Review

Survey of SNPs Associated with Total Number Born and Total Number Born Alive in Pig

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Abstract: Reproductive productivity depend on a complex set of characteristics. The number of piglets at birth (Total number born, Litter size, TNB) and the number of alive piglets at birth (Total number born alive, NBA) are the main indicators of the reproductive productivity of sows in pig breeding. Great hopes are pinned on GWAS (Genome-Wide Association Studies) to solve the problems associated with studying the genetic architecture of reproductive traits of pigs. This paper provides an overview of international studies on SNP (Single nucleotide polymorphism) associated with TNB and NBA in pigs presented in PigQTLdb as “Genome map association”. Currently on the base of Genome map association results 306 SNPs associated with TNB (218 SNPs) and NBA (88 SNPs) have been identified and presented in the Pig QTLdb database. The results are based on research of pigs such as Large White, Yorkshire, Landrace, Berkshire, Duroc and Erhualian. The presented review shows that most SNPs found in chromosome areas where candidate genes or QTLs (Quantitative trait locus) have been identified. Further research in the given direction will allow to obtain new data that will become an impulse for creating breakthrough breeding technologies and increase the production efficiency in pig farming.

Keywords: pig; litter size; total number born alive; SNP (single nucleotide polymorphism); GWAS (Genome-Wide Association Studies)

1. Introduction

In the early 1990s the work on mapping the pig genome started and maps containing more than 1200 microsatellite markers appeared due to the development of the international project “PiGMMap” and projects of the US Department of Agriculture and American agricultural institutes. These maps were used to identify the Quantitative Trait Loci (QTL) underlying the genetic architecture of pig productivity traits [1–3]. To date, an extended database has been created—Pig Quantitative Trait Locus Database (PigQTLdb), which presents 30170 QTLs for 688 pig trait of deferent classes [4].

The sows’ reproductive potential is the basis for continuous and efficient production. In recent decades, the BLUP (Best linear unbiased prediction) method has made a significant contribution to improving reproduction rates [5,6]. However, low heritability coefficients of reproductive traits and their sex-limited phenotypic exhibition lead to developing new approaches revealing the biological nature of reproductive performance. Great hopes are pinned on GWAS (Genome-Wide Association Studies) to solve the problems associated with studying the genetic architecture of reproductive traits of pigs [7–10].
GWAS results can be represented by the information on detected associations with various genetic aberrations: chromosomal mutations (whole chromosomes or their fragments), large inserts or deletions (100–100,000 nucleotides), small inserts or deletions (1 to 100), single nucleotide polymorphisms (SNP) [11]. Each SNP is represented by at least two alleles: minor (rarer) and major. Genetic variations with minor allele frequency exceeding 0.01% are numbered and assigned to rs index [12].

Currently, SNP BeadChip technology is more affordable for genome-wide research than sequencing is. SNP BeadChips have been developed to include high (HD), medium (MD), or low (LD) genome distribution of markers. Rigid structure is noted as a disadvantage, which allows us to analyze only what is already predetermined by the BeadChip design and in this connection the potentially important information can be omitted [13]. Markers do not have the same density across all chromosomes and not fully track structural genetic variations such as insertions and deletions [13]. However, despite these shortcomings, SNP BeadChip has recently gained great popularity in studies of the genetic architecture of quantitative traits of farm animals and pigs in particular [14–16].

The first SNP BeadChips with a resolution of about 60 thousand markers covering all autosomal and X chromosome genes PorcineSNP60 BeadChip v2 were presented by the American company Illumina (San Diego, CA, USA). In addition to SNP BeadChip with high density, LD SNP BeadChip with low density have been proposed to reduce genotyping costs. Commercial LD SNP BeadChip «GeneSeek/Neogen GPP-Porcine LD Illumina Bead Chip panel» were also developed by «GeneSeek/Neogen» (Lincoln, NE, USA). Besides this, the company introduced HD SNP BeadChips with a higher density (about 70 thousand markers). HD SNP BeadChips containing about 650 thousand markers and including all markers of the «Illumina PorcineSNP60 BeadChip v2» array, were produced by «Affymetrix» (Santa Clara, CA, USA). It should be noted that SNP BeadChip can be custom made including specific SNPs associated with given traits of productivity.

Reproductive productivity depend on a complex set of characteristics. The number of piglets at birth (Total number born, Litter size, TNB) and the number of alive piglets at birth (Total number born alive, NBA) are the main indicators of the reproductive productivity of sows in pig breeding [17–21]. These indicators reflect the level of all physiological processes associated with fertilization, intrauterine development of the fetus and a sow’s labor, and are also quite easy to account for.

2. SNPs Associated with Total Number Born Alive

Currently on the base of Genome map association results 88 SNPs associated with NBA have been identified and presented in the Pig QTLdb database (Table 1). The results are based on a study of pigs such as Large White, Large White, Yorkshire, Landrace [7,14,22–26] Duroc [27] and Erhualian [28]. SNPs, associated with the NBA are represented in all Sus scrofa chromosomes (SSC) except SSCY.
Table 1. SNPs (Single nucleotide polymorphism) associated with NBA (Total number born alive) presented in the PigQTLdb (Pig Quantitative Trait Locus Database). Ensembl db, Sus Scrofa 11.1 (NA—This variant has not been mapped on Ensembl db, Sus Scrofa 11.1).

