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# Polymorphism of Kappa-Casein, Somatotropin, Beta-Lactoglobulin, Prolactin, and Thyreoglobulin Genes of Black and White Cattle of North Kazakhstan

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**Abstract**

At present black and white cattle of new Karatomar interbreeding type in farms of North Kazakhstan is characterized as follows: milk yield 5612 kg±114, fat 3.78%±0,01, protein 3.24%±0,004. In terms of main gene markers it has been established than for kappa casein gene (CSN3) the frequency of allele A is 0.833; B – 0.167; Ho – 0.293; He – 0.278; Fis – 0.055, Ae – 1.358. Genotype AA is more advantageous in comparison with BB in terms of content of total fat and protein in milk. In terms of beta-lactoglobulin (BLG) about 40% of animals are characterized by allele variant BB, which provides higher milk yield, content of fat and protein, genotypes AB and BB: pA = 0.323, pB=0.677, Ho 0.434, He 0.438, Fis 0.007, Ae 1.778. In terms of somatotropin or growth hormone (GH) the variant LL has 82%, pL = 0.914, pV=0.086, Ho 0.141, He 0.157, Fis 0.099, Ae 1.186. Prolactin gen (PRL) has pG 0.914 and pA0.086, Ho 0.152, He 0.157, Fis 0.035, Ae 1.186, in terms of thyroglobulin (TG) - pC0.884 and pT0.116, Ho 0.192, He 0.205, Fis 0.065, Ae 1.258. Genotype CC has higher indices in terms of milk yield, content of fat and milk, and growth rate in comparison with genotype CT.

**Key words:** gene, efficiency, DNA, marker, prolactin, kappa-casein, beta-lactoglobulin, thyroglobulin, somatotropin, interbreeding type.

## INTRODUCTION

Present-day concept of cattle breeding in Kazakhstan is oriented at significant increase in yield of agriculture products, in particular, milk yield. It is mainly based on determination and maximum use of genetic potential of animals.

Analysis of genes in selection, responsible for quantitative characters or of appropriate genes, has some advantages in comparison with conventional selection. Such selection is directly based on analysis of genotype and does not consider the variety of useful properties stipulated by environment. This facilitates selection among young animals and irrespective of their sex, which increases selection efficiency.

Marker genes are selected among genes influencing on biochemical and physiological processes in organism and possessing polymorphism (various allele variants) usually stipulated by point mutation. Mutations can be located both in coding sequence, exon, and lead to variations in aminoacid composition of proteins, and in regulatory elements, thus influencing of gene transcription.

Polymorphism of genes, associated with parameters of milk yield, makes it possible to carry out selection of cattle with consideration for valuable genotypes regarding useful properties. The list of candidate genes for cattle with regard to properties of milk yield includes genes of major milk proteins (lactalbumines and caseins), hormone genes stimulating their expression, as well as genes the products of which regulate exchange of proteins and lipids in organism [1,2]. Peculiar position in this group is occupied by genes of kappa-casein, growth hormone, beta-lactoglobulin, prolactin and thyroglobulin [3, 4, 5, 6, 7, 8, 9]. Kappa-casein provides optimum technological properties of milk in cheese production, hence, its gene is considered as one of main markers of cattle breeding value. Kappa-casein gene (CSN3) of Bostaurus L. is located on the 6th chromosome. Among ten described alleles of this gene the most frequent are the allele variants A and B, which are distinguished by two aminoacid substitutions in the 136–th Thr(A)/Ile(B) and the 148–th Asp(A)/Ala(B) positions of polypeptide chain. Numerous researches detected association of B allele of CSN3 gen with higher content of protein in milk and cheese yield, as well as with better coagulation properties of milk [10, 11, 12, 13, 14]. Somatotropin or growth hormone GH is peptide hormone synthesized by hypophysis. Growth hormone (GH) is required for regulation of postnatal growth, hydrocarbon, lipid, nitrogen, and mineral exchange, it influences the amount and quality of produced milk. It is localized in chromosome

