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Effect of single nucleotide polymorphism on the total number of piglets born per parity of three different pig breeds

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Objective: To determine the effects of genomic breeding values (GBV) and single nucleotide polymorphisms (SNP) on the total number of piglets born (TNB) in 3 pig breeds (Berkshire, Landrace, and Yorkshire).
Methods: After collecting genomic information (Porcine SNP BeadChip) and phenotypic TNB records for each breed, the effects of GBV and SNP were estimated by using single step best linear unbiased prediction (ssBLUP) method.
Results: The heritability estimates for TNB in Berkshire, Landrace, and Yorkshire breeds were 0.078, 0.107, and 0.121, respectively. The breeding value estimates for TNB in Berkshire, Landrace, and Yorkshire breeds were in the range of –1.34 to 1.47 heads, –1.79 to 1.87 heads, and –2.60 to 2.94 heads, respectively. Of sows having records for TNB, the reliability of breeding value for individuals with SNP information was higher than that for individuals without SNP information. Distributions of the SNP effects on TNB did not follow gamma distribution. Most SNP effects were near zero. Only a few SNPs had large effects. The numbers of SNPs with absolute value of more than 4 standard deviations in Berkshire, Landrace, and Yorkshire breeds were 11, 8, and 19, respectively. There was no SNP with absolute value of more than 5 standard deviations in Berkshire or Landrace. However, in Yorkshire, four SNPs (ASGA 0089457, ASGA0103374, ALGA0111816, and ALGA0098882) had absolute values of more than 5 standard deviations.
Conclusion: There was no common SNP with large effect among breeds. This might be due to the large genetic composition differences and the small size of reference population. For the precise evaluation of genetic performance of individuals using a genomic selection method, it may be necessary to establish the appropriate size of reference population.

Keywords: Berkshire; Genomic Breeding Value; Landrace; Single Nucleotide Polymorphism; Total Number of Piglets Born; Yorkshire

INTRODUCTION

Since the deoxyribonucleic acid (DNA) structure was identified in 1950s, exploration technology for genetic variation of organisms has been developed rapidly due to rapid development of molecular biology technology with many genome projects to identify genome-wide base pair sequence. Due to the development of DNA chip technology using microarray which enables exhaustive analysis of several hundreds to millions of single nucleotide polymorphism (SNP) markers through selective hybridization on solid surface based on by genotype, many genes can be identified in a short period. Currently, the imputation of genotypes using higher density chips from low-density chips is being undertaken. Meuwissen et al [1] and Van Eenennaam et al [2] have proposed the genomic selection method using genome-wide high-density SNP markers for the first time.

Genetic performance of individuals can be predicted by genomic selection through marker

mapping with dense interval. This is more accurate than conventional breeding value estimation method. Especially, it is highly accurate for breeding value estimation of young animals without phenotypic data, thus enabling juvenile selection [1]. Gengler et al [3] have proposed an algorithm to predict genomic information of animals without phenotypic data. VanRaden [4] has suggested an algorithm to calculate genomic relationship coefficient matrix and estimate genomic breeding value (GBV). Also, Misztal et al [5] have reported an algorithm that combines the conventional pedigree information with genomic information. Recently, Liu et al [6] have developed an SNP Single-step genomic model as a method to estimate SNP effects directly from the analysis model.

In this experiment, genomic information and phenotypic data on the total number of piglets born were collected from Berkshire, Landrace, and Yorkshire breeds. Their GBVs were estimated and the accuracies of these estimated breeding values were compared. In addition, SNP effects on total number of piglets born (TNB) by pig breed were investigated.

MATERIALS AND METHODS

SNP data and quality control

Using porcine SNP60 (v1, v2) manufactured by Illumina company and genomic profiler for porcine high density (GGP Porcine HD) genotyping BeadChip manufactured by GeneSeek company, genomic information for 3,998 breeding pigs was collected for Berkshire (1,903 heads), Landrace (1,041 heads), and Yorkshire (1,054 heads) breeds.

