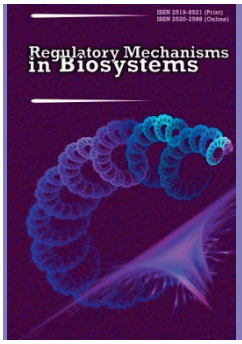

Regulatory Mechanisms in Biosystems

ISSN 2519-8521 (Print)
ISSN 2520-2588 (Online)
Regul. Mech. Biosyst.,
2022, 13(3), 225–230
doi: 10.15421/022229

Association of Fut1 and Slc11a1 gene polymorphisms with productivity traits of Large White pigs

V. V. Sukhno*, P. A. Vashchenko**, A. M. Saenko*, O. M. Zhukorskyi***, O. M. Tserenyuk*, N. V. Kryhina*

*Institute of Pig Breeding and Agroindustrial Production of National Academy of Agrarian Sciences of Ukraine, Poltava, Ukraine
**Poltava State Agrarian University, Poltava, Ukraine
***National Academy of Agrarian Sciences of Ukraine, Kyiv, Ukraine

Article info

Received 22.06.2022
Received in revised form 19.07.2022
Accepted 20.07.2022

Institute of Pig Breeding and Agroindustrial Production of National Academy of Agrarian Sciences of Ukraine, Shvedska Mohyla st., 1, Poltava, 36000, Ukraine. Tel.: +38-066-727-24-93. E-mail: pigbreeding@ukr.net

Poltava State Agrarian University, Skovorody st., 1/3, Poltava, 36003, Ukraine. Tel.: +38-096-944-98-12. E-mail: pavlo.vashchenko@pdaa.edu.ua

National Academy of Agrarian Sciences of Ukraine, Mikhail Omelyanovich-Pavlenko st., 9, Kyiv, 01010, Ukraine. Tel.: +38-044-521-92-77. E-mail: prezid@naas.gov.ua

Sukhno, V. V., Vashchenko, P. A., Saenko, A. M., Zhukorskyi, O. M., Tserenyuk, O. M., & Kryhina, N. V. (2022). Association of Fut1 and Slc11a1 gene polymorphisms with productivity traits of Large White pigs. Regulatory Mechanisms in Biosystems, 13(3), 225–230. doi:10.15421/022229

The purpose of our work was to study the polymorphism of genes associated with disease resistance and to search for their associations with productive traits in the population of the Ukrainian Large White pigs. For this study, 50 pigs were used, observations and measurements were carried out at the age from birth to 180 days. Genetic studies were carried out in a certified laboratory of the Institute of Pig Breeding and Agroindustrial Production. In the study of fucosyltransferase 1 and solute carrier family 11 member 1 genes, polymorphism was found in three of the five analyzed loci. In the Ukrainian Large White subpopulation of pigs the informativeness of these gene polymorphisms was at the optimal level for associative analysis, Polymorphism Information Content was greater than 0.3 in two loci. A sufficiently high level of Polymorphism Information Content indicates the value of this breed to preserve the biodiversity of pigs. The distribution of genotypes at some loci of the solute carrier family 11 member 1 gene was characterized by a deviation from the theoretically expected one due to the increase in the frequency of the heterozygous genotype. There was also a statistically confirmed deviation of the genotypes' distribution from the normal and polymorphism fucosyltransferase 1 gene, but in this case in the direction of increasing the frequency of both homozygous variants. These results indicate the presence of a certain selection pressure on the mentioned polymorphisms and their possible impact on productive traits. The influence of solute carrier family 11 member 1 gene polymorphism on the weight of pigs at the age of 120 and 180 days, the average daily gain recorded in the period 28–120 days and from birth to 180 days, as well as on the backfat thickness, was established. The preferred genotype is TT, which can be used in breeding to obtain more productive animals with increased disease resistance, but in the selection of animals at this locus, it is necessary to control the backfat thickness and prevent breeding of pigs that may worsen this trait.

Keywords: pig breeding; genomic selection; DNA-markers; disease resistance; animal growth; average daily gain; body development; backfat thickness.

Introduction

Despite research having confirmed the influence of the genetic component on the resistance of animals to infectious diseases, this aspect has not been given enough attention until recently (Adams & Templeton, 1998; Xie et al., 2018). The issue of finding and using methods of animal disease prevention without the use of antibiotics has become particularly relevant after the adoption of Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC (http://data.europa.eu/eli/reg/2019/6/oj).

Pig breeding practice shows that clinically healthy and resistant animals generally have higher productivity compared to animals prone to various diseases (Rudoman et al., 2017a). Susceptibility to infectious diseases depends more or less on the genetic component of the animals. Infectious diseases are difficult to cure and cause significant economic losses in livestock species. Selective breeding is used to increase resistance against infectious disease and it may prove to be an economical and sustainable practice. Genetic methods, such as selection of disease resistance in the pig, have not been widely used (Devi et al., 2018). Among the genes associated with animal resistance, solute carrier family 11 member 1 gene (*SLC11A1*) and fucosyltransferase 1 gene (*FUT1*) are studied well enough. *SLC11A1* is a candidate gene that affects the overall resistance of pigs to disease (Cellier et al., 1994; Bhanita Devi et al., 2017). It is a member of the solute carrier family 11 encoding a multi-domain integral membrane protein (Fleming et al., 1997; Braliou et al., 2019) and is involved in iron metabolism and host resistance to certain pathogens (Gunshin et al., 1997; Braliou et al., 2019). It is a divalent metal ion (Fe^{2+}, Zn^{2+}, and Mn^{2+}) transporter located in the membranes of early and late endosomes/ phagosomes and lysosomes in macrophages. From there, it pumps the metal ions out of the microbiophorous phagosomes (Blackwell et al., 2003; Braliou et al., 2019). Various polymorphisms in *SLC11A1* have been investigated regarding their role in disease susceptibility to tuberculosis (Holder et al., 2020; Li et al., 2022), brucellosis (Sahraoui et al., 2020) but insufficient research has been conducted on the relationship of these polymorphisms and the productive qualities of animals (Pires et al., 2021).

