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The Effects of Polymorphisms in *Growth Hormone* and *Growth Hormone Receptor* Genes on Production and Reproduction Traits in Aberdeen-Angus Cattle (*Bos taurus* L., 1758)

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Abstract—The study was aimed to analyze the relation between individual genotypes and allelic variants of SNPs *g.2141C>G* of growth hormone gene, *g.914T>A* and *g.257A>G* of growth hormone receptor gene with growth and reproduction traits and to evaluate the populationgenetic structure in Aberdeen-Angus cattle (*Bos taurus* L., 1758) sample of Eastern Ukraine according SNPs studied. Allele *C* of SNP *g.2141C>G* has a positive correlation with birth weight, body stature, bigger rump, udder and total exterior evaluation score, shorter calving interval and better calve birth weight and negative correlation with calve average daily gain. Allele *T* of SNP *g.914T>A* has positive correlation with the muscle and udder size; live weight in each age, average daily gain, weight and average daily gain of calves born conform to the principle *AA>TT⩾TA*. SNP *g.257A>G* showed a positive correlation for *G* allele with muscle size. The population is in equilibrium for SNPs *g.2141C>G* and *g.257A>G*, and in disequilibrium for SNP *g.914T>A*. The analysis showed no linkage disequilibrium between SNPs *g.914T>A* and *g.257A>G*. Inbreeding coefficient F_{ST} in Aberdeen-Angus group studied was 16.1%.

Keywords: polymorphic variant, GH gene, GHR gene, *g.2141C>G*, *g.257A>G*, *g.914T>A*, Aberdeen-Angus breed
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INTRODUCTION

Growth hormone (GH), also known as somatotropin, is secreted by the acidophilic cells of the anterior pituitary gland in mammals. This hormone plays a key role in the regulation of metabolism, growth processes, cell differentiation and affects fertility, lactogenesis, and mammary gland development. As evident from the spectrum of hormone action, the growth hormone gene (BTA 19, NCBI Reference Sequence AC_000176.1) can be considered as promising marker of animal productivity. The effect of growth hormone is mediated by the interaction with a specific receptor (GHR) encoded by the growth hormone receptor gene (BTA 20, NCBI Reference Sequence: AC_000177.1). Growth hormone receptors consist of several domains (the transmembrane domain, the extracellular domain, and the cytoplasmic domain), present almost in all tissues, and belong to the cytokine receptor family. A signaling pathway that is activated upon the binding of the hormone to the receptor induces multiple gene transcription and cellular metabolism regulation [1].

Most studies of *GH* and *GHR* structure related to animal husbandry are focused on the search for single nucleotide polymorphisms and the analysis of the association between these polymorphisms and productivity traits. By now, the single nucleotide polymorphisms (SNPs) in bovine *GH* and *GHR* genes are associated with birth weight, average daily gain [2], stature [1], milk yield, milk composition (fat content, protein content, and somatic cell count) [3, 4], the onset of reproductive age, fertility, predisposition to mastitis [3, 5], and the taste characteristics of meat, such as juiciness, marbling, and odor [6, 7]. The molecule formed upon the expression of *G* allele of the polymorphic variant *g.2141C>G* (*L127V*, *rs41923484*) in the fifth exon of the *GH* gene is characterized by lower affinity to the receptor [3]. The reactive hydroxyl group in the aromatic ring of tyrosine at the position 279 in the transmembrane domain of *GHR* reduces the hydrophobicity of the molecule relative to that associated with the presence of the neutral phenylalanine. The replacement of phenylalanine by tyrosine occurs upon the expression of the *A* allele in SNP *g.914T>A* (*F279Y*, *rs385640152*) in the eighth exon [8]. Another

Table 1. Allele and genotype frequencies for SNPs *g.2141C> G*, *g.914T> A*, and *g.257A> G*, growth and reproduction parameters in Aberdeen-Angus cattle

