UDC 636.92.033:575.113/.22

GENETIC ASPECTS OF THE REPRODUCTIVE ABILITY OF DOE RABBITS: THE ROLE OF POLYMORPHISM IN GROWTH HORMONE GENE

*** V. V. Dzitsiuk[1], O. V. Boiko[2], O. F. Honchar[3], O. M. Havrysh[4], O. J. Guzevatiy[5], T. V. Lytvynenko[6], O. P. Vergeles[7]**

[1]The M.V. Zubets Institute of Animal Breeding and Genetics of the National Academy of Agrarian Sciences of Ukraine, 1, Pohrebniaka Str., Chubynske village, Boryspil District, Kyiv Region, 08321, Ukraine

[2–4]The Cherkasy Experimental Station of Bioresources of the National Academy of Agrarian Sciences of Ukraine, 76, Pasterivska Str., Cherkasy, 18036, Ukraine

[5]The M.F. Ivanov Institute of Animal Husbandry of Steppe Regions, "Askania-Nova" — the National Scientific Breeding and Genetic Center for Sheep Breeding of the National Academy of Agrarian Sciences of Ukraine, 1, Pohrebniaka Str., Chubynske village, Boryspil District, Kyiv Region, 08321, Ukraine

[6, 7]The National University of Life and Environmental Sciences of Ukraine of the Ministry of Education and Science of Ukraine, 16, Vystavochna Str., acad. bldg. 12D, Kyiv, Ukraine

*E-mail: *[1]valentynadzitsiuk@gmail.com, [2]aleksboy18@meta.ua, [3]of.gonchar@gmail.com, [4]gavrish.olexandr@gmail.com, [5]oleg_guzevatiy@ukr.net, [6]tvpptvergeles@gmail.com*

ORCID: 10000-0001-9697-4165, 20000-0002-3917-5583, 30000-0003-2269-9767, 40000-0002-8632-6508, 50000-0002-2470-5430, 6 0000-0003-0415-5264

The aim of the study was to analyze the parameters of the reproductive ability of Chinchilla doe rabbits with different genotypes by locus GH (mutation c.-78C>T). **Methods.** The genotypes of animals were determined by PCR-RFLP. The amplification was conducted in the programmed thermocycler Applied Biosystems MiniAmp (Thermo Scientific, the USA) using specific primers. The amplicons were cleaved with the endonuclease *Bst*UI (Thermo Scientific, the USA), and the fragments were separated in 2 % agarose gel supplemented with ethidium bromide. The following indices were used to evaluate the reproductive ability of doe rabbits: milk production (kg), number of litter kits, birth and weaning weight of litter (kg), and average daily gain of infant rabbits (g). The population and genetic indices were assessed using common methods. The impact of the genotype of GH locus on the parameters of the reproductive function of doe rabbits with different genotypes by locus GH was analyzed using ANOVA. **Results.** The investigated sampling of Chinchilla doe rabbits (34 animals) was found to have *Bst*UI-polymorphism in position -78 of the start codon of exon I of gene GH (c.-78C>T). The analysis of associations demonstrated that the doe rabbits with the heterozygous genotype CT in locus GH had higher indices of milk production, number of litter kits and live weight of the litter, average daily gain, and live weight of one animal at the age of 35 days. Statistically significant differences were found between genotypes CT and TT in terms of milk production ($p<0.001$) and live birth and weaning weight of the litter ($p<0.05$). **Conclusions.** The results obtained demonstrated the promising perspectives of the use of *Bst*UI-polymorphism of locus GH (c.-78C>T) as a genetic marker in the breeding programs, aimed at enhancing the fecundity of rabbits.

Keywords: polymorphism, gene GH, genotype, prolificacy, rabbit.

DOI: https://doi.org/10.15407/agrisp12.01.037

INTRODUCTION

Rabbit breeding is a high-value branch of the animal breeding industry due to the rapid reproduction of livestock, efficient use of fodder, and very low production costs (El-Sabry et al., 2021, Wongnaa et al., 2023, Siddiqui et al., 2023; Wang et al., 2022).

The efficiency of industrial rabbit breeding depends on their reproductive potential, including the number and survival rate of the newborns (Helal et al., 2024). However, the traditional methods of rabbit breeding demonstrate limited efficiency in improving reproductive traits. Firstly, it is conditioned by their dependence on gender which complicates the selection, and secondly, by a low coefficient of heritability for these traits. The resulting genetic progress, achieved using traditional breeding, is often insignificant (Sosa-Madrid et al., 2020).

The use of genomic information and marker-associated selection (MAS) to enhance the efficiency of breeding provides for a considerable acceleration of genetic progress tempo in industrial rabbit breeding (Bozhilova-Sakova et al., 2022; Kyselová et al., 2021). Among potential genes-candidates, associated with productive and reproductive traits in farm animals, including rabbits, special attention is paid to the growth hormone gene (GH).

Growth hormone gene (GH) is located on chromosome 19 of rabbits, and consists of 5 exons and 4 introns, encoding the protein of 216 aminoacids. The main physiological function of gene GH is to regulate the post-natal growth, metabolism of lipids, and formation of the muscle bulk in mammals (Fontanesi, 2012).