| SNP       | SSC | Location | Allele | Consequence       | SYMBOL | Trait | Breed            | Reference |
|-----------|-----|----------|--------|-------------------|--------|-------|------------------|-----------|
| rs339929690 | 1   | 59515751 | C      | intergenic_variant | -      | NBA   | Landrace/Yorkshire | [14]      |
| rs329624627 | 1   | 72605122 | C      | intron_variant    | CRYBG1 | NBA   | Landrace/Yorkshire | [14]      |
| rs338462676 | 1   | 74750265 | T      | intron_variant    | -      | NBA   | Landrace/Yorkshire | [14]      |
| rs80982567  | 1   | 99668135 | G      | intron_variant    | -      | NBA   | Landrace/Yorkshire | [14]      |
| rs329761313 | 1   | 116715803| C      | intron_variant    | -      | NBA   | Landrace/Yorkshire | [14]      |
| rs329145797 | 1   | 116791808| T      | intron_variant    | -      | NBA   | Landrace/Yorkshire | [14]      |
| rs80830052  | 1   | 139481542| A      | intron_variant    | ALDH1A3| NBA   | Landrace/Large White | [26] |
| rs80930659  | 1   | 139579572| G      | intron_variant    | LRRK1  | NBA   | Landrace/Large White | [26] |
| rs8084265   | 1   | 139608452| A      | intron_variant    | LRRK1  | NBA   | Landrace/Large White | [26] |
| rs80862569  | 1   | 139636710| C      | intergenic_variant| -      | NBA   | Landrace/Large White | [26] |
| rs80846651  | 1   | 139655026| A      | intergenic_variant| -      | NBA   | Landrace/Large White | [26] |
| rs81348779  | 1   | 141989297| G      | intron_variant    | UBE3A  | NBA   | Large White       | [22]      |
| rs329931325 | 1   | 144835089| T      | intergenic_variant| -      | NBA   | Landrace/Yorkshire | [14]      |
| rs326961952 | 1   | 145395812| G      | intergenic_variant| -      | NBA   | Landrace/Yorkshire | [14]      |
| rs336474421 | 1   | 145452726| T      | intergenic_variant| -      | NBA   | Landrace/Yorkshire | [14]      |
| rs322202112 | 1   | 146334522| C      | intergenic_variant| -      | NBA   | Landrace/Yorkshire | [14]      |
| rs332924521 | 1   | 239558816| C      | intron_variant    | XPA    | NBA   | Landrace/Yorkshire | [14]      |
| rs330585697 | 1   | 239775818| T      | intron_variant    | TRMO   | NBA   | Landrace/Yorkshire | [14]      |
| rs34029855  | 1   | NA       |        |                   |        | NBA   | Landrace/Yorkshire | [14]      |
| rs81291755  | 2   | 20563683 | G      | intergenic_variant| -      | NBA   | Landrace/Yorkshire | [26]      |
| rs81355894  | 2   | 20637563 | C      | intergenic_variant| -      | NBA   | Landrace/Large White | [26] |
| rs81359903  | 2   | 20665892 | T      | intergenic_variant| -      | NBA   | Landrace/Large White | [26] |
| rs81359915  | 2   | 20717076 | G      | intergenic_variant| -      | NBA   | Landrace/Large White | [26] |
| SNP       | SSC | Location     | Allele | Consequence       | SYMBOL | Trait | Breed                  | Reference |
|-----------|-----|--------------|--------|-------------------|--------|-------|------------------------|-----------|
| rs81356698 | 2   | 28380318     | G      | intron_variant    | EIF3M  | NBA   | Large White            | [22]      |
| rs81265647 | 2   | 125660328    | T      | upstream_gene_var | -      | NBA   | Landace/Large White    | [26]      |
| rs328177895 | 2   | NA           |        |                   |        | NBA   | Large White            | [23]      |
| rs81379421 | 3   | 27307613     | G      | intron_variant    | XYLT1  | NBA   | Landace/Large White    | [7]       |
| rs334867206 | 3   | 43312168     | T      | intergenic_variant | -      | NBA   | Large White            | [23]      |
| rs319494663 | 3   | 43463318     | C      | upstream_gene_var | ssc-let-7a-2 | NBA | Large White            | [23]      |
| rs80927364  | 4   | 130597207    | A      | intron_variant    | DDAH1  | NBA   | Erhualian              | [28]      |
| rs80890206  | 5   | 31022891     | C      | upstream_gene_var | GRIP1  | NBA   | Erhualian              | [28]      |
| rs80867243  | 5   | 87337099     | C      | intron_variant    | ELK3   | NBA   | Landace/Large White    | [7]       |
| rs81279319  | 5   | NA           |        |                   |        | NBA   | Landace/Large White    | [7]       |
| rs81383147  | 5   | NA           |        |                   |        | NBA   | Landace/Large White    | [7]       |
| rs81320475  | 6   | 70313133     | A      | upstream_gene_var | RBP7   | NBA   | Landace/Large White    | [26]      |
| rs81285644  | 6   | 70323076     | G      | intron_variant    | RBP7   | NBA   | Landace/Large White    | [26]      |
| rs81275494  | 6   | 70408106     | G      | intron_variant    | UBE4B  | NBA   | Landace/Large White    | [26]      |
| rs81279050  | 6   | 70418172     | A      | intron_variant    | UBE4B  | NBA   | Landace/Large White    | [26]      |
| rs81270030  | 6   | 70428427     | T      | intron_variant    | UBE4B  | NBA   | Landace/Large White    | [26]      |
| rs81388947  | 6   | 80229040     | A      | intergenic_variant | -      | NBA   | Duroc                  | [27]      |
| rs704072370 | 6   | 80388745     | A      | intergenic_variant | -      | NBA   | Duroc                  | [27]      |
| rs81332505  | 6   | 83142163     | A      | intron_variant    | MAN1C1 | NBA   | Duroc                  | [27]      |
| rs81476037  | 6   | 83545020     | T      | intron_variant    | PDK1L  | NBA   | Duroc                  | [27]      |
| rs328276462 | 6   | 83863384     | G      | downstream_gene_var | HMGN2 | NBA | Duroc                  | [27]      |
| rs335265547 | 6   | 83871998     | C      | upstream_gene_var | -      | NBA   | Duroc                  | [27]      |
| rs81287462  | 6   | 83986459     | A      | intergenic_variant | -      | NBA   | Duroc                  | [27]      |
### Table 1. Cont.