Parameter	*GH, g.2141C>G*			*GHR, g.914T>A*			*GHR, g.257A>G*		
	Allele, frequency								
	C, 0.333	*G*, 0.667		*T*, 0.667	*A*, 0.333		*A*, 0.856	*G*, 0.144	
	Genotype, *n* (%)								
	CC, 5 (9.6)	*CG*, 25 (48.1)	*GG*, 22 (42.3)	*TT*, 32 (61.5)	*TA*, 6 (11.5)	*AA*, 14 (27.0)	*AA*, 38 (73.1)	*AG*, 13 (25.0)	*GG* 1 (1.9)
Live weight (kg) dynamics									
At birth	35.2 ± 1.3*	30.4 1.0*	29.9 ± 0.9*	30.2 ± 0.7	31.7 ± 0.4	31.3 ± 1.9	30.5 ± 0.7	31.6 ± 1.6	24
Average daily gain, g/day	763 ± 54	771 ± 15	774 ± 19	758 ± 14*	718 ± 33*	811 ± 24*	767 ± 14	782 ± 23	814
8 months	220.8 ± 15.3	213.3 ± 4.7	208.7 ± 4.1	211.2 ± 3.9*	193.8 ± 5.7*	222.5 ± 7.3*	212.1 ± 3.5	213.9 ± 8.6	205
12 months	288.8 ± 18.6	280.4 ± 4.4	272.8 ± 6.0	278.7 ± 5.0	262.4 ± 6.0	280.7 ± 6.0	278.0 ± 4.8	277.6 ± 5.2	290
15 months	342.0 ± 19.8	324.0 ± 4.9	318.9 ± 4.4	325.6 ± 4.7	305.0 ± 5.3	325.6 ± 7.7	323.4 ± 4.3	323.5 ± 7.0	338
18 months	380.8 ± 24.9	369.1 ± 6.2	362.6 ± 4.1	368.2 ± 5.0	346.5 ± 9.1	374.5 ± 10.1	367.1 ± 5.3	368.4 ± 7.2	375
2 years	421.4 ± 19.0	416.2 ± 6.6	413.1 ± 7.1	417.8 ± 5.5*	385.2 ± 3.3*	423.8 ± 11.0*	417.8 ± 5.3	410.3 ± 10.5	427
3 years	460.3 ± 22.8	446.9 ± 8.5	446.8 ± 10.3	443.7 ± 6.9	424.7 ± 10.3	461.9 ± 14.5	449.8 ± 7.2	446.9 ± 14.8	450
4 years	505.0 ± 18.1	488.7 ± 9.8	479.9 ± 10.9	484.0 ± 7.4	462.0 ± 1.7	497.1 ± 16.0	490.2 ± 8.0	476.9 ± 14.9	500
5 years	588.0 ± 40.0	557.0 ± 19.8	579.8 ± 21.8	570.9 ± 16.6	652.5 ± 30.0	522.1 ± 15.3	569.3 ± 14.9	586.0 ± 34.3	565
Characteristics of exterior parameters (score)									
Stature	12.2 ± 0.5	12.0 ± 0.1	11.9 ± 0.2	12.1 ± 0.1	11.7 ± 0.3	11.8 ± 0.2	11.9 ± 0.1	11.9 ± 0.2	13
Musculature	8.6 ± 0.2	8.1 ± 0.2	8.1 ± 0.1	8.3 ± 0.1	8.1 ± 0.2	7.9 ± 0.3	8.1 ± 0.1	8.3 ± 0.1	9
Head and neck	4.0 ± 0.0	4.0 ± 0.1	4.0 ± 0.1	4.0 ± 0.1	4.0 ± 0.0	4.0 ± 0.1	4.1 ± 0.1	3.9 ± 0.1	5
Thorax	7.8 ± 0.2	8.0 ± 0.1	7.9 ± 0.1	7.9 ± 0.1	7.7 ± 0.2	8.1 ± 0.1	7.9 ± 0.1	7.9 ± 0.2	9
Withers, back, coupling	12.2 ± 0.5	11.6 ± 0.2	11.9 ± 0.2	11.9 ± 0.2	11.5 ± 0.3	11.6 ± 0.2	11.8 ± 0.1	11.6 ± 0.3	12
Sacrum	8.2 ± 0.2	8.0 ± 0.1	8.0 ± 0.1	8.0 ± 0.1	8.0 ± 0.0	8.1 ± 0.1	8.0 ± 0.1	8.1 ± 0.1	9
Hind quarter	8.4 ± 0.4	8.5 ± 0.1	8.5 ± 0.1	8.6 ± 0.1	8.0 ± 0.3	8.3 ± 0.2	8.5 ± 0.1	8.4 ± 0.1	9
Udder	12.8 ± 0.5	12.4 ± 0.1	12.3 ± 0.2	12.6 ± 0.1	12.3 ± 0.3	12.1 ± 0.1	12.4 ± 0.1	12.4 ± 0.2	12
Limbs	8.0 ± 0.0	8.0 ± 0.1	7.9 ± 0.1	8.0 ± 0.1	8.0 ± 0.0	7.9 ± 0.1	7.8 ± 0.1	8.0 ± 0.0	8
Total score	82.2 ± 2.2	80.7 ± 0.8	80.5 ± 0.7	81.5 ± 0.7	79.7 ± 61.6	79.9 ± 0.9	80.7 ± 0.6	80.5 ± 0.9	86
Characteristics of the reproduction									
Calving interval, months	12.6 ± 0.3	14.3 ± 0.4	14.6 ± 0.4	14.3 ± 0.3*	13.6 ± 0.5*	14.5 ± 0.6*	14.1 ± 0.3	14.7 ± 0.6	127
n	37	149	127	202	34	76	229	76	7
Calf birth weigth, kg	29.3 ± 0.7	29.0 ± 0.3	28.9 ± 0.3	28.9 ± 0.2*	27.8 ± 0.8*	29.4 ± 0.3*	28.9 ± 0.2	29.2 ± 0.4	31.0
Calf average daily gain, g/day	737 ± 5	743 ± 10	748 ± 8	733 ± 5*	734 ± 14*	761 ± 15*	743 ± 7	748 ± 11	696

Here and in Table 2, data are represented as $\bar{x} \pm s_x$ (mean value ± error of the mean). * The factor has a statistically significant effect, $p < 0.05$. *n*—number of animals in the group.

polymorphic variant *g.257A>G* (*S555G*, *rs109300983*) in the promoter region of the tenth exon is associated with changes in the configuration of the cytoplasmic domain [1]. Thus, expression of functional molecules of growth hormone and growth hormone receptor is expected for genotypes that include the wild-type alleles (*g.2141C>G*), *C* (*g.914T>A*), and *A* (*g.257A>G*).