The studies on different allelic variants of GH and their association with productive and reproductive traits of farm animals are conducted in different countries, using different species and breeds. For instance, the associations between gene GH and performance were studied in bovine cattle (Cruz et al., 2022; Dzitsiuk, Guzevatiy, 2024), goats (Buranakarl et al. 2024), sheep (Al-Muhsen et al., 2019; Kumar et al., 2024), pigs (Kmieć et al., 2007), and rabbits (Garcia, Argente, 2020).

The studies of Abdel-Kafy et al. (2015) determined the impact of *Bst*UI-polymorphism of gene GH (c.-78C>T) on the live weight of rabbits. In addition, in rabbits, gene GH plays a considerable part in the complex regulation of reproductive processes (Gencheva et al., 2022; Migdal et al., 2019). It modulates gametogenesis, for instance, it stimulates the development and maturity of spermatogonia (Zachmann, 1992) and impacts such parameters of ejaculate as volume, concentration, and motility of spermatozoa (Khalil et al., 2021; Zachmann, 1992; Tusell et al., 2012). In doe rabbits, gene GH impacts the development of follicles (Downing and Scaramuzzi, 1991), stimulates the maturity of oocytes (Silva et al., 2009) and regulates lactogenesis (Fontanasi et al., 2012; Tusell et al., 2012; Amalianingsih i Brahmantiyo, 2014). A relevant criterion of reproductive ability in selecting maternal lines in rabbit breeding is the number of litter kits at birth and weaning (Garreau H., et al., 2004). In this context, the genes, impacting the ability of a doe to reproduce, are of special relevance.

Considering the role of the growth hormone in the reproduction processes of rabbits, we studied the possible association between a single nucleotide polymorphism (SNP) c.-78C>T of gene GH and the reproductive characteristics of Chinchilla doe rabbits. This study is a logical continuation of the study of the polymorphism of gene GH, initiated in our previous publication in *Visnyk ahrarnoi nauky* scientific journal (Dzitsiuk et al., 2025).

MATERIALS AND METHODS

The studies were conducted at the Genetics Laboratory of the M.V. Zubets Institute of Animal Breeding and Genetics, the NAAS, and the experimental farm of the Cherkasy Experimental Station of Bioresources, the NAAS. The experimental group of 5-month-old Chinchilla doe rabbits (34 animals) was used as the study object.

The investigated doe rabbits were kept in one-storied cage complexes. Each animal was identified with an ear tag and kept in group cages of 4 animals in each, and after giving birth — in individual cages. The cage size was 80×60×35 cm which ensured the minimal area of 0.14–0.22 sq.m. per animal and corresponded to the age and weight norms. The animals were fed with commercial complete pelleted feed.

Peripheral blood of doe rabbits taken from the ear vein into blood collection tubes with the anticoagulant EDTA was used as a source of biological material.

DNA extraction was conducted using the DNA extraction kit *Quick-DNA Miniprep Plus* (Zymo Research, the USA). The efficiency of DNA extraction was defined by electrophoretic separation in 0.7% agarose gel at 200 V for 10 min.

The genotypes of animals in the experimental population were determined by PCR-RFLP. The analysis of the allelic frequencies of the locus of gene GH was conducted along with the determination of *Bst*UI-polymorphism of the start codon of exon I, caused by replacing cytosine with thymine.

The PCR was conducted in the programmed thermocycler Applied Biosystems MiniAmp (Thermo Scientific, the USA). The reaction mixture (the volume of 10 µl) contained the fivefold PCR buffer with ammonium sulfate, 2.5 mmol MgCl2, 50 ng DNA, 1 µM of each primer, 0.2 mm of each dNTP, 0.5 un. of DreamTaq polymerase (TermoFisher, the USA). The following primers were used for the amplification of DNA fragments: GTA TAG TGG GAT GGG GTT GG; TTA CGC TCC CAT TCA GAA GC (Fontanesi et al., 2012; Migdal et al., 2019). The amplification was conducted according to the following protocol: primary denaturation (95°C) — 2 min; 34 amplification cycles (denaturation at 95°C — 30 s, hybridization of primers at 59°C — 30 s, elongation at 72°C — 45 s); final elongation at 72°C for 5 min, retention at 15°C.

The size of the amplified fragment was 231 bp. The amplicons were cleaved with the endonuclease *Bst*UI (Thermo Scientific, the USA) at 37°C/15 min. The restriction products were separated in 2.5 % agarose gel at 90 V for 90 min.

The indices of milk production, number of litter kits, live weight of the litter at birth and weaning, and the average daily gain of young rabbits were used as experimental traits of the reproductive function of doe rabbits. The amount of milk, produced by the feeding breeding rabbit (the milk production of does), was determined by the formula:

$$M = (W_1 - W_2) \times C,$$

where M — milk production of a doe with young rabbits; W_1 — live weight of the litter of young rabbits at the age of 35 days, g; W_2 — live weight of the litter of newborn rabbits, g; C — coefficient of converting live weight of young rabbits into milk production of a doe rabbit (Boiko et al., 2024).