For quality control, SNPs on sex chromosome, SNPs without location information on chromosome, markers with more than 10% of missing rate, markers without polymorphism (homo or hetero genotype markers), markers with less than 1% of minor allele frequency, and markers with more than 23.93 ($p<10^{-6}$) of Hardy-Weinberg disequilibrium chi-square value, and genomic information of animals with more than 10% of SNP missing rate were excluded.

After performing quality control, the number of effective SNPs used for the analysis was 31,354 for Berkshire, 36,392 for Landrace, and 40,783 for Yorkshire. The numbers of pigs with genomic information for Berkshire, Landrace, and Yorkshire breeds were 1,871, 1,038, and 1,035 heads, respectively. Of sows with genomic information, the numbers of pigs with phenotypic data for Berkshire, Landrace, and Yorkshire breeds were 546, 836, and 898 heads, respectively (Table 1). Boars and candidate pigs only had SNP information. Phenotypic data were unavailable.

Phenotypic data

A total of 17,007 records of phenotypic data for the TNB were collected from Berkshire (4,504 records from 1,106 heads), Landrace (5,178 records from 1,498 heads), and Yorkshire (7,325 records from 1,923 heads) breeds. The total number of pigs was 3,600 Berkshires, 1,952 Landraces, and 2,424 Yorkshires. The average TNB for Berkshire, Landrace, and Yorkshire breeds were 8.58, 11.92, and 12.66 heads, respectively.

Table 1. Description of single nucleotide polymorphism (SNP) dataset

Description	Breed		
	Berkshire	Landrace	Yorkshire
Total No. of animals	1,903	1,041	1,054
No. of animals with missing over 10%	32	3	19
No. of selected animals	1,871	1,038	1,035
No. of sows with record	546	836	898
No. of common markers on autosome	42,276	48,245	51,984
No. of selected (useful) markers	31,354	36,392	40,783

Statistical model

Estimation of genomic breeding values: For fixed effect, parity and farrowing year-month-week were included and the following analysis model was used:

$$y = Xb+Za+Wp+e$$

Where, y = n×1 vector of observation, b = p×1 vector of fixed effect, a = q×1 vector of additive genetic random effect, p = q×1 vector of permanent environmental random effect, e = n×1 vector of residual effect, X(n×p), Z(n×q), and W(n×q) were known incidence matrix corresponding to b, a, and p, respectively.

Mixed model equation was as follows:

$$\begin{bmatrix} X'X & X'Z & X'W \\ Z'X & Z'Z+\alpha_1 H^{-1} & Z'W \\ W'X & W'Z & W'W+\alpha_2 I \end{bmatrix} \begin{bmatrix} \hat{b} \\ \hat{a} \\ \hat{p} \end{bmatrix} = \begin{bmatrix} X'y \\ Z'y \\ W'y \end{bmatrix}$$

Where, $\alpha_1 = \sigma_e^2/\sigma_a^2$, $\alpha_2 = \sigma_e^2/\sigma_{pe}^2$, $H^{-1} = A^{-1}+\begin{bmatrix} 0 & 0 \\ 0 & G^{-1}-A_{22}^{-1} \end{bmatrix}$, A^{-1} = inverse matrix of numerator relationship matrix, G^{-1} = inverse matrix of genomic relationship matrix and A_{22}^{-1} = inverse matrix of numerator relationship matrix of pigs with genomic information. Reliability (r^2) of breeding value was calculated using the prediction error variance (PEV) value. $r^2 = 1-(PEV/\sigma_a^2)$.

SNP effect: The SNP effect of each marker was estimated through reverse operation method of GBVs. When $\widehat{a_g} = Z\hat{u}$, $\widehat{a_g}$ = GBV vector, Z = coefficient matrix of SNP, $\hat{u}$ = vector of SNP effects.