The geographical range of the studies on these SNPs in different dairy and beef cattle breeds includes the countries of Europe [1, 4–6, 8–15], North [7, 16–19] and South America [20], and the Middle [3] and Far East [2, 21–23]. The SNP *g.2141C>G* of the *GH* gene was studied in small samples of selected beef [24–27] and dairy [24, 27, 28] cattle breeds in Ukraine. Comprehensive studies of *GHR* gene polymorphic variants in Ukrainian cattle breeds have not been conducted yet, and only occasional reports are available [29].

The present study was aimed to analyze the relation between individual genotypes and allelic variants by SNPs *g.2141C>G* of the *GH* gene, *g.914T>A* and *g.257A>G* of the *GHR* gene with growth and reproduction traits and to evaluate the population-genetic structure in Aberdeen-Angus cattle sample of Eastern Ukraine according SNPs studied.

MATERIALS AND METHODS

Animals used in the study belonged to the nuclear stock of the Aberdeen-Angus cattle population of the Kharkiv region, Ukraine ($n = 58$: 52 cows and 6 bulls). Live body weight was determined at birth and at the age of 8, 12, 15, and 18 months and 2, 3, 4, and 5 years. Exterior evaluation of the 3–4-year-old animals followed the regulatory documents; the maximal score was 100 [30]. The parameters evaluated included general appearance–development and the intensity of exterior features typical for the breed, such as body stature (15 points) and state of the musculature (10 points), exterior dimensions—head and neck (5 points), thorax (10 points), withers, back, and coupling (15 points), sacrum (10 points), hind quarter (10 points), udder (15 points), and limbs (10 points). Genealogical analysis showed that the animals belonged to seven breeding lines [31].

Molecular genetic analysis involved the isolation of DNA from venous blood of the animals using Diatom DNA Prep 100 DNA extraction kits (Izogen, Russia), PCR-RFLP genotyping [3, 5, 8] using AluI and VspI restriction endonucleases (Fermentas, Lithuania), and electrophoretic analysis in a 2% agarose gel.

The genetic distance between the group of animals studied and the animals described in earlier publications was determined according to Nei [32]. The values of D' and r^2 were calculated to assess the linkage disequilibrium [33]. Values of the random inbreeding coefficient F_{ST} [34] were calculated in order to assess the genetic structure of the population.

Asymmetry and excess parameters were calculated during statistical analysis in order to check whether the data followed the normal distribution law. Student's method was used to compare the arithmetic means, and Pearson's correlation analysis was used to assess the relationships between the traits. One-way analysis of variation was used upon the comparison of three or more groups. Statistical hypotheses were checked using the t test and the χ^2 criterion at significance levels of 0.05 and 0.01, respectively [35].

RESULTS AND DISCUSSION

The genotype and allele frequencies of the SNPs studied in the entire sample of animals were: for *g.2141C>G*, *CC* = 8.6%, *CG* = 46.6%, and *GG* = 44.8%; *C* = 0.319 and *G* = 0.681; for *g.914T>A*, *TT* = 62.1%, *TA* = 13.8%, and *AA* = 24.1%; *T* = 0.690 and *A* = 0.310; for *g.257A>G*, *AA* = 74.1%, *AG* = 24.1%, and *GG* = 1.8%; *A* = 0.862, and *G* = 0.138. Genotype and allele frequencies in the bulls were: for *g.2141C>G*, *CC* = 0.0%, *CG* = 33.3%, and *GG* = 66.7%; *C* = 0.167 and *G* = 0.833; for *g.914T>A*, *TT* = 66.7%, *TA* = 33.3%, and *AA* = 0.0%; *T* = 0.833 and *A* = 0.167; and for *g.257A>G*, *AA* = 83.3%, *AG* = 16.7%, and *GG* = 0.0%; *A* = 0.917 and *G* = 0.083. Allele frequencies, genotype frequencies for *g.2141C>G*, *g.914T>A*, and *g.257A>G*, and quantitative characteristics of the cows are listed in Table 1.

The reported *C* allele frequency of the polymorphic variant *g.2141C>G*, being preferable based on cattle quantitative characteristics and the duration of the calving interval, ranged from 0.590 to 0.800, with 0.590 in Japan, $n = 6$ [23], 0.620 in the United States, $n = 468$ [16], 0.770 in Brazil, $n = 52$ [20], and 0.800 in Ukraine, $n = 10$ [24]. Genetic distances between the group studied and the groups listed above were calculated as described by Nei [32] and were 0.145, 0.180, 0.407, and 0.460, respectively.