The study results were used to determine the general population and genetic parameters: observed (Ho) and expected (He) heterozygosity, frequencies of alleles and genotypes, correspondence of the genetic equilibrium state by Hardy-Weinberg, Wright's fixation index according to the general methods, using POPGENE32 software (https://sites.ualberta.ca/~fyeh/popgene_download.html). The reproductive parameters of doe rabbits with different genotypes by locus GH were analyzed using ANOVA.

RESULTS

*Bst*UI-polymorphism in the start codon of exon I of the growth hormone locus leads to the occurrence of two allelic variants, C (restriction site is absent) and T (restriction site is present). The size of the amplicon is 231 bp.

In the experimental sampling of Chinchilla doe rabbits, the study results revealed individuals with all possible genotype variants — CC, CT, TT. The homozygous TT genotype is characterized by the presence of a non-cleaved DNA fragment of 231 bp. The CC homozygous genotype after treatment with restriction endonuclease *Bst*UI demonstrated two DNA fragments of 169 bp and 62 bp, indicating the presence of a cleavage site. The heterozygous CT genotype is characterized by the presence of all three fragments: one non-cleaved (231 bp) and two cleaved ones (169 bp and 62 bp).

It was determined that animals with heterozygous genotype CT prevailed in the experimental sampling of doe rabbits by the growth hormone locus. The share of CC homozygotes is 26.5 %; the animals with TT genotype make up 20.6 % of the total number of genotyped animals. The frequencies of alleles C and T were 0.529 and 0.471, respectively (**Fig. 1**).

To evaluate the genetic equilibrium of the sampling, we conducted the comparative analysis of the empirically determined frequencies of alleles and the frequencies, expected according to Hardy-Weinberg law. The statistical processing of the data using criterion χ^2 did not find statistically significant deviations from the expected values ($p > 0.1$).

The results confirm that the investigated sampling is in the state of genetic equilibrium, and one may assume that either the selection does not impact the investigated locus considerably or its impact is insufficient to disturb the equilibrium. In the investigated sampling of animals, the level of observed heterozygosity (Ho = 0.52) somewhat exceeds the expected heterozygosity (Ne = 0.49). The negative value of Fisher's coefficient (Fis = –0.06) demonstrates the excess of heterozygotes, which may be an indicator of outbreeding. The polymorphic information content (PIC), which is an index of genetic diversity, is 0.50 which demonstrates a high level of diversity in the investigated population of rabbits. The effective

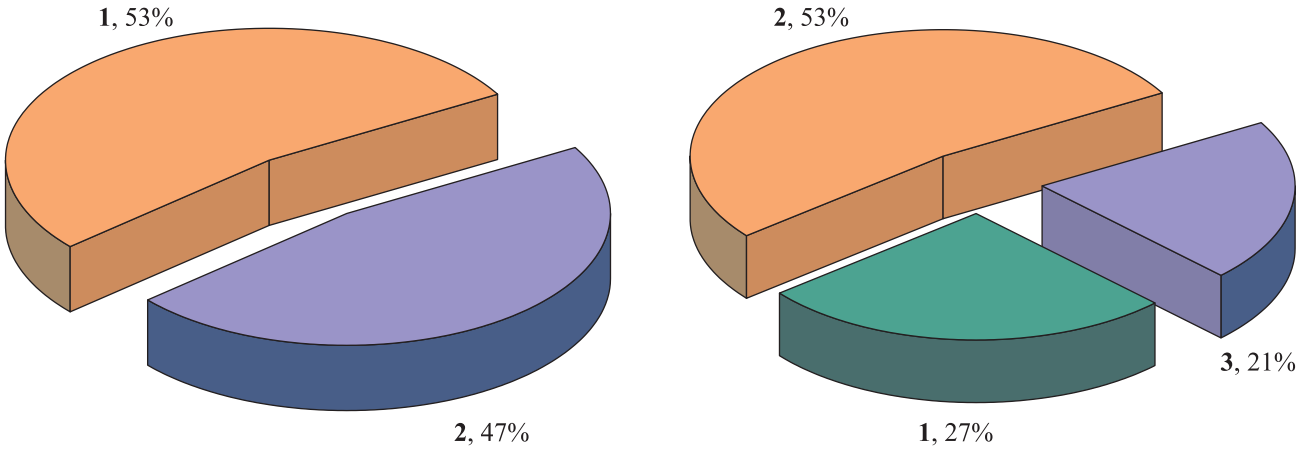

Fig. 1. The frequencies of alleles and genotypes in the investigated population of Chinchilla rabbits

number of alleles (ne = 2.0) reaches the threshold value, which is an index of efficient participation of both alleles in genotyping, typical for diallelic systems (**Table 1**).

The locus of the growth hormone gene was used to analyze the parameters of the reproductive ability of doe rabbits in the experimental group with all the determined genotypes — CC, CT, TT (**Table 2**).

The results of the study of milk production of doe rabbits demonstrated that the animals with heterozygous genotype CT were characterized by the highest indices of the milk production index, which were reli-

Table 1. The main genetic and population characteristics of the Chinchilla rabbit population by locus CH

Breed, n	Ho	He	nc	Ca	PIC	Fis	χ^2
Chinchilla, 34 animals	0,529	0,498	2,0	0,47	0,50	–0,06	0,42

He — expected heterozygosity; Ho — observed heterozygosity; nc — effective number of alleles; Ca — homozygosity coefficient; PIC — polymorphic information content.

