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STUDY OF WUR10000125 POLYMORPHISM ASSOCIATION WITH MEAT, FATTENING AND REPRODUCTIVE TRAITS OF LANDRACE AND LARGE WHITE PIG BREEDS

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Abstract

Integration of DNA markers associated with disease resistance into breeding programs is one of the most promising approaches to control infections of livestock. The identification and implementation of such a marker for the porcine reproductive and respiratory syndrome is particularly topical. The disease causes significant economic losses in the industry, and the proposed vaccines against PRRS are ineffective and associated with a risk of developing viremia after immunization. A promising DNA marker of resistance to this disease is the single nucleotide polymorphism WUR10000125 (*WUR*) localized in the *GBP1* gene. The aim of the study was to assess the reproductive, fattening and meat qualities of Large White and Landrace pigs bred in PRRS-free nucleus farms, considering the genetic variant of the WUR gene. Studies were conducted in 2018-2019 on pigs of Large White and Landrace pigs reared in Selection and Hybrid Center LLC (Voronezh region). Genotypes of 206 sows of Large White and 112 sows of Landrace pig breeds were determined by PCR with using the QuantStudio 5 Real-Time PCR System (Thermo Fisher Scientific, USA). The reproductive qualities of sows (number of piglets born alive per litter; total litter weight at birth; number of stillborn pigs per litter; number of mummified pigs per litter; total number born per litter) were estimated based on the first three litters: for Large White pig breed in the period from 2008 to 2018 and for Landrace pig breed in the period from 2010 to 2018. Characteristics of meat and fattening qualities, including the age of 100 kg of body weight, the back-fat thickness, measured in three points, muscle depth (lifetime measurements), were evaluated. To assess the effect of genotype on *WUR* on the productivity traits the model equations for multivariate analysis of variance were used. The results of animal genotyping showed that the studied pigs were characterized by relatively low frequencies of the "desirable" allele *G* responsible of resistance to PRRS (2.9 and 13.4 %) and *GG* genotype (0.49 and 4.46 %) in pigs of Large White and Landrace breeds, respectively. The analysis of values of estimates of the *WUR* genotypes obtained by the least square means (LSM) method showed a statistically significant superiority of carriers of the *AA* genotype over animals with *AG* variant by the total number born per litter, prolificacy and total litter weight at birth in pigs of Large White breed, but the similar tendency in Landrace pigs breed was not found. We noted some superiority of the *AA* genotype carriers over the *AG* genotype carriers among sows of Large White breed by EBV of total litter weight at birth. Comparison of meat and fattening parameters did not reveal significant differences either by direct phenotypic estimates or by EBV values. Thus, assessment of the productive traits of Large White and Landrace pigs from PRRS-free nucleus farms did not show a significant effect of the *WUR* genotypes on the meat and fattening parameters, as well as on the reproductive qualities of Landrace pigs. The increasing of the *G* allele and *GG* genotype frequencies under nucleus conditions will lead to an increase in the number of animals with preferable character-

istics under PRRS conditions.

Keywords: *Sus scrofa*, pigs, large white breed, landrace, WUR10000125, reproductive-respiratory syndrome, linear regression, productivity, evaluation of breeding value, DNA marker.

The integration of DNA markers associated with disease resistance into breeding programs is a promising approach to control infections of livestock [1]. Porcine reproductive and respiratory syndrome (PRRS), a highly contagious viral disease caused by a small virus with single-stranded non-segmented RNA (PRRSV), is a widespread disease that causes significant economic damage to pig breeding [2]. PRRSV disrupts the cellular immune response and damages mucosal surfaces. Clinical signs of the reproductive and respiratory syndrome are infertility, agalactia, lower conception frequency, a significant increase in the number of abortions in the late stages and the presence of stillborn, mummified or weakened piglets [3-5]. The economic loss is caused by the death of sows and young animals, early forced slaughter during fattening, reduced meat and fattening productivity, and lower sanitary quality of meat.