The *FUT1* gene is primarily associated with resistance to colibacteriosis. This disease is one of the most common infectious diseases in pig breeding in Ukraine (Rudoman et al., 2017a; Matsenko et al., 2019). According to the results of studies conducted in different years, the proportion of colibacteriosis among other infectious diseases ranges from 11.3 (Golovko et al., 2019) to 23.8% (Yakubchak et al., 2014). In addition to pig production, colibacteriosis is also a significant problem in the poultry and livestock industries (Vasylieva, 2016). The problem of colibacteriosis is

also dealt with in other countries with a high level of management in the pig industry (Richards et al., 2005). The disease is widespread both in traditional and industrial pig farms and causes great economic damage. Antimicrobials used in animal production in Europe are often the same or belong to the same classes as those used in human medicine. Therefore, antimicrobial resistance is a major undesirable side effect of antimicrobial drugs' use both in humans and animals. In this regard, some *Escherichia coli* strains are an example of zoonotic bacteria that can be ingested by humans with food of animal origin. It was found that from 2005 to 2015 the number of most commonly used antimicrobial drugs to which *E. coli* strains isolated from pigs developed resistance increased from 5 to 11 (generally 24 antimicrobial drugs were tested). Among the drugs to which high resistance was developed were amoxicillin, cefquinome, cefotaxime, nalidixic acid, colistin, tiamulin, flumequine and streptomicin (Dimitrova & Yordanov, 2020). Treatment and control of colibacillosis in animals is mainly based on antibiotic therapy, the result of the widespread use of antibiotics is the emergence of resistance among bacterial strains. The main factor in the pathogenicity of enteropathogenic *E. coli* is intimin (Kupczyński et al., 2019). It is an adhesive protein of a pathogenic strain that allows close adherence of bacterial cells to the intestinal villi and causes obstruction of their structure and intestine inflammation. Currently, the phenomenon of resistance among bacterial strains is a serious problem in the treatment of both humans and animals and is widely publicized. There is a growing need for alternative and effective methods, such as a vaccine or plant extracts, to cope with these problems and to reduce the use of antibiotics (Kupczyński et al., 2019). Another promising way to solve the problem is to use genomic selection to create populations of animals resistant to this disease (Tait-Burkard et al., 2018). Genome-wide association studies have attempted to confirm associations found and identify new genes involved in pathogenesis and susceptibility. Selection of disease resistant animals for breeding might be the prophylactic measure of first choice (Devi et al., 2018).

Associations of the mentioned genes with disease resistance can affect animal productivity and be breed-specific (Vashchenko et al., 2019). However, the problem of the influence of resistance-related genes on the productivity of pigs has not been sufficiently studied. Therefore, our purpose was to study polymorphism of these genes and to search for their associations with productive qualities in pigs of the Ukrainian Large White breed.

Materials and methods

The study was performed using 50 pigs of the Ukrainian Large White breed of the breeding herd at the "Plekhiv-Agro" farm. The farm is located in Poltava Region of Ukraine. All experiments were conducted in compliance with the requirements of the European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes (Strasburg, 1985) and the Order of the First National Congress of the Bioethics (Kyiv, 2001), as well as the law of Ukraine "On the protection of animals against ill-treatment" No. 3447-IV as of 21/02/2006 last amended on 04/08/2017. The study was approved by the Committee for the Maintenance and Use of Animals of the Institute of Pig Breeding and Agroindustrial Production.

The farm used fodder of its own production. Pigs were fed a diet in accordance with the norms of feeding young breeding animals (Provatorov et al., 2007). Suckling piglets were fed prestarter feed which contained 15.4 MJ/kg of metabolic energy, 231 g of crude protein and 11.1 g of lysine per 1 kg of dry matter. When growing from 20 to 40 kg of live weight, the animals were given feed containing per 1 kg of dry matter: 14.4 MJ/kg metabolic energy, 200 g crude protein, 9.0 g lysine. When growing from 40 to 80 kg of live weight the animals were given feed containing per 1 kg of dry matter: 13.5 MJ/kg metabolic energy, 174 g crude protein, 7.3 g lysine. Animals weighing more than 80 kg were fed feed containing 1.2 MJ/kg metabolic energy, 163 g crude protein and 6.9 g lysine per 1 kg dry matter. Piglets were weaned from the sow when they reached the age of 28 days. Backfat thickness was measured by a portable digital Renco Lean-Meter device (Renco Corporation, USA) at the level of 6–7th rib (Zhang et al., 2018). The measurement was carried out when the pigs reached a weight of 100 kg. The average daily gains were calculated for the periods from birth to 180 days, 28–120 days and 120–180 days. The body length of pigs was measured from the occipital crest to the root of the tail.