Table 2. The indices of reproductive ability in doe rabbits with different genotypes by growth hormone gene

Parameters	Female genotype		
	CC (n=9)	CT (n=18)	TT (n=7)
Milk production, kg	4.520±0.50	5.650±0.34*	2.350±0.46*
Liveborn kits/litter, n	6.22±0.52	7.26±0.54	5.4±1.20
Stillborn kits/litter, n	0	0.35±0.08	2.6±1.02
Weaned rabbits, n	6.22±0.52	6.70±0.60	3.94±1.20
Percentage of survival of rabbits until weaning at the age of 35 days, %	100.0	92.93±3.82	73.06±5.41
Live weight of litter at birth, kg	0.38±0.078	0.49±0.030**	0.30±0.050**
Live weight of litter at weaning, kg	5.12±0.012	6.96±0.022**	3.95±0.028**
Live weight of one animal at 35 days, kg	0.86±0.032	0.89±0.029	0.80±0.038
Average daily gain of a young rabbit, g	0.022±0.0007	0.026±0.0009	0.021±0.0019

* ($p < 0.01$); ** ($p < 0.05$).

ably higher than those of homozygotes TT ($p < 0.01$). The analysis of variation coefficients (Cv) for milk production parameters demonstrated a low level of variability in the investigated groups, where Cv values did not exceed 12.5 %. As for the size of the litter (the number of young rabbits), higher indices at birth were registered for heterozygous animals with genotype CT as compared to the carriers of homozygous genotypes CC and TT, by 14.3 % and 25.6, respectively. Similarly, the animals with genotype CT prevailed in terms of the litter size at weaning. However, no statistically significant differences between genotypes were found for this index. The value of the variation coefficients among the indices of litter size demonstrated that the variability level was above average, in a wide range of 10.01–33.60 %. The highest variation index was observed for homozygotes TT, while in heterozygotes, it was closer to the average one. No stillborns were registered in the group of doe rabbits with genotype CC, which demonstrated a high survival rate of the progeny. In the group with genotype CT, there was an insignificant decrease in the progeny survival — about 4 % of non-viable newborns.

The most manifested decrease in survival rate with the statistically significant difference ($p < 0.01$) was observed in the groups with genotype TT, where 40 % of young rabbits did not survive after birth. 100 % survival of young rabbits until weaning at the age of 35 days was observed in the group of doe rabbits with genotype CC, while in the group with genotype TT, this index was much lower — 73.06 %, and in the group of genotype CT, it had an intermediate value — 92.93 %. Noteworthy is a group of doe rabbits with genotype TT which was characterized by the smallest litter size, a high percentage of stillborn animals, and the lowest survival rate of young rabbits until weaning, which may indirectly demonstrate that their performance is not high. The analysis of the distribution of genotypes by live birth weight of the litter indicates that genotype CT is associated with a larger litter weight as compared to TT (by 30 g) and CC (by 50 g). This tendency was preserved in the analysis of the live litter weaning weight, when the difference between genotypes CT and TT was statistically significant ($p < 0.05$). The doe rabbits with genotype CT have some advantages over animals with other genotypes in terms of the live weight of one animal at the age of 35 days and the average daily gain. Yet the differences, found in terms of the live weight of young rabbits at birth and weaning are statistically insignificant, which may be caused by a considerable range of variation (the variation coefficient is almost 22 %).

DISCUSSION

In this study, we analyzed *Bst*UI-polymorphism (c.-78C>T) in the start codon of exon I of the growth hormone gene (GH) to investigate its possible association with the reproductive function traits of Chinchilla doe rabbits. The review of the literature showed that most published data indicate a higher frequency of allele C as compared to allele T in this polymorphic locus. For instance, in the population of Harnali rabbits, the frequency of allele C was 0.630, and that of allele T — 0.370 (Ramadan et al. 2020). Similar results were obtained in the population of New Zealand white rabbits (NZW), where the frequencies of alleles C and T were 0.613 and 0.387, respectively, and the frequency of the homozygous genotype CC exceeded the frequency of TT (0.300 against 0.075) with the frequency of the heterozygous genotype CT — 0.625 (Gencheva et al., 2018). In Flemish giant rabbits, the frequencies of alleles C and T were 0.68 and 0.32, respectively, and those of genotypes — CC — 0.449, CT — 0.457, TT — 0.093 (Migdał et al. 2019).

Similar results were obtained with New Zealand white rabbits, where the frequency of heterozygous genotype CT was 0.615, while the frequencies of homozygous genotypes CC and TT were much lower — 0.270 and 0.115, respectively, which demonstrates the prevalence of allele C (0.577) over allele T (0.423) (Hristova D., et al., 2017). A higher distribution of allele C as compared to allele T (0.625 against 0.375) was also reported by Fontanasi et al. (2012) and Amalianingsih et al. (2014) in New Zealand white rabbits and Californian breeds. The communications of the same authors show that Champange d`Argent has only allele C, and in Satin breed, the frequencies of alleles C and T are the same.