The use of vaccines against PRRS is not effective enough, which, most likely, is associated with different virulence and degree of antigenic relationship of vaccine and field viruses [6, 7]. Vaccination with a live modified vaccine provides effective protection against genetically homologous wild-type PRRSV strains, but only partially protects or completely does not protect against heterologous strains [8, 9]. Another disadvantage of vaccination is the possibility of isolating persistent virus strains from vaccinated animals. It was shown that viremia may develop in pigs vaccinated with live modified vaccine within 4 weeks after immunization, which leads to the spread of the vaccine virus among uninfected animals [8, 10]. There is also evidence of recombination between a live modified vaccine strain and wild-type strains [10, 11].

The selection of pigs that are genetically more resistant to PRRS is attractive to improve herd health [12]. As a result of genome-wide association studies (GWAS), single nucleotide polymorphism (SNP) WUR10000125 (*WUR*) was identified which is located next to the putative polyadenylation site in the 3′-untranslated region of the *GBP1* gene (interferon-inducible guanylate-binding protein-1-encoding gene). *WUR* may affect the stability of the transcript with consequences for protein synthesis and expression [13]. It was shown that pigs with a susceptible genotype (allele A of WUR10000125) expressed less GBP5 than pigs with a resistant genotype, and truncated protein was produced as a result of alternative splicing [14]. This polymorphism was responsible for 13.2% of the viremia variability and 9.1% of the variability in the average daily gain of pigs under viral load [15]. The discovered effect of *WUR* was successfully confirmed in pig populations of various genetic origins [16, 17]. GWAS studies conducted before and after the outbreak of PRRS revealed a close relationship between *WUR* polymorphism and the number of stillborn and non-viable piglets, as well as the presence of antibodies to PRRSV [18]. Different ($p < 0.05$) expression of *GBP5* gene, a member of the family of interferon-activated guanylate binding protein (*GBP*) genes located next to the *WUR* [14], in pigs with different genotypes on *WUR* confirms that the *WUR* is a DNA marker. The *WUR* effect was validated in pigs of different breeds vaccinated against PRRSV, infected with various PRRSV isolates, and also coinfected with PRRSV and pig type 2b circovirus (PCV2b) [19-21].

WUR polymorphism is due to the A→G nucleotide substitution at the position 139666819 SSC4 (rs80800372, Sscrofa10.2). Dominant G allele is desirable under the viral load due to both infection and vaccination. A study of *WUR* polymorphism showed a relatively low frequency of the desired G allele in pigs of the Large White (0.08), Landrace (0.02-0.22) and Duroc (0.08-0.12) breeds of

foreign breeding [17]. In pigs of Russian selection, the frequency of the G allele was also relatively low, 0.03 in animals of the Large White breed, 0.18 in Landrases, and 0.07 in Duroc pigs [22]. Considering that pure-bred pigs are used in an industrial cross-breeding (hybridization) system, and the young animals obtained are raised in commercial herds, with a significantly higher pathogenic load and vaccination against PRRS, selection of carriers of the *G* allele of *WUR* is relevant. The use of *WUR* as a DNA marker in pig breeding should be preceded by an assessment of the *WUR* effects on the most important economically useful traits. Based on the relatively low frequency of the *G* allele in various pig breeds, a negative relationship was suggested between the *G* allele and the most important economically significant traits and, as a result, selection against this allele was characteristic of breeding herds with a high health status [23]. Thus, in the absence of the virus, a higher fattening rate was established in pigs with the *WUR AA* genotype [24]. However, another investigation of cross-breed pigs (Yorkshire × Landrace) in the presence of pathogenic microflora revealed a significant superiority in the growth rate before weaning in piglets with the *G* allele.

Comprehensive studies of the reproductive, fattening and meat qualities of pigs in relation to the *WUR* genotype have not yet been conducted.

In this work we have found for the first time that the *WUR* genotype is not associated with productivity traits in Landrace pigs. The Large White pigs showed some superiority of the *AA* genotype carriers over heterozygous individuals in larger litter size and in the number of piglets born per farrow. It was found that the *WUR* DNA marker can be used to obtain fattened pigs on pedigree farms free from PRRS infection.

Our purpose was to study the influence of the *WUR* genotype on the reproductive, fattening, and meat qualities of the Large White and Landrace pigs under the conditions of nucleus farms free from pig reproductive and respiratory syndrome (PRRS).

Techniques. The investigations were carried out on Large White and Landrace sows (*Sus scrofa*) (Selective Hybrid Center LLC, Voronezh Region, 2018-2019).