Genetic studies were carried out in a certified laboratory of the Institute of Pig Breeding and Agroindustrial Production. Genomic DNA was isolated from 400 μL of blood using "Chelex 100" (Walsh et al., 1991). DNA typing was performed using PCR-RFLP technique (Hlazko et al., 2001). A fragment of the *SLC11A1* gene consisting of 536 bp was amplified using a pair of specific primers: forward: 5'-GCGTCAGTCTTCCCTGCTCAG -3' and reverse: 5'-ACGGCAGTTACCACTCTCCATCT -3' (Tuggle et al., 2005). For *FUT1* gene PCR amplification primers of the following structure were used: forward: 5'- CCAACGCCTCCGATTCCTGT -3' and reverse: 5'-GTGCATGGCAGGCTGGATGA-3' (Rudoman et al., 2017b). PCR reactions were performed in 25 μL (final volume) of the mixture containing 10–100 mg of genomic DNA, 200 nM of forward and reverse primers, 2.5 mM $MgCl_2$, 0.25 mM of each of the dNTPs and one unit of the recombinant Taq DNA Polymerase (Thermoscientific (EU). PCR amplification program: 94 °C – 5 minutes; 35 cycles: 94 °C – 40 s, annealing of primers for *SLC11A1* 60 °C – 40 s, annealing of primers for *FUT1* 62 °C – 40 s, 72 °C – 60 s; 72 °C – 5 min. PCR was performed in thermocycler "Tertsyk-2" (DNA Technology, RF). AvaII and HinfI enzymes were used to restrict SLC11A1. When using the enzyme HinfI genotypes at positions 176 and 334 bp (counting from the beginning of the amplified fragment) were determined using the patterns shown in Table 1, composed of data (Tuggle et al., 2005) and information presented in NCBI GenBank (*Sus scrofa* isolate, T. J. Tabasco, breed Duroc, chromosome 15, Sscrofa11.1, whole genome shotgun sequence https://www.ncbi.nlm.nih.gov/nuccore/NC_010457.5?report=genbank&from=120434100&to=120446396).

Table 1
Patterns for identification of genotypes according to the length of restriction DNA fragments *SLC11A1* gene

Length of DNA fragments, bp	Alleles of the first chromosome, allele name (nucleotide in position 176 … nucleotide in position 334)	Alleles of the second chromosome, allele name (nucleotide in position 176 … nucleotide in position 334)	Genotype in position 176	Genotype in position 334
76, 100, 360	A (G…C)	A (G…C)	GG	CC
76, 100, 155, 205, 360	A (G…C)	B (G…T)	GG	CT
76, 100, 155, 205	B (G…T)	B (G…T)	GG	TT
76, 100, 360, 436	D (A…C)	A (G…C)	AG	CC
76, 100, 155, 205, 436	D (A…C)	B (G…T)	AG	CT
76, 100, 205, 231, 360	C (A…T)	A (G…C)	AG	CT
76, 100, 155, 205, 231	C (A…T)	B (G…T)	AG	TT
100, 436	D (A…C)	D (A…C)	AA	CC
100, 205, 231, 436	D (A…C)	C (A…T)	AA	CT
100, 205, 231	C (A…T)	C (A…T)	AA	TT

The amplification fragment of the *FUT1* gene was restricted with the enzyme HspAI (Thermo Fisher Scientific, Lithuania), which caused the appearance of restriction fragments corresponding to the following genotypes of the *FUT1* gene: AA – 161 bp, GA – 161, 117, 44 bp, GG – 117, 44 bp. The allele frequencies, genotype frequencies and Polymorphic Information Content (PIC) were calculated using GenAlEx 6.0 software (Peakall, 2012). Reliability of the differences between the observed genotypes frequencies and expected genotypes' frequencies was calculated

using Chi-square test. Data processing was performed using SAS/STAT(R) 15.1 statistical software (SAS Institute Inc. (2018). SAS/STAT(R) 15.1 User's Guide. Cary, NC). The tables show the arithmetic mean values and their standard errors (x ± SE). The significant of differences between the genotypes was assessed using single-factor analysis of variance (ANOVA). Fisher's F-test was used to assess the ratio of intergroup and intragroup variability. Differences were considered significant at $P < 0.05$.

Results

In the Ukrainian Large White pig subpopulation, the HinfI restriction sites at positions 176 and 334 bp in the amplified fragment of the *SLC11A1* gene was characterized by polymorphism. At the same time, in the AvaII restriction site of the studied gene fragment in Ukrainian Large White polymorphism was not detected. The *FUT1* gene was also characterized by polymorphism with a predominance of the allele G (Table 2).

Table 2
Distribution of allele and genotype frequencies and the level of heterozygosity for the studied genes in the subpopulation of Ukrainian large white pigs

Locus/polymorphism	Distribution of allele frequencies	Distribution of genotype frequencies			χ^2	Polymorphism Information Content
SLC11A1/HinfI Position 176 *G > A*	A = 0.11 G = 0.89	AA = 0.00 (0.01)	AG = 0.22 (0.20)	GG = 0.78 (0.79)	0.382	0.180
SLC11A1/HinfI Position 334 *C > T*	C = 0.35 T = 0.65	CC = 0.02 (0.12)	CT = 0.66 (0.46)	TT = 0.32 (0.42)	10.150**	0.350
SLC11A1 /AvaII Position 72 *G > A*	A = 0.00 G = 1.00	AA = 0.00	AG = 0.00	GG = 1.00	–	–
SLC11A1 /AvaII Position 364 *G > A*	A = 1.00 G = 0.00	AA = 1.00	AG = 0.00	GG = 0.00	–	–
FUT1 g.307 G > A	A = 0.27 G = 0.73	AA = 0.14 (0.07)	GA = 0.26 (0.40)	GG = 0.60 (0.53)	5.795*	0.320

Notes: 1) the expected frequency of the genotype, calculated according to Hardy-Weinberg's law, is given in parentheses; 2) values of χ^2 were determined to assess the probability of deviation in the actual frequency distribution of genotypes from the expected one; * $P < 0.05$; ** $P < 0.01$; 3) for loci *SLC11A1 /AvaII* Position 72 and *SLC11A1 /AvaII* Position 364 calculation of χ^2 and Polymorphism Information Content is not possible due to lack of polymorphism.

