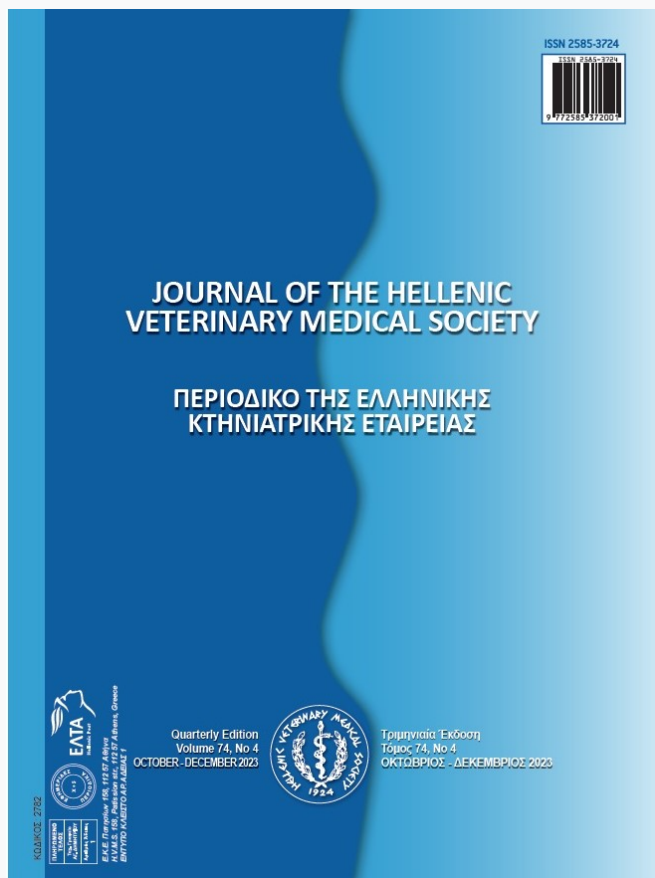


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## The Effects of Somatotropic Axis Gene Polymorphisms on Milk Yields in Simmental Cattle

Z. Sönmez<sup>1</sup>, S. Kopuzlu<sup>2</sup>, M. Özdemir<sup>2</sup>

*1Department of Agricultural Biotechnology, Faculty of Agriculture, Ataturk University, Erzurum, Turkey*

*2Department of Animal Science, Faculty of Agriculture, Ataturk University, Erzurum, Turkey*

**ABSTRACT:** Due to the increasing world population, scientists aim to obtain high-yield products using new techniques and methods to meet needs in the fields of food, agriculture, and livestock. It is very important to select the candidate genes and markers correctly, especially in the QTL and MAS techniques in livestock. Somatotropic axis genes affect yield traits, growth, reproduction, and milk production in cattle. In the study, we determined GH/AluI and IGFI/SnaBI gene polymorphisms using the PCR-RFLP technique in DNA samples obtained from 70 Simmental cattle. The allele frequencies of the genes were in the same proportion as 0.62 and 0.38, L and V for the GH gene and T and C for the IGFI gene. There was no significant relationship between the polymorphic genotypes of the genes we examined and lactation milk yields, 305-day milk yields, daily milk yields, and lactation periods of Simmental cattle. The probability of using bGH/AluI and IGFI/SnaBI genetic variations as markers in association studies with milk yield in cattle is extremely low.

**Keywords:** Axis genes; RFLP; MAS; Simmental; milk yield

*Corresponding Author:*

Z.Sonmez, Ataturk University, Department of Agricultural Biotechnology, Erzurum, Turkey  
E-mail address: zeynepsonmez@atauni.edu.tr

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## INTRODUCTION

Nowadays, genome sequencing of organisms and the development of comprehensive single-nucleotide polymorphism (SNP) data, along with advancements in genotype identification technologies, have made genetic association maps in the entire genome possible. Somatotrophic axis genes, consisting mainly of growth hormone (GH), insulin-like growth factors (IGF I and II), carrier proteins and receptors associated with them (GHR, IGFR, IGFBP), take part in metabolism and physiological processes. They also play a role in many physiological processes, including the regulation of ionic and osmotic balance, the regulation of lipid, carbohydrate and protein metabolisms, growth, reproduction, immune function and behaviour (Renaville et al., 2002; Gabillard et al., 2003; Besseau et al., 2013; Hax et al., 2017).