Genomic DNA was isolated from tissue samples (ear pluck) using the DNA Extran-2 Reagent Kit (Syntol LLC, Russia). DNA quality and concentration were determined on a Qubit 2.0 fluorimeter (Invitrogen/Life Technologies, USA) and a NanoDrop8000 spectrophotometer (Thermo Fisher Scientific, USA).

WUR genotypes (A→G at the position 139666819 SSC4, rs80800372, Sscrofa10.2) (https://www.ncbi.nlm.nih.gov/assembly/GCF_000003025.5/) were determined by the real-time PCR method (PCRq) (a QuantStudio 5, Thermo Fisher Scientific, USA) with a test system based on the use of two specific primers WUR-SN-F and WUR-SN-R and two allele-specific fluorescently labeled probes, a probe for identifying *G* allele associated with pig resistance to PRRS was labeled with FAM, and a probe for allele *A* with CY5.

The reproductive traits of Large White sows (n = 206) and Landrace sows (n = 112) were evaluated for the first three farrowing: for the Large White sows from 2008 to 2018, and for the Landrace sows from 2010 to 2018. The meat and fattening qualities of the Large White (n = 200) and Landrace (n = 108) pigs, including early maturity (age of 100 kg body weight), fat thickness at three points, and muscle depth (intravital measurements) were also measured.

Descriptive statistical parameters were determined to characterize the studied productivity indicators, i.e. M — arithmetic mean for the trait in the sample, ±SEM — standard error of the mean; the standard deviation for the trait in the sample (σ) was used in the calculations.

In assessing the breeding value of animals for reproduction traits, the equation of the BLUP-AM model was used:

$$y = YM + b_1Par + animal + pe + e,$$

where y is the productivity indicator for the traits: the number of live piglets born per farrow (TBA), the weight of the nest at birth (BW), the number of stillborn piglets per farrow (SB), the number of mummified piglets per farrow (MUM), the total number of all piglets born per farrow (TNB); YM — "year-month of farrowing" factor; b_1Par — regression effect of "farrowing number" and regression coefficient; animal — a randomized effect of an animal; pe — permanent environmental effects; e — residual effects not included in the model.

The following models of assessing the breeding value of sows according to their own indicators of meat and fattening qualities were applied:

$$y = YM + b_1W + animal + e,$$

where y is the weighing age for calculating precocity estimates; b_1W — regression effect of "live weight during weighing" and regression coefficient;

$$y = YM + b_1Age + animal + e,$$

where y is the phenotypic indicator of the traits: the thickness of the fat at the first measurement point (the 6th-7th rib, mm) (BF1), the thickness of the fat at the second measurement point (the 1st rib, mm) (BF2), the thickness of the fat at the third measurement point (the 14th rib, mm) (BF3), muscle depth (LD); b_1Age — regression effect of "age at weighing" and regression coefficient.

When assessing the effect of the *WUR* genotype on reproductive traits, the model equation was used for multivariate analysis of variance without interaction:

$$y = YM + b_1Par + G + e,$$

where y is the evaluated trait; *G* is the effect due to the influence of the *WUR* factor. The effect of the *WUR* genotype on meat and fattening qualities was evaluated using the model equation for multivariate analysis of variance without interaction:

$$y = YM + A + G + e,$$

where y is the evaluated parameter; A — age at weighing (for traits BF1, BF2, BF3, LD) and live weight at weighing (for Age100, the precocity trait).

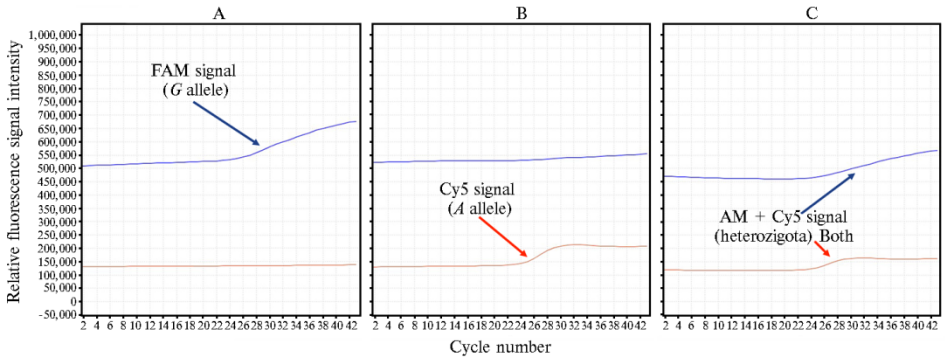
To assess the statistical significance of the influence of the factors taken into account, we used the Fisher test (the ratio of the variance of the factor taken into account to the residual variance) for the corresponding number of degrees of freedom (df). The significance of differences in the average values of traits in the compared groups of genotypes was determined using Student's *t*-test for the corresponding number of degrees of freedom and levels of confidence probability $P > 0.95$; $P > 0.99$; $P > 0.999$. Calculations for analysis of variance and the LSM method (Least Square Means) were performed using the STATISTICA 10 software (StatSoft, Inc., USA). The assessment of the breeding value of animals and the analysis of variants were carried out using the BLUPF90 family programs [26].

