Agronomy Research **18**(3), 2156–2165, 2020
https://doi.org/10.15159/AR.20.171

'GENETIC LOAD' and changes in the chronology of early mortality in mini-pigs of ICG SB RAS

S.V. Nikitin[1], K.S. Shatokhin[2,*], V.I. Zaporozhets[1], N.N. Kochnev[2], D.S. Bashur[1], A.V. Khodakova[2] and V.I. Ermolaev[1]

[1]Institute of Cytology and Genetics of Siberian Department of Russian Academy of Sciences, RU630090 Novosibirsk, Russia
[2]Novosibirsk State Agrarian University, RU630039 Novosibirsk, Russia
[*]Correspondence: true_genetic@mail.ru

Abstract. This paper describes the study of the common factors of mortality of suckling piglets. It is assumed that this parameter is influenced by recessive lethal factors of the genetic load in population. An immediate subject of study was the chronological analysis of mortality in piglets from the breeding group of mini-pigs of ICG SB RAS (Institute of Cytology and Genetics Siberian Branch of Russian Academy of Sciences) for the period from 2013 through 2019. The results revealed increased number of dead piglets in the early postnatal period (first five days after farrowing) over this time period. This observation was confirmed by a statistically significant correlation coefficient between the year of birth and the number of animals that died during the first five days of life. Mortality in the period from the 6th day to weaning, on the contrary, decreased to probable accidental death which was non-related to genetic causes. Observed redistribution of mortality may be associated with increased general homozygosity in population and, in part, with the optimization of the excessive for mini-pigs multiple fertility. It is possible that the consequence of the second cause is an increase in mortality and a decrease in multiple pregnancy. It is assumed that in the breeding group of mini-pigs of the ICG SB RAS, there is the process of eliminating excessive lethal 'genetic load' and optimizing homozygosity to a level ensuring maximum survival of piglets on the 6th day after birth. Results of regression analysis showed that the mortality of piglets in 2018 reached its maximum level and in future a decrease to the optimum level which is typical for domestic pigs is possible. In general, results of this study suggest that newborn piglets are represented by two types. The first type includes animals whose viability potential determined by recessive lethal 'genetic load' is zero – they cannot live outside mother's body. The second type is represented by animals with a genetic viability potential equal to one –they can die only from accidental death.

Key words: mini-pigs of ICG SB RAS, 'genetic load', homozygosity, inbreeding, mortality, optimization of piglets number, genetic viability potential, agriculture.

INTRODUCTION

Gene pool of a domestic pig, as well as of on any other species, has the so-called 'genetic load' which includes neutral and lethal components (Ingue-Vechtomov, 1989; Lyons et al., 2009). Domestic pigs exist somehowin isolated populations (herds) with limited number of members (Bekenev, 2012; Christensen et al., 2019) where genetic processes typical forsuch populations take place; one of these is an increase in homozygosity. This is caused by both random stochastic processes, such as gene drift, and elimination of lethal and semi-lethal mutations through selection (Li, 1976; Ingue-Vechtomov, 1989; Nikitin & Knyazev, 2015). Depletion of gene pool due to gene drift is somewhat balanced by the selection vector for adaptive heterozygosity, as well as due to continuous mutagenesis of the satellite DNA (Ollivier, 2007; Jaeger et al., 2016). At the same time, protein-coding fragments of genome are subject to elimination which depletes not only gene pool, but also population phenofund (Markov & Naimark, 2015). The rate of these processes depends on the size of population and the presence of inbreeding (Li, 1976; Huisman et al., 2016). Moreover, if there is inbreeding in the population, then not only separate loci but the entire genomes (Severtsov, 1990) or, what is obviously more true, their rather large fragments, become homozygous.

The aim of this research is to study the process of elimination 'genetic load' from the breeding group of mini-pigs of the ICG SB RAS associated with early mortality. During the study period, this group was 'closed' (isolated), small in number, and there was a systematic planned inbreeding in it. Herd homozygosity increased from 0.25 in 2012 to 0.90 in 2018 (Nikitin et al., 2014 and 2018). 'Genetic load' of the breeding group of mini-pigs of the ICG SB RAS should be very high and various since four initial breeds were used for its forming – Svetlogorsk mini pigs, Large White, Landrace and Vietnamese breeds (Nikitin et al., 2014). Moreover, it should be taken into account that the allele pool of mini-pigs of the ICG SB RAS was formed not by the general gene pool of these breeds, but rather by total genomes of the founders (Shatokhin et al., 2014). Ultimately, a unique gene pool, different from other forms of domestic pig, has developed in this population what is confirmed by the unique sets of frequencies of erythrocyte antigens of blood groups, allotypes of serum proteins (Shatokhin et al., 2019), endogenous retroviruses (Aitnazarov et al., 2014) and microsatellites (Traspov et al., 2016). Each of the founders, accordingly, brought its share of genetic load into the herd. Studying of the variety of colors of mini-pigs of the ICG SB RAS showed the presence of 'hidden' variants in the initial forms (Nikitin et al., 2016 and 2017) which are obviously a manifestation of a neutral recessive 'genetic load', however, the question about the presence of early mortality lethal 'genetic load' remained unanswered.