19q22 and has five exons. Genotype L of GH gene is related with increased milk yield, yield of fat and protein [3, 14], as well as with increased growth energy of young cattle and fat content [15, 16, 17]. Beta-lactoglobulin gene (LGB) is responsible for protein content in milk and is an index of milk biological value, variant LGB0 is related with high content of casein protein in milk, high fat percentage, and variant LGBA is characterized by high content of whey proteins. Differences between variants A and B are stipulated by substitution of nucleotides in exons 3 and 4 and respective aminoacids in position 64 (asparagine for variant A and glycine for variant B) and in position 118 (variant B has valine and variant A alanine) (Kučerová et al., 2006). Prolactin gene (PRL) participates actively in formation of properties of milk yield. Positive interrelation between allele G and milk yield, yield of milk fat and protein has been revealed [3]. It is localized in chromosome 23 and has five exons. Existence of alleles A and G of PRL gene is stipulated by synonymic A–G transition in position 8398 of exon 3, corresponding to codon 103 [18, 19, 20, 21]. Gene of thyroglobulin hormone (TG5) was previously considered as functional and positional gene, candidate of intramuscular fat [20]. Currently, on the basis of QTL (quantitative trait loci) studies performed on cattle of milk breeds as well as due to the influence of this gene on fat metabolism it is considered that the gene of thyroglobulin hormone is related with milk yield and qualitative composition of milk [22].

## EXPERIMENTAL

The studies were performed with approximately 100 animals of Karatomar black and white interbreeding cattle. The animals were selected with assistance from experts and graders of leading farms of Kostanai oblast, Kazakhstan. Measurements of dimensions, live weight and individual efficiency were obtained from Kazakhstan IAS data analytical system. Genetic studies were performed in Kazak tulpary laboratory certified according to **ISO/IEC 17025**KZ.И.11.1585. Polymorphism of gene of productivity was estimated using conventional procedure: PCR–RFLP (polymerase chain reaction and restriction fragment length polymorphism). Blood of animals for analysis was sampled into sealed tubes with EDTA (K2E, Belgium). DNA was purified using ExtraGenDNAPrep sets (OOO Isogen, Moscow). DNA fragments obtained after DNA amplification and segregation by restriction endonuclease were separated in 3% agar gel. Electrophoresis was performed at 100 V in 60–90 min. DNA ladder was added into a gel cavity (molecular weight: 100–1000 bp, NPO SibEnzim, Novosibirsk). Results of PCR splitting were estimated by electrophoresis in 3% agar gel colored with ethidium bromide using transilluminator in UV light. Distribution of DNA restriction fragments was estimated by means of Infinity Capt. software. Individual analyses were performed using primers (ZAO Sintol. Mosocw), sequences of amplification and restrictase (NPO SibEnzim, Novosibirsk): *kappa-casein CSN3* – nucleotide sequence of primers for CSN3: F:5'–ata–gcc–aaa–tat–atc–cca–att–cag–t–3', R:5'–ttt–att–aat–aag–tcc–atg–aat–ctt–g–3' [29]. Hot start – 5 min at 93°C; 35 cycles: denaturation – 30 sec at 93°C, annealing – 1 min at 60°C, synthesis – 1 min at 72°C; fill-in – 5 min at 72°PP. Hind III restrictase (site A↑AGCTT TTCGA↓A). *Somatotropin or growth hormone GH* – nucleotide sequence of primers for GH–L127V [30]: F:5' – tag–ggg–agg–gtg–gaa–aat–gga–3', R:5' – gac–acc–tac–tca–gac–aat–gcg–3'. Hot start – 5 min at 94 °C; 30 cycles: denaturation – 30 sec at 94°C, annealing – 30 sec at 57°C, synthesis – 40 sec at 72°C; fill-in – 5 min at 72°PP. Restrictase (site AluIAG↑CTTC↓GA) *beta-lactoglobulin BLG* – nucleotide sequence of primers for BLG [31]: F:5'–gtc–ctt–gtg–ctg–gac–acc–gac–tac–a – 3', R: 5'–cag–gac–acc–ggc–tcc–cgg–tat–atg–a – 3'. Hot start – 5 min at 94°C; 35 cycles: denaturation – 60 sec at 94°C, annealing – 60 sec at 60°C, synthesis – 60 sec at 72°C; fill-in – 5 min at 72°PP. Restrictase Hae III (GG↑CC CC↓GG). *Prolactin PRL* – mutation detection – PCR–RFLP. Nucleotide sequence of primers PRL [32]: F:5'–cga–gtc–ctt–atg–agc–ttg–att–ctt–3', R:5'–gcc–ttc–cag–aag–tcg–ttt–gtt–ttc–3'. Hot start – 3 min at 94°C; 30 cycles: denaturation – 60 sec at 94°C, annealing – 60 sec at 59°C, synthesis – 60 sec at 72°C; fill-in – 10 min at 72°PP. Restrictase RsaI (GT↑AC CA↓TG). *Thyroglobulin TG* – nucleotide sequence of primers [33]: F:5' – ggg–gat–gac–tag–gag–tat–gac–tg–3', R:5' – gtg–aaa–atc–ttg–agg–ctg–ta–3'. Hot start – 5 min at 94°C; 30 cycles: denaturation – 30 sec at 94°C, annealing – 60 sec at 59°C, synthesis – 40 sec at 72°C; fill-in– 5 min at 72°PP. Restrictase BstX2I (R↑GATCY YCTAG↓R).