| SNP          | SSC | Location     | Allele | Consequence   | SYMBOL | Trait | Breed                      | Reference |
|--------------|-----|--------------|--------|---------------|--------|-------|----------------------------|-----------|
| rs81332455   | 6   | 84069079     | G      | intron_variant| ARID1A | NBA   | Duroc                      | [27]      |
| rs336670754  | 6   | 84118086     | C      | synonymous_variant| ARID1A | NBA   | Duroc                      | [27]      |
| rs342908929  | 6   | 159933806    | T      | intron_variant| ZFYVE9 | NBA   | Commercia                  | [25]      |
| rs81345088   | 6   | 168897980    | A      | intron_variant| ZMYND12| NBA   | Landace/Large White        | [26]      |
| rs81259198   | 6   | 168899114    | A      | intron_variant| ZMYND12| NBA   | Landace/Large White        | [26]      |
| rs81245903   | 6   | 168916590    | T      | intron_variant| RIMKLA | NBA   | Landace/Large White        | [26]      |
| rs81237774   | 6   | 168931165    | C      | intron_variant| RIMKLA | NBA   | Landace/Large White        | [26]      |
| rs80882306   | 7   | 11003222     | G      | upstream_gene_var | - | NBA   | Erhualian                  | [28]      |
| rs325729252  | 7   | 109101108    | C      | intergenic_variant | - | NBA   | Landace/Large White        | [7]       |
| rs81397142   | 7   | NA           |        |                |        | NBA   | Large White                | [22]      |
| rs81397215   | 7   | NA           |        |                |        | NBA   | Large White                | [22]      |
| rs318557169  | 8   | 95381096     | G      | intergenic_variant | - | NBA   | Landrace/Yorkshire         | [14]      |
| rs327655683  | 8   | 95402330     | A      | intergenic_variant | - | NBA   | Landrace/Yorkshire         | [14]      |
| rs81257618   | 9   | 13492371     | A      | intergenic_variant | - | NBA   | Landace/Large White        | [7]       |
| rs81417393   | 9   | 126541658    | C      | intron_variant | -    | NBA   | Landace/Large White        | [7]       |
| rs81421148   | 10  | 16506621     | C      | intron_variant| AKT3   | NBA   | Landace/Large White        | [7]       |
| rs80978601   | 10  | 25256004     | G      | intergenic_variant | - | NBA   | Landace/Large White        | [7]       |
| rs81255997   | 10  | 28330355     | C      | intergenic_variant | - | NBA   | Landace/Large White        | [7]       |
| rs81243666   | 10  | 57593745     | G      | intron_variant| PARD3  | NBA   | Erhualian                  | [28]      |
| rs81236069   | 10  | 58288430     | A      | intergenic_variant | - | NBA   | Landace/Large White        | [7]       |
| rs81302230   | 10  | 58290108     | G      | intergenic_variant | - | NBA   | Landace/Large White        | [7]       |
| rs81430147   | 11  | 836702       | C      | downstream_gene_var | - | NBA   | Landace/Large White        | [7]       |
Table 1. Cont.

| SNP          | SSC | Location  | Allele | Consequence         | SYMBOL | Trait | Breed                | Reference |
|--------------|-----|-----------|--------|---------------------|--------|-------|----------------------|-----------|
| rs81430859   | 11  | 4296303   | C      | intron_variant      | WASF3  | NBA   | Landace/Large White  | [7]       |
| rs81242222   | 11  | 67129570  | A      | intergenic_variant  | -      | NBA   | Landace/Large White  | [7]       |
| rs81434499   | 12  | 36207006  | G      | intergenic_variant  | -      | NBA   | Erhualian            | [28]      |
| rs80962240   | 13  | 52784022  | C      | intron_variant      | FOXP1  | NBA   | Large White          | [23]      |
| rs81215583   | 13  | 71905692  | C      | synonymous_variant  | RPN1   | NBA   | Erhualian            | [28]      |
| rs81447100   | 13  | 80866929  | A      | intron_variant      | CLSTN2 | NBA   | Erhualian            | [28]      |
| rs81447231   | 13  | 82603578  | A      | intron_variant      | GRK7   | NBA   | Erhualian            | [28]      |
| rs319258722  | 14  | 123766842 | T      | intergenic_variant  | -      | NBA   | Large White          | [23]      |
| rs45435330   | 15  | 118847390 | A      | intron_variant      | IGFBP2 | NBA   | Berkshire            | [24]      |
| rs324003968  | 15  | NA        |        |                     |        | NBA   | Commercia            | [25]      |
| rs81459590   | 16  | 6025546   | A      | intron_variant      | MYO10  | NBA   | Landace/Large White  | [7]       |
| rs80952566   | 17  | 27123793  | T      | intron_variant      | -      | NBA   | Erhualian            | [28]      |
| rs81469701   | 18  | 42920811  | T      | upstream_gene_var   | SCRN1  | NBA   | Landace/Large White  | [7]       |
| rs81471172   | 18  | 51640938  | T      | intron_variant      | HECW1  | NBA   | Large White          | [23]      |
| rs81473442   | X   | 91880535  | C      | intron_variant      | TRPC5  | NBA   | Landace/Large White  | [26]      |
| rs81323503   | X   | 92070342  | A      | intergenic_variant  | -      | NBA   | Landace/Large White  | [26]      |
| rs81283192   | X   | 92244402  | A      | intron_variant      | RTL4   | NBA   | Landace/Large White  | [26]      |
| rs337547716  | X   | 92330719  | A      | intron_variant      | RTL4   | NBA   | Landace/Large White  | [26]      |
| rs80834138   | X   | 92447181  | A      | intron_variant      | LHFPL1 | NBA   | Landace/Large White  | [26]      |
| rs81339510   | X   | 118854990 | T      | intergenic_variant  | -      | NBA   | Landace/Large White  | [26]      |
Search for SNPs associated with NBA of Chinese Erhualian pigs was carried out by Ma et al. [28]. Sows with high and low estimated breeding values (EBVs) were selected for genotyping. According to the research results, 9 SNPs associated with Pig QTLDdb with NBA were presented. The greatest effect was found for SNP rs81447100 (SSC13), which was additionally tested on Erhualian pigs (n = 313), Sutai (n = 173) and Yorkshire (n = 488). In all groups under study, a significant association between allelic variants of SNP rs81447100 (SSC13) and NBA was determined. However, allele A was desirable for the Erhualian pigs and allele G for the Sutai and Yorkshire pigs.