MATERIALS AND METHODS

The studies were carried out according to the data of zootechnical registration of farrowing in the breeding group of mini-pigs of the ICG SB RAS for the period of 2013–2019. The number of animals in reproductive group during each coupling campaign in the study period ranged from 5 to 10 boars and from 20 to 30 sows (Nikitin et al., 2018). In the period from 01.01.2013 to 31.12.2019 were conducted 14 coupling campaigns. There was culling of small and weak at birth animals in the first five days of their life. All animals were separately weighed at birth and 1 month age. Upon the each fact of mortality of an animal, the date and reason for it was specified in the zootechnical document.

Mini-pigs of the ICG SB RAS is kept in 'Mini-pigs farm' of the Federal State Budget Scientific Institution 'Federal Research Center Institute of Cytology and Genetics of the Siberian Branch of the Russian Academy of Sciences' (ICG SB RAS) in the suburban area of Novosibirsk, in the village of Kainskaya Zaimka, Russia. Animals are kept in unheated pig house, on concrete floors, using sawdust as bedding (Sada & Reppo, 2011). Feeding of animals carried out with concentrates consisting of bran, wheat stock feed and boiled meat waste. The content and ratio of nutrients in the feeding corresponded to the standards for feeding pigs with calculation on a live weight of 50–80 kg (Vladimirov et al., 2003). Currently, mini-pigs of the ICG SB RAS are used as a model for cardiac surgery experiments conducted at Meshalkin National Medical Research Center (Chepeleva et al., 2017).

In domestic pigs, early mortality of piglets is commonly divided into two main periods (Topchin, 2012):

1. Before registration in zootechnical journal, i.e. first five days after birth. This group includes stillborn, dead at birth, small, weak and ugly pigs.

2. After registration, on the sixth day after birth and before weaning to sows.

Mortality was estimated as the ratio of the number of deaths during the first of second period to the total number of birth expressed as a percentage. Thus, three parameters were used:

1. Total mortality –ratio of the number of deaths before weaning to sows, including stillborn and ugly ones, to the number of births (%);

2. Mortality before the 6^{th} day – ratio of the number of deaths during first five days, including stillbirths and ugly ones, to the number of births (%);

3. Mortality of sucklings – ratio of the number of deaths starting from the 6^{th}day until weaning to the number of births (%).

For plottingin accordance to studied parameters, we used Microsoft Excel. Regression and correlation analyses were carried out according to recommendation (Lakin, 1990). Significance of differences in statistical parameters was evaluated using Student's test (Lakin, 1990). The trend was calculated by using software Microsoft Exel 2007.

RESULTS

Six-year dynamics of changes in mortality of piglets of mini-pigs in the ICG SB RAS can be described by linear regression equations (Fig. 1); it allows estimating the significance of these changes through correlation coefficients between the year of birth and the proportion of dead piglets (Table 1).

These changes show a relevant increased death rate of piglets until the 6^{th} day after birth with a relevant decreased mortality starting from the 6^{th}day. In general, mortality growth from birth to weaning is statistically insignificant (Table 1). This combination of changesin three mortality parameters allows suggesting that there is a shift in the time of piglets' death to the earlier period, i.e. first five days after birth. If this assumption is true, changes in mortality before the 6^{th}day after birth and starting from it should be:

1) symmetrical,

2) with a negative correlation between them.

Symmetry of the changesobserved means the symmetry of their linear trends, through the intersection of which and parallel to *x* axis, the line of symmetry will run. To determine the y coordinate of this line, we used linear regressionequationsfor mortality before the 6^{th}day and starting from it (Fig. 1). The equations were reduced to $x = \frac{y+6472.2}{3.2225}$ and $x = \frac{-y+4491.7}{2.2238}$ and, and then combined into equation $\frac{y+6472.2}{3.2225} = \frac{-y+4491.7}{2.2238}$ from which $y \approx 14.99$ (Fig. 1).