The IGF I hormone consisting of 70-amino-acid with a weight of 7649 kilodaltons connected by disulfide bridges in the form of A and B chains. The cleavage sites of the SnaBI restriction enzyme, recognized by Ge et al. (2001), the C>T cleavage site at base 512 in the regulatory region of the IGFI gene, have been studied extensively. The IGF-I hormone is functionally separated since it is released by two different tissues. First, it is released by the liver and acts as an extension of the GH axis through the tonic pituitary stimulation of hepatic synthesis (Oster et al., 1995). Second, the GH hormone determines the level

of IGF-I in circulation along with nutritional factors (Laron, 2001; Delafontaine et al., 2004).

The bovine growth hormone (bGH) represents a single-chain polypeptide hormone weighing 22 kDa produced in the pre-pituitary gland and comprising 191 amino acids. Studies on bGH polymorphism-shave intensely determined L (leucine at codon 127) and V (valine at codon 127) allelic polymorphisms located on the 5th exon and coinciding with the recognition region of the AluI (GH-AluI) restriction enzyme (Zhang et al., 1993). The hormone bGH is known to play an essential role in biological processes, including breast development, lactation, ageing, growth and regulation of metabolism, ovulation in female individuals, and control of sexual behaviours (Ge et al., 2003). Polymorphisms in the GH gene are known to correlate with different production yields, such as milk yield and quality, growth (Pal et al., 2005; Kovacs et al., 2006; Zhou et al., 2006), carcass composition and quality (Grochowska et al., 2001). Furthermore, this gene also plays an important role in postpartum growth and overall metabolism, as well as lactation in cattle (Fedota et al., 2016).

Studies on various cattle breeds have generally reported the L allele in the GH/Alu gene polymorphism and the B (T) allele in the IGFI/SnaBI gene polymorphism at higher frequencies. Tables 1 and 2 present some studies on the GH/AluI and IGFI/SnaBI genes.

**Table 1.** Summary of the results obtained from the literature and the current study on the frequency of IGFI/SnaBI

| Breeds                       | N         | Allele frequencies |             | References                 |
|------------------------------|-----------|--------------------|-------------|----------------------------|
|                              |           | A                  | B           |                            |
| <b>IGF-I/SnaBI</b>           |           |                    |             |                            |
| South Anatolian Red (SAR)    | 50        | 0.23*              | 0.77*       | Akis et al., 2010          |
| East Anatolian Red (EAR)     | 50        | 0.38*              | 0.62*       | Akis et al., 2010          |
| Charolais (Coahuila)         | 68        | 0.26               | 0.74        | Reyna et al., 2010         |
| Charolais (Nuevo León)       | 68        | 0.46*              | 0.54*       | Reyna et al., 2010         |
| Beefmaster (Tamaulipas)      | <b>25</b> | <b>0.03</b>        | <b>0.97</b> | Reyna et al., 2010         |
| Angus                        | 275       | 0.40               | 0.60        | Rogberg-Muñoz et al., 2013 |
| Charolais                    | 238       | 0.47               | 0.53        | Jeanmasset et al., 2014    |
| Black Hereford               | 36        | 0.48               | 0.52        | Daşet al., 2019            |
| Limousin                     | 34        | 0.42               | 0.58        | Daşet al., 2019            |
| Brahman                      | 24        | 0.34               | 0.66        | Daş et al., 2019           |
| Holstein                     | 250       | 0.46*              | 0.54 *      | Bonakdar et al., 2010      |
| <b>IGF-1/SnaBI (Eco105I)</b> |           |                    |             |                            |
| Montbeliarde                 | 163       | 0.67*              | 0.33*       | Szewczuk, 2016             |
| Necdi                        | 84        | 0.10               | 0.90        | Yazdanpanah et al., 2013   |
| Pesisir cattle               | 183       | 0.02               | 0.98        | Putra et al., 2017         |
| Jersey                       | 227       | 0.52*              | 0.48 *      | Piątkowska et al., 2021    |
| Polish Holstein              | 147       | 0.56*              | 0.44 *      | Piątkowska et al., 2021a   |
| Polish Holstein              | 181       | 0.52*              | 0.48 *      | Piątkowska et al., 2021b   |

|   |     |          |          |                       |
|---|-----|----------|----------|-----------------------|
| Holstein–Friesian bulls                 | 296 | 0.44 *   | 0.56 *   | Ardicli et al., 2018  |
| Kazakhstan Holstein                     | 100 | 0.58*    | 0.42*    | Beishova et al., 2019 |
| Holstein                                | 95  | 0.59*    | 0.41 *   | Silveira et al., 2019 |
| Native Sudanese Baggaracattle (Nyalawi) | 64  | 0.93     | 0.07     | Omer et al., 2018     |
| Native Sudanese Baggaracattle (Mesairi) | 63  | 0.92     | 0.08     | Omer et al., 2018     |
| Holstein-Friesian                       | 70  | 0.59*    | 0.41 *   | Nicolini et al., 2013 |
| Iranian Holstein                        | 60  | 0.40*    | 0.60*    | Araroutı et al., 2013 |
| Polish Holstein                         | 191 | 0.54*    | 0.46 *   | Szewczuk et al., 2013 |
| Holstein                                | 381 | 0.4(-/-) | 0.6(+/+) | Hax et al., 2017      |
| Kazakhstan black and white tawny        | 99  | 0.55*    | 0.45*    | Ulyanov et al., 2021  |