According to research work of Wu et al. [14], conducted on Landrace and Yorkshire pigs the database contains 15 SNPs localized on SSC1 and SSC8 and associated with NBA. 11 of these SNPs are located in the QTL regions annotated earlier, and 4 SNPs are presented for the first time. All these 4 SNPs (rs329624627, rs339929690, rs322202112 and rs330585697) are located on the SSC1. The most significant effect was established for SNP rs81397421 (SSC1).

Coster et al. [23] conducted associative studies on Large White pigs from two commercial lines of «Hypor» and «Topigs», and revealed 4 SNPs associated with NBA located on SSC7 (rs81397142 and rs81397215), SSC1 (rs81348779) and SSC2 (rs81356698).

Bergfelder-Drüing et al. [7] conducted research using Large White and Landrace pigs. Preliminary calculations based on graphs of multidimensional scaling showed the genetic distance between the breeds. For analysis pigs were divided into two clusters taking into account the breed and intra-breed clusters taking into account the breeding economy. As a result, 17 SNPs associated with NBA were identified, 5 of these SNPs had a minor allele frequency less than 1%. The study of Bergfelder-Drüing et al. [7] was the first to show an association with NBA for SNP rs81430147 (SSC11). All other SNPs were found in chromosome regions where candidate genes or QTLs affecting pig reproductive traits have already been identified. It should be noted that different SNPs were established for each breed cluster, and no associative communications were established simultaneously in two breeds. 13 SNPs were identified for Large White sows, and 4 SNPs for Landrace sows. In sows Landrace SNPs are localized on SSC7, SSC9, SSC11 and SSC16. Large White on SSC3, SSC5, SSC9, SSC10, SSC11 and SS18. The most significant effects on NBA of Large White sows are found for 4 SNPs: rs81379421 (SSC3), rs81417393 (SSC9), rs81417393 (SSC9), rs81242222 (SSC11) and rs81469701 (SSC18).

Research carried out by Wang et al. [22] on Large White pigs identified 6 SNPs associated with NBA located on SSC2, SSC3, SSC13, SSC14 and SSC18. The most significant effect was determined for SNP rs334867206 (SSC3), according to which pigs of AA genotype had more NBA, compared with analogues of GG genotype.

Suwannasing et al. [26] investigated Large White and Landrace pigs and established 25 SNPs for the NBA. Of these, 11 SNPs located in SSC1 and SSCX were defined for Large White pigs, 14 SNPs for Landrace pigs in SSC2 and SSC6. It is remarkable that SNPs on SSCX showed significance only at the NBA for Large White sows.

In the course of research on commercial pigs, Li et al. [25] established 2 SNPs (rs342908929 (SSC6) and rs324003968 (SSC15)) associated with NBA. According to the results of Chen et al. [27] obtained from the sows of Duroc in the database presents 9 SNPs and all of them are localized on SSC6.

An et al. [24] studied the IGFBP2 (SSC15) and IGFBP3 (SSC18) genes in Berkshire pigs. Their results showed significant SNPs in these genes. This work also analyzed the expression levels of IGFBP2 and IGFBP3 mRNA in the endometrium in pigs of various genotypes. Homozygous GG pigs expressed higher levels of IGFBP3 mRNA in the endometrium than pigs of other genotypes, and a positive correlation was observed between litter size traits and IGFBP3 but not IGFBP2 expression level. These results suggest that SNPs in the IGFBP2 and the IGFBP3 gene are useful biomarkers for the little traits of pigs. According to the results of this work 2 SNPs are included in PigQTLDdb rs45435330 on SSC15 as Genome map association for NBA and TNB.
3. SNPs Associated with Total Number Born

In general, in Pig QTLdb for TNB showed 218 SNPs (as Genome map association), of which 155 SNPs were detected by He et al. [8] and Ma et al. [28] in Erhualians, 52 SNPs are defined in Large White, Yorkshire, Landrace, 1 SNP in Berkshire and 10 SNPs in Duroc (Table 2) [14,18,22–25,29–33]. SNPs associated with TNB are represented in all Sus Scrofa Chromosome except for SSCY.

For an associative study He et al. [8] selected Erhualan sows with high and low EBV values. According to the results of their work, the most significant SNPs were detected on SSC2 chromosomes (rs81367039), SSC7 (rs80891106), SSC8 (rs81399474), SSC12 (rs81434499), SSC14 (rs80938898). Among them SNPs on chromosomes SSC2, SSC7, and SSC12 were annotated for the first time. To study the effect of significant SNPs additional studies were conducted on a livestock of 331 Erhualan sows. According to the results of additional testing, significant differences in TNB were found only for SNP rs81399474 (SSC8). In the studies of Ma et al. [28] 8 SNPs were identified as associated with TNB in Erhualian sows and located on SSC1, SSC4, SSC7, SSC8, SSC10, SSC12, SSC13 and SSC16.

