journal of Ecology, 9(1): 251-261. https://www.researchgate.net/publication/332819579

Li J, Zhang S, Shen C, Niu Z, Yang H, Zhang K, et al. (2021). Indel mutations within the bovine HSD17B3 gene are significantly associated with ovary morphological traits and mature follicle number. The Journal of Steroid Biochemistry and Molecular Biology, 209:105833. DOI: https://doi.org/10.1016/j.jsbmb.2021.105833

Liefers SC, Veerkamp RF, Te Pas MFW, Chilliard Y, and Van der Lende T (2005). Genetics and physiology of leptin in periparturient dairy cows. Domestic Animal Endocrinology, 29(1): 227-238. DOI: https://doi.org/10.1016/j.domaniend.2005.02.009

Lu X, Abdalla IM, Nazar M, Fan Y, Zhang Z, Wu X, and Yang Z (2021). Genome-Wide Association Study on Reproduction-Related Body-Shape Traits of Chinese Holstein Cows. Animals, 11(7): 1927. DOI: https://doi.org/10.3390/ani11071927

Lund MS, de Roos AP, de Vries AG, Druet T, Ducrocq V, Fritz S, and Su G (2011). A common reference population from four European Holstein populations increases reliability of genomic predictions. Genetics Selection Evolution, 43(1): 1-8. DOI: https://doi.org/10.1186/1297-9686-43-43

Machulnyi VV (2018). Productivity of cows of Ukrainian black-and-white and red-and-white dairy breeds. Animal Breeding and Genetics, 51: 112-118. DOI: https://doi.org/10.31073/abg.51.15

Mattos KKD, Del Lama SN, Martinez ML, and Freitas AF (2004). Association of bGH and Pit-1 gene variants with milk production traits in dairy Gyr bulls. Pesquisa Agropecuária Brasileira, 39(2): 147-150. DOI: https://doi.org/10.1590/S0100-204X2004000200007

Miluchová M, Gábor M, Candrák J, Trakovická A, and Candráková K (2018). Association of HindIII-polymorphism in kappa-casein gene with milk, fat and protein yield in holstein cattle. Acta Biochimica Polonica, 65(3): 403-407. DOI: https://doi.org/10.18388/abp.2017_2313

Morkūnienė K, Baltrėnaitė L, Puišytė A, Bižienė R, Pečiulaitienė N, Makštutienė N, and Kerzienė S (2016). Association of kappa casein polymorphism with milk yield and milk protein genomic values in cows reared in Lithuania. Veterinarija ir Zootechnika, 74(96): 27-32. https://vetzoo.lsmuni.lt/data/vols/2016/74/pdf/morkuniene.pdf

Hartati H, Anwar S, and Soewandi BDP (2018). Genetic polymorphism of Pit-1| HinfI gene in Grati-Ongole Grade cattle at Indonesian Beef Cattle Research Station. Journal of the Indonesian Tropical Animal Agriculture, 43(4): 315-322. DOI: https://doi.org/10.14710/jitaa.43.4.315-322

Ng-Kwai-Hang KF, Hayes JF, Moxley JE, and Monardes HG (1984). Association of genetic variants of casein and milk serum proteins with milk, fat, and protein production by dairy cattle. Journal of dairy science, 67(4): 835-840. DOI: https://doi.org/10.3168/jds.S0022-0302(84)81374-0

Ozdemir M, Kopuzlu S, Topal M, and Bilgin OC (2018). Relationships between milk protein polymorphisms and production traits in cattle: a systematic review and meta-analysis. Archives Animal Breeding, 61(2): 197-206. DOI: https://doi.org/10.5194/aab-61-197-2018

Oztabak K, Un C, Tesfaye D, Akis I, and Mengi A (2008). Genetic polymorphisms of osteopontin (OPN), prolactin (PRL) and pituitary-specific transcript factor-1 (PIT-1) in South Anatolian and East Anatolian Red cattle. Acta Agriculturae Scand Section, 58(2): 109-112. DOI: https://doi.org/10.1080/09064700802357771

Pedrosa VB, Schenkel FS, Chen SY, Oliveira HR, Casey TM, Melka MG, and Brito LF (2021). Genomewide Association Analyses of Lactation Persistency and Milk Production Traits in Holstein Cattle Based on Imputed Whole-Genome Sequence Data. Genes, 12(11): 1830. https://doi.org/10.3390/genes12111830

Putra WPB, Anwar S, Said S, Indarto RAA, and Wulandari P (2019). Genetic characterization of thyroglobulin and leptin genes in Pasundan cattle at West Java. Buletin Peternakan, 43(1): 1-7. DOI: https://doi.org/10.21059/buletinpeternak.v43i1.38227

Seo D, Lee DH, Jin S, Won JI, Lim D, Park M, et al (2022). Long-term artificial selection of Hanwoo (Korean) cattle left genetic signatures for the breeding traits and has altered the genomic structure. Scientific reports, 12: 6438. DOI: https://doi.org/10.1038/s41598-022-09425-0

Soltani-Ghombavani M, Ansari-Mahyari S, and Edriss MA (2013). Association of a polymorphism in the 3'untranslated region of the OLR1 gene with milk fat and protein in dairy cows. Archives Animal Breeding, 56(1): 328-334. DOI: https://doi.org/10.7482/0003-9438-56-032

Wang H, Jiang L, Wang W, Zhang S, Yin Z, Zhang Q, and Liu JF (2014). Associations between variants of the HAL gene and milk production traits in Chinese Holstein cows. BMC genetics, 15(1): 1-9. DOI: https://doi.org/10.1371/journal.pone.0168316

Yurnalis Y, Sarbaini S, Arnim A, Jamsari J, and Nellen W (2013). Identification of single nucleotide polymorphism of growth hormone gene exon 4 and intron 4 in Pesisir cattle, local cattle breeds in West Sumatera Province of Indonesia. African Journal of Biotechnology, 12(3): 249-252. DOI: https://doi.org/10.5897/AJB12.2690

Zhang M, Luo H, Xu L, Shi Y, Zhou J, Wang D, and Wang Y (2022). Genomic Selection for Milk Production Traits in Xinjiang Brown Cattle. Animals, 12(2): 136. DOI: https://doi.org/10.3390/ani12020136

Zhou J, Liu L, Chen CJ, Zhang M, Lu X, Zhang Z, and Shi Y (2019). Genome-wide association study of milk and reproductive traits in dual-purpose Xinjiang Brown cattle. BMC genomics, 20(1): 1-11. DOI: https://doi.org/10.1186/s12864-019-6224-x