The *T* allele frequency of the SNP *g.914T>A*, being preferable based on milk quality, in beef breeds were 0.870 in a breeds group from Ireland, $n = 22$ [1], 0.87 in Aberdeed Angus-cross beef cattle from Scotland, $n = 438$ [6], and 0.115 and 0.104 in two beef breed populations from the United States, $n = 556$ and $n = 609$ [17]. Genetic distances between the group studied and the groups listed above were 0.038, 0.038, 0.664, and 0.669. The frequency of the *A* allele of the SNP *g.257A>G*, being preferable based on milk quality, was 0.780 in a beef breeds sample from the United States, $n = 472$ [19] and 0.880 in a beef breeds sample from Ireland, $n = 22$ [1], whereas the genetic distances between these samples and the sample studied were 0.013 and 0.001, respectively. These data indicated greater variability in preferred alleles frequencies in the polymorphic variants *g.2141C>G* and *g.914T>A*

(CV = 15.2 and 36.8%) compared to that in SNP *g.257A>G* (CV = 1.0%). High conservatism of the cytoplasmic domain sequence and the secondary character of the activation of this domain relative to transmembrane domain activation provide an explanation for the fact presented above [36].

The live weight parameters of the animals with different genotypes with regard to the SNP *g.2141C>G* followed the *CC* > *CG* > *GG* pattern at almost all ages. The intergroup differences in birth weight ranged from 4.8 to 5.2 kg, which is equivalent to 14.6–16.1% (p = 0.044). The differences in live weight decreased as the animals matured and ranged from 3 to 25 kg (1–5%) between *CC* and CG groups and from 10 to 25 kg (2–7%) between *CC* and *GG* groups.

The data obtained in the present study are comparable with the results reported by other researchers with regard to the body weight of *CC* animals (at birth and in general) being greater than that of the animals with a *CG* or *GG* genotype [2, 18, 25]. The *C* allele of the SNP *g.2141C>G* was associated with higher body weight and beef marble score in beef cattle breeds [6]. The average daily gain of the endemic Hanwoo cattle in Korea reported by Lee et al. [2] followed the *CC* < *CG* < *GG* pattern established in the present study (*CC*: 0.73 ± 0.01 kg, *CG*: 0.74 ± 0.02 kg, and *GG*: 0.81 ± 0.03 kg; p = 0.038). However, the pattern was reversed in the Southern beef breed: *CC* > *CG* > *GG* [25]. Unfortunately, we could not compare our data for older animals with the results obtained by other researchers, since their studies were limited to productive populations of cattle younger than 2 years.

Analysis of the SNP *g.914T>A* showed that the animals' body weight decreased according to the *AA* > *TT* > *TA* pattern at each age. The average daily gain in animals with *AA* genotype was higher than in animals of other genotypes by 40–100 g (p = 0.045). The body weight of 8-month-old and 2-year-old cows in the *AA* group was 30–35 kg higher (p = 0.026 and 0.032, respectively) than in the *TA* group, whereas intermediate values of body weight were characteristic of the cows with the *TT* genotype.

However, the wild-type *T* allele of the SNP *g.914T>A* was reportedly preferable. Animals of American beef breeds group that were carriers of the *AA* genotype yielded carcasses of lower quality characterized by a smaller amount of fat tissue, higher bone weight, and taste properties inferior to those registered in animals with the *TA* genotype [17]. Tait et al. [7] recommended selection directed towards the increase in the frequency of the *TT* genotype.

Analysis of SNP *g.257A>G* effects was limited to carriers of the *AA* and *AG* genotypes in the present study, since the *GG* group was small. However, the growth dynamics was comparable in the groups selected. The difference in body weight in the carriers of different genotypes ranged from 1 to 20 kg (up to 3% of body weight). These results are comparable to the data concerning the absence of association between *g.257A>G* and quantitative characteristics, such as average daily gain and body weight [37].

Low *G* allele frequency of the SNP *g.257A>G* was reported for other populations as well: G = 0.22 in Aberdeen Angus cattle from the United States (n = 472) [19], G = 0.12 in the beef breed group from Ireland (n = 22) [1], G = 0.049 in Holstein breed from Germany (n = 315) [13], G = 0.168/0.109 for Holstein-Frisian cows and bulls from Poland (n_{cows} = 395/n_{bulls} = 477) [10], and G = 0.13 in the Ayrshire breed from Finland (n = 1528) [8].

Thus, the *g.914T>A* SNP was more informative than the *g.257A>G* SNP considering the effects on body weight dynamics.

Analysis of the exterior parameters showed that the animals corresponded to the breed standard and had a body shape characteristic of beef breeds. The musculature scored approximately eight points, the trunk was wide and deep with a flat top line (approximately 12 points), the sacrum was distinct (approximately eight points), and the hind quarter muscles were well developed (approximately 8.5 points).