Results. Using the developed test system, genetic variants of Large White pigs and Landrace pigs by the WUR marker were identified (Fig.).

The studied sample of pigs had relatively low frequencies of the allele desirable for resistance to PRRS (2.9% and 13.4% in Large White and Landrace pigs, respectively) and the *GG* genotype (0.49% and 4.46%) (Table 1).

The analysis of the weighted values of the *WUR* genotype estimates obtained by the least squares (LSM) method for sow fertility revealed a statistically significant superiority of carriers of the *AA* genotype over animals with *AG* in

terms of the total number of piglets per farrow and multiple pregnancy in Large White pigs (Table 2). Comparison with productivity indices for carriers of the *GG* genotype was not possible as there was only one Large White sow with the *GG* genotype in the studied sample. In Landrace pigs, there were no statistically significant differences between groups with different *WUR* genotypes.



The results of genotyping Large White and Landrace sows (*Sus scrofa*) for *WUR* using real-time PCR (QuantStudio 5, Thermo Fisher Scientific, USA): A — *GG*, B — *AG*, C — *AA* (Selective Hybrid Center LLC, Voronezhskaya Province, 2018-2019).

1. **Frequencies of *WUR* genotypes and alleles in the studied samples of Large White and Landrace sows (*Sus scrofa*)** (Selective Hybrid Center LLC, Voronezhskaya Province, 2018-2019)

Breed	Frequency of genotypes			Frequency of alleles	
	AA	*AG*	*GG*	*A*	*G*
Large White	94.66	4.85	0.49	0.971	0.029
Landrace	77.68	17.86	4.46	0.866	0.134

2. **Weighted values of the *WUR* genotype estimates obtained by the least squares** (LSM) **for fertility traits of Large White and Landrace sows (*Sus scrofa*)** (*M*±SEM, Selective Hybrid Center LLC, Voronezhskaya Province, 2018-2019)

Genotype	TBA	BW	SB	MUM	TNB
		Large White (n = 206)			
AA	14.18±0.40[a]	19.29±0.51	1.82±0.15	0.17±0.07	16.17±0.44[a]
AG	12.30±0.66[a]	17.55±0.85	1.58±0.25	0.19±0.11	14.07±0.73[a]
GG	14.47±1.71	18.88±2.18	1.41±0.66	0.01±0.30	15.89±1.88
F-test	5.96*	3.09*	0.83	0.18	6.05*
		Landrace (n = 112)			
AA	12.41±0.48	17.90±0.62	1.41±0.27	0.20±0.09	14.02±0.53
AG	12.90±0.56	18.72±0.73	1.57±0.31	0.14±0.10	14.61±0.62
GG	12.02±0.82	17.25±1.06	1.50±0.46	0.12±0.15	13.63±0.90
F-test	1.13	1.89	0.35	0.55	1.30

Note. TBA — the number of live piglets born per farrow, BW — the weight of the nest at birth, SB — the number of stillborn piglets per farrow, MUM — the number of mummified piglets per farrow, TNB — the total number of all piglets born per farrow; [a] — differences between the marked genotypes are statistically significant at $p \le 0.05$.
* The value of the Fisher test is statistically significant at $p \le 0.05$.

A study of the breeding value of sows depending on the WUR genotype showed a statistically significant effect of variant *AA* on the estimation of breeding value (EBV) of nest weight at birth ($F = 3.33$) in Large White pigs. No significant differences in other reproductive traits were found in sows with unequal *WUR* genotypes (Table 3).