The maximum G allele frequency was observed in positions 72 (*SLC11A1/AvaII*) and 176 (*SLC11A1/HinfI*) of the amplified fragment. In position 334 (*SLC11A1/HinfI*), the maximum frequency of heterozygotes was found. The established distribution of genotypes by *SLC11A1/HinfI* 334 was characterized by a deviation from the theoretically expected one due to the increase in the frequency of the heterozygous genotype. The *FUT1* g.307 G > A polymorphism also showed a statistically confirmed deviation of the genotype distribution from the normal in the direction of increasing the frequency of both homozygous variants. These results indicate the presence of a certain selection pressure on the above polymorphisms, their possible impact on the manifestation of productive traits. Informativeness of the *SLC11A1/HinfI* 334 and *FUT1* g.307 G > A polymorphisms in the Ukrainian Large White subpopulation was at the optimal level for associative analysis, Polymorphism Information Content = 0.350 and 0.320, accordingly. At the same time, all other polymorphisms could not be involved in the associative study in this Ukrainian Large White subpopulation due to their homozygosity or low level of polymorphism.

The results of the association analysis polymorphism of the *SLC11A1* (HinfI position 334) and *FUT1* (SNP g.307 G > A) genes with the productivity traits of Ukrainian large white pigs are presented in Table 3. In the Ukrainian large white subpopulation the CC genotype for the *SLC11A1 / HinfI* 334 polymorphism was represented by only one animal and was not included in the association analysis.

Table 3
Association of *SLC11A1/HinfI* 334 and *FUT1* g.307 G >A polymorphisms with productivity traits of Ukrainian Large White pigs (x ± SE)

Productive traits	*SLC11A1* at position 334				*FUT1*				
	Genotype		F	P	Genotype			F	P
	CT (n = 33)	TT (n = 16)			AA (n = 7)	AG (n = 13)	GG (n = 30)		
Weight at birth, kg	1.476 ± 0.044	1.506 ± 0.060	1.45	0.245	1.343 ± 0.111	1.531 ± 0.071	1.513 ± 0.043	1.54	0.225
Weight at 28 days, kg	7.883 ± 0.163	8.046 ± 0.202	0.57	0.567	7.919 ± 0.371	7.698 ± 0.288	8.017 ± 0.149	0.57	0.568
Weight at 120 days, kg	50.38 ± 0.49	52.14 ± 0.62	4.44	0.017	51.09 ± 1.35	49.99 ± 0.72	51.15 ± 0.52	0.75	0.476
Weight at 180 days, kg	93.60 ± 1.10	98.64 ± 2.31	3.66	0.033	97.60 ± 2.55	94.22 ± 1.85	94.77 ± 1.55	0.46	0.634
Average gain from birth to weaning at 28 days, g	228.84 ± 5.27	235.85 ± 6.91	1.42	0.252	234.87 ± 13.56	220.25 ± 8.45	233.49 ± 5.10	1.00	0.376
Average daily gain for the period 28–120 days, g	548.09 ± 5.37	565.80 ± 4.62	3.89	0.027	550.86 ± 12.44	545.14 ± 7.85	556.67 ± 5.26	0.72	0.490
Average daily gain for the period 120–180 days, g	716.72 ± 18.26	770.00 ± 33.86	1.43	0.250	765.95 ± 30.39	736.54 ± 34.15	722.72 ± 22.33	0.39	0.678
Body length at 180 days, cm	117.73 ± 1.18	117.31 ± 2.41	0.36	0.697	117.43 ± 1.77	118.00 ± 2.27	117.23 ± 1.51	0.04	0.958
Withers height at 180 days, cm	70.61 ± 1.15	72.13 ± 1.79	0.52	0.596	70.71 ± 2.55	69.46 ± 1.76	72.07 ± 1.27	0.69	0.506
Chest circumference at 180 days, cm	101.73 ± 1.41	97.06 ± 1.84	1.96	0.153	100.57 ± 2.57	102.31 ± 1.96	99.30 ± 1.59	0.63	0.535
Backfat thickness at weight of 100 kg, mm.	19.26 ± 0.56	22.82 ± 0.81	7.22	0.002	20.89 ± 1.53	20.40 ± 0.81	20.19 ± 0.71	0.10	0.903
Average daily gain from birth to 180 days, g	510.82 ± 6.03	537.98 ± 12.33	3.71	0.032	532.39 ± 13.57	514.39 ± 10.17	516.92 ± 8.39	0.45	0.638
Age of reaching weight of 100 kg, days	190.23 ± 1.82	183.79 ± 3.20	2.85	0.068	183.78 ± 3.44	189.32 ± 2.87	189.18 ± 2.32	0.65	0.529

The influence of the *SLC11A1/HinfI* 334 polymorphism on the weight of pigs at the age of 120 and 180 days, the average daily gain recorded in the period 28–120 days and from birth to 180 days, as well as on the backfat thickness, measured at a live weight of 100 kg, was established. Regarding *FUT1* g.307 G > A no statistically confirmed effect of this polymorphism was detected on any of the studied features.

Discussion

Allele A of *FUT1* gene is prevalent in the native wild boar population with a frequency of 65.12% (Le et al., 2021). In breeds that are more adapted to improved technologies, the frequency of the A allele is reduced. When studying the *FUT1* gene on 174 Pudong white pigs, the results showed that their respective genotype frequencies AA, AG, and GG were 0.052, 0.448, and 0.500. The frequency of the A allele is 0.276 and the frequency of the G allele is 0.724 (Zhang et al., 2013). In experiments on Yorkshire piglets (Luc et al., 2020) AA genotype was found in six animals from 613 (0.98%), GG in 470 (76.67%), and AG in 137 (22.35%). Consequently, the frequency for allele A was 12.15%, whereas the frequency for allele G was 87.85%. Research conducted in Italy (Geraci et al., 2019) found the frequency of the resistance-associated alleles for the four polymorphisms was usually higher in all local pig breeds,

indirectly supporting a higher rusticity of autochthonous breeds, compared to commercial populations.