Analysis of the *g.2141C>G* SNP showed that carriers of the *CC* genotype had a better-developed musculature than the animals with the *GG* genotype (*CC* = 8.6, *GG* = 8.1, $p < 0.01$). The number of *C* alleles showed a positive correlation with a larger body (r = 0.99, $p < 0.01$), sacrum (r = 0.94, $p < 0.05$), udder (r = 0.93, $p < 0.05$), and the total exterior evaluation score (r = 0.91, $p < 0.05$), whereas the correlation with head and neck dimensions was negative (r = –0.91, p < 0.01). The association of the *C* allele with a larger body size was demonstrated for two dairy breeds: the *C* allele occurred more frequently in the larger Holstein animals (*C*: G = 0.70: 0.30) than in Jersey animals (*C*: G = 0.53: 0.47) [38].

Assessment of *TT* genotype carriers for the SNP *g.914T>A* showed that these animals had a larger body and a better developed musculature, hind quarter, and udder than the carriers of other genotypes. The genotype had a significant effect on hind quarter size (F_{fact} = 4.4, F_{stat} = 3.2, $p < 0.05$). The number of *T* alleles showed a positive correlation with the size of the musculature (r = 0.97, $p < 0.05$) and udder size (r = 0.99, $p < 0.01$). This is consistent with the data reported by other authors [7, 17]. Waters et al. [1] reported an effect of SNP *g.914T>A* on thorax width, but a similar effect was not observed in the present study.

Analysis of the SNP *g.257A>G* revealed a negative correlation between the *A* allele and musculature size (r = –0.96, $p < 0.05$), although the individual characteristics of the animals appeared comparable. The absence of a clearly pronounced effect of the SNP *g.257A>G* on the exterior parameters examined can be due to the location of this polymorphic variant on the periphery of a conserved region, which is indicative of a low structural or functional significance of the single

nucleotide substitution [8]. However, Waters et al. [1] reported the effects of the SNP *g.257A>G* on stature, offspring stature, and angularity.

Analysis of the reproductive characteristics in Aberdeen Angus cows showed that the calving interval in the cows that carried the *CC* genotype of the *g.2141C>G* SNP was, on average, 2 months shorter than the interval in cows that carried other genotypes. The number of *C* alleles showed a correlation with the decrease of the calving interval ($r = 0.94$, $p < 0.05$) and a higher calf birth weight ($r = 0.94$, $p < 0.05$).

Hadi et al. [3] stated that the birth of large calves from cows with the *CC* genotype could be expected, since a higher concentration of the growth hormone in the mother's blood led to suppression of insulin-mediated lipolysis, increased glucose concentration in the mother's blood, and improved fetal nutrition, regardless of the inability of the growth hormone to cross the placental barrier. The association of the SNP *g.2141C>G* with reproductive characteristics (fertility and calving intervals) reported by certain authors is mediated by the secretion of IGF-1. The secretion of IGF-1 is enhanced upon more efficient binding of the growth hormone with leucine in the position 127 (formed upon the expression of the normal *C* allele) to the growth hormone receptors in the liver [5].

Birth weight and average daily gain of calves born from the cows studied followed the *AA* > *TT* > *TA* pattern with regard to the SNP *g.914T>A*. The effect of the factor was significant for all parameters at the level of significance $p < 0.05$ ($F_{stat} = 3.2$, $F_{fact} = 3.25$ for calving interval, $F_{fact} = 6.5$ for calf birth weight, and $F_{fact} = 6.1$ for calf average daily gain).

The expression of the *G* allele of the *g.257A>G* SNP showed a positive correlation with the higher calf birth weight ($r = 0.92$, $p < 0.05$). The weight and average daily gain of the calves produced by cows with the *AA* and *AG* genotypes of *g.257A>G* were comparable in the sample studied, whereas the calving interval was 0.6 months shorter in the *AA* group, but calf birth weight and calf average daily gain were higher in the *AG* group (by 0.3 kg).

We could not find any publications concerning the dynamics of growth of the calves born from cows that were genotyped with regard to these SNPs. We assume that the average daily gain or the growth rate of calves of beef breeds can be regarded as a characteristic of milk quality.

A positive correlation between the average daily gain and the number of *G* alleles of the SNP *g.2141C>G* was established ($r = 0.99$, $p < 0.01$). Therefore, calf growth dynamics with *GG* and *CG* genotypes may be a factor that enables the preservation of high frequency of the *G* allele in the population.

Only part of milk yield and milk quality parameters have been reported for cattle of beef breeds genotyped for all the SNPs in *GH* and *GHR* genes analyzed in the present study. Comparison of the results of the present study with the published reports that traced the connections between these SNPs and milk parameters in cows of dairy breeds showed that the *CC* genotype for the SNP *g.2141C>G* was associated with higher milk yields [3], but discordant data were obtained for different breeds. Polish cows of the Black-and-White dairy breed that carried the *CC* genotype were characterized by higher milk yields, as well as a higher fat and protein content [5], as compared to the animals that carried the *GG* and *CG* genotypes. Belarusian cows of the Black-and-White breed showed an association of high milk yields with the *CG* genotype, whereas the fat and protein content was higher in animals with a *GG* genotype [29]. Fat and protein content in the milk of Holstein cows from Ukraine was the highest in the carriers of the *CC* genotype [28]. Milk yields were also higher in carriers of the *CC* genotype [28], although the difference between these animals and the carriers of *CG* and *GG* genotypes decreased with each subsequent lactation. Milk yield at first lactation was higher in Holstein cows that carried a *GG* genotype than in the animals that carried a *CC* genotype [27].