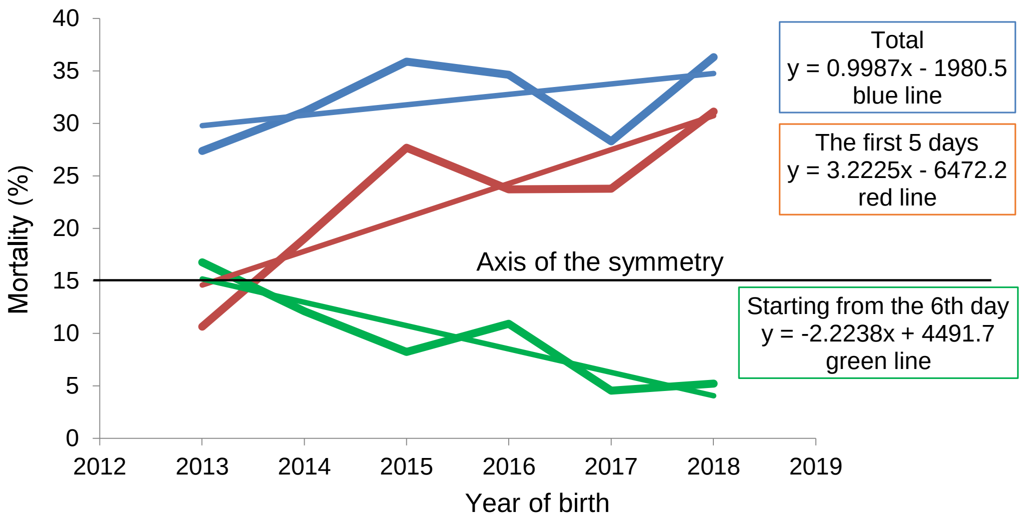

Figure 1. Changes in postnatal mortality of piglets of mini-pigs at the ICG SB RAS during the period from 2013 to 2018.

Table 1. Changes in mortality of piglets of mini-pigs in ICG SB RAS

Parameter			Year						Correlation coefficient
			2013	2014	2015	2016	2017	2018	
Born	total	heads	555	331	365	413	265	212	–
Died	total	heads	152	103	131	143	75	77	–
		%	27.38 ± 1.89	31.12 ± 2.54	35.89 ± 2.51	34.62 ± 2.34	28.30 ± 2.77	36.32 ± 3.30	0.48
	before the 6th day	heads	59	63	101	98	63	66	–
		%	10.63 ± 1.31	19.03 ± 2.16	27.67 ± 2.34	23.73 ± 2.09	23.77 ± 2.61	31.13 ± 3.18	0.84 *P* < 0.05
		trend	14.69	17.92	21.14	24.36	27.58	30.81	–
	After the 6th day	heads	93	40	30	45	12	11	–
		%	16.76 ± 1.59	12.08 ± 1.79	8.22 ± 1.44	10.90 ± 1.53	4.53 ± 1.28	5.19 ± 1.52	-0.90 *P* < 0.01
		trend	15.19	12.97	10.74	8.52	6.30	4.07	–
Trend deviation from the line of symmetry	before the 6th day	%	0.30	2.93	6.15	9.37	12.59	15.82	–
	Afterthe 6th day	%	0.20	2.02	4.25	6.47	8.69	10.92	–
	difference	%	0.10	0.91	1.90	2.90	3.90	4.90	–
Difference between actual proportions of died before and after the 6th day		%	-6.13	6.95	19.45	12.83	19.24	25.94	0.89 *P*< 0.01
Average weight at birth		g	701.29	709.28	669.05	682.31	706.75	651.39	-0.56

Paired values of deviations of trend lines from the line of symmetry should be equal in absolute values, and their difference should be equal to zero, both in each comparison pair and in general. However, the absolute values of deviations were actually not equal (Table 1), and their average value over six measurements, 2.435 ± 0.742, is definitely

(P < 0.01) not equal to zero. Thus, the changesin mortality before and after the 6th day after birth are not symmetrical, however, relevant negative correlation is observed between them (r = -0.98, P < 0.01). This result showed that, along with a redistribution of the death time of piglets, there was a direct increase in their mortality up to the 6th day after birth, as it is indicated by a relevant positive correlation between the year of birth and the difference between observed mortality values before the 6th days after birth and starting from it (Table 1).