The low frequency of *FUT1* A allele was observed in Duroc, Landrace, and Large White pigs (Ruan et al., 2013) with values of 0.278, 0.061, and 0.092, respectively. However, the AA genotype was absent in Asian local pigs breeds that did not have a high growth rate and thin backfat (Cuong et al., 2012) and the statement that low frequencies of resistant animals with AA genotype is characteristic of pigs from western countries alone is unreasonable. The relative low frequency of the A allele in animals of more productive breeds created the prerequisites for testing the effect of the allele on productivity. However, selection during 6 years for the resistant allele of *FUT1* AA and increasing the proportion of resistant animals from 8 to 35% in commercial pig herds of the Pig Improvement Company did not lead to a decrease in productivity (van der Steen et al., 2005).

Pigs of the Ukrainian Large White breed used in our research belong to the group of breeds with improved productivity, adapted to breeding in large pig farms. That explains why the observed highest frequency of the *FUT1* GG genotype was expected. The frequency of AA genotype in our research was 7.5 times less compared to frequency of GG genotype. The frequency of the A allele compared to the G allele was 2.7 times less. This is consistent with data from other researchers.

The *Slc11a1* genotypes' and alleles' frequency has been studied less compared to *FUT1*. According to studies (Tuggle et al., 2005), 176 pigs were tested; as a result, the following allele frequencies were established: in the *Slc11a1* HINF 176 locus, the frequency of the A allele was 0.540, and that of the G allele was 0.460; in the *Slc11a1* HINF 334 locus, the frequency of the C allele was 0.09, and that of the T allele was 0.91. In our studies, allele C also had a lower frequency compared to T, but only by 1.86 times, the difference between frequencies was not as large as in Tuggle's studies.

There is a large number of studies researching the effect of *SLC11A1* and *FUT1* genes polymorphism on animal immunity (Dai et al., 2017; Liu et al., 2017; Prajapati et al., 2017, Bosewell et al, 2018; Wen et al., 2018; Ardiyana et al., 2020). It is well known that pigs with better disease resistance may have better growth, greater weight and better feed conversion (Tuggle et al., 2005), but the question of the relationship between the polymorphism of these genes and pig productivity has not been studied enough, the studies are fragmentary.

In the experiments, a positive effect of the *FUT1* AA genotype on the reproductive qualities of sows was also established (Kim et al., 2013). The survival rate of piglets with genotype AA was almost two times greater than piglets with GG genotype. This study gave reason to use the *FUT1* polymorphism as a marker for selection programs to improve post-weaning piglet survival.

Also, the positive effect of the *FUT1* AA genotype was observed in studies on Yorkshire pigs (Zhu et al., 2014). The age of reaching 100 kg of AA genotype pigs was shorter by 4.23 days ($P < 0.05$) than that of animals with AG genotype, whereas backfat thickness and depth of longissimus dorsi were similar. On the contrary, in another experiment on Yorkshire pigs (Luc et al., 2020), no significant effect of gene polymorphism on different types of productivity was found. In research the body weights at birth, weaning, initial fattening period, and final fattening period were collected from 611, 516, 479, and 418 animals, respectively, whereas backfat thickness, depth of longissimus dorsi, and lean meat percentage were recorded from 328 animals. The effect of *FUT1* genotype was not observed for all production traits ($P > 0.05$), whereas final body weight and depth of longissimus dorsi were significantly different between females and males ($P < 0.05$).

FUT1 was used in marker-assisted selection (MAS) in a few pig populations of Italian Large White pigs (Geraci et al., 2019). After that, since interactions or antagonism between growth, innate immunity and disease resistance traits could exist, their work investigated whether disease resistance gene markers could affect seven production traits (average daily gain, back fat thickness, lean meat cuts, feed gain ratio, ham weight, visible intermuscular fat and ham weight loss at first salting) and 15 hematological parameters in about 550 performance tested Italian Large White pigs. Association analyses carried out in Italian Large White pigs for production traits, meat quality or haematological parameters under investigation showed no significant effect of any genotyped polymorphisms (Geraci et al., 2019).

Among the works in which the *FUT1* gene was studied we can note the work (Rudoman et al., 2017b) in experiments on the Ukrainian Large White breed of pigs, the same breed of pigs as in our research. The correlation was established of SNP g.307 G > A locus *FUT1* with the average daily gain of animals, the age of achieving live weight of 100 kg and the fat depth at the level of 6–7th rib, as well as the correlation of individual genotypes of the mucin 4 gene with the average daily gain and the age of reaching live weight of 100 kg.

However, in our research, the effect of *FUT1* SNP g.307 G > A on all studied productive traits was not detected. This fact can be explained by a certain dynamic of the genetic markers' associations with productive traits, which is connected with different selection methods used in different periods of population existence.

At the same time, the *SLC11A1/HinfI* 334 polymorphism was found to be associated with the average daily gain of pigs and their weight at 120 and 180 days of birth, and the preferred genotype to improve these traits is TT. However, pigs with this genotype were characterized by the largest fat depth, which negatively affects their breeding value. Our results, which indicate a relationship between greater fat depth and better disease resistance, are consistent with data from other researchers who argue that aboriginal breeds often have better resistance (Wu et al., 2008; Proudfoot et al., 2019; Huang et al., 2020) but bigger fat depth (Chen et al., 2012; Nevrkla et al., 2017).

The high level polymorphism in 3 loci out of 5 studied in pigs of the Ukrainian LW breed is consistent with studies (Yan et al., 2004; Wu et al., 2007; Vashchenko et al., 2019) which indicate that local breeds of pigs are characterized by greater genetic variability compared to industrial breeds.