**Table 2.** Summary of the results obtained from the literature and the current study on the frequency of GH/AluI

| Breeds                              | N   | Allele frequencies |       | References               |
|-------------------------------------|-----|--------------------|-------|--------------------------|
|                                     |     | L                  | V     |                          |
| <i>bGH</i>                          |     |                    |       |                          |
| Native Antioquia (Colombia)         | 178 | 0.87               | 0.13  | Echeverri et al., 2015   |
| Italian Holstein                    | 695 | 0.86               | 0.14  | Fontanesi et al., 2015   |
| Grey steppe                         | 76  | 0.79               | 0.21  | Özdemir, 2011            |
| Holstein                            | 177 | 0.90               | 0.10  | Özdemir, 2011            |
| Brown Swiss                         | 177 | 0.90               | 0.10  | Özdemir, 2011            |
| East Anatolian Red                  | 51  | 0.95               | 0.05  | Özdemir, 2011            |
| East Anatolian Red                  | 76  | 0.84               | 0.16  | Özkan et al., 2009       |
| South Eastern Red                   | 180 | 0.44*              | 0.56* | Yardibiet al., 2009      |
| East Anatolian Red                  | 76  | 0.84               | 0.16  | Özkan et al., 2009       |
| East Anatolian Red                  | 50  | 0.43*              | 0.57* | Yardibiet al., 2009      |
| Holstein                            | 410 | 0.87               | 0.13  | Amiri et al., 2018       |
| Holstein Friesian                   | 578 | 0.87               | 0.13  | Pal et al., 2020         |
| Kazakhstan Holstein                 | 100 | 0.82               | 0.18  | Beishova et al., 2019    |
| Pesisir cattle                      | 175 | 0.79               | 0.21  | Afriani, 2018            |
| Holstein                            | 158 | 0.90               | 0.10  | Gilmanov et al., 2021    |
| Holstein's calves                   | 59  | 0.96               | 0.04  | Çınar et al., 2018       |
| Slovak spotted ows                  | 110 | 0.68*              | 0.32* | Hazuchova et al., 2013   |
| Egyptian water buffaloes            | 200 | 0.80               | 0.20  | El-Komy et al., 2021     |
| Slovak spotted black-and-white cows | 58  | 0.64*              | 0.36* | Moravcikova et al., 2012 |
| Limousin                            | 114 | 0.71,              | 0.29  | Sedykh et al., 2020      |
| Hereford                            | 115 | 0.69*              | 0.31* | Sedykh et al., 2020      |
| Kazakhstan black and white tawny    | 99  | 0.7                | 0.3   | Ulyanov et al., 2021     |
| Holstein                            | 186 | 0.82               | 0.18  | Özdemir et al., 2015     |
| Holstein                            | 115 | 0.65*              | 0.35* | Sönmez et al., 2018      |

Our study aimed to identify the genotypes of somatotrophic axis genes in 70 heads of Simmental cattle by the RFLP method and correlate the genotype polymorphisms of the relevant gene regions with milk yield traits

## MATERIALS AND METHODS

### Animal care, Animal DNA isolation and Primer Sets

In the present study, we collected blood samples from 70 heads of Simmental cattle with low degrees of relatedness for analysis. Animals were raised on a private Simmental cattle farm in Erzurum province.

DNA was isolated from whole blood using the Puregene DNA kit following the manufacturer's instruction (Gentra Systems Minnesota USA). In the PCR step, for growth hormone (bGH)-AluI, the 245-bp DNA region, the primers F: 5'-GTA GGG GAG GGT GGAAA TG -3 and R: 5' TGA CCCTCA GGT ACG TCT CC -3 (Özdemir, 2011), and for the 249-bp IGF1/SnaBI gene, F: 5'-ATT-ACA-AAG-CTG-CCT-GCC-CC-3' and R: 5'-ACC-TTA-CCC-GTA-TGA-AAG-GAA-TAT-ACG Primers -T-3' (Ge et al., 2001) were used.