If this equation is converted into variance equation, then $G^* = ZDZ'\lambda$, where D was weighted vector. Using the above two equations, it can be converted into $\hat{u} = \lambda DZ'G^{*-1}\widehat{a_g} = DZ'(ZDZ)^{-1}\widehat{a_g}$, where $\hat{u}$ = vector of SNP effects, $\widehat{a_g}$ = vector of GBV, Z = coefficient matrix of SNP, D = weighted vector

[7,8].

RESULTS AND DISCUSSION

Genetic parameter

The heritability estimates for TNB of Berkshire, Landrace, and Yorkshire breeds were 0.078, 0.107, and 0.121, respectively. The repeatability estimates for TNB of Berkshire, Landrace, and Yorkshire breeds were 0.176, 0.190, and 0.188, respectively (Table 2). Su et al [9] and Chen et al [10] have reported that the heritability estimates for TNB of Landrace breed is 0.08. The heritability estimates for TNB of Yorkshire and Duroc breeds have been reported to be 0.10 and 0.09, respectively [10]. It is 0.07 in Berkshire breed [11]. Therefore, the heritability for TNB seems to be low or around 0.1, depending on genetic characteristics of the population [12].

Table 2. Additive genetic (σ^2_a), permanent environmental (σ^2_{pe}), residual (σ^2_e) variance components, heritabilities (h^2), standard error (SE), and repeatabilities (r) for the total number of piglets born (TNB) by breed

Breed	Variance component			h^2±SE	r
	σ^2_a	σ^2_{pe}	σ^2_e		
Berkshire	0.6024	0.7516	6.3597	0.078±0.021	0.176
Landrace	0.9861	0.7641	7.4400	0.107±0.024	0.190
Yorkshire	1.4545	0.8143	9.7902	0.121±0.021	0.188

Breeding value and reliability

The breeding value estimates for TNB of Berkshire, Landrace, and Yorkshire breeds were in the range of –1.34 to 1.47, –1.79 to 1.87, and –2.60 to 2.94 heads, respectively. The reliabilities for the estimated breeding values depended on the number of records, pedigree information, and heritability. Reliability for the breeding value was estimated after classifying sows into two groups (with or without SNP information). Of sows with records for the TNB, the reliability of the breeding value for individuals with SNP information was higher than that for individuals without SNP information (Table 3).

This result was in agreement with that of Forni et al [13] showing that higher reliability is obtained for individuals with SNP information. When genomic information is used, reliability is increased. Especially, when breeding values for the progeny without phenotypic data are estimated using conventional BLUP method, their breeding values are equal to the average of breeding values of their parents. Breeding values for all progenies from the same parents are the same. On the other hand, for the estimation of GBV, genomic information of individuals considering Mendelian sampling is used. Therefore, more precise breeding value can be obtained. This seems to be very efficient for the selection of candidate pigs [14].

SNP effects

In ssBLUP, both phenotypic data of individuals with genomic information and phenotypic data of individuals with only pedigree information can be used [15,16]. For ssBLUP, since the estimated effects from the model are the pedigree and GBVs of the individuals, conventional breeding value and GBV can be estimated simultaneously by one analysis. Through back solution, the effects of SNPs can be estimated reversely [7,8].

After absolute values for the estimated SNP effects were taken, optimal histograms fitted with real estimated values were drawn using the estimated parameters for gamma distribution (Figure 1). They were distributions for SNP effects on TNB. Most SNP effects were near zero. Only a few SNPs had large effects.

Meuwissen et al [1] have reported that the distribution of quantitative trait locus follows Gamma distribution. However, in this study, we performed Goodness-of-Fit tests for gamma distribution and found that the distribution of estimated SNP effects on TNB did not follow Gamma distribution (Table 4).