The significant deviation of the observed distribution of genotypes by *SLC11A1/HinfI* 334 polymorphism from the expected greater number of hybrids (Table 2) may be explained by the fact that hybrid animals combine higher average daily gains with low backfat depth (Berezovskyy et al., 2021) and such animals are given priority in further breeding.

Conclusions

It was found that the *SLC11A1* gene polymorphism affects the average daily gain of pigs and their weight at 120 and 180 days after birth. The preferred genotype at position 334 restricted by *HinfI* is TT, which can be used in breeding to obtain more productive animals with increased resistance to disease, but pigs with this genotype was characterized by the largest backfat depth, which adversely affects their breeding value. Therefore, when selecting animals for this locus, it is necessary to control the fat depth and not to allow the breeding of those pigs that may worsen this trait.

The Ukrainian Large White breed has a fairly high level of polymorphism by the genetic markers *SLC11A1/HinfI* 334 and *FUT1* SNP g.307 G > A. Polymorphism Information Content > 0.3 indicates the value of this breed to preserve the genetic diversity of pigs.

This study was carried out with the support of the National Academy of Agrarian Sciences of Ukraine funded by the budget project "Innovative technologies of breeding, industrial and organic production of pig products." The subproject was "To develop modern systems of selection and hybridization using molecular genetics methods", state registration No. 0116U005008.

The authors declare no conflicts of interest.

References

Adams, L. G., & Templeton, J. W. (1998). Genetic resistance to bacterial diseases of animals. Revue Scientifique et Technique – Office International des Epizooties, 17(1), 200–219.

Ardiyana, M., Gunawan, A., Murtini, S., Sartika, T., & Sumantri, C. (2020). Polymorphisms and associations of the NRAMP-1 and iNOS genes on Newcastle disease and *Salmonella enteritidis* resistances in SenSi-1 Agrinak Chickens. Tropical Animal Science Journal, 43(2), 95–102.

Berezovskyy, M. D., Narizhna, O. L., Vashchenko, P. A., Shostya, A. M., Usenko, S. O., Kuzmenko, L. M., & Slynko, V. H. (2021). Terminal boars and other