### PCR conditions

Ten pmol/μL of each primer and 2.5 μL of dNTP-

mix (D7595: Sigma, St. Louis, MO, USA, 0.25mM), 0.5 units of Taq DNA polymerase (D1806: Sigma), 100 ng of template DNA, 5 µL of 10x PCR Buffer (100 mM Tris-HCl, pH 8.3, 500 mM KCl, 15 mM MgCl<sub>2</sub> and 0.01% gelatin), 1.5 µL of 0.25 mM MgCl<sub>2</sub>, and dH<sub>2</sub>O making the total volume of 30 µL were used for PCR amplification.

PCR amplification conditions for GH were as follows: 5 min at 94°C, 50 s at 94°C, and 50 s at 58°C; PCR amplification conditions for the IGFI gene were as follows: 5 min at 94°C, 30 s at 94°C, and 50 s at 61°C, and 30 cycles for both genes, with the final elongation temperature set at 72°C for 5 min and 1 cycle.

For the amplified IGFI and bGH genes, 2-5 U of the AluI and SnaBI restriction enzymes were added to each 7 µL PCR product and incubated at 37°C for 12 hours. After incubation, the samples were run on 3.0% agarose gel at 45 Volts for 2.5 hours, and bands were observed under UV light. The bGH and IGFI allele gene frequencies of each Simmental breed were calculated by counting. POPGENE software v1.32 (Yeh et al., 1999) was utilized to reveal whether the genotype frequencies were in Hardy-Weinberg equilibrium. SPSS 21.0 software program was used to analyze the association of genotypes with the population's milk data.

To research the impacts of IGFI and GH gene polymorphisms on lactation and some other milk yield traits in Simmental cattle raised on a private enterprise in Erzurum, a correlation analysis was conducted between the relevant polymorphic regions and the milk yield records of animals in different lactations, whose yield records were systematically kept between 2017 and 2020.

The statistical association analysis used milk yield traits, including real milk yield, 305-day milk yield, lactation period, and daily milk yield of the Simmental cattle breed. Data were analyzed by the SPSS 25.0 statistics package program (IBM SPSS 25.0 Corp. Inc.) based on the general linear model (Harvey, 1994). The analysis evaluated the effects of environmental factors, e.g., genotype, lactation order, and calving seasons, thought to affect the relevant yield trait.

According to the yield traits in the research, the following statistical model was employed.

$$Y_{ijk} = \mu + a_i + b_j + c_k + e_{ijk}$$

Where

$Y_{ijk}$  is any of the milk yield traits (real milk yield, 305-day milk yield, lactation period, and daily milk yield),

$\mu$  is the population average,

$a_i$  is the  $i^{\text{th}}$  genotype effect,

$b_j$  is the effect of the  $j^{\text{th}}$  lactation order ( $j$ : 3; 1<sup>st</sup> Lactation: 1, 2<sup>nd</sup> Lactation: 2, 3<sup>rd</sup> Lactation: 3, 4<sup>rd</sup> Lactation: 4, 5<sup>th</sup> Lactation: 5, 6<sup>th</sup> Lactation: 6, 7<sup>th</sup> Lactation: 7),

$c_k$  is the effect of the  $k^{\text{th}}$  calving season ( $k$ : 2; 1: winter-spring, 2: summer-autumn),

$e_{ijk}$  is the margin of error.

## RESULTS

The figures show the PCR amplification results and base sizes of PCR products (Figure 1).

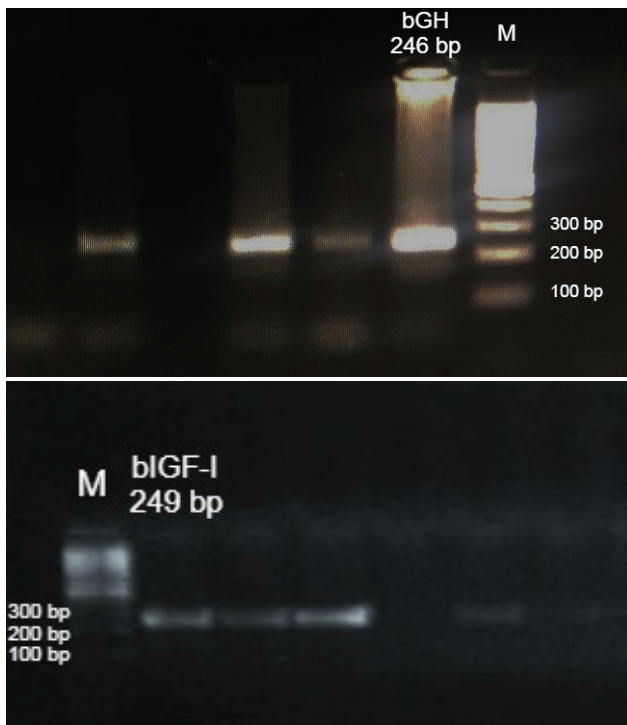
The 249 bp PCR products were digested by SnaBI for the IGFI gene, and the result of digestion was one band (249 bp) for the CC genotype, three bands (249, 223, and 26 bp) for the TC genotype, and two bands (223 and 26 bp) for the TT genotype (Figure 2).