## RESULTS

Saturation of market with high quality domestic products in sufficient amounts is impossible without intensification of cattle breeding. Selection on the basis of marker technologies is required. This makes it possible to forecast cattle productivity after birth irrespective of sex, age, physiological state of animals and to eliminate unpromising ones. However, there exist contradictory opinions relating usage of restriction polymorphism of some genes as accurate criterion.

As a consequence of diagnostics of cows in terms of CSN3 gene, it was revealed that 33% of animals are characterized by allele B, which, according to some data, is associated with higher protein content in milk, shorter coagulation time under action of enzyme rennet, higher quality of coagulant and higher yield of high quality milk protein products [23, 24, 25, 26]. Herewith, only three animals had genotype BB. Frequency of allele AA in selection was 0.833, allele B – 0/167. The observed heterozygosis Ho 0.293 was higher than calculated He 0.278, with fixation index Fis –0.055, Ae 1.358. The indices of cattle efficiency in terms of genotypes of gene CSN3 are summarized in Table 1.

**Table 1. Efficiency of cows of various genotypes in terms of *CSN3* gene**

| No. | Genotype, animals | Index | | Milk yield, kg | Fat, % | Protein, % | Fat, kg | Protein, kg |
|---|---|---|---|---|---|---|---|---|
| 1 | BB (3) | M | average | 5302 | 3.78 | 3.21 | 200 | 170 |
| | | STD | standard deviation | 1516.74 | 0.04 | 0.02 | 55.38 | 47.49 |
| | | Cv | variation coefficient | 28.609 | 0.936 | 0.662 | 27.710 | 27.974 |
| | | m | error | 152.439 | 0.004 | 0.002 | 5.5661 | 4.773 |
| 2 | AB (29) | M | average | 5577 | 3.78 | 3.24 | 211 | 181 |
| | | STD | standard deviation | 1150.84 | 0.10 | 0.04 | 44.81 | 37.39 |
| | | Cv | variation coefficient | 20.634 | 2.575 | 1.223 | 21.239 | 20.681 |
| | | m | error | 115.663 | 0.009 | 0.004 | 4.503 | 3.7579 |
| 2 | AA (67) | M | average | 5634 | 3.77 | 3.24 | 212 | 183 |
| | | STD | standard deviation | 1149.39 | 0.08 | 0.04 | 41.95 | 37.96 |
| | | Cv | variation coefficient | 20.402 | 2.241 | 1.312 | 19.753 | 20.778 |
| | | m | error | 115.518 | 0.009 | 0.004 | 4.2160 | 3.815 |