The analysis of variance did not reveal a statistically significant effect of the *WUR* genotype on meat and fattening productivity traits both in Large White and in Landrace pigs (Table 4). A study of the breeding value of sows with different *WUR* genotypes did not show a statistically significant effect of *WUR* genotypes on EBV for meat and fattening productivity (Table 5).

3. Association of breeding value estimates for fertility in Large White and Landrace sows (*Sus scrofa*) depending on the *WUR* genotype (*M*±SEM, Selective Hybrid Center LLC, Voronezhskaya Province, 2018-2019)

Genotype	TBA	BW	SB	MUM	TNB
		Large White (n = 206)			
AA	0.003±0.06	0.02±0.10	–0.01±0.02	0.003±0.003	0.003±0.07[a]
AG	–0.59±0.26	–0.52±0.43	–0.23±0.11	0.02±0.01	–0.87±0.33[a]
GG	–0.00±0.83	–0.27±1.37	–0.11±0.34	–0.02±0.04	–0.13±1.04
F-test	2.42	0.75	1.98	0.67	3.33*
		Landrace (n = 112)			
AA	–0.02±0.03	–0.00±0.00	0.07±0.05	–	0.05±0.10
AG	0.01±0.06	0.01±0.01	0.21±0.10	–	0.34±0.22
GG	–0.04±0.12	–0.01±0.01	–0.00±0.20	–	–0.08±0.44
F-test	0.10	1.36	0.87		0.81

Note. TBA — the number of live piglets born per farrow, BW — the weight of the nest at birth, SB — the number of stillborn piglets per farrow, MUM — the number of mummified piglets per farrow, TNB — the total number of all piglets born per farrow; [a] — differences between the marked genotypes are statistically significant at $p \le 0.05$. Dashes mean that in the studied sample the variability is completely due to the individual characteristics of individuals, that is, non-additive genetic effects.
* The value of the Fisher test is statistically significant at $p \le 0.05$.

4. Weighted values of the *WUR* genotype estimates obtained by the least squares (LSM) **for meat and fattening productivity of Large White and Landrace sows (*Sus scrofa*)** (*M*±SEM, Selective Hybrid Center LLC, Voronezhskaya Province, 2018-2019)

Genotype	$Age100_{corr}$	BF1	BF2	BF3	LD
		Large White (n = 200)			
AA	152.98±0.68	14.83±0.37	11.93±0.29	11.89±0.27	56.76±0.58
AG	152.44±2.57	15.10±1.20	12.17±0.93	11.85±0.88	56.15±1.68
GG	148.00±7.46	17.83±3.57	12.30±2.76	14.11±2.61	55.50±5.54
F-test	0.24	0.38	0.04	0.37	0.08
		Landrace (n = 108)			
AA	155.50±0.94	14.52±0.63	12.59±0.50	11.61±0.46	55.16±0.94
AG	158.01±2.02	13.82±1.27	10.30±1.00	10.60±0.93	50.49±1.88
GG	152.34±3.51	11.75±2.04	10.34±1.60	11.26±1.49	58.54±3.02
F-test	1.24	0.94	2.76	0.50	3.89

Note. $Age100_{corr}$ — precocity, adjusted for a mass of 100 kg, BF1 — the thickness of the fat at the first measurement point (in the region of the 6th-7th rib, mm), BF2 — the thickness of the fat at the second measurement point (in the region of the 10th rib, mm), BF3 — the thickness of the fat at the third measurement point (in the region of the 14th rib, mm) (BF3), LD — muscle depth.

5. Association of breeding value estimates for meat and fattening productivity in Large White and Landrace sows (*Sus scrofa*) depending on the *WUR* genotype (*M*±SEM, Selective Hybrid Center LLC, Voronezhskaya Province, 2018-2019)