The results of the studies, conducted by Rogel-Gaillard et al. (2009) demonstrated an opposite tendency: the frequency of allele T (0.594) exceeded that of allele C (0.406) in Strokach breed of rabbits. Similar data were obtained by Hussein et al. (2015), where the rabbits of the APRI line had the same distribution of frequencies of alleles T and C (0.540 and 0.460, respectively). According to numerous studies, gene GH plays a key role in the regulation of reproduction processes in rabbits (Fontanasi et al., 2008,

2012; Amalianingsih and Brahmantiyo, 2014; Abdel-Kafy et al., 2015; Migdal et al., 2019).

In these studies, this gene is mostly viewed as a promising candidate for the identification of molecular markers, associated with quantitative and qualitative traits of sperm in rabbits (Fontanesi et al., 2012; Abdel-Kafy et al., 2015; Migdal et al., 2019). At present, there are rare studies on the possible association between the polymorphism in gene GH and reproductive function traits in doe rabbits. For instance, Ramadan et al. (2020) conducted a study of the reproductive function of doe rabbits with different genotypes by gene GH and determined that the animals with the heterozygous genotype CT had more litter kits and a higher live weight of young rabbits at the age of 8 and 12 weeks, as compared to the homozygous genotypes CC and TT.

The results of the study, conducted by Abdel-Kafy et al. (2015), demonstrated the association between genotype CC by mutation c.-78C>T of gene GH with the earlier age of sexual maturity in rabbits. The studies of Silva et al. (2009) showed the impact of gene GH on folliculogenesis and ovulation of doe rabbits via the induction of the development of small antral follicles and stimulation of oocyte maturity. The confirmation of the involvement of gene GH in the reproductive function of doe rabbits is found in the results of the studies, conducted by Sirotkin et al., (2003), which demonstrated the impact of allele C on the reproductive function via the regulative GH-pituitary axis (hypothalamo-pituitary-somatotropic axis), which may be related to the key role of GH in the processes of oogenesis and folliculogenesis (Silva et al., 2009).

In addition, based on the results of their studies, Alsat et al. (1997) reported that gene GH impacts the development of mammary glands in mammals, including doe rabbits. The results of the studies of Abdel-Kafy et al. (2015) demonstrated a statistically significant additive impact of allele C on milk production of APRI doe rabbits, and the heterozygous genotype CT demonstrated higher milk productivity, which may illustrate the effect of domination of allele C over allele T.

The single nucleotide polymorphism (SNP) c.-78C>T, localized in the flanking region of the growth hormone gene (GH), is known not to cause changes in the aminoacid sequence of the relevant protein, which classifies it as “silent mutation”. However, even “silent” mutation may impact the regulatory expression of the gene at the post-transcription level (Roos, de Boer, 2021).

From here, SNPs, localized in the non-coding sites of gene GH, may impact the transport mRNA from the nucleus into the cytoplasm, which is a critical stage of gene expression (Neilson JR, Sandberg R. 2010). In its turn, it impacts the regulation of the protein level and its conformation (three-dimensional structure) (Sauna and Kimchi-Sarfaty, 2011).

Anandakumar et al. (2017) also report in their publication that non-coding single nucleotide polymorphisms (SNPs) are capable of inducing changes in DNA loci, increasing their polymorphism, which, in turn, impacts the formation of phenotypic traits in mammals. It may explain the role of mutation c.-78C>T of the growth hormone gene in the formation of the reproductive function of animals, including rabbits, in the ontogenesis.

The studies of Helal et al. (2024) demonstrated that non-coding SNPs were capable of impacting the milk productivity of rabbits, which confirmed the hypothesis about their role in regulating the phenotypic traits.

Our results of the studies on the association between SNP c.-78C>T in gene GH and the reproductive traits of rabbits are in agreement with these conclusions.

CONCLUSIONS

The presence of *Bst*UI-polymorphism (c.-78C>T) in the start codon of exon I of the growth hormone gene (GH) was found in the sampling of Chinchilla doe rabbits.

It was determined that animals with heterozygous genotype CT prevailed in the experimental sampling by the locus of growth hormone (GH); the frequencies of alleles C and T were 0.529 and 0.471, respectively. The analysis of associations determined higher indices of milk production, number of litter kits, live weight of the litter, average daily gain, and live weight of one animal at the age of 35 days, in the doe rabbits with heterozygous genotype CT by locus GH (polymorphism c.-78C>T).

Statistically significant differences were found between genotypes CT and TT in terms of milk production ($p<0.001$) and live birth and weaning weight of the litter ($p<0.05$). The results of the study demonstrated that *Bst*UI-polymorphism (c.-78C>T) in locus GH may be a promising marker in the evaluation of

reproductive traits of doe rabbits with its potential application in MAS-selection.

However, prior to the practical application of this polymorphism as a marker, its efficiency should be assessed more accurately and checked using a larger number of animals.

Adherence to ethical principles. All the studies were conducted with the consideration of the requirements of the Council Directive 98/58/EU dated July 20, 1998, regarding the protection of animals, kept for farming, "General ethical principles of experiments involving animals", approved by the First National Bioethics Congress (Kyiv, September 20, 2001) and the Law of Ukraine "On Protection of Animals from Cruelty", 2021.