Genome-wide association study

To compare the relative magnitude of estimated SNP effects, absolute values of estimated SNP effects were taken after standardization (Figure 2). If we assume that 99.74% of values drawn from a normal distribution are within 3 standard deviations, selection threshold should be more than 4 standard deviations as useful markers (Table 5). For TNB, the numbers of SNPs with absolute value of more than 4 standard deviations in Berkshire, Landrace, and Yorkshire breeds were 11, 8, and 19, respectively. There was no SNP with absolute value of more than 5 standard deviations in Berkshire or Landrace breed. However, in Yorkshire, four SNPs (ASGA0089457 [5,20], ASGA0103374 [5.11], ALGA0111816 [5.32], and ALGA 0098882 [5.79]) had absolute values of more than 5 standard deviations (Table 5). No SNP had large effects for all breeds.

Table 3. Reliabilities (r_2) on the estimated breeding values of animals with SNPs or without SNPs in sows with total number of piglets born (TNB) records by breed

Breed	Overall		Without SNPs		with SNPs	
	Animals	r^2±SD	Animals	r^2±SD	Animals	r^2±SD
Berkshire	1,106	0.33±0.08	564	0.30±0.08	542	0.35±0.08
Landrace	1,498	0.41±0.10	662	0.33±0.08	836	0.48±0.07
Yorkshire	1,923	0.45±0.11	1,025	0.39±0.10	898	0.53±0.07

SNPs, single nucleotide polymorphisms; SD, standard deviation.