The 246 bp products were acquired after the PCR process, and PCR products were digested by the AluI restriction enzyme for the GH gene. At the end of digestion, one band (246 bp) for the VV genotype, three bands (246, 171, and 52 bp) for the LV genotype, and two bands (171 and 52 bp) for the LL genotype were expected. The band of 52 bp could not be observed on agarose gel electrophoresis (Figure 3).

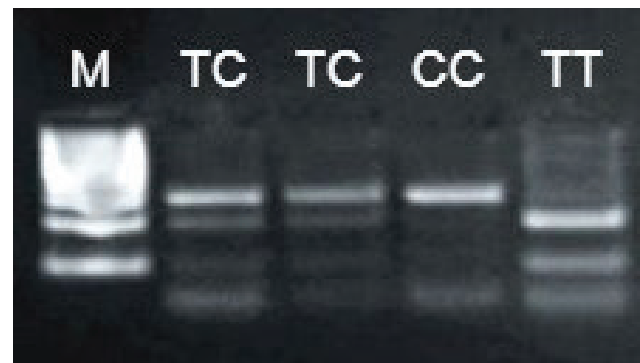
As a result of determining allele and genotype frequencies in Simmental cattle, it was found that the LL, LV, and VV genotype frequencies for the GH gene were 0.33, 0.57, and 0.10, respectively, while the TT, CT, and CC genotype frequencies for the IGFI gene were 0.35, 0.55, and 0.10, respectively. The LL and VV allele frequencies for the GH gene and the TT and CC allele frequencies for the IGFI gene were measured similarly as 0.62 and 0.38 (Table 3).

Hardy-Weinberg genetic equilibrium test showed that the distributions of these genotype frequencies were not in equilibrium in the analysed breed ( $P > 0.05$ ).

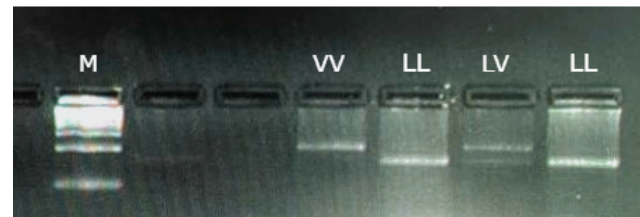
The overall averages for milk yield, 305-day milk yield, daily milk yield, real milk yield, and lactation



**Figure 1.** PCR results of the bGH and IGFI gene regions (1<sup>st</sup> primer pair 246, 2<sup>nd</sup> primer pair 249, with Standard GENESTA 100 bp DNA marker images, respectively)



**Figure 2.** IGFI-SnaBI RFLP results (CC, CT, and TT genotypes with Standard GENESTA100 bp DNA marker images, respectively)



**Figure 3.** GH-AluI RFLP results (VV, LV, and LL genotypes with Standard GENESTA 100 bp DNA marker images)

**Table 3.** The genotype and allele frequencies and H-W equilibrium IGFI-SnaBI and GH-AluI genes

| IGFI allele and genotype frequencies |     |      |      |             |                  | GH allele and genotype frequencies |     |      |      |             |                  |
|--------------------------------------|-----|------|------|-------------|------------------|------------------------------------|-----|------|------|-------------|------------------|
| Genotype                             | N   | T    | C    | % Frequency | H-W <sup>a</sup> | Genotype                           | N   | L    | V    | % Frequency | H-W <sup>a</sup> |
| TT                                   | 23  | 46   | 0    | 34.85       | 0.20             | LL                                 | 23  | 46   | 0    | 33.33       | 0.11             |
| CT                                   | 36  | 36   | 36   | 54.55       |                  | LV                                 | 39  | 39   | 39   | 56.52       |                  |
| CC                                   | 7   | 0    | 14   | 10.61       |                  | VV                                 | 7   | 0    | 14   | 10.14       |                  |
| Total                                | 66  | 82   | 50   | 100.00      |                  | Total                              | 69  | 85   | 53   | 100.00      |                  |
| P                                    | 132 | 0.62 | 0.38 |             |                  | P                                  | 138 | 0.62 | 0.38 |             |                  |

a. P-value for the test for Hardy-Weinberg equilibrium, in which P>0.05 indicates that the sampled population is not in Hardy-Weinberg equilibrium.