To assess the nature of changes in the growth rate of piglet mortality during the first five days after birth, the dynamics of this process was developed (Fig. 2) showing that although this process can be described by linear regression equation in the time period under study, it can be more adequately expressed by parabolic equation (Fig. 2). According to parabolic equation, in 2018, the death rate of piglets in the first five days after birth reached its maximum and will continue to decline. It is known that low weight of newborn piglets (less than 600 g) is accompanied by their reduced life and competitiveness (Pond & Houpt, 1978; Nikitin & Knyazev, 2015). Correlation between mortality from birth to weaning and average birth weight during this year was statistically significant (r = -0.87, P < 0.05). At the same time, in this research, the correlation between the year of birth and the average weight of piglet born this year is statistically insignificant (Table 1). That is, the variation in average birth weight, unlike mortality, is not related to the year of birth. Therefore, the correlation between mortality and average birth weightis not indirect (mediated by year of birth), but a direct one.

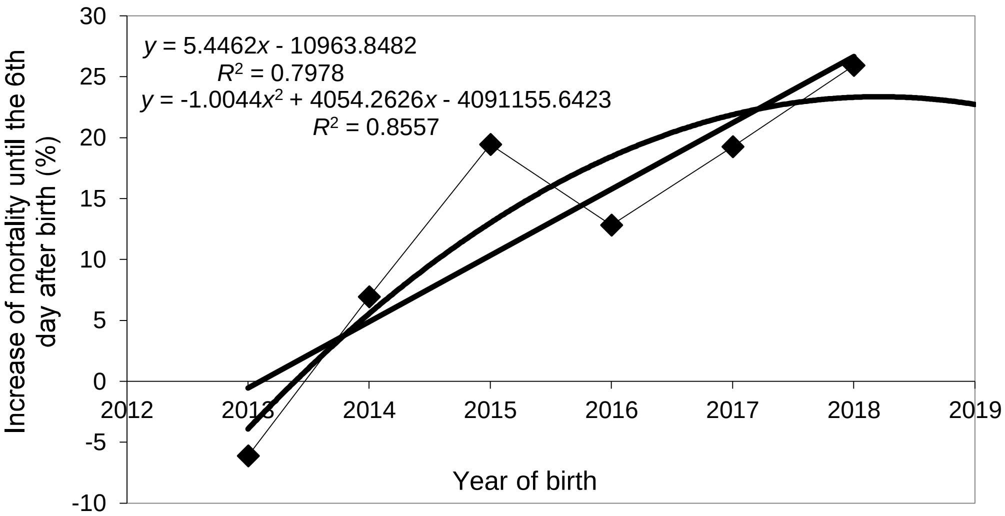

Figure 2. Increase in mortality of piglets of mini-pigs at the ICG SB RAS during the first five days after birth in the period from 2013 to 2018.

Piglets mortality from birth to weaning will result in a reduction in the number of piglet reared from sow (live on the 6th day after birth) and in the number of weaned piglets received on average from one sow. Since it cannot be excluded out that a shift in mortality can also affect prenatal period, a decrease in total number of piglets (including stillborn piglets) is possible.

To assess these parameters, the dynamics of their changes were plotted (Fig. 3). It turned out that although a decrease in multiple pregnancy was observed for six years, correlation coefficient between it and the year of birth of piglets is statistically insignificant and equals to -0.64. However, for parameters directly related to mortality, it is statistically significant ($P < 0.01$) and amounts to:

1) for the number of born piglets on the 6th day after birth $r = -0.98$;
2) for the number of piglets at weaning $r = -0.91$.

Statistical insignificance of correlation between multiple pregnancy and the year of birth suggests that there is no shift in mortality to prenatal period. However, there is a parallelism in the trends of multiple pregnancy and the number of piglets in a litter at weaning (Fig. 3), but at the same time, correlation coefficient between these parameters is irrelevant ($r = 0.70$). Since the inclination of line is determined by regression coefficient, the absence of significant differences between two regression coefficients indicates their possible parallelism. Regression coefficient for multiple pregnancy is -0.1591 ± 0.0954, for the number of live piglets before weaning -0.1771 ± 0.0395 (Fig. 3). Difference between them is irrelevant (Student's criterion is 0.17). Parallelism of trends, one of which is statistically significant and the other irrelevant, as well as irrelevant correlation between them indicate a greater exposure of the second parameter to the influence of random factors. Thus, there is reason to believe that a shift in mortality to prenatal period exists, and itmakes sense much more than the absence of such shift.