In literature the association with the parameters of milk quality was reported for the SNP *g.914T>A*. Polish cows of the Jersey breed showed higher milk yield and a higher fat and protein content in the milk for the *TT* genotype as compared to the *AA* genotype [5]. However, an association of the *A* allele of the SNP *g.914T>A* with an increase in milk yield and lactose content and a decrease in the content of fat, protein, casein, and somatic cell count was reported for German Holstein cows [4]. Animals of the Jersey breed are generally smaller (the weight of a cow is 300–400 kg and that of a bull is 600–700 kg) than those of the Holstein breed (the weight of a cow is 680–770 kg, and that of a bull is 1000–1200 kg), and, therefore, the effects of a specific allele of a single polymorphic variant may vary and depend on the presence of coadaptive gene complexes characteristic of each breed.

Our results revealed comparable values of the average daily gain in *AA* and *AG* groups of the SNP *g.257A>G*. Oleński et al. [10] reported an association between the *A* allele of the SNP *g.257A>G* and an increased fat and protein content in milk.

Growth hormone is directly involved in interactions with the transmembrane domain of the specific receptor, and, therefore, it appeared reasonable to analyze the data for the combination of the two SNPs *g.2141C>G* and *g.914T>A* (Table 2). The wild-type *C* and *T* alleles are preferred for these polymorphic variants, since they correspond to functional molecules of the growth hormone and the receptor. However, our data revealed an advantage of the animals that carried the *AA* genotype in the SNP *g.914T>A* over the carriers of the *TT* genotype.

The animals with *CCTT* genotype were characterized by the highest body weight at the age younger than

Table 2. Growth and reproduction parameters of Aberdeen-Angus cows by SNPs *g.2141C>G* in the *GH* gene and *g.914T>A* in the *GHR* gene

Parameter	Genotype, *n* (%)							
	CCTT, 3 (5.8)	CCTA 2 (3.8)	CGTT, 17 (32.6)	CGTA, 1 (1.9)	CGAA, 7 (13.5)	GGTT, 12 (23.1)	GGTA, 3 (5,8)	GGAA, 7 (13,5)
	Live weight (kg) dynamics							
At birth	37 ± 1.1	32.5 ± 0.5	28.6 ± 0.2	30	34.7 ± 1.0	30.7 ± 0.2	31.7 ± 0.3	27.8 ± 0.8
Average daily gain, g/day	814 ± 77	686 ± 38	758 ± 3	652	820 ± 13	761 ± 7	762 ± 55	802 ± 14
8 months	241.7 ± 15.3	189.5 ± 2.5	207.9 ± 0.9	184.0	233.3 ± 4.8	209.4 ± 2.1	203.0 ± 13.0	209.6 ± 0.9
12 months	320.0 ± 25.0	257.5 ± 3.5	277.8 ± 1.2	256.0	297.5 ± 1.6	276.0 ± 3.1	270.5 ± 15.5	267.2 ± 2.2
15 months	370.0 ± 17.8	300.0 ± 7.0	318.9 ± 1.2	304.0	339.0 ± 4.0	326.5 ± 1.7	308.7 ± 10.4	310.0 ± 3.2
18 months	413.7 ± 23.2	331.5 ± 23.5	363.4 ± 1.3	350.0	385.9 ± 6.2	365.2 ± 1.5	355.3 ± 10.7	361.2 ± 3.8
2 years	447.3 ± 19.2	382.5 ± 2.5	408.8 ± 1.1	380.0	439.4 ± 6.8	423.0 ± 3.2	388.7 ± 6.3	405.7 ± 3.0
3 years	479.0 ± 18.3	404	432.6 ± 1.4	–	485.2 ± 8.7	454.8 ± 4.8	435.0 ± 0.0	434.0 ± 4.8
4 years	519.0 ± 16.2	463	475.9 ± 2.3	–	520.8 ± 8.6	492.8 ± 5.5	461.7 ± 1.7	461.5 ± 4.0
5 years	548.3 ± 7.3	707	562.2 ± 7.7	619.0	527.5 ± 13.1	589.7 ± 10.7	642.0 ± 57.0	515.0 ± 8.7
	Characteristics of exterior parameters (score)							
Stature	13.0 ± 0.0	11.0 ± 0.0	12.0 ± 0.1	12.0	12.0 ± 0.1	12.0 ± 0.1	12.0 ± 0.6	11.5 ± 0.1
Musculature	9.0 ± 0.0	8.0 ± 0.0	8.2 ± 0.1	8.0	7.8 ± 0.2	8.0 ± 0.1	8.3 ± 0.3	8.0 ± 0.0
Head and neck	4.0 ± 0.0	4.0 ± 0.0	4.0 ± 0.1	4.0	4.0 ± 0.1	4.1 ± 0.1	4.0 ± 0.0	4.0 ± 0.0
Thorax	8.0 ± 0.0	7.5 ± 0.5	7.9 ± 0.1	8.0	8.2 ± 0.1	7.9 ± 0.1	7.7 ± 0.3	8.0 ± 0.0
Withers, back, coupling	13.0 ± 0.0	11.0 ± 0.0	11.6 ± 0.1	12.0	11.6 ± 0.1	12.0 ± 0.1	11.7 ± 0.7	11.7 ± 0.2
Sacrum	8.3 ± 0.3	8.0 ± 0.0	8.0 ± 0.1	8.0	8.1 ± 0.1	8.0 ± 0.0	8.0 ± 0.0	8.0 ± 0.1
Hind quarter	9.0 ± 0.0	7.5 ± 0.5	8.5 ± 0.1	8.0	8.4 ± 0.1	8.7 ± 0.1	8.3 ± 0.3	8.1 ± 0.1
Udder	13.3 ± 0.3	12.0 ± 1.0	12.5 ± 0.1	12.0	12.1 ± 0.1	12.3 ± 0.1	12.7 ± 0.3	12.1 ± 0.1
Limbs	8.0 ± 0.0	8.0 ± 0.0	8.0 ± 0.1	8.0	8.0 ± 0.0	8.0 ± 0.0	8.0 ± 0.0	7.9 ± 0.1
Total score	85.7 ± 0.3	77.0 ± 2.0	80.8 ± 0.2	80.0	80.4 ± 0.5	81.1 ± 0.3	80.7 ± 1.8	79.4 ± 0.5
	Characteristics of reproduction							
Calving interval, months	12.9 ± 0.5	12.3 ± 0.4	14.1 ± 0.1	13.0	14.7 ± 0.3	14.8 ± 0.1	14.6 ± 0.1	14.3 ± 0.3
n	25	12	103	4	42	75	18	34
Calf birth weigth, kg	30.1 ± 0.3	28.1 ± 1.3	29.1 ± 0.1	25.0	29.5 ± 0.2	28.9 ± 0.1	28.7 ± 1.1	29.2 ± 0.1
Calf average daily gain, g/day	777 ± 9	738 ± 0	730 ± 2	671	786 ± 10	754 ± 4	752 ± 11	736 ± 4