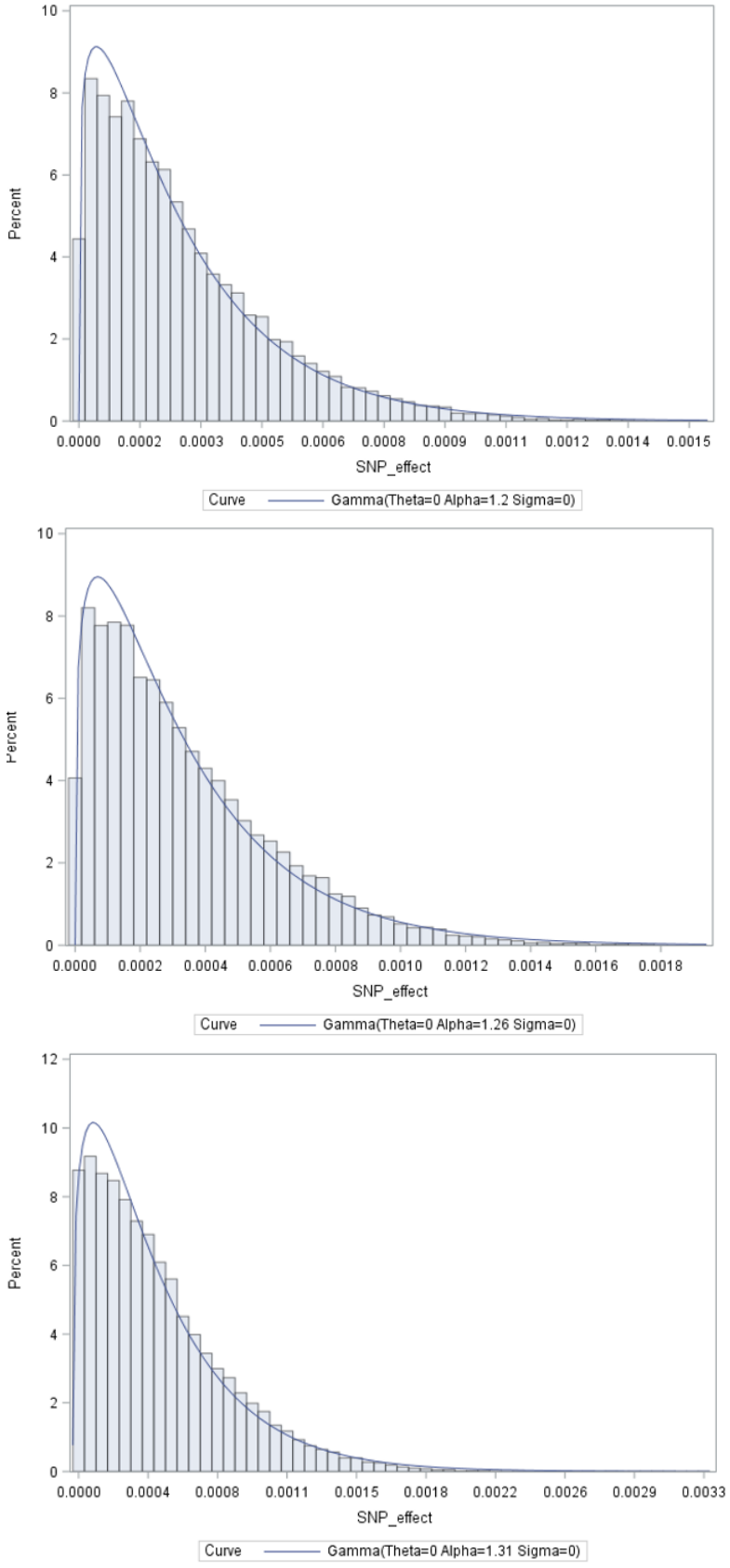

Figure 1. Distribution of estimated single nucleotide polymorphism (SNP) effects for the total number of piglets born (TNB) in Berkshire, Landrace, and Yorkshire breeds (from left to right).

Table 4. Goodness-of-fit tests for gamma distribution of estimated single nucleotide polymorphism (SNP) effects for the total number of piglets born (TNB) by breed

Breed	Test method (statistics)		
	Kolmogorov-Smirnov (D)	Cramer-von Mises (W-Sq)	Anderson-Darling (A-Sq)
Berkshire	0.0241**	5.7569**	33.9518**
Landrace	0.0240**	8.1674**	49.8215**
Yorkshire	0.0285**	10.5087**	60.4243**

** $p < 0.01$.

This might be due to the large genetic composition differences among breeds.

Only a few markers had large effects on the TNB. Due to linkage disequilibrium, some markers in regions adjacent to markers with large effects also had large effects. For TNB, SNPs in chromosome number 2 (MARC0046316, ASGA0101159), chromosome number 6 (ALGA0114670, H3GA0055046), and chromosome number 17 (ALGA0093629, ASGA0075678, ALGA0093681) in Berkshire, SNPs in chromosome number 7 (ASGA0036842, ALGA0045470) in Landrace, and SNPs in chromosome number 3 (MARC0053067, MARC0034058, ASGA0089809, H3GA0009642), chromosome number 8 (ASGA0089457, ASGA0103374, ALGA0111816, H3GA0025815), and chromosome number 18 (M1GA0023425, ALGA0098863, H3GA0051231, ALGA0109739, ALGA0098882, ALGA

Table 5. Single nucleotide polymorphism (SNP) name, chromosome number (Chr.), position, SNP effect and absolute standardized SNP effect of more than 4.0 STD value for the total number of piglets born by breed