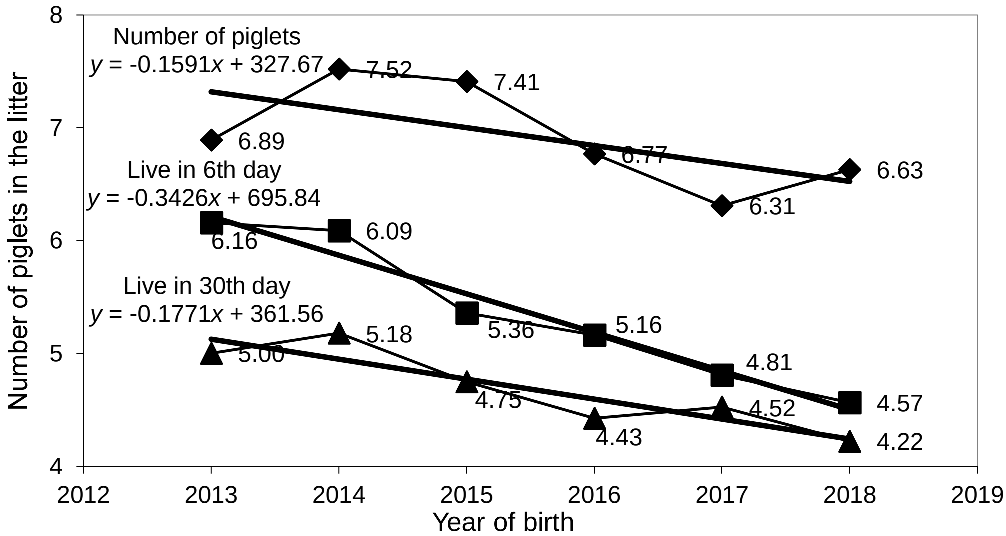

Figure 3. Dynamics of changes in total multiple pregnancy; piglets reared from mother and the number of piglets at weaning per sow.

DISCUSSION

This study showed the relevancy of common division of piglets' mortality into two periods:

1) before the 6thday after birth;
2) starting from the 6th day after birth.

Genetic background of this dividing is obvious. It is due to genetically determined viability potential of newborns which are naturally divided into two types (Rosendo et al., 2007; Andersen et al., 2011; Topchin, 2012; Nikitin & Knyazev, 2015):

1) Animals whose genetic viability potential (the probability of surviving until weaning) is equal to zero. Their genotype and, accordingly, phenotype are incompatible with life outside mother's body. The proportion of such animals shows the level of burdening the reproductive part of population with lethal 'genetic load' but is not related to the viability of young animals during suckling period.

2) Animals whose genetic viability potential in early postnatal period of ontogenesis can be considered as equal to one. In them, just accidental death can happen which is not related to their genetic characteristics.

The features of mortality changes are obviously associated with increased homozygosity in a limited population with systematic inbreeding hat was observed earlier (Dubinin & Glembotskiy, 1967). Was shown that the maximum frequency of lethal alleles can reach 10%, after which these alleles were eliminated by selection (Derks et al., 2019). Since each dying and naturally not leaving offspring animal reduces the frequency of allele responsible for its death (Li, 1976; Altukhov, 2003), this should form the dynamics of increased mortality described by parabolic equation (Fig. 2). Increased homozygosity of selection group is also associated with redistribution of mortality to an earlier period. This seems quite logical given the four-factor system of piglets ' safety, which consists of feeding sows, their maternal qualities, size of the litter and genetic components (Andersen et al., 2011). Moreover, the latter is also very difficult (Rothschild et al., 2007; Wang et al., 2016; Stafuzza et al., 2019) and it in turn can be decomposed into the presence of alleles that reduce viability, homozygosity and genes that determine the live weight, since it is also a factor of survival (Pond & Houpt, 1978; Smith et al., 2007). With constant litter size and feeding conditions, as well as with the elimination of sublethal alleles and a decrease in homozygosity, the shift in mortality terms to an earlier period can be explained by the fact that the proportion of mortality of small-weight piglets in the herd increases.