Studies of Large White pigs conducted by Sell-Kubiak et al. [30] allowed the identification of 10 SNPs associated with the number of piglets at birth and located on SSC1, SSC5, SSC8, SSC11, SSC13 and SSC18. SNPs (rs80989787 and rs81289355) located on SSC11 were annotated for the first time in this paper. The most significant effect has been determined for SNP rs80989787 (SSC11). According to the results of associative studies conducted by Uimari et al. [18] on Finnish Landrace pigs 10 SNPs were identified. All established SNPs are located on SSC9.

The most significant effect was established for SNP rs81300575 (SSC9), which amounted to about 1 piglet between two homozygous genotypes. In the studies of Uimari et al. [18] it was also noted that in the past 15 years the frequency of the desired SNP rs81300575 (SSC9) genotype in the studied population has increased from 0.14 to 0.22.

Zhang et al. [29] conducted research on Duroc pigs and identified 10 SNPs associated with TNB. The most significant SNPs were rs80979042 and rs80825112 located on SSC14. In addition, the remaining potential SNPs were located on SSC5, SSC6, SSC12 and SSC17.

In the studies of Coster et al. [23], Wu et al. [14], Wang et al. [22] and Li et al. [25] the effects of SNPs on TNBs were investigated along with the search of SNPs associated with NBAs. So according to the results of Coster et al. [23] the database contains 16 SNPs defined on SSC1, SSC2, SSC7, SSC14 and SSC18. Wu et al. [14] established 5 SNPs associated with TNB located on SSC8 and SSC14. Wang et al. [22] identified 11 SNPs for TNB on SSC1-SSC5, SSC13 and SSC18, and Li et al. [25] 2 SNPs (rs342908929 (SSC6) and rs324003968 (SSC15)). Besides this, Pig QTLdb presents SNPs associated with TNB according to the studies of Onteru et al. [31]—SNP rs81452018 SSC15, Wang et al. [32]—SNP rs345476947 SSC6 and Liu et al. [33]—rs rs55618224 SSC6.
Table 2. SNPs (Single nucleotide polymorphism) associated with TNB (Total number born alive) presented in the Pig QTLdb (Pig Quantitative Trait Locus Database). Ensembl db, Sus Scrofa 11.1 (NA—This variant has not been mapped on Ensembl db, Sus Scrofa 11.1).

| No | SNP         | SSC | Location | Allele | Consequence                  | SYMBOL | Trait | Breed  | Reference |
|----|-------------|-----|----------|--------|------------------------------|--------|-------|--------|-----------|
| 1  | rs80972494  | 1   | 7262020  | C      | intergenic_variant           | -      | TNB   | Large White | [22]     |
| 2  | rs80787893  | 1   | 14869534 | C      | intron_variant               | ZBTB2  | TNB   | Large White | [30]     |
| 3  | rs80851003  | 1   | 20072414 | G      | intergenic_variant           | -      | TNB   | Erhualian  | [8]       |
| 4  | rs80970692  | 1   | 97934013 | A      | intron_variant               | ZBTB7C | TNB   | Large White | [23]     |
| 5  | rs80845110  | 1   | 139993309| A      | intron_variant               | GABRG3 | TNB   | Large White | [22]     |
| 6  | rs80933698  | 1   | 140097794| G      | intron_variant               | GABRG3 | TNB   | Large White | [22]     |
| 7  | rs80869858  | 1   | 140178409| T      | intron_variant               | GABRG3 | TNB   | Large White | [22]     |
| 8  | rs80999701  | 1   | 140290677| A      | intron_variant               | GABRG3 | TNB   | Large White | [22]     |
| 9  | rs81348717  | 1   | 140463533| G      | intron_variant               | GABRG3 | TNB   | Large White | [22]     |
| 10 | rs81348724  | 1   | 140550299| A      | intron_variant               | GABRA5 | TNB   | Large White | [22]     |
| 11 | rs81348751  | 1   | 140808020| A      | intron_variant               | GABRB3 | TNB   | Large White | [22]     |
| 12 | rs80989931  | 1   | 140896691| A      | intron_variant               | GABRB3 | TNB   | Large White | [22]     |
| 13 | rs81348779  | 1   | 141989297| G      | downstream_gene_var         | UBE3A  | TNB   | Large White | [22]     |
| 14 | rs80912860  | 1   | 164637575| C      | intergenic_variant           | -      | TNB   | Large White | [30]     |
| 15 | rs80956812  | 1   | 164674664| A      | intron_variant               | SMAD6  | TNB   | Large White | [30]     |
| 16 | rs81267574  | 1   | 222278217| G      | intron_variant               | PIP5K1B| TNB   | Erhualian  | [8]       |
| 17 | rs80938435  | 1   | 245222778| T      | intergenic_variant           | -      | TNB   | Erhualian  | [8]       |
| 18 | rs81296573  | 1   | 263022859| A      | intergenic_variant           | -      | TNB   | Erhualian  | [8]       |
| 19 | rs80913204  | 1   | 270166629| T      | intron_variant               | FNBP1  | TNB   | Erhualian  | [8]       |
| 20 | rs81367039  | 1   | NA       |        |                              |        | TNB   | Erhualian  | [8]       |
| 21 | rs81330112  | 2   | 3058633  | A      | upstream_gene_var           | CTTN   | TNB   | Erhualian  | [8]       |
| 22 | rs81214065  | 2   | 7420349  | A      | missense_variant            | PYGM   | TNB   | Erhualian  | [8]       |
| 23 | rs81474834  | 2   | 9252507  | T      | intron_variant               | -      | TNB   | Erhualian  | [8]       |
Table 2. Cont.