2 years and the most advantageous exterior parameters. Comparison of the *CCTT* group with the most numerous *CGTT* group revealed differences in live weight at almost all ages. The difference was 8 kg (25%) at birth ($p < 0.01$), 32 kg (15%) at 8 months ($p < 0.01$), 33 kg (14%) at 12 months ($p < 0.05$), 52 kg (15%) at 15 months ($p < 0.01$), 50 kg (13%) at 18 months ($p < 0.01$), 39 kg (9%) at 2 years ($p < 0.05$), and 47 kg (10%) at 3 years ($p < 0.01$), with the *CCTT* genotype always associated with a higher weight. Carriers of this genotype also had 8% higher scores for stature ($p < 0.05$), 9% higher scores for musculature development ($p < 0.05$), and 11% higher scores for the withers, back, and coupling ($p < 0.05$).

Comparison of the groups with the preferred *CCTT* genotype and the *GGAA* group with all alternative alleles revealed the following statistically significant differences in weight between the animals: 9 kg (28%) at birth ($p < 0.05$), 32 kg (14%) at 8 months ($p < 0.05$), 53 kg (14%) at 12 months ($p < 0.05$), 60 kg (15%) at 15

months ($p < 0.01$), 50 kg (13%) at 18 months ($p < 0.01$), 42 kg (10%) at 2 years ($p < 0.05$), and 58 kg (12%) at 4 years ($p < 0.01$). The udders of the animals with the *CCTT* genotype were, on average, 9% larger ($p < 0.05$), and the total evaluation score was higher by 8% ($p < 0.05$). The reproductive characteristics were comparable in all groups, although the calving interval was 14.8 ± 0.1 months in animals with *GGTT* genotype and 12.3 ± 0.4 months in animals with *CCTA* genotype, with the latter group characterized by the lowest live weight values and exterior evaluation scores. The values of the investigated parameters were similar in the most numerous groups *CGTT* and *GGTT*.

The differences in the quantitative characteristics of the animals with different genotypes are probably due to a change in the affinity of the receptor to the effector and to increased competition for normal receptors [36] that leads to a decrease in the growth rate of the individual parts of the animal's body.

The frequencies of the genotypes for the SNPs *g.2141C>G* and *g.257A>G* corresponded to the Hardy–Weinberg equation; that is, the population was in equilibrium. Equilibrium was not observed for *g.914T>A* ($\chi^2_{fact} = 17.79$, $\chi^2_{st} = 13.82$, $p < 0.001$). The investigated population did not exhibit equilibrium for the polymorphic variants *g.914T>A* and *g.2141C>G* ($\chi^2_{fact} = 65.85$; $\chi^2_{st} = 26.12$; $p < 0.001$) and *g.914T>A* and *g.257A>G* ($\chi^2_{fact} = 28.54$; $\chi^2_{st} = 26.12$; $p < 0.001$) due to the low number of animals heterozygous for the SNP *g.914T>A*. Low frequency of the *TA* genotype can be due to low values of the body weight dynamics parameters prior to the age of 2–3 years and unfavorable exterior features that predispose towards the elimination of the carriers of this genotype from the population in the course of selection.