Statement about the conflict of interests. Being the corresponding author, I declare the absence of any conflicts of interests between the co-authors of this article.

Financing. The study was conducted within the state financing framework of the NAAS of Ukraine according to the schedule of scientific and research work of the M.V. Zubets Institute of Animal Breeding and Genetics, the NAAS, and the Cherkasy Experimental Station of Bioresources, the NAAS.

REFERENCES

Abdel-Kafy EM, Hussein BA, Abdel-Ghany SM, El-Din A, Badawi Y. (2015). Single nucleotide polymorphisms in growth hormone gene are associated with some performance traits in rabbits. *Int. J. Biol. Pharm. Allied Sci*. 4:490–504

Al-Muhsen F, Al-Nassir H, Mirza S, Mnati A. (2019). Association of Growth Hormone Gene Polymorphism with Birth and Weaning Weight of Nuimi and Awassi Sheep at Kerbala Province. *Indian Journal of Public Health Research & Development*. 10:936. doi:https://doi.org/10.5958/0976-5506.2019.00181.

Alsat E, Guibourdenche J, Luton D, Frankenne F, Evain-Brion Dv. (1997). Human placental growth hormone. *American Journal of Obstetrics and Gynecology* 177: 1526–1534. doi:https://doi.org/10.1016/s0002-9378-(97)70103-0

Amalianingsih T, Brahmantiyo B, Jakaria J. (2014) The Variability of Growth Hormone Gene Associated with Ultrasound Imaging of Longissimus Dorsi Muscle and Perirenal Fat in Rabbits. *Media Peternakan*, 37:1–7. doi:https://doi.org/10.5398/medpet.2014.37.1.1

Anandakumar S, Nagarajan A, Pramanayagam S. (2017). Non-coding DNA-a brief review. 5:42–47. doi:https://doi.org/10.7324/JABB.2017.50507

Boiko O.V., Umanets RM, Honchar OF, Zlamaniuk LM, Umanets DP. Tekhnolohiia vyrobnytstva produktsii krolivnytstva ta zvirivnytstva. Navchalnyi posibnyk. Kyiv: NUBiP Ukrainy. 2024. 488 s

Bozhilova M, Viryanski D, Dimitrova I, Ignatova M, Stoykova-Grigorova R. (2022). Genetic factors influencing rabbit breeding. An overview. *Zhivotnovadni Nauki*, 59(6): 46–56

Buranakarl C, Chamsuwan S, Thammacharoen S, Ratchakom P, Chuaypen N. (2024). Single-Nucleotide Polymorphisms of Growth Hormone Gene and Its Relationship with Growth Traits in Black Bengal Goats. *Animals* (Basel). 8. 14(6):834. doi:https://doi.org/10.3390/ani14060834

Cruz G, Correa R, Macedo D et al. (2022) Association between somatotropic axis gene polymorphisms and reproductive efficiency of bovine females: a review. *Ciência Animal Brasileira*. 23. doi:https://doi.org/10.1590/1809-6891v23e-72386E

Roos D, de Boer M. (2021) Mutations in cis that affect mRNA synthesis, processing and translation, *Biochimica et Biophysica Acta (BBA) — Molecular Basis of Disease*. 1867(9):166. doi:https://doi.org/10.1016/j.bbadis.2021.166166

Downing J, Scaramuzzi R. (1991). Nutrient effects on ovulation rate, ovarian function and the secretion of gonadotrophic and metabolic hormones in sheep. *Journal of reproduction and fertility*. Supplement. 43:209–227. doi:https://doi.org/10.1530/biosciprocs.2.017.

Dzitsiuk V, Boyko O, Gonchar O, Gavrish O, Guzevaty O. (2025) Polymorphism of the growth hormone gene in populations of rabbits of the Chinchilla and Poltava silver breeds. *Bulletin of Agricultural Science*. 1(862): 43–49.

Dzitsiuk V, Guzevatiy O. (2024). Polymorphism of the Growth Hormone Gene (G.2141C>G) in Cattle Populations: Analysis of Reproductive Traits. *Cytology and Genetics*. 3: 225–233. doi:https://doi.org/10.3103/S0095452724030046

El-Sabry M, Zaki M, Elgohary F, Helal M. (2021). Sustainable Rabbit Production under the Global Warming Conditions in Southern Mediterranean Region. *World's Veterinary Journal*, 11:543–548. doi:https://dx.doi.org/10.54203/scil.2021.wvj69

Fontanesi L, Dall'Olio S., Spaccapaniccia E. et al. (2012) A single nucleotide polymorphism in the rabbit growth hormone (GH1) gene is associated with market weight in a commercial rabbit population. *Livest. Sci*. 147:84–88. doi:https://doi.org/10.1016/j.livsci.2012.04.006

Garcia M, Argente M. (2020). The Genetic Improvement in Meat Rabbits. In book: Lagomorpha Characteristics [Working Title] doi:https://doi.org/10.5772/intechopen.93896

Garreau H, Piles M, Larzul C, Baselga M, de Rochambeau H. (2005) Book chapter Conference paper, France,

Corronsac, Proceedings of the 8th World Rabbit Congress, September 7–10, 2004, Pueblo, Mexico, (14-), World Rabbit Science Association (WRSA), Selection of maternal lines: last results and prospects.