Studies of cattle selection in terms of ***GH gene*** revealed 82% of animals are characterized with variant LL, undesirable variant VV was not observed. The frequencies of allele occurrence pL = 0.914, pV=0.086. The observed heterozygosis of GH gene is lower than the calculations Ho 0.141 and He 0.157, respectively, at fixation index Fis 0.099, Ae 1.186. Cattle efficiency in terms of GH gene as a function of genotype was traced from birth to end of the first lactation and summarized in Table 2.

Analysis of cattle efficiency in terms of ***BLG gene*** revealed that about 40% of animals in general selection are characterized by allele variant BB, Table 3. Variant AB with intermediate level constitutes 52%, only 6% of animals are characterized by variant AA. The frequencies of allele occurrence are pA = 0.323, pB=0.677. Ho and He are 0.434 and 0.438, respectively, at fixation index Fis 0.007, Ae 1.778.

The studies demonstrated that the frequencies of allele occurrence G and A of ***PRL gene*** among animals of new Karatomar black and white interbreeding cattle was 0.914 and 0.086, respectively. The observed heterozygosis of PRL gene is at the level of calculations Ho 0.152 and He 0.157, respectively, at fixation index Fis 0.035, Ae 1.186. Efficiency of cows in terms of genotypes is summarized in Table 4.

The frequencies of allele occurrence C and T of ***TG5 gene*** were 0.884 and 0.116, respectively. Herewith, Ho and He constituted 0.192 and 0.205, respectively, at fixation index Fis 0.065, Ae 1.258. One of cows had genotype TT, not characteristic for milk efficiency of cattle. Efficiency of cows of various genotypes in terms of ***TG gene is*** summarized in Table 5.

**Table 2. Efficiency of cows of various genotypes in terms of GH gene**

| Genotype, animals | | Live weight, kg | | | | | Milk yield, kg | Fat, % | Protein, % |
|---|---|---|---|---|---|---|---|---|---|
| | | at birth | 6 mo. | 12 mo. | 15 mo. | 18 mo. | | | |
| LL (82) | M | 28 | 180 | 267 | 319 | 378 | 5602 | 3.78 | 3.24 |
| | STD | 2.21 | 19.60 | 10.86 | 12.05 | 16.39 | 1183.08 | 0.09 | 0.04 |
| | Cv | 7.754 | 10.884 | 4.068 | 3.777 | 4.338 | 21.118 | 2.3513 | 1.261 |
| | m | 0.222 | 1.969 | 1.091 | 1.211 | 1.647 | 118.905 | 0.009 | 0.0041 |
| LV (17) | M | 29 | 184 | 268 | 317 | 382 | 5659 | 3.76 | 3.23 |
| | STD | 2.23 | 18.98 | 11.66 | 15.40 | 18.16 | 916.71 | 0.08 | 0.04 |
| | Cv | 7.668 | 10.349 | 4.351 | 4.857 | 4.757 | 16.199 | 2.068 | 1.278 |
| | m | 0.2244 | 1.908 | 1.172 | 1.548 | 1.826 | 92.132 | 0.008 | 0.004 |