male parents in hybridization system. Bulletin of Poltava State Agrarian Academy, 3, 135–141.
Blackwell, J. M., Searle, S., Mohamed, H., & White, J. K. (2003). Divalent cation transport and susceptibility to infectious and autoimmune disease: Continuation of the Ity/Lsh/Bcg/Nramp1/Slc11a1 gene story. Immunology Letters, 85, 197–203.
Bosewell, A., Naicy, T., Aravindakshan, T. V., & Kurian, E. (2018). Sequence characterization, structural analysis, SNP detection and expression profiling of SLC11A1 gene in Indian goats. Small Ruminant Research, 164, 15–21.
Botstein, D., White, R. L., Skolnick, M., & Davis, R. W. (1980). Construction of a genetic linkage map in man using restriction fragment length polymorphisms. American Journal of Human Genetics, 32(3), 314–331.
Braliou, G. G., Kontou, P. I., Boleti, H., & Bagos, P. G. (2019). Susceptibility to leishmaniasis is affected by host SLC11A1 gene polymorphisms: A systematic review and meta-analysis. Parasitology Research, 118(8), 2329–2342.
Cellier, M., Govoni, G., & Vidal, S. (1994). Human natural resistance associated macrophage protein: cDNA cloning, chromosomal mapping, genomic organization and tissue-specific expression. Journal of Experimental Medicine, 180, 1741–1752.
Chen, C., Deng, B., Qiao, M., Zheng, R., Chai, J., Ding, Y., & Jiang, S. (2012). Solexa sequencing identification of conserved and novel microRNAs in backfat of Large White and Chinese Meishan pigs. PLoS One, 7(2), e31426.
Cuong, N. V., Thu, N. T., Thoa, T. T., Hoan, T. X., Thuy, N. T., & Thuy, N. T. D. (2012). Polymorphisms of candidate genes associated with meat quality and disease resistance in indigenous and exotic pig breeds of Vietnam. South African Journal of Animal Science, 42, 221–231.
Dai, C. H., Wu, J. Y., Zhao, C. X., Yu, L. H., Bao, W. B., & Wu, S. L. (2017). Nramp1 gene expression in different tissues of Meishan piglets from newborn to weaning. Genetics and Molecular Research, 16, 19288.
Devi, B., Laskar, S., Borah, P., & Bharti, P. (2018). Cloning and polymorphism of disease resistance SLC11A1 gene in pig (*Sus scrofa*): A review. International Journal of Livestock Research, 8(9), 36–48.
Devi, B., Laskar, S., Borah, P., Hussain, I., & Bharti, P. K. (2017). Sequencing and phylogenetic analysis of the SLC11A1 gene in pigs. Journal of Applied Animal Research, 45(1), 494–497.
Dimitrova, A., & Yordanov, S. (2020). Sensitivity of *Escherichia coli* strains isolated from pigs in the period 2006–2015 to antimicrobial drugs. Acta Microbiologica Bulgarica, 36(1), 9–18.
Fleming, M. D., Trenor, C. C. 3rd, Su, M. A., Foernzler, D., Beier, D. R., Dietrich, W. F., & Andrews, N. C. (1997). Microcytic anaemia mice have a mutation in Nramp2, a candidate iron transporter gene. Nature Genetics, 16, 383–386.
Geraci, C., Varzandi, A. R., Schiavo, G., Bovo, S., Ribani, A., Utzeri, V. J., Galimberti, G., Buttazzoni, L., Ovilo, C., Gallo, M., Dall'Olio, S., & Fontanesi, L. (2019). Genetic markers associated with resistance to infectious diseases have no effects on production traits and haematological parameters in Italian Large White Pigs. Livestock Science, 223, 32–38.
Golovko, V. O., Severin, R. V., Voitenko, R. V., Kochmarski, V. A., Ivanchenko, I. M., Gontar, A. M., & Kuzmenko, M. V. (2019). PRRS in the nozoprofile of infectious diseases in pigs in Chornuhynsky District of Poltava Region. Veterinary Science, Technologies of Animal Husbandry and Nature Management, 3, 243–249.
Gunshin, H., Mackenzie, B., Berger, U. V., Gunshin, Y., Romero, M. F., Boron, W. F., Nussberger, S., Gollan, J. L., & Hediger, M. A. (1997). Cloning and characterization of a mammalian proton-coupled metal-ion transporter. Nature, 388, 482–488.
Hlazko, V. Y., Shulha, E. V., Dyman, T. N., & Hlazko, H. V. (2001). DNK-tekhnolohii i bioinformatika v reshenii problem byotekhnologii mlekopitaiushchykh [DNA technologies and bioinformatics in solving the problems of mammalian biotechnologies]. BSAU, Belaya Tserkov (in Russian).
Holder, A., Garty, R., Elder, C., Mesnard, P., Laquerbe, C., Bartens, M. C., Salavati, M., Tzelos, T., Connelley, T., Villarreal-Ramos, B., & Werling, D. (2020). Analysis of genetic variation in the bovine SLC11A1 gene, its influence on the expression of NRAMP1 and potential association with resistance to bovine tuberculosis. Frontiers in Microbiology, 11, 1420.
Huang, M., Yang, B., Chen, H., Zhang, H., Wu, Z., Ai, H., & Huang, L. (2020). The fine-scale genetic structure and selection signals of Chinese indigenous pigs. Evolutionary Applications, 13(2), 458–475.
Kim, K., Nguyen, D. T., Choi, M., & Kim, J. H. (2013). Alpha (1,2)-fucosyltransferase M307A polymorphism improves piglet survival. Animal Biotechnology, 24, 243–250.
Kupczyński, R., Szumny, A., Bednarski, M., Piasecki, T., Śpitalniak-Bajerska, K., & Roman, A. (2019). Application of *Pontentilla anserina*, *Polygonum aviculare* and *Rumex crispus* mixture extracts in a rabbit model with experimentally induced *E. coli* infection. Animals, 9(10), 774.
Le, T. T. H., Tran, T. H. G., & Nghia, S. H. (2021). Fertility, growth rate, polymorphism of GH and FUT1 genes of hybrid between wild boars and indigenous breeds. Chemical Engineering Transactions, 89, 109–114.
Li, T., Wang, L., Guo, C., Zhang, H., Xu, P., Liu, S., Hu, X., & Gao, Q. (2022). Polymorphisms of SLC11A1 (NRAMP1) rs17235409 associated with and susceptibility to spinal tuberculosis in a Southern Han Chinese population. Infection, Genetics and Evolution, 98, 105202.
Liu, K., Zhang, B., Teng, Z., Wang, Y., Dong, G., Xu, C., & Zhang, Y. (2017). Association between SLC11A1 (NRAMP1) polymorphisms and susceptibility to tuberculosis in Chinese Holstein Cattle. Tuberculosis, 103, 10–15.
Luc, D. D., Thinh, N. H., Bo, H. X., Vinh, N. T., Manh, T. X., Hung, N. V., Ton, V. D., & Famir, F. (2020). Mutation c. 307G> A in FUT1 gene has no effect on production performance of Yorkshire Pigs in the tropics: The case of Vietnam. Canadian Journal of Animal Science, 100(3), 426–431.
Matsenko, O. V., Mogilyovskyy, V. M., Mitrofanov, O. V., Maslak, Y. V., Shchepetilnikov, Y. O., Pasechnik, V. A., & Furda, I. V. (2019). The complex scheme of prevention of gastrointestinal diseases of piglets in farm condition. Veterinary Science, Technologies of Animal Husbandry and Nature Management, 3, 144–153.
Nevrkla, P., Kapelański, W., Václavková, E., Hadaš, Z., Cebulska, A., & Horký, P. (2017). Meat quality and fatty acid profile of pork and backfat from an indigenous breed and a commercial hybrid of pigs. Annals of Animal Science, 17(4), 1215–1227.
Peakall, R., & Smouse, P. E. (2012). GenAlEx 6.5: Genetic analysis in Excel. Population genetic software for teaching and research – an update. Bioinformatics, 28, 2537–2539.
Pires, V. S., Fernando, A. D. O., Minozzo, G. A., de Castro, L. L. D., Moncada, A. D., Klassen, G., Ramos, E. A. S., & Molento, M. B. (2021). Epigenetic regulation of SLC11a1 gene in horses infected with cyathostomins. Gene Reports, 25, 101410.
Prajapati, B. M., Gupta, J. P., Pandey, D. P., Parmar, G. A., & Chaudhari, J. D. (2017). Molecular markers for resistance against infectious diseases of economic importance. Veterinary World, 10(1), 112–120.
Proudfoot, C., Lillico, S., & Tait-Burkard, C. (2019). Genome editing for disease resistance in pigs and chickens. Animal Frontiers, 9(3), 6–12.
Provatorov, H. V., Ladyka, V. I., & Bondarchuk, L. V. (2007). Normy hodivli, ratsiony i pozhyvnist' kormiv dlia riznykh vydiv silskohospodarskykh tvaryn [Feeding norms, rations and nutritional value of feed for different species of farm animals]. Sumy (in Ukrainian).
Richards, J. D., Gong, J., & de Lange, C. F. M. (2005). The gastrointestinal microbiota and its role in monogastric nutrition and health with an emphasis on pigs: Current understanding, possible modulations, and new technologies for ecological studies. Canadian Journal of Animal Science, 85(4), 421–435.
Ruan, G. R., Xing, Y. Y., Fan, Y., Qiao, R. M., He, X. F., Yang, B., Ding, N. S., Ren, J., Huang, L. S., & Xiao, S. J. (2013). Genetic variation at RYR1, IGF2, FUT1, MUC13, and KPL2 mutations affecting production traits in Chinese commercial pig breeds. Czech Journal of Animal Science, 58, 65–70.
Rudoman, H. S., Balatsky, V. M., Nor, V. Y., & Vovk, V. O. (2017a). Zviazok polimorfizmu 1849 G>C henu mutsyn 4 iz hospodarsko-korysnymy oznakamy svynei Velykoi Biloi porody [Association of 1849g>c polymorphism of the mucin 4 gene with economicaly important traits in the Large White pig breed]. Scientific and Technological Bulletin, 117, 142–147 (in Ukrainian).
Rudoman, H. S., Balatsky, V. M., Nor, V. Y., & Vovk, V. O. (2017b). Zviazok polimorfizmu g307 G>A SNP henu alfa-fukozyltrasferazy 1 iz hospodorsko-korysnymy oznakamy svynej velykoji biloji porody [Association of g307 G> A SNP polymorphism of alpha-fucosyltransferase 1 gene with economically useful traits of large white pigs]. Animal Breeding and Genetics, 54, 134–140 (in Ukrainian).
Sahraoui, H., Madani, T., Fantazi, K., Khouane, A. C., Ameur, A. A., Paschino, P., & Dettori, M. L. (2020). Genetic variability in the A microsatellite at SLC11A1 gene and possible implications with innate resistance against brucellosis in Algerian native goats. Biodiversitas Journal of Biological Diversity, 21(12), 5630–5636.
Tait-Burkard, C., Doeschl-Wilson, A., McGrew, M. J., Archibald, A. L., Sang, H. M., Houston, R. D., Whitelaw, C. B., & Watson, M. (2018). Livestock 2.0 – genome editing for fitter, healthier, and more productive farmed animals. Genome Biology, 19, 204.
Tuggle, C. K., Marklund, L., Stabel, T. J., Mellencamp, M. A., & Stumbaugh, A. (2005). Genetic markers for screening animals for improved disease resistance (NRAMP). United States Patent, 6844159B2.
van der Steen, H. A. M., Prall, G. F. W., & Plastow, G. S. (2005). Application of genomics to the pork industry. Journal of Animal Science, 83(13), 1–8.
Vashchenko, P. A., Balatsky, V. M., Pocherniaev, K. F., Voloshchuk, V. M., Tsybenko, V. H., Saenko, A. M., Oliynychenko, Y. K., Buslyk, T. V., & Rudoman, H. S. (2019). Genetic characterization of the Mirgorod pig breed, obtained by analysis of single nucleotide polymorphisms of genes. Agricultural Science and Practice, 6(2), 47–57.
Vasilyeva, T. B. (2016). The monitoring of epizootic situation of colibacteriosis in Ukraine during 2004–2015. Scientific Messenger of Lviv National University of Veterinary Medicine and Biotechnologies, Series Veterinary Sciences, 18(66), 30–34.
Walsh, P. S., Metzger, D. A., & Higuchi, R. (1991). Chelex 100 as a medium for extraction of DNA for PCR-based typing from forensic material. BioTechniques, 10, 506–509.