**Table 4.** Effects of IGFI/SnaBI genotypes on milk yields in Simmental cattle

| Variation Sources | N               | Daily milk yield  |                   | Lactation milk yield |                   | 305-day milk yield |                   | Lactation period |  |
|-------------------|-----------------|-------------------|-------------------|----------------------|-------------------|--------------------|-------------------|------------------|--|
|                   |                 | $\bar{X} \pm S_x$ | $\bar{X} \pm S_x$ | $\bar{X} \pm S_x$    | $\bar{X} \pm S_x$ | $\bar{X} \pm S_x$  | $\bar{X} \pm S_x$ |                  |  |
| IGFI/SnaBI        | CC              | 36                | 18,279±0,702      | 5468,285±283,960     | 5571,231±218,310  | 301,822±13,997     |                   |                  |  |
|                   | CT              | 39                | 18,265±0,690      | 5085,252±279,220     | 5515,907±214,666  | 282,320±13,763     |                   |                  |  |
|                   | TT              | 8                 | 17,044±1,483      | 4916,054±600,087     | 5286,936±461,350  | 304,416±29,579     |                   |                  |  |
|                   | <b>P</b>        |                   | <b>0,732</b>      | <b>0,536</b>         | <b>0,857</b>      | <b>0,545</b>       |                   |                  |  |
| Calving season    | 1               | 48                | 17,742±0,786      | 4783,274±318,281     | 5228,148±244,696  | 278,548±15,688     |                   |                  |  |
|                   | 2               | 35                | 17,984±0,809      | 5529,786±327,522     | 5687,901±251,801  | 313,824±16,144     |                   |                  |  |
|                   | <b>P</b>        |                   | <b>0,817</b>      | <b>0,081</b>         | <b>0,160</b>      | <b>0,094</b>       |                   |                  |  |
|                   | Lactation order | 2                 | 10                | 17,026±1,439         | 4994,060±582,260  | 5272,492±447,645   | 297,624±28,700    |                  |  |
| 3                 |                 | 17                | 18,423±1,067      | 5300,083±432,062     | 5677,206±332,172  | 290,881±21,297     |                   |                  |  |
| 4                 |                 | 18                | 17,422±1,085      | 5577,652±438,982     | 5493,044±337,492  | 332,631±21,638     |                   |                  |  |
| 5                 |                 | 18                | 18,687±0,983      | 5294,563±397,867     | 5674,684±305,882  | 280,223±19,611     |                   |                  |  |
| 6                 |                 | 14                | 17,440±1,165      | 5044,346±471,381     | 5327,560±362,400  | 298,212±23,235     |                   |                  |  |
| 7                 |                 | 6                 | 18,177±1,745      | 4728,477±706,436     | 5303,162±543,112  | 277,545±34,821     |                   |                  |  |
| <b>P</b>          |                 |                   | <b>0,876</b>      | <b>0,893</b>         | <b>0,924</b>      | <b>0,502</b>       |                   |                  |  |
| Total             | 83              | 17,863±0,605      | 5156,530±244,727  | 5458,025±188,148     | 296,186±12,063    |                    |                   |                  |  |

$\bar{X}$ : General Means,  $S_x$ : Standard deviation

period were 5458,025kg, 17,863 kg, 5156,530 kg, and 296,186days, respectively. Among the polymorphic regions, the highest average for all milk yield values was obtained with the CC genotype and the lowest value was obtained with the TT genotype for the IGFI/SnaBI polymorphic region, while the difference between the highest and lowest average milk yield values was not insignificant.

The differences between the genotype according to the GH/AluI fragment differences and the milk

yield averages of 91 Simmental cattle in 6 lactations and the genotype, calving season, and lactation order factors were statistically insignificant ( $p>0.05$ ). The overall averages for milk yield, 305-day milk yield, daily milk yield, real milk yield, and lactation period were 5443,264 kg, 18,355 kg, 5619,733 kg, and 301,545days, respectively. Among the yield records, the highest genotype average was observed in the LL genotype, while the lowest yield average was observed in the LV genotype.