Culling of weak newborns could simulate shifting mortality to an earlier period but such cases are recorded as culling, and not as death, so this assumption is untenable. At the same time, cumulative effect of homozygosity in many loci that reduce viability should shift the time of death to an earlier period. It is known that one of the significant factors of animal mortality in a highly inbreed population is the homozygous state of lethal and sublethal alleles (Latter, 1998; Charlesworth & Willis, 2009). Therefore, the more such loci are homozygous, the earlier the animal will die. Shift in mortality to the first five days after birth has led to minimal mortality of piglets during later period; during last two years, it has stabilized and amounts to about 5%. This value is consistent with the probability of accidental death non-dependent of genetic factors (Muns et al., 2016). Therefore, there is reason to believe that, other things being equal, achieved level will remain such in the future.

The idea that a negative 'genetic load' can also perform positive functions seems to be very interesting. If multiple pregnancy is excessive, homozygosity for recessive lethal and sublethal alleles reduces its size and, thereby, reducing the 'damage' to mother's body and competition between littermates, increases the possibility of survival of the remaining animals. Breeding mini-pigs aimed at downsizing is, in fact, an artificially created situation when multiple fertility inherited from large pigs is clearly excessive. A rapid decrease in actual multiple pregnancy (the number of ovulated eggs) is hardly possible, therefore, the optimization of the number of offspring in litter (bringing it in line with the size of mother) is achieved by increasing homozygosity for the alleles of early death. Moreover, the sooner this death occurs, the more beneficial it will be, both for mother and for remained piglets. Mortality changes observed in the breeding group of mini-pigs of the ICG SB RAS are consistent with this hypothesis. They show a rapid increase in early mortality (the whole process took just six years), with the same rapid decrease in mortality during later period. At the same time, the number of piglets survived to weaning is reduced what can be considered as an adaptively determined tendency for an optimal number for breeding group. It should be noted that a decrease in the number of piglets at weaning to the value obtained in 2018 (4.22 piglets per sow) is not critical for mini-pigs at the ICG SB RAS. Much more important is the positive effect of this reduction, i.e. lesser burden on sows, their better development, fatness, and health of piglets; the latter, therefore, in less age become ready for use in surgical experiments.

CONCLUSION

In general, results of this study show that in the breeding group of mini-pigs of the Institute of Cytology and Genetics of SB RAS, the process of removing 'genetic load' and optimization of multiple pregnancy has reached its completion stage. A herd of mini-pigs at the ICG SB RAS is highly inbred. According to 2018 data, similarity index forthe animals of reproductive core calculated on the basis of the 'blood share' of founder is close to the figure of one, that is, genetic similarity between them is close to that between siblings. It is clear that the level of homozygosity with this genetic background is rapidly growing including this in the alleles that form 'genetic' load which caused increased mortality. However, death of young animals from the 6^{th}day until weaning in 2017–2018 stopped at a value close to 5%, that is, it obviously does not have genetic background and is due to random reasons. The shift of death to the first days after birth and achievement of maximal annual increase in mortality during this period indicate that in the future, a decrease in piglet mortality is expected to reach the level optimal for the breeding group of mini pigs of the Institute of Cytology and Genetics SB RAS.

ACKNOWLEDGEMENTS. This study was supported by budget financing on a state assignment (project No. AAAA-A17-117071240065-4).

REFERENSES

Aitnazarov, R.B., Yudin, N.S., Nikitin, S.V., Ermolayev, V.I. & Voevoda, M.I. 2014. Identification of whole genomes of endogenous retroviruses in Siberian miniature pigs. */Vavilovskii Zhurnal Genetiki i Selektsii/ Vavilov Journal of Genetics and Breeding* **18**(2), 294–297 (in Russian).

Altukhov, Yu.P. 2003. *Genetic processes in populations: Manual*. 3ed. Moscow, Academkniga, 431 pp. (in Russian).

Andersen, I.S., Naevdal, E. & Bøe, K.E. 2011. Maternal investment, sibling competition, and offspring survival with increasing litter size and parity in pigs (*Sus scrofa*). *Behav Ecol Sociobiol.* **65**(6), 1159–1167. doi: 10.1007/s00265-010-1128-4

Bekenev, V.A. 2012. *Technology of Pig Keeping and Breeding*. St. Petersburg: Lan Publ., 416 pp. (in Russian).

Charlesworth, D. & Willis, J.H. 2009. The genetics of inbreeding depression. *Nat Rev Genet*. **10**, 783–796. doi: 10.1038/nrg2664

Chepeleva, E.V., Balashov, V.A., Dokuchaeva, A.A., Korobejnikov, A.A., Strelnikov, A.G., Lependin, S.O., Pavlova, S.V., Agladze, K.I., Sergeevichev, D.S. & Pokushalov, E.A. 2017. Analyis of biological compatibility of polylactidenanofibrous matrix vitalized with cardiac fibroblasts in a porcine model. /*Geny I kletki* / *Genes & Cells* **XII**(4). doi: 10.23868/201707031 (in Russian).