**Table 3. Efficiency of cows of various genotypes in terms of *BLG* gene**

| No. | Genotype, animals | Indices | | Milk yield, kg | Fat, % | Protein, % | Fat, % | Protein, % |
|---|---|---|---|---|---|---|---|---|
| 1 | BB (39) | M | average | | | 3.24 | 220 | 189 |
| | | STD | standard deviation | 1330.15 | 0.09 | 0.04 | 48.19 | 43.31 |
| | | Cv | variation coefficient | 22.755 | 2.394 | 1.371 | 21.873 | 22.869 |
| | | m | error | 133.685 | 0.009 | 0.004 | 4.8434 | 4.353 |
| 2 | AB (53) | M | average | 5469 | 3.77 | 3.24 | 206 | 177 |
| | | STD | standard deviation | 964.61 | 0.09 | 0.04 | 37.25 | 32.27 |
| | | Cv | variation coefficient | 17.637 | 2.269 | 1.183 | 18.069 | 18.187 |
| | | m | error | 96.947 | 0.009 | 0.004 | 3.744 | 3.244 |
| 2 | AA (7) | M | average | 5392 | 3.83 | 3.23 | 206 | 174 |
| | | STD | standard deviation | 1132.98 | 0.07 | 0.05 | 42.06 | 36.13 |
| | | Cv | variation coefficient | 21.011 | 1.791 | 1.533 | 20.410 | 20.734 |
| | | m | error | 113.869 | 0.007 | 0.005 | 4.227 | 3.631 |

**Table 4. Efficiency of cows of various genotypes in terms of *PRL* gene**

| No. | Genotype, animals | Indices | | Milk yield, kg | Fat, % | Protein, % | Fat, % | Protein, % |
|---|---|---|---|---|---|---|---|---|
| 1 | AG (15) | M | average | 5353 | 3.76 | 3.23 | 201 | 173 |
| | | STD | standard deviation | 819.54 | 0.10 | 0.04 | 29.94 | 26.64 |
| | | Cv | variation coefficient | 15.310 | 2.594 | 1.3394 | 14.9024 | 15.3845 |
| | | m | error | 82.367 | 0.009 | 0.004 | 3.009 | 2.677 |
| 2 | GG (84) | M | average | 5628 | 3.78 | 3.24 | 212 | 182 |
| | | STD | standard deviation | 1180.71 | 0.08 | 0.04 | 43.79 | 38.72 |
| | | Cv | variation coefficient | 20.9798 | 2.250 | 1.247 | 20.622 | 21.229 |
| | | m | error | 118.666 | 0.009 | 0.004 | 4.401 | 3.892 |

**Table 5. Efficiency of cows of various genotypes in terms of *TG* gene**

| No. | Genotype, animals | Indices | | Milk yield, kg | Fat, % | Protein, % | Fat, % | Protein, % |
|---|---|---|---|---|---|---|---|---|
| 1 | CC (78) | M | average | 5664 | 3.77 | 3.24 | 213 | 184 |
| | | STD | standard deviation | 1134.26 | 0.09 | 0.04 | 42.614 | 37.107 |
| | | Cv | variation coefficient | 20.026 | 2.343 | 1.269 | 19.940 | 20.219 |
| | | m | error | 113.997 | 0.009 | 0.004 | 4.283 | 3.729 |
| 2 | CT (21) | M | average | 5282 | 3.78 | 3.24 | 198 | 169 |
| | | STD | standard deviation | 997.54 | 0.08 | 0.04 | 37.840 | 34.233 |
| | | Cv | variation coefficient | 18.887 | 2.202 | 1.231 | 19.124 | 20.195 |
| | | m | error | 100.256 | 0.008 | 0.004 | 3.803 | 3.441 |

## DISCUSSION

The obtained results mainly agree with published data on frequency of occurrences of allele variants of genes and their association with the considered efficiency indices of various cattle breeds. Herewith, restriction polymorphism not of all genes is accompanied by reliable difference of efficiency indices.

In particular, analysis of own cattle efficiency of genotype AA of ***CSN3 gene*** concerning content of fat and total protein revealed statistically reliable advantage in comparison with BB (Student t–test, $p \leq 0.05$), but did not detect reliable difference for milk yield.