Breed	SNP name	Chr.	Position	SNP effect	|STD value|
Berkshire	MARC0046316	2	2216738	0.00140875	4.39
	ASGA0101159	2	2224107	0.00135236	4.22
	H3GA0056247	3	101704758	–0.00149613	4.40
	ALGA0114670	6	74627362	–0.00138505	4.06
	H3GA0055046	6	74682817	–0.00138505	4.06
	DRGA0012350	13	53111671	0.00128118	4.01
	ASGA0096197	16	77537650	0.00130050	4.06
	ALGA0105626	17	18894036	0.00145942	4.54
	ALGA0093629	17	21259716	–0.00145520	4.28
	ASGA0075678	17	21701959	0.00129377	4.04
	ALGA0093681	17	22559386	–0.00154334	4.54
Landrace	H3GA0016445	5	45404530	–0.00193198	4.37
	ASGA0036842	7	126525777	0.00171787	4.01
	ALGA0045470	7	126664035	0.00173147	4.04
	MARC0043234	13	119326691	–0.00179717	4.06
	H3GA0038201	13	211949439	0.00175716	4.10
	DIAS0003382	15	83795094	–0.00179399	4.05
	ALGA0103750	15	142396418	0.00177819	4.14
	ASGA0075659	17	21411732	–0.00177623	4.01
Yorkshire	M1GA0002671	2	10286572	0.00228474	4.10
	MARC0053067	3	56950047	–0.00280437	4.93
	MARC0034058	3	57211150	–0.00240863	4.23
	ASGA0089809	3	58664523	–0.00243213	4.27
	H3GA0009642	3	58873656	–0.00277533	4.88
	ASGA0089457	8	146074727	–0.00295488	5.20
	ASGA0103374	8	146101319	–0.00290477	5.11
	ALGA0111816	8	146216038	–0.00302276	5.32
	H3GA0025815	8	146688242	–0.00233696	4.11
	CASI0008334	9	116927941	0.00227066	4.07
	DRGA0010231	10	9488500	–0.00246896	4.34
	H3GA0038333	14	2865914	–0.00251473	4.42
	ALGA0098185	18	45821014	0.00233614	4.19
	M1GA0023425	18	57244090	–0.00233631	4.10
	ALGA0098863	18	57260307	–0.00250486	4.40
	H3GA0051231	18	57292109	–0.00250486	4.40
	ALGA0109739	18	57411145	0.00252987	4.53
	ALGA0098882	18	57936786	–0.00328544	5.79
	ALGA0098883	18	57957917	–0.00266136	4.68