Wen, Y., Cheng, X., & Zhao, S. (2018). Nucleotide variants of the Nramp1 gene in pigs and their effects on disease resistance. Indian Journal of Animal Research, 52(4), 8491.
Wu, H. M., Wang, L. X., Cheng, D. X., & Ma, X. J. (2008). Relationship between polymorphisms of Nramp1 gene and immune function of pig. Zhongguo Nong Ye Ke Xue, 41, 215–220.
Wu, Z. F., Luo, W. H., Yang, G. F., & Zhang, X. Q. (2007). Genomic organization and polymorphisms detected by denaturing high-performance liquid chromatography of porcine SLC11A1 gene. DNA Sequence, 18(5), 327–333.
Xie, Z., Pang, D., Yuan, H., Jiao, H., Lu, C., Wang, K., & Ouyang, H. (2018). Genetically modified pigs are protected from classical swine fever virus. PLoS Pathogens, 14(12), e1007193.
Yakubchak, O. M., Obshtat, S. V., Mukovoz, V. M., Karpulenko, M., & Gavrylenko, O. (2014). The analysis of the epizootic situation of infectious diseases of pigs in Ukraine. Bulletin of Poltava State Agrarian Academy, 3, 82–85 (in Ukrainian).
Yan, X. M., Ren, J., Ai, H. S., Ding, N. S., Gao, J., Guo, Y. M., Chen, C. Y., Ma, J. W., Shu, Q. L., & Huang, L. S. (2004). Genetic variations analysis and characterization of the fifth intron of porcine NRAMP1 gene. Asian-Australasian Journal of Animal Sciences, 17, 1183–1187.
Zhang, G. H., Gao, W. L., Tao, S., Yu, L. N., Zhang, G. F., & Luo, X. (2018). Online ultrasonic terminal for measuring pig backfat thickness. International Journal of Agricultural and Biological Engineering, 11(2), 190–195.
Zhang, Y., Wang, M., Yu, X. Q., Ye, C. R., & Zhu, J. G. (2013). Analysis of polymorphisms in the FUT1 and TAP1 genes and their influence on immune performance in Pudong White Pigs. Genetics and Molecular Research, 14(4), 17193–17203.
Zhu, S., Liu, Y., Dong, W., Zheng, X., Zhu, G., Wu, S., & Bao, W. (2014). Polymorphism of FUT1 Gene M307 and its relationship with partial immune indexes and economic traits in Yorkshire Pigs. Asian Journal of Animal and Veterinary Advances, 9, 253–261.