Genotype	$Age100_{corr}$	BF1	BF2	BF3	LD
		Large White (n = 200)			
AA	0.08±0.13	–0.00±0.07	0.00±0.02	–0.03±0.04	–0.09±0.03
AG	–0.00±0.58	–0.31±0.29	–0.01±0.07	–0.04±0.19	–0.11±0.13
GG	–1.61±1.82	1.04±0.93	0.04±0.22	0.29±0.59	–0.03±0.41
F-test	0.44	1.15	0.02	0.15	0.03
		Landrace (n = 108)			
AA	0.00±0.00	0.10±0.07	0.05±0.04	0.06±0.04	0.07±0.05
AG	0.01±0.01	0.23±0.16	0.00±0.09	0.18±0.09	0.03±0.11
GG	–0.01±0.01	–0.03±0.30	–0.08±0.17	0.04±0.18	0.23±0.21
F-test	1.02	0.40	0.33	0.72	0.37

Note. $Age100_{corr}$ — precocity, adjusted for a mass of 100 kg, BF1 — the thickness of the fat at the first measurement point (in the region of the 6th-7th rib, mm), BF2 — the thickness of the fat at the second measurement point (in the region of the 10th rib, mm), BF3 — the thickness of the fat at the third measurement point (in the region of the 14th rib, mm) (BF3), LD — muscle depth.

Pig reproductive and respiratory syndrome, which has a significant negative impact on the economic efficiency of the industry, causes a significant increase in mortality rates (up to 30-50% of suckling pigs and 4-20% of piglets after weaning), and also leads to the manifestation of clinical signs (shortness of breath, anorexia, lethargy, skin hyperemia, weight loss) in animals after weaning and growing [2]. It also causes changes in the reproductive system of young animals associated with the chronic PRRS, which, in turn, reduce fertility [5].

The use of a DNA marker in breeding, which is associated with leveling the negative effects of vaccination or increasing the ability of an animal to be less affected by viruses, is of great practical importance. However, a limitation for the large-scale introduction of this marker may be its connection with the fertility traits, meat and fattening productivity. Our studies of the Large White and Landrace sows did not reveal such a relationship. However, these findings are consistent with the studies of Dunkelberger et al. [23] who did not note a significant effect of *WUR* genotypes on the reproductive and fattening traits of Landrace and Large White pigs. The authors showed the effect of this marker ($p < 0.001$) on the survival of Pietrain piglets. In terminal pigs, a correlation was found between the *G* allele, which is desirable for resistance to PRRSV, with significantly lower feed intake ($p = 0.004$) and, consequently, a decrease in daily gain during life ($p = 0.001$) and daily gain during testing ($p = 0.002$). An opposite relationship was found for the Pietrain pig line, where the *G* allele was associated with significantly higher feed intake ($p < 0.001$) and a tendency to increase average daily growth during testing ($p = 0.09$). The influence of *WUR* on the values of the breeding index for all indicators was not significant for any of the studied breeds ($p \geq 0.15$) [23]. At the same time, another study of contact of cross-bred pigs (Yorkshire × Landrace) with pathogenic microflora establishes significant superiority in the growth rate before weaning in piglets carrying the *G* allele: the average daily increase in *AA* piglets was 339 g versus 365 g in *AG* piglets ($p = 0.013$) [25].

Thus, the investigations of the productive indicators in Large White and Landrace pigs under the conditions of nucleus farms free of pig reproductive and respiratory syndrome (PRRS) did not show a significant effect of the *WUR* genotype on meat and fattening traits, as well as the reproductive qualities of Landrace pigs. The obtained relationships between *WUR* genetic variants and reproductive qualities of Large White pigs should be clarified on a large number of carriers of the *GG* genotype. Selection for the *G* allele is expected to lead to an increase in the number of livestock that has more preferable parameters under PRRS infection, and is not inferior in productivity to other genetic variants for *WUR* in conditions free of viral load. It will also contribute to an increase in the frequency of the desired genotype in herds that are most vulnerable and susceptible to diseases, since it is in them that the degree of pathogenic load is significantly higher.