It is advisable to maintain two directions of selection in the Angus group, with the breeding direction intended for the reproduction of the future generations of animals and the production direction intended for the production of meat, and, therefore, the preferable genotypes should be defined by the objectives of the selection. Cows with the *CCTA* genotype with regard to the SNPs *g.2141C>G* and *g.914T>A* should be selected for the breeding core, since these animals have a short calving interval, whereas the bulls used for the breeding should carry the *CCTT* genotype to maximize the production of calves with the *CCTT* genotype that will have the best weight and exterior parameters for meat production. The use of bulls from other lines is reasonable, since it will improve the productive characteristics and minimize the risk of inbreeding.

The inbreeding coefficient increase is known to be associated with deterioration of a number of cattle economically significant characteristics [39, 40]. An at least 1% increase in the inbreeding rate in beef breeds is associated with a 0.06-kg decrease of birth weight, a 0.44-kg decrease of weaning body weight, a 0.69-kg decrease of first year body weight, and a 1.3-kg decrease of mature body weight. Burrow [39] reported a decrease of milk yield and reproductive potentials in breeding cows upon an increase of the inbreeding coefficient. The decrease was manifested as a 0.3-kg decrease of calf weight at weaning and a 0.21-kg decrease at the age of 1 year. An increase of the inbreeding coefficient in Angus cattle population was associated with a decrease of body weight and daily average gain. The changes were mediated by a decrease in the concentration of IGF-1 in the blood. The values of the inbreeding coefficient were 4.20 and 6.82% for the cows and the calves, respectively, and increased every year by 0.25 and 0.36%, respectively [40].

The F_{ST} coefficient for the entire sample of Aberdeen-Angus cattle used in the present study was 16.1%, and the values for the five breeding lines Ilinmera Leda, Prospector, McHeary, Southhome Extra and Brialhill South [31] were 28.3, 20.7, 14.7, 10.5, and 6.4%, this being indicative of high inbreeding levels.

The inbreeding coefficient of the Brialhill South and Southhome Extra, the two lines characterized by rather high values of the quantitative parameters, were lower than in the other lines, which is in agreement with the data reported in [39, 40].

Pronounced linkage disequilibrium of individual markers is characteristic of mixed populations with a low random inbreeding index [41]. The SNPs *g.914T>A* and *g.257A>G* were used to assess linkage disequilibrium (LD), since they are located in the eighth and tenth exons of the *GHR* gene and the LD calculation method is only applicable for limited genetic distances (not more than 19 kb in cattle [1]). The SNPs under investigation occupied the positions 31909478 (*g.914T>A*) and 31891050 (*g.257A>G*) on the chromosome, and, thus, the distance was approximately 18 kb.

The value of 0.108 obtained for the coefficient *D'* shows that certain alleles are inherited together in approximately 11% of all cases. This estimate is not sufficient, since *D'* is sensitive to low frequency of any of the alleles, and, therefore, a risk of a false conclusion on linked inheritance exists. We used the r^2 index to normalize *D'* in the set of alleles investigated. The r^2 index for the sample investigated had a value of 0.004, which is indicative of the absence of linked inheritance.

Linkage of the SNP *g.914T>A* with five genetic markers was demonstrated in four groups of Holstein-Frisian cattle and two groups of Jersey cattle [42], but the distance between the markers investigated was less than between the SNPs *g.914T>A* and *g.257A>G*. Waters et al. [1] demonstrated the linkage of alleles of nine loci in the tenth exon of the *GHR* gene in Holstein-Frisian cows from Great Britain and Ireland.

Linkage of individual loci can be attained if systematic selection based on quantitative characteristics is performed. However, selection and an increase of the

inbreeding coefficient can disrupt the linkage due to the increase of the number of contact sites during crossingover, especially in highly inbred animals [43]. The LD value is expected to decrease upon an increase of the inbreeding coefficient. Thus, a low LD value for markers located at a distance of 18 kb is probably due to a high index of random inbreeding in the Aberdeen Angus population investigated in the present work.

CONCLUSIONS

A direct correlation of the *C* allele of *g.2141C>G* in the *GH* gene with birth weight, a generally larger body and better exterior characteristics, a shorter calving interval, and the birth of larger calves was established upon the analysis of the SNPs *g.2141C>G* of the *GH* gene and *g.914T>A* and *g.257A>G* of the *GHR* gene in a group of animals of the Aberdeen-Angus breed. A positive correlation of the *T* allele of the SNP *g.914T>A* and the *G* allele of the SNP *g.257A>G* with muscle size was observed. The population was in equilibrium with regard to the SNPs *g.2141C>G* and *g.257A>G*, whereas the lack of equilibrium was observed for the SNP *g.914T>A*. No interallele linkage was observed for the SNPs *g.914T>A* and *g.257A>G* ($D' = 0.108$, $r^2 = 0.004$). This finding was in agreement with the high inbreeding rate of the population investigated as inferred from the value of the random inbreeding index $F_{ST} = 16.1\%$.

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