Gencheva D.G., Velikov K.P., Veleva P.M. 2022. Association analysis of nucleotide polymorphisms in growth hormone (GH) and its receptor (GHR) with body weight in Californian rabbits. *World Rabbit Sci*., 30:95–102. doi:https://doi.org/10.4995/wrs.2022.13127

Gencheva D, Tanchev S, Krasimir V, Gonchev P, Georgieva S. (2018). Single nucleotide polymorphism of the growth hormone (GH) encoding gene in inbred and outbred domestic rabbits. *World Rabbit Science*. 26:49. doi:https://doi.org/10.4995/wrs.2018.7211

Helal M, Sameh J, Gharib S. Merghany RM, Bozhilova-Sakova M, Ragab M. (2024). Candidate genes associated with reproductive traits in rabbits. *Trop Anim Health Prod*. 56:94. doi:https://doi.org/10.1007/s11250-024-03938-8

Hussein B, Abdel-Kafy E, Abdel-Ghany S, Gamal A, Badawi Y. (2015). Single nucleotide polymorphisms in growth hormone gene are associated with some performance traits in rabbits. *Int. J. Biol. Pharm. Allied Sci*., 4:490–504.

Hristova D, Tanchev S, Velikov K, Gonchev P and Georgieva S. (2017) Rabbit Growth Hormone and Myostatin Gene Polymorphisms. *J Agri Res*. 2(3). doi:https://doi.org/10.23880/oajar-16000133

Khalil M, Zaghloul A, Iraqi M, El Nagar A, Ramadan S. (2021). Association of GH gene polymorphism with growth and semen traits in rabbits. *World Rabbit Science*, 29:31–40. doi:https://doi.org/10.4995/wrs.2021.13001

Kmieć M, Terman A, Wierzbicki H, Zych S. (2007), Association of GH gene polymorphism with semen parameters of boars. *Acta Veterinaria Brno*. 76:41–46. doi:https://doi.org/10.2754/avb200776010041

Kumar S, Yadav A, Magotra A, Bangar Y, Garg A, Kumar N. (2024). Polymorphism of growth hormone (GH) gene and its association with performance and body conformation of Harnali sheep. *Tropical Animal Health and Production*. 56. https://doi.org/10.1007/s11250-024-03968-2

Kyselová J, Tichý L, Jochová K. (2021) The role of molecular genetics in animal breeding: A minireview. *Czech J. Anim. Sci*. 66(4):107–111. doi:https://doi.org/10.17221/251/2020-CJAS

Migdal L, Palka S, Kmiecik M, Derewicka O. (2019). Association of polymorphisms in the GH and GHR genes with growth and carcass traits in rabbits (*Oryctolagus cuniculus*). *Czech J. Anim. Sci*., 64:255–264. doi:https://doi.org/10.17221/27/2019-CJAS

Neilson JR, Sandberg R. (2010) Heterogeneity in mammalian RNA 3' end formation. *Exp Cell Res*. 1. 316(8):1357–64. doi:https://doi.org/10.1016/j.yexcr.2010.02.040.

Ramadan S., Manaa E, El-Attrony M, El Nagar A. (2020). Association of growth hormone (GH), insulin-like growth factor 2 (IGF2) and progesterone receptor (PGR) genes with some productive traits in Gabali rabbits. *World Rabbit Science*, 28:135–144. doi:https://doi.org/10.4995/wrs.2020.12610

Rogel-Gaillard C, Ferrand N., Hayes H. (2009). Genome Mapping and Genomics in Domestic Animal. Chapter 7: Rabbit. Editor: Noelle E. Cockett, Chittaranjan Kole. Springer- Verlag Berlin Heidberg. www.springer.com

Sauna ZE, Kimchi-Sarfaty C. (2011). Understanding the contribution of synonymous mutations to human disease. *Nat Rev Genet*. 31.12(10):683–91. doi:https://doi.org/10.1038/nrg3051.

Siddiqui SA, Gerini F, Ikram A, Saeed F, Feng X, Chen Y. (2023). Rabbit meat production, consumption and consumers' attitudes and behavior. *Sustainability* 15:2008. doi:https://doi.org/10.3390/su15032008

Silva J, Figuieredo J, van den Hurk R. (2009). Involvement of growth hormone (GH) and insulin-like growth factor (IGF) system in ovarian folliculogenesis. *Theriogenology*. 71:1193–1208. doi:https://doi.org/10.1016/j.theriogenology.2008.12.015

Sirotkin AV, Mertin D, Süvegová K, Makarevich AV, Mikulová E. (2003), Effect of GH and IGF-I treatment on reproduction, growth, and plasma hormone concentrations in domestic nutria (*Myocastor coypus*). *Gen. Comp. Endocrinol*. 131296-301. doi:https://doi.org/10.1016/S0016-6480(03)00024-8.