Christensen, O.F., Nielsen, B., Su, G., Xiang, T., Madsen, P., Ostersen, T., Velander, I. & Strathe, A.B. 2019. A bivariate genomic model with additive, dominance and inbreeding depression effects for sire line and three-way crossbred pigs. *Genet SelEvol*. **51**, 45. doi: 10.1186/s12711-019-0486-2

Derks, M.F.L., Gjuvsland, A.B., Bosse, M., Lopes, M.S., van Son, M., Harlizius, B., Tan, B.F., Hamland, H., Grindflek, E., Groenen, M.A.M. & Megens, H.-J. 2019. Loss of function mutations in essential genes cause embryonic lethality in pigs. *PLoS Genet*. **15**(3), e1008055. doi: 10.1371/journal.pgen.1008055

Dubinin, N.P. & Glembotskiy, Ya.L. 1967. *Population genetics and selection*. Moscow, Nauka, 592 pp. (in Russian).

Huisman, J., Kruuk, L.E.B., Ellis, P.A., Clutton-Brock, T. & Pemberton, J.M. 2016. Inbreeding depression across the lifespan in a wild mammal population. *Proc Natl AcadSci*. **113**(13), 3585–3590. doi: 10.1073/pnas.1518046113

Ingue-Vechtomov, S.G. 1989. *Genetics with the basics of breeding*. Moscow, Vyshayashkola, 591 pp. (in Russian).

Jaeger, C.P., Duvall, M.R., Swanson, B.J., Phillips, C.A., Dreslik, M.J., Baker, S.J. & King, R.B. 2016. Microsatellite and major histocompatibility complex variation in an endangered rattlesnake, the Eastern Massasauga (*Sistruruscatenatus*). *EcolEvol*.**6**(12), 3991–4003. doi: 10.1002/ece3.2159

Lakin, G.F. 1990. *Biometrics. Fourth edition revised and expanded*. Moscow, Vysshayashkola, 352 pp. (in Russian).

Latter B.D. 1998. Mutant alleles of small effect are primarily responsible for the loss of fitness with slow inbreeding in Drosophila melanogaster. *Genetics*; **148**(3), 1143–1158.

Li, C.C. 1976. *First course in population genetics.* The Boxwood Press Pacific Grove, California, 556 pp.

Lyons, E.J., Amos, W., Berkley, J.A., Mwangi, I., Shafi, M., Williams, T.N., Newton, C.N., Peshu, N., Marsh, K., Scott, J.A.G. & Hill, A.V.S. 2009. Homozygosity and risk of childhood death due to invasive bacterial disease. *BMC Med Genet*. **10**, 55.doi: 10.1186/1471-2350-10-55

Markov, A. & Naimark, E. 2015. Evolution. Classical Ideas in the Light of New Discoveries. Moscow, ACT: CORPUS, 656 pp. (in Russian).

Muns, R., Nuntapaitoon, M. & Tummaruk, P. 2016. Non-infectious causes of pre-weaning mortality in piglets. *Livestock Science* **184**, 46–57. doi: 10.1016/j.livsci.2015.11.025

Nikitin, S.V. & Knyazev, S.P. 2015. *Selection and Adaptation in Domestic Pig Populations.* Saarbrucken, Lambert Academy, 228 pp. (in Russian).

Nikitin, S.V., Knyazev, S.P. & Shatokhin, K.S. 2014. Miniature pigs of ICG as a model object for morphogenetic research. *Russ. J. Genet.: Appl. Res*. **4**(6), 511–522. doi: 10.1134/S207905971406015X

Nikitin, S.V., Knyazev, S.P., Shatokhin, K.S., Goncharenko, G.M., Zaporozhets, V.I. & Ermolayev, V.I. 2017. Juvenile coat colours in mini-pigs at ICG. /*Vavilovskii Zhurnal Genetiki i Selektsii / Vavilov Journal of Genetics and Breeding* **21**(6), 638–645. doi: 10.18699/VJ17.280 (in Russian).

Nikitin, S.V., Knyazev, S.P., Shatokhin, K.S., Zaporozhets, V.I. & Ermolaev, V.I.2018.Breeding and selection of mini-pigs in the ICG SB RAS. /*Vavilovskii Zhurnal Genetiki i Selektsii / Vavilov Journal of Genetics and Breeding* **22**(8), 922–930. doi: 10.18699/ VJ18.434 (in Russian).