**Table 5.** Effects of GH/AluI genotypes on milk yields in Simmental cattle

| Variation Sources |          | N  | Daily milk yield<br>$\bar{X} \pm S_{\bar{x}}$ | Lactation milk yield<br>$\bar{X} \pm S_{\bar{x}}$ | 305-day milk yield<br>$\bar{X} \pm S_{\bar{x}}$ | Lactation period<br>$\bar{X} \pm S_{\bar{x}}$ |
|-------------------|----------|----|---|---|---|---|
| GH/AluI           | LL       | 33 | 18,349±0,728                                  | 5541,241±292,225                                  | 5624,453±228,070                                | 304,904±14,130                                |
|                   | LV       | 47 | 18,167±0,623                                  | 5059,354±250,305                                  | 5499,343±195,353                                | 282,277±12,103                                |
|                   | VV       | 11 | 18,549±1,215                                  | 5729,198±487,804                                  | 5735,402±380,712                                | 317,454±23,587                                |
|                   | <b>P</b> |    | <b>0,954</b>                                  | <b>0,290</b>                                      | <b>0,824</b>                                    | <b>0,273</b>                                  |
| Calving period    | 1        | 54 | 18,447±0,672                                  | 5262,943±269,631                                  | 5508,863±210,436                                | 289,717±13,037                                |
|                   | 2        | 37 | 18,262±0,742                                  | 5623,586±297,773                                  | 5730,602±232,400                                | 313,374±14,398                                |
|                   | <b>P</b> |    | <b>0,847</b>                                  | <b>0,350</b>                                      | <b>0,461</b>                                    | <b>0,206</b>                                  |
| Lactation order   | 2        | 10 | 17,306±1,332                                  | 5093,744±534,652                                  | 5297,029±417,275                                | 295,945±25,852                                |
|                   | 3        | 17 | 18,875±1,040                                  | 5584,882±417,492                                  | 5817,002±325,836                                | 297,047±20,187                                |
|                   | 4        | 20 | 18,008±0,970                                  | 5689,066±389,565                                  | 5602,114±304,040                                | 326,819±18,836                                |
|                   | 5        | 21 | 18,983±0,965                                  | 5408,306±387,470                                  | 5738,397±302,405                                | 283,487±18,735                                |
|                   | 6        | 16 | 17,388±1,046                                  | 5304,829±419,796                                  | 5345,561±327,634                                | 312,241±20,298                                |
|                   | 7        | 7  | 19,570±1,552                                  | 5578,758±623,270                                  | 5918,292±486,438                                | 293,732±30,137                                |
|                   | <b>P</b> |    | <b>0,681</b>                                  | <b>0,940</b>                                      | <b>0,794</b>                                    | <b>0,600</b>                                  |
| Total             |          | 91 | 18,355±0,522                                  | 5443,264±209,579                                  | 5619,733±163,568                                | 301,545±10,134                                |

$\bar{X}$ : General Means,  $S_{\bar{x}}$ : Standard deviation

## DISCUSSION

The study carried out in the Simmental breed because of LL and CC genotypes are seen at the same rate distributions so allele frequencies are similar for GH/AluI and IGFI/SnaBI genes. Tables 1 and 2 present the allele and genotype frequencies obtained in previous polymorphic studies on the GH and IGFI genes in cattle. Among these studies, those that show similarities and differences with our studies are marked. The distributions of allele and genotype frequencies for both genes are generally similar to previous studies, and it is seen that the L allele is dominant for the GH hormone, while the T allele is dominant for the IGFI gene. According to the Hardy-Weinberg equilibrium test, the distributions of genotype frequencies in the herd were estimated to be in not balanced because the herd was raised in a closed barn environment, external migration was absent, and there was high mortality due to uncontrolled breeding.

In two different studies in which we correlated the

yields of GH/AluI gene polymorphisms in 118 and 186 numbers of Holstein cattle breeds from different farms, no significant relationship was found between genotypes and milk yields. A similar relationship could not be found between GH-AluI and IGFI-SnaBI gene polymorphisms and milk yield in Simmental cattle (Sönmez et al., 2018; Özdemir et al., 2018). Therefore, considering our three association studies, we examined previous studies to determine the potential for these gene regions to be used as markers.

In our study of associating the IGFI/SnaBI gene polymorphism with milk yield in 70 cattle breeds, we thought that the relevant polymorphic gene marker was not associated with milk yields may be due to a small number of samples. However, similar results were obtained in previous milk yield association studies on different breeds and with a large number of samples. Studies on milk yield generally report that the IGFI/SnaBI gene polymorphism does not have a significant effect. Similar to our study, in the study