REFERENCES

1. Prajapati B.M., Gupta J.P., Pandey D.P., Parmar G.A., Chaudhari J.D. Molecular markers for resistance against infectious diseases of economic importance. *Veterinary World*, 2017, 10(1): 112-120 (doi: 10.14202/vetworld.2017.112-120).
2. Dietze K., Pinto J., Wainwright S., Hamilton C. Porcine reproductive and respiratory syndrome (PRRS): virulence jumps and persistent circulation in Southeast Asia. In: *Focus on...* Food and Agriculture Organization of the United Nations, Rome, 2011, Iss. 5: 1-8.
3. Zimmerman J., Benfield D.A., Murtaugh M.P., Osorio F., Stevenson G.W., Tottemorell M. Porcine reproductive and respiratory syndrome virus (porcine arterivirus). In: *Diseases of Swine, 9th Edition.* B.E. Straw J.J. Zimmerman, S. D'Allaire, D.J. Taylor (eds.). Blackwell Publishing Professional, Ames, 2006: 387-417.
4. Rowland R.R., Lunney J., Dekkers J. Control of porcine reproductive and respiratory syndrome (PRRS) through genetic improvements in disease resistance and tolerance. *Frontiers in Genetics*, 2012, 3: 260 (doi: 10.3389/fgene.2012.00260).
5. Verkhneva D.A., Semenova N.N. *Agrarnyi vestnik Urala*, 2012, 10-2(105): 12-13 (in Russ.).
6. Hurd H.S., Bush E.J., Losinger W., Corso B., Zimmerman J.J., Wills R., Swenson S., Pyburn D., Yeske P., Burkgren T. Outbreaks of porcine reproductive failure: report on a collaborative field investigation. *Journal of Swine Health and Production*, 2001, 9(3): 103-108.
7. Mengeling W.L., Lager K.M., Vorwald A.C., Koehler K.J. Strain specificity of the immune response of pigs following vaccination with various strains of porcine reproductive and respiratory syndrome virus. *Veterinary Microbiology,* 2003, 93(1): 13-24 (doi: 10.1016/S0378-1135(02)00427-3).
8. Charerntantanakul W. Porcine reproductive and respiratory syndrome virus vaccines: immunogenicity, efficacy and safety aspects. *World J. Virol.,* 2012, 1(1): 23-30 (doi: 10.5501/wjv.v1.i1.23).
9. Roca M., Gimeno M., Bruguera S., Segalés J., Díaz I., Galindo-Cardiel I.J., Martínez E.,