Nikitin, S.V., Shatokhin, K.S., Knyazev, S.P., Goncharenko, G.M., Zaporozhets, V.I. & Ermolayev, V.I. 2016. Polymorphic loci of coat color inmini-pigs. /*Vavilovskii Zhurnal Genetiki i Selektsii / Vavilov Journal of Genetics and Breeding* **20**(5), 584–595. doi: 10.18699/VJ16.180 (in Russian).

Ollivier, L. 2007. Analyses of the European pig diversity using genetic marcers. In: *Proceedings of 6th International Symposium on the Mediterranean Pig* (Ed. L. Nanni, Costa, P. Zambonelli, V. Russo). October 11–13, 2007. Messina - Capo d'Orlando (ME), Italy, pp. 10–22.

Pond, W.G. & Houpt, K.A. 1978. *The Biology of the Pig*. Cornell University Press, Ithaca, New York, 356 pp.

Rosendo, A., Druet, T., Gogué, J., Canario, L. & Bidanel, J.P. 2007. Correlated responses for litter traits to six generations of selection for ovulation rate or prenatal survival in French Large White pigs. *J Anim Sci*. **85**(7), 1615–1624. doi: 10.2527/jas.2006-690

Rothschild, M.F., Zhi-Liang, H. & Zhihua, J. 2007. Advances in QTL mapping pigs. *Internation J. Biological Sci.* **3**, 192–197. doi: 10.7150/ijbs.3.192

Severtsov, A.S. 1990. *The direction of the evolution*. Moscow State Univercity Publ., 272 pp. (in Russian).

Sada, O. & Reppo, B. 2011. Indoor climate in pigsty with deep litter system in winter. *Agronomy Research* **9**(Special Issue 1) 203–212.

Shatokhin, K.S., Knyazev, S.P., Goncharenko, G.M., Nikitin, S.V. 2014. The effect of allele introduction on the status of the allele pool of blood group system loci in the population of minipigs in the Institute of Cytology and Genetics, Novosibirsk. /*Vestnik NGAU / Bulletin of the Novosibirsk State Agrarian University* **33**(4), 119–124 (in Russian).

Shatokhin, K.S., Nikitin, S.V., Knyazev, S.P., Goncharenko, G.M., Ermolaev, V.I. & Zaporozhets, V.I. 2019. Livestock, physiology and genetic of the mini-pigs of ICG SB RAS. Novosibirsk, Siberian Federal Research Centre for AgroBiotechnology Publ.URL: https://elibrary.ru/ author_items.asp? authorid=805266 (in Russian).

Smith, A.L., Stalder, K.J., Serenius, T.V., Baas, T.J. & Mabry, J.W. 2007. Effect of piglet birth weight on weights at weaning and 42 days post weaning. *J Swine Health Prod*. **15**(4), 213–218.

Stafuzza, N.B., de Oliveira Silva, R.M., de Oliveira Fragomeni, B., Masuda, Y., Huang, Y., Gray, K., Lino Lourenco, D.A. 2019. A genome-wide single nucleotide polymorphism and copy number variation analysis for number of piglets born alive. *BMC Genomics* **20**, 321. doi: 10.1186/s12864-019-5687-0

Topchin, A.V. 2012. Safety of young animals– the most important factor in increasing profitability in pig farming. /*VestnikVNIMZh / Journal of VNIIMZH* **3**(7), 38–42 (in Russian).

Traspov, A., Deng, W., Kostyunina, O., Ji, J., Shatokhin, K., Lugovoy, S., Zinovieva, N., Yang, B. & Huang, L. 2016. Population structure and genome characterization of local pig breeds in Russia, Belorussia, Kazakhstan and Ukraine. *Genet SelEvol*. **48**(16) doi: 10.1186/s12711-016-0196-y

Vladimirov, N.I., Cheremnyakova, L.N., Lunicyn, V.G., Kocarev, A.P. & Popelyaev, A.S. 2008. *Feeding of farm animals*. Barnaul, Russia, Altai State Agricultural University Publ., 212 pp. (in Russian).

Wang, X., Liu, X., Deng, D., Yu, M. & Li, X. 2016. Genetic determinants of pig birth weight variability. *BMC Genet*. **17**(1), 15. doi:10.1186/s12863-015-0309-6