| No | SNP       | SSC | Location   | Allele | Consequence          | SYMBOL | Trait | Breed       | Reference |
|----|-----------|-----|------------|--------|----------------------|--------|-------|-------------|-----------|
| 24 | rs81273273| 2   | 24914867   | G      | intron_variant       | LDLRAD3| TNB   | Erhualian   | [8]       |
| 25 | rs81356698| 2   | 28300318   | G      | downstream_gene_var  | TNB    | TNB   | Large White | [22]      |
| 26 | rs346316162| 2  | 84269464   | T      | intron_variant       | ANKRD31| TNB   | Erhualian   | [8]       |
| 27 | rs81360234| 2   | 85003252   | G      | intron_variant       | SV2C   | TNB   | Erhualian   | [8]       |
| 28 | rs81270902| 2   | 136051929  | G      | intron_variant       | FSTL4  | TNB   | Erhualian   | [8]       |
| 29 | rs81307772| 2   | 142675693  | C      | intron_variant       | PCDHAC2| TNB   | Erhualian   | [8]       |
| 30 | rs81366836| 2   | 145019988  | C      | intergenic_variant   | -      | TNB   | Erhualian   | [8]       |
| 31 | rs81367208| 2   | 146880995  | T      | intergenic_variant   | -      | TNB   | Erhualian   | [8]       |
| 32 | rs81346993| 2   | 148668538  | G      | intron_variant       | DPYSL3 | TNB   | Erhualian   | [8]       |
| 33 | rs328177895| 2  | NA         |        |                      |        | TNB   | Large White | [23]      |
| 34 | rs81367039| 2   | NA         |        |                      |        | TNB   | Erhualian   | [8]       |
| 35 | rs81367039| 2   | NA         |        |                      |        | TNB   | Erhualian   | [8]       |
| 36 | rs334519198| 3  | 5376605    | T      | intron_variant       | LMTK2  | TNB   | Large White | [23]      |
| 37 | rs81243084| 3   | 14585248   | T      | intron_variant       | AUTS2  | TNB   | Erhualian   | [8]       |
| 38 | rs81318451| 3   | 20859502   | T      | intron_variant       | HS3ST4 | TNB   | Erhualian   | [8]       |
| 39 | rs81319541| 3   | 23688143   | G      | downstream_gene_var  | IGSF6  | TNB   | Erhualian   | [8]       |
| 40 | rs81379942| 3   | 30034842   | A      | intron_variant       | SHISA9 | TNB   | Erhualian   | [8]       |
| 41 | rs81369361| 3   | 43227069   | A      | intergenic_variant   | -      | TNB   | Large White | [23]      |
| 42 | rs334867206| 3  | 43312168   | T      | intergenic_variant   | -      | TNB   | Large White | [23]      |
| 43 | rs319494663| 3  | 43463318   | C      | upstream_gene_variant| ssc-let-7a-2| TNB | Large White | [23]      |
| 44 | rs338135576| 3  | 52266739   | T      | intron_variant       | IL1R1  | TNB   | Erhualian   | [8]       |
| 45 | rs81370592| 3   | 53699303   | C      | intergenic_variant   | -      | TNB   | Erhualian   | [8]       |
| 46 | rs81377897| 3   | 124275280  | G      | upstream_gene_variant| -      | TNB   | Erhualian   | [8]       |
| 47 | rs81272059| 3   | 125892592  | G      | intron_variant       | NOL10  | TNB   | Erhualian   | [8]       |
### Table 2. Cont.

| No | SNP          | SSC | Location   | Allele | Consequence           | SYMBOL | Trait | Breed              | Reference |
|----|--------------|-----|------------|--------|-----------------------|--------|-------|--------------------|-----------|
| 48 | rs81319839   | 4   | 18194352   | A      | intergenic_variant    | -      | TNB   | Large White        | [23]      |
| 49 | rs81312912   | 4   | 18196598   | A      | intergenic_variant    | -      | TNB   | Large White        | [23]      |
| 50 | rs80986621   | 4   | 87990037   | C      | missense_variant      | UAP1   | TNB   | Erhualian          | [8]       |
| 51 | rs80860510   | 4   | 89154886   | A      | intron_variant        | SDHC   | TNB   | Erhualian          | [8]       |
| 52 | rs80987610   | 4   | 89242132   | G      | downstream_gene_var   | APOA2  | TNB   | Erhualian          | [8]       |
| 53 | rs80910021   | 4   | 96557774   | C      | intergenic_variant    | -      | TNB   | Erhualian          | [8]       |
| 54 | rs80999559   | 4   | 98260992   | C      | downstream_gene_var   | CERS2  | TNB   | Erhualian          | [8]       |
| 55 | rs80927364   | 4   | 130597207  | A      | intron_variant        | DDAH1  | TNB   | Erhualian          | [8]       |
| 56 | rs81385465   | 5   | 4131296    | G      | intergenic_variant    | -      | TNB   | Large White        | [30]      |
| 57 | rs336638152  | 5   | 11274122   | A      | intron_variant        | -      | TNB   | Duroc              | [29]      |
| 58 | rs327336155  | 5   | 31752997   | G      | intergenic_variant    | -      | TNB   | Large White        | [23]      |
| 59 | rs80890539   | 5   | 49084918   | T      | intergenic_variant    | -      | TNB   | Erhualian          | [8]       |
| 60 | rs80999110   | 5   | 65577418   | T      | intergenic_variant    | -      | TNB   | Duroc              | [29]      |
| 61 | rs328217833  | 5   | 78953555   | C      | intergenic_variant    | -      | TNB   | Erhualian          | [8]       |
| 62 | rs81303269   | 5   | 79020148   | A      | intergenic_variant    | -      | TNB   | Erhualian          | [8]       |
| 63 | rs81236331   | 6   | 4395948    | T      | intron_variant        | WFDC1  | TNB   | Erhualian          | [8]       |
| 64 | rs81307446   | 6   | 4817058    | T      | intron_variant        | CDH13  | TNB   | Erhualian          | [8]       |
| 65 | rs81393472   | 6   | 21728055   | A      | intergenic_variant    | -      | TNB   | Erhualian          | [8]       |
| 66 | rs345476947  | 6   | 54042595   | T      | intron_variant        | FUT2   | TNB   | Large White        | [32]      |
| 67 | rs81322640   | 6   | 74250906   | T      | intron_variant        | KAZN   | TNB   | Erhualian          | [8]       |
| 68 | rs81283746   | 6   | 78467732   | C      | downstream_gene_var   | UBXN10 | TNB   | Erhualian          | [8]       |
| 69 | rs55618224   | 6   | 80088638   | C      | 3_prime_UTR_variant   | -      | TNB   | Yorkshire          | [33]      |
| 70 | rs81318862   | 6   | 82375634   | A      | intergenic_variant    | -      | TNB   | Duroc              | [29]      |
### Table 2. Cont.