Darwich L., Fang Y., Maldonado J., March R., Mateu E. Effects of challenge with a virulent genotype II strain of porcine reproductive and respiratory syndrome virus on piglets vaccinated with an attenuated genotype I strain vaccine. *The Veterinary Journal,* 2012, 193(1): 92-96 (doi: 10.1016/j.tvjl.2011.11.019).
10. Wang C., Wu B., Amer S., Luo J., Zhang H., Guo Y., Dong G., Zhao B., He H. Phylogenetic analysis and molecular characteristics of seven variant Chinese field isolates of PRRSV. *BMC Microbiology*, 2010, 10: 146 (doi: 10.1186/1471-2180-10-146).
11. Wenhui L., Zhongyan W., Guanqun Z., Zhili L., JingYun M., Qingmei X., Baoli S., Yingzuo B. Complete genome sequence of a novel variant porcine reproductive and respiratory syndrome virus (PRRSV) strain: evidence for recombination between vaccine and wild-type PRRSV strains. *Journal of Virology*, 2012, 86(17): 9543 (doi: 10.1128/JVI.01341-12).
12. Lewis C.R.G., Ait-Ali T., Clapperton M., Archibald A.L., Bishop S.C. Genetic perspectives on host responses to porcine reproductive and respiratory syndrome (PRRS). *Viral Immunology*, 2007, 20(3): 343-358 (doi: 10.1089/vim.2007.0024).
13. Gol S., Estany J., Fraile L.J., Pena R.N. Expression profiling of the *GBP1* gene as a candidate gene for porcine reproductive and respiratory syndrome resistance. *Animal Genetics*, 2015, 46: 599-606 (doi: 10.1111/age.12347).
14. Koltes J.E., Fritz-Waters E., Eisley C.J., Choi I., Bao H., Kommadath A., Serão N.V., Boddicker N.J., Abrams S.M., Schroyen M., Loyd H., Tuggle C.K., Plastow G.S., Guan L., Stothard P., Lunney J.K., Liu P., Carpenter S., Rowland R.R., Dekkers J.C., Reecy J.M. Identification of a putative quantitative trait nucleotide in guanylate binding protein 5 for host response to PRRS virus infection. *BMC Genomics*, 2015, 16: 412 (doi: 10.1186/s12864-015-1635-9).
15. Boddicker N., Waide E.H., Rowland R.R.R., Lunney J.K., Garrick D.J., Reecy J.M., Dekkers J.C.M. Evidence for a major QTL associated with host response to porcine reproductive and respiratory syndrome virus challenge. *Journal of Animal Science*, 2012, 90(6): 1733-1746 (doi: 10.2527/jas.2011-4464).
16. Boddicker N.J., Garrick D.J., Reecy J.M., Rowland B., Lunney J.K., Dekkers J.C.M. Quantitative trait locus on *Sus scrofa* chromosome 4 associated with host response to experimental infection with porcine reproductive and respiratory syndrome virus. *Animal Industry Report*, 2013, AS 659: ASL R2823 (doi: 10.31274/ans_air-180814-1255).
17. Boddicker N.J., Bjorkquist A., Rowland R.R.R., Lunney J.K., Reecy J.M., Dekkers J.C.M. Genome-wide association and genomic prediction for host response to porcine reproductive and respiratory syndrome virus infection. *Genetics Selection Evolution*, 2014, 46: 18 (doi: 10.1186/1297-9686-46-18).
18. Serão N.V.L., Matika O., Kemp R.A., Harding J.C.S., Bishop S.C., Plastow G.S., Dekkers JC. Genetic analysis of reproductive traits and antibody response in a PRRS outbreak herd. *Journal of Animal Science*, 2014, 92(7): 2905-2921 (doi: 10.2527/jas.2014-7821).
19. Hess A.S., Islam Z., Hess M.K., Rowland R.R.R., Lunney J.K., Wilson A.D., Plastow G.S., Dekkers J.C. Comparison of host genetic factors influencing pig response to infection with two North American isolates of porcine reproductive and respiratory syndrome virus. *Genetics Selection Evolution*, 2016, 48: 1-20 (doi: 10.1186/s12711-016-0222-0).
20. Waide E.H., Tuggle C.K., Serro N.V.L., Schroyen M., Hess A., Rowland R.R.R., Lunney J.K., Plastow G., Dekkers J.C. Genomewide association of piglet responses to infection with one of two porcine reproductive and respiratory syndrome virus isolates. *Journal of Animal Science*, 2017, 95: 16-38 (doi: 10.2527/jas2016.0874).
21. Dunkelberger J.R., Serro N.V.L., Niederwerder M.C., Kerrigan M.A., Lunney J.K., Rowland R.R.R., Lunney J.K., Plastow G., Dekkers J.C. Effect of a major quantitative trait locus for porcine reproductive and respiratory syndrome (PRRS) resistance on response to coinfection with PRRS virus and porcine circovirus type 2b (PCV2b) in commercial pigs, with or without prior vaccination for PRRS. *Journal of Animal Science*, 2017, 95: 584-598 (doi: 10.2527/jas2016.1071).
22. Fornara M.S., Bardukov N.V., Kostyunina O.V., Sadkova Ya.A., Kaz'mina N.A., Zinov'eva N.A. *Svinovodstvo,* 2018, 5: 17-19 (in Russ.).
23. Dunkelberger J., Mathur P.K., Lopes M.S., Knol E.F., Dekkers J.C.M. Pigs can be selected for increased natural resistance to PRRS without affecting overall economic value in the absence of PRRS. *Animal Industry Report*, 2017, AS 663: ASL R3192 (doi: 10.31274/ans_air-180814-378).
24. Abella G., Pena R.N., Nogareda C., Armengol R., Vidal A., Moradell L., Tarancon V., Novell E., Estany J., Fraile L. A WUR SNP is associated with European Porcine Reproductive and Respiratory Virus Syndrome resistance and growth performance in pigs. *Research in Veterinary Science*, 2016, 104: 117-22 (doi: 10.1016/j.rvsc.2015.12.014).
25. Jeon R.L., Putz A.M., Dyck M., Harding J.C.S., Fortin F., Plastow G.S., Kemp B., Dekkers J.C.M. PSIII-10 Effect of WUR genotype on resilience to a polymicrobial natural disease challenge in pigs. *Journal of Animal Science*, 2019, 97(Supplement_2): 165 (doi: 10.1093/jas/skz122.291).
26. Salajpal K., Đikić M., Karolyi D., Šurina J., Matković M., Liker B. Effect of MC4R polymorphism on physiological stress response in pigs. *Poljoprivreda*, 2007, 13(1): 46-50.