Frequency of occurrence of allele L of ***GH gene*** of various cattle breeds varies in the range from 0.520 to 0.867. Herewith, the frequency of allele V of black and white, Kholmogorskaya, Yaroslavskaya, Simmental breeds is lower than that of Holstein [27]. Frequency of occurrence of alleles is pL = 0.914, pV=0.086. The observed heterozygosis of GH gene is lower than calculations Ho 0.141 and He 0.157, respectively, at fixation index Fis 0.099, Ae 1.186. Analysis of own efficiency of animals regarding genotype in terms of ***GH gene*** did not reveal reliable difference of milk yield, content of fat and protein (Student t–test, $p \geq 0.05$). In addition, no significant differences of growth rate were detected in groups with different genotypes.

Existence of one variant (A or B) of **BLG gene** influences on protein content in milk, biological value and physicochemical properties of milk, as well as increases actual content of beta-lactoglobulin [27]. Higher content of casein and fat in milk of cows with variant B of beta-lactoglobulin stipulates better technological properties upon production of dairy food, and existence of variant A determines higher content of whey protein.

Efficiency with regard to genotypes of ***BLG gene*** demonstrated that animals of BB type have significantly advantageous difference (Student t–test, $p \leq 0.05$) with genotype groups AB and AA in terms of milk yield, content of fat and protein both measured as percentage or as quantity. About 40% of animals from general selection are characterized by allele variant BB. Variant AB of intermediate level is detected by 52% of animals, variant AA is observed only for 6% of animals. Frequency of occurrences of alleles for general selection are pA = 0.323, pB=0.677, Ho 0.434 and He 0.438, respectively, at fixation index Fis 0.007, Ae 1.778.

Frequency of occurrences of allele G of ***PRL gene*** in black and white, Jersey, Kholmogorskaya, Yaroslvskaya, Simmental cattle breeds is 0.308–0.853. Higher frequency of occurrence of allele G of PRL gene was observed for black and white breed: 0.853, herewith, the lowest frequency of allele was observed for Jersey cattle: 0.308 [18, 28]. In our studies frequency of occurrence of alleles G and A of PRL gene among animals of new Karatomar black and white interbreeding type was 0.914 and 0.086, respectively. Despite the existing difference in product qualities between animal groups, only difference in fat content can be considered as reliable (Student t–test, $p \leq 0.05$).

In published data on allele polymorphism of ***TG gene*** among cross breeds of Czech black spotted × black and white Holstein and red and white Holstein cattle the frequency of allele *C* is 0.77, allele T – 0.23, respectively (Kaplanová*et.al*, 2009). According to our results, the frequency of alleles C and T of ***TG gene*** was 0.884 and 0.116, respectively. Analysis of own efficiency of cows with regard to genotypes revealed significantly advantageous difference of CC type in terms of milk yield, content of fat and total protein (Student t–test, $p \leq 0.01$). The group with CC variant is also characterized by high growth energy. Therefore, those advantages promote monomorphism of subpopulation with regard to allele C of thyroglobulin gene.

## CONCLUSIONS

In general, restriction fragments of DNA are targeted genetic markers and at the same time phenotypic characters closely related with organism genotype. This facilitates monitoring of spreading of such markers in populations, their transfer from parents to kids upon interbreeding and use in selection programs aiming at increase in herd efficiency.

It has been established that black and white cattle of new Karatomar type in leading dairy farms of North Kazakhstan is characterized by dominating allele A (pA frequency 0.833) and genotype AA of CSN3 gene which differs by statically significant advantages with respect to genotype in terms of content of total fat and protein in milk. In GH gene allele L (pL 0.914) and genotype LL dominate, genotype VV has not been detected. BLG gene is characterized by frequency of allele B – 0.677, A–0.323. Animals of genotype BB (less than 40% in herd) have advantage in comparison with genotypes AB and AA in terms of milk yield, content of fat and protein. Frequency of allele G of PRL gene is slightly higher than respective published data p 0.914; frequency of alleles C and T of TG gene was 0.884 and 0.116, respectively; herewith genotype CC in terms of content of fat and total protein, growth rate was superior to genotype CT.

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