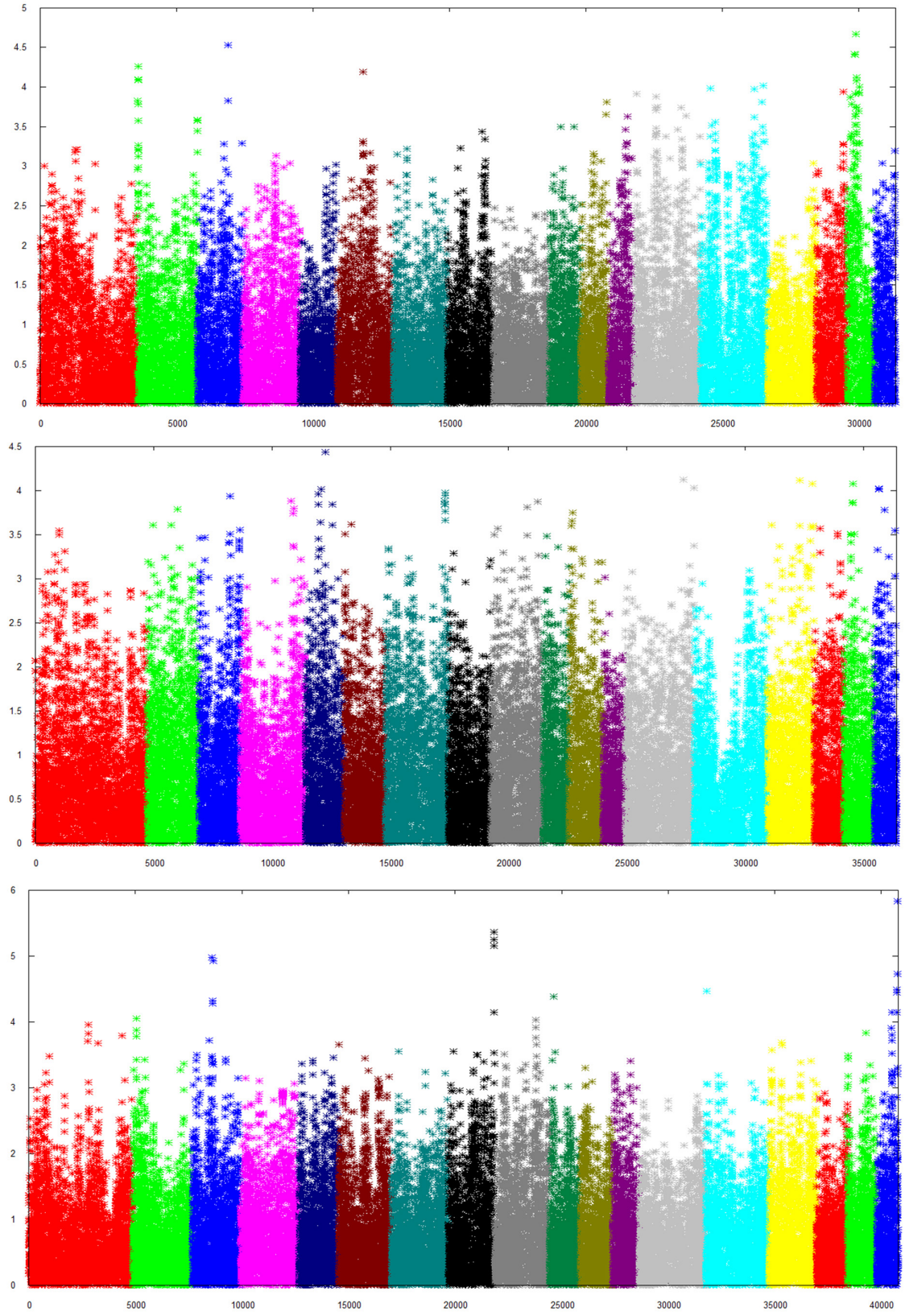

Figure 2. Manhattan plots for standardized single nucleotide polymorphism (SNP) effects on the total number of piglets born (TNB) in Berkshire, Landrace, and Yorkshire breeds (from upper to lower).

0098883) in Yorkshire were in linkage disequilibrium blocks.

Guo et al [17] reported that in Landrace, 18 SNPs on chromosome 2, 5 SNPs on chromosome 3, 7 SNPs on chromosome 6, 1 SNP on chromosome 13, and 3 SNPs on chromosome 14 had effects on the TNB, while in Yorkshire, 9 SNPs on chromosome 1 and 2 SNPs on chromosome 3 had effects on the TNB. Also, it was reported that in Landrace, 5 SNPs on chromosome 9 had effects on the total number of piglets born [18]. However, SNPs which were identified to have effects on the TNB in this experiment were not reported in other experiments.

It has been known that in Berkshire, complement C1q B chain gene (ALGA0114670) with high SNP effect is the candidate gene which is associated with the immune responses to porcine reproductive and respiratory syndrome virus infection and affects reproductive immunity in pigs [19,20], and in Landrace, phospholipase D1 gene (MARC0043234) controls the mTORC1 regulators which play a crucial role for the regulation of skeletal muscle protein synthesis in neonatal pigs [21]. Also, it was reported that in Yorkshire, CD6 molecule gene (M1GA0002671) regulates the cell adhesion molecules expression in the biological pathways including the development of embryonic cells and nerve tissues, and protein kinase, cGMP-dependent, type II (ASGA0089457, ASGA0103374) is involved in the secretion of luteinizing hormone beta polypeptide and progesterone [22].

There was no common SNP with large effect among breeds. This might be due to the large genetic composition differences among breeds. If we analyze again after deleting markers in the linkage disequilibrium blocks, the effect will be clearer. The main reason for that may be the small size of reference population used in this study, which could happen in any study when the size of reference population is small. For the precise evaluation of genetic performance of individuals using a genomic selection method, it may be necessary to establish the appropriate size of reference population.

CONFLICT OF INTEREST

We certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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