| No | SNP         | SSC | Location | Allele | Consequence         | SYMBOL | Trait | Breed            | Reference |
|----|-------------|-----|----------|--------|---------------------|--------|-------|------------------|-----------|
| 71 | rs329711941 | 6   | 84156205 | C      | intron_variant      | ZDHHC18| TNB   | Duroc            | [29]      |
| 72 | rs81391439  | 6   | 129931172| A      | intergenic_variant  | -      | TNB   | Erhualian        | [8]       |
| 73 | rs342908929 | 6   | 159933806| T      | intron_variant      | ZFYVE9 | TNB   | Commercia        | [25]      |
| 74 | rs81319462  | 6   | 163598597| G      | intergenic_variant  | -      | TNB   | Erhualian        | [8]       |
| 75 | rs81319428  | 6   | 163598619| C      | intergenic_variant  | -      | TNB   | Erhualian        | [8]       |
| 76 | rs80882306  | 7   | 11003222 | G      | upstream_gene_variant| -    | TNB   | Erhualian        | [28]      |
| 77 | rs80813007  | 7   | 21583296 | G      | downstream_gene_var| -     | TNB   | Erhualian        | [8]       |
| 78 | rs80938431  | 7   | 22008244 | G      | intron_variant      | -      | TNB   | Erhualian        | [8]       |
| 79 | rs80933422  | 7   | 27905935 | T      | intergenic_variant  | -      | TNB   | Erhualian        | [8]       |
| 80 | rs80797074  | 7   | 29268803 | G      | synonymous_variant  | DST    | TNB   | Erhualian        | [8]       |
| 81 | rs340672537 | 7   | 38439290 | T      | intron_variant      | ABCC10 | TNB   | Erhualian        | [8]       |
| 82 | rs81398070  | 7   | 58232894 | C      | intron_variant      | SIN3A  | TNB   | Erhualian        | [8]       |
| 83 | rs80824208  | 7   | 63161681 | G      | intron_variant      | SLC25A21 | TNB    | Erhualian        | [8]       |
| 84 | rs32644823  | 7   | 63618208 | A      | downstream_gene_var| -     | TNB   | Erhualian        | [8]       |
| 85 | rs80867516  | 7   | 70133128 | G      | downstream_gene_var| -     | TNB   | Erhualian        | [8]       |
| 86 | rs80891106  | 7   | 73467314 | A      | intergenic_variant  | -      | TNB   | Erhualian        | [8]       |
| 87 | rs81295302  | 7   | 74333495 | T      | intron_variant      | STXBP6 | TNB   | Erhualian        | [8]       |
| 88 | rs81398127  | 7   | 75705436 | G      | 3_prime_UTR_variant | CMTM5  | TNB   | Erhualian        | [8]       |
| 89 | rs336977324 | 7   | 81077680 | T      | intron_variant      | RYR3   | TNB   | Erhualian        | [8]       |
| 90 | rs80927564  | 7   | 108030803| C      | intergenic_variant  | -      | TNB   | Erhualian        | [8]       |
| 91 | rs80942529  | 7   | 110057727| G      | intergenic_variant  | -      | TNB   | Erhualian        | [8]       |
| 92 | rs80969683  | 7   | NA      |        |                     | TNB    | Large White |               | [22]     |
| 93 | rs81397215  | 7   | NA      |        |                     | TNB    | Large White |               | [22]     |
| No | SNP          | SSC | Location | Allele | Consequence         | SYMBOL | Trait | Breed               | Reference |
|----|--------------|-----|----------|--------|---------------------|--------|-------|---------------------|-----------|
| 94 | rs81397142   | 7   | NA       |        |                     |        | TNB   | Large White         | [22]      |
| 95 | rs81403620   | 8   | 15474371 | T      | intron_variant      | KCNIP4 | TNB   | Erhualian           | [8]       |
| 96 | rs81405013   | 8   | 16400498 | C      | intergenic_variant  |        | TNB   | Erhualian           | [8]       |
| 97 | rs81342198   | 8   | 16560870 | C      | intergenic_variant  |        | TNB   | Erhualian           | [8]       |
| 98 | rs81406385   | 8   | 17782561 | C      | intron_variant      |        | TNB   | Erhualian           | [8]       |
| 99 | rs81343566   | 8   | 18863902 | C      | intron_variant      | CCDC149| TNB   | Erhualian           | [8]       |
| 100| rs81399474   | 8   | 32370687 | C      | downstream_gene_var | UCHL1  | TNB   | Erhualian           | [8]       |
| 101| rs81399527   | 8   | 32800253 | G      | intergenic_variant  |        | TNB   | Erhualian           | [8]       |
| 102| rs81399633   | 8   | 33508704 | A      | splice_region_variant | ATP8A1 | TNB   | Erhualian           | [8]       |
| 103| rs81227962   | 8   | 34380373 | A      | intergenic_variant  |        | TNB   | Erhualian           | [8]       |
| 104| rs81476987   | 8   | 34885027 | C      | intron_variant      | KCTD8  | TNB   | Erhualian           | [8]       |
| 105| rs81399897   | 8   | 36628170 | C      | intergenic_variant  |        | TNB   | Erhualian           | [8]       |
| 106| rs81400131   | 8   | 38946698 | A      | downstream_gene_var | CWIH43 | TNB   | Erhualian           | [8]       |
| 107| rs81400868   | 8   | 63262973 | A      | downstream_gene_var | U6     | TNB   | Erhualian           | [8]       |
| 108| rs81401375   | 8   | 73118551 | A      | intergenic_variant  |        | TNB   | Erhualian           | [8]       |
| 109| rs339466191  | 8   | 80345448 | A      | intron_variant      | NR3C2  | TNB   | Landrace/Yorkshire  | [14]      |
| 110| rs33905163   | 8   | 80589152 | A      | intergenic_variant  | NR3C2  | TNB   | Landrace/Yorkshire  | [14]      |
| 111| rs81294311   | 8   | 88225561 | T      | intergenic_variant  |        | TNB   | Erhualian           | [8]       |
| 112| rs319272490  | 8   | 103706053| C      | intergenic_variant  |        | TNB   | Landrace/Yorkshire  | [14]      |
| 113| rs81403286   | 8   | 107008700| T      | intergenic_variant  |        | TNB   | Erhualian           | [8]       |
| 114| rs81403527   | 8   | 112530303| A      | downstream_gene_var | CASP6  | TNB   | Erhualian           | [8]       |
| 115| rs81403538   | 8   | 112566311| T      | intron_variant      | MCUB   | TNB   | Erhualian           | [8]       |
| 116| rs334180816  | 8   | 115856336| C      | intron_variant      | NPNT   | TNB   | Landrace/Yorkshire  | [14]      |
| 117| rs80834695   | 8   | 120291881| A      | intergenic_variant  |        | TNB   | Erhualian           | [8]       |
Table 2. Cont.