that examined the impact of the IGFI gene polymorphism on milk yield in three breeds (227 Jersey, 147 Polish Holstein-Friesian black-and-white (HO) and 181 Polish Holstein-Friesian red-and-white (RW)) in different lactations, the average milk yield was high in individuals with the CC genotype, but there was no significant difference between this average and other genotype averages (Piałkowska et al., 2021). The study in which the serum IGF-I concentration and reproductive performance of Holstein dairy cows were associated with IGF-I gene polymorphisms reported no significant relationship between milk production and body condition score and IGF-I genotypes (Silveira et al., 2019). In different studies conducted on a number of which is over 100 Holstein cattle showed that the IGFI/SnaBI polymorphism did not significantly affect milk yield, but the fat and protein ratios in milk were high, especially in individuals with the AB (CT) genotype (Bonakdar et al., 2010; Zhang et al., 2018; Beishova et al., 2017; Beishova et al., 2018; Beishova et al., 2019). For the IGFI gene, Ge et al. (2001) reported that the c. 512 C>T polymorphic marker defined by studies on milk yield in cattle breeds was generally not associated with milk yield. However, it was reported that different SNPs identified for the IGFI gene were associated with milk yield (Mullen et al., 2011; Lynch et al., 2010; Gui et al., 2018). The IGFI-SnaBI polymorphism studies conducted in different cattle breeds reported that the CC genotype was positively associated with the meat and fat weight of the carcass (Ge et al., 2001; Reyna et al., 2010; Siadkowska et al., 2006). Especially among studies on meat yield, studies are showing that the IGFI gene affects meat quality parameters and meat colour change, positively associated with live body weight at slaughter, cold carcass weight, meat and fat weight in valuable cuts, body weight, subcutaneous back fat, and waist circumference musculature (Curi et al., 2005; Siadkowska et al., 2006; Ardicli, 2018; Szwczuk et al., 2013). In the study determining the effects of the IGFI gene polymorphism on the reproductive data of different cattle breeds, it was revealed that the genotypes defined with IGF-SnaBI were effective on reproductive data but did not affect milk yield. Studies on reproductive data associated the SNP identified in the IGF-1 gene with the resumption of the postpartum lying phase and affected reproductive parameters in Holstein cows (Nicolini et al., 2013; Ararouti et al., 2013). In another study, the SNP within the GH/IGF-1 pathways was associated with the reproductive performance of Holstein cows under

heat stress conditions and associated with services per conception (SPC) (Leyva-Corona et al., 2018). While most studies have reported that the IGFI gene affects reproductive data, some studies have reported no significant relationship between IGF-I SnaBI genotypes in Holstein cattle kept under different breeding conditions and the fertility of Holstein cows raised in semi-intensive or intensive regimens (Hax et al., 2017).

Studies have demonstrated that the GH/AluI gene polymorphism, like the IGFI/SnaBI gene polymorphism is more effective on growth data and body weight than milk yield, especially in cattle. Similar to our study among the association studies on the GH hormone, a study conducted on black and white calico heifers reported that the amount of milk and the protein and fat ratios in milk were high in LL genotype heifers (Gilmanov et al., 2021) but the difference between the highest and lowest average milk yield values was not significant. In the studies GH-AluI gene polymorphism was determined in different breeds and the relationships between the obtained genotype data and body weight gain and body measurements were investigated genotype data showed that the GH-AluI polymorphism was related to the weaning body weights and the length of the chest circumference (Çınar et al., 2018; Afriani and Putra, 2018). In the association analyses conducted milk production length according to GH-AluI genotypes was not found significant, however, other SNPs identified in the GH gene were found to be associated with milk yields. (Zhou et al., 2006; Maylinda, 2011; Moravcikova et al., 2012; Hazuchova et al., 2013). Studies conducted on different cattle types and buffaloes have reported that GH-AluI gene polymorphisms affect meat yield, pre-slaughter body weight, carcass meat weight, slaughter weight and growth data (Pereira et al., 2005; Curi et al., 2006; Sedykh et al., 2020; El-Komy et al., 2021)

Parallel to our research, polymorphic association studies analyzing somatotrophic axis genes together have generally associated these genes with growth and reproduction data but not with milk yield, especially GH/AluI and IGFI/SnaBI (Balogh et al., 2008; Ulyanov et al., 2021). The two different META analysis studies show that the common L allele was dominant and no significant difference was found in the results of the meta-analysis and subgroup analysis for the milk yields in the LL, LV, and VV genotypes Akcay et al., 2020; Bangar et al., 2021). The results of the

meta-analysis on bGH/AluI and IGFI/SnaBI genetic variations in cattle confirm the results of our study.

In association analysis studies published to determine the potential of the gene polymorphisms to be used as markers in cattle breeding, the above-mentioned genes appear to have significant implications for body weight, meat yield, and reproductive performance in general. Studies to be conducted in the field of animal breeding estimate the effects of the determined bGH/AluI and IGFI/SnaBI genetic variations on different breeds with different performance traits and their potential to be used as markers in breeding

programs. However, previous studies and our work have shown that bGH/AluI and IGFI/SnaBI genetic variations in cattle are less likely to be used as markers in milk data analyses.

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## CONFLICTS OF INTEREST

The Authors have no conflict of interest to declare

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