Sosa-Madrid B, Santacreu M, Blasco A, Fontanesi L, Pena R, Ibáñez-Escriche N. (2020). A genome-wide association study in divergently selected lines in rabbits reveals novel genomic regions associated with litter size traits. *Journal of Animal Breeding and Genetics*, 137:123–138. doi:https://doi.org/10.1111/jbg.12451.

Tusell L, Legarra A, García-Tomás M, Rafel O, Ramon J, Piles M. (2012). Genetic basis of semen traits and their relationship with growth rate in rabbits. *J. Anim. Sci*. 90:1385–1397. doi:https://doi.org/10.2527/jas.2011-4165

Wang H, Jing Liu, Jinhua Li, Zhibin Jia, Chonglei Li (2022). Comparative life cycle assessment of rex rabbit breeding industry chains: benefits of a circular industry chain. *The International Journal of Life Cycle Assessment*. 27:366–379. doi:https://doi.org/10.1007/s11367-022-02036-x

Wongnaa CA., Afful-Kwadam K, Asempah MK, Hagan MAS, Awunyo-VD. (2023). Is it profitable and viable to invest in commercialization of rabbit production? Implication on rural enterprise development. *Sustain. Technol. Entrepreneurship* 2:100048. doi:https://doi.org/10.1016/j.stae.2023.100048

Zachmann M. (1992). Interrelations between growth hormone and sex hormones: physiology and therapeutic consequences. *Horm. Res. Paediat*., 38:1–8. doi:https://doi.org/10.1159/000182562

УДК 636.92.033:575.113/.22

ГЕНЕТИЧНІ АСПЕКТИ РЕПРОДУКТИВНОЇ ЗДАТНОСТІ КРОЛИЦЬ: РОЛЬ ПОЛІМОРФІЗМУ ГЕНА ГОРМОНУ РОСТУ

* В.В. Дзіцюк[1], О.В. Бойко[2], О.Ф. Гончар[3], О.М. Гавриш[4], О.Є. Гузеватий[5], Т.В. Литвиненко[6], О.П. Вергелес[7]

[1] Інститут розведення і генетики тварин імені М.В. Зубця Національної академії аграрних наук України вул. Погребняка, 1, с. Чубинське Київської обл., 08321, Україна

[2–4] Черкаська дослідна станція біоресурсів Національної академії аграрних наук України вул. Пастерівська, 76, Черкаси,18036, Україна

[5] Інститут тваринництва степових районів імені М.Ф. Іванова «Асканія-Нова» — Національний науковий селекційно-генетичний центр з вівчарства вул. Погребняка, 1, с. Чубинське Київської обл., 08321, Україна

[6-7] Національний університет біоресурсів і природокористування України Міністерства освіти і науки України 16, вул. Виставкова, буд. 12Д, Київ, Україна, 03041

E-mail: * [1]valentynadzitsiuk@gmail.com, [2]aleksboy18@meta.ua, [3]of.gonchar@gmail.com, [4]gavrish.olexandr@gmail.com, [5]oleg_guzevatiy@ukr.net, [6]tvpptvergeles@gmail.com, [7]tvpptvergeles@gmail.com

orcid: 10000-0001-9697-4165, 20000-0002-3917-5583, 30000-0003-2269-9767, 40000-0002-8632-6508, 50000-0002-2470-5430, 60000-0002-0405-3367, 70000-0003-0415-5264

Мета. Проаналізувати параметри відтворної здатності кролиць породи шиншила з різними генотипами за локусом GH (мутація c.-78C>T). **Методи.** Визначення генотипів тварин проводили за використання методу PCR-RFLP. Ампліфікацію здійснювали у програмованому термоциклері Applied Biosystems MiniAmp (Thermo Scientific, США) з використанням специфічних праймерів. Амплікони розщеплювали ендонуклеазою *Bst*UI ((Thermo Scientific, США), фрагменти розділяли у 2,0 % агарозному гелі з додаванням бромистого етидію. Для оцінки репродуктивної здатності кролиць використовували показники: молочність (кг), розмір і живу масу гнізда при народженні та відлученні (кг), середньодобовий приріст кроленят (г). Популяційно-генетичні показники розраховували за загальноприйнятими методиками. Аналіз впливу генотипу локусу GH на параметри репродуктивної функції кролиць з різними генотипами за локусом GH здійснювали за допомогою однофакторного дисперсійного аналізу (ANOVA). **Результати.** У досліджуваній вибірці кролиць (34 голови) породи шиншила виявлено *Bst*UI-поліморфізм у позиції -78 стартового кодону екзону I гена GH (c.-78C>T). Аналіз асоціацій показав, що у кролиць з гетерозиготним генотипом CT у локусі GH виявився вищі показники молочності, розміру та живої маси гнізда, середньодобового приросту та живої маси однієї особини у 35-денному віці. Встановлено статистично значущі відмінності між генотипами CT і TT за молочністю ($p < 0,001$) та живою масою гнізда при народженні та відлученні ($p < 0,05$). **Висновок.** Отримані результати свідчать про перспективність використання *Bst*UI-поліморфізму локусу GH (c.-78C>T) як генетичного маркера в селекційних програмах для підвищення продуктивності кролів.

Ключові слова: поліморфізм, ген GH, генотип, плодючість, кріль.