| No  | SNP             | SSC | Location   | Allele | Consequence          | SYMBOL | Trait | Breed       | Reference |
|-----|-----------------|-----|------------|--------|----------------------|--------|-------|-------------|-----------|
| 118 | rs81317149      | 8   | 127090631  | G      | intergenic_variant   | -      | TNB   | Large White | [30]      |
| 119 | rs81413855      | 9   | 8393770    | G      | 3_prime_UTR_variant  | C2CD3  | TNB   | Erhualian   | [8]       |
| 120 | rs81416386      | 9   | 11655571   | G      | intron_variant       | MYO7A  | TNB   | Erhualian   | [8]       |
| 121 | rs81407589      | 9   | 21695319   | C      | intron_variant       | -      | TNB   | Erhualian   | [8]       |
| 122 | rs81408950      | 9   | 34248222   | G      | intergenic_variant   | -      | TNB   | Erhualian   | [8]       |
| 123 | rs81409102      | 9   | 35438101   | C      | upstream_gene_variant| GRIA4  | TNB   | Erhualian   | [8]       |
| 124 | rs81413928      | 9   | 84593678   | A      | intron_variant       | AGMO   | TNB   | Landrace    | [18]      |
| 125 | rs81413949      | 9   | 85057918   | C      | intergenic_variant   | -      | TNB   | Landrace    | [18]      |
| 126 | rs81287478      | 9   | 85128043   | T      | intergenic_variant   | -      | TNB   | Landrace    | [18]      |
| 127 | rs81223525      | 9   | 85362483   | G      | intergenic_variant   | -      | TNB   | Landrace    | [18]      |
| 128 | rs81260290      | 9   | 87932749   | G      | intron_variant       | HDAC9  | TNB   | Erhualian   | [28]      |
| 129 | rs81414623      | 9   | 96283483   | C      | intron_variant       | SEMA3A | TNB   | Erhualian   | [8]       |
| 130 | rs81300575      | 9   | 102308556  | T      | intron_variant       | PHTF2  | TNB   | Landrace    | [18]      |
| 131 | rs81331059      | 9   | 137095797  | G      | intron_variant       | -      | TNB   | Erhualian   | [8]       |
| 132 | rs81419264      | 9   | 137162279  | G      | non_coding_transcript| -     | TNB   | Erhualian   | [8]       |
| 133 | rs81419315      | 9   | 137216947  | G      | upstream_gene_variant| U6    | TNB   | Erhualian   | [8]       |
| 134 | rs81315852      | 9   | 138107624  | T      | intergenic_variant   | -      | TNB   | Erhualian   | [8]       |
| 135 | rs81332239      | 9   | 138462123  | C      | intergenic_variant   | -      | TNB   | Erhualian   | [8]       |
| 136 | rs81417713      | 9   | NA         |        |                      |        | TNB   | Erhualian   | [8]       |
| 137 | rs81429231      | 10  | 10002753   | G      | intron_variant       | MARK1  | TNB   | Erhualian   | [8]       |
| 138 | rs80895456      | 10  | 26509297   | T      | intergenic_variant   | -      | TNB   | Erhualian   | [8]       |
| 139 | rs341908955     | 10  | 48658434   | T      | intergenic_variant   | -      | TNB   | Erhualian   | [8]       |
| 140 | rs81329283      | 10  | 56421545   | A      | intron_variant       | NRP1   | TNB   | Erhualian   | [8]       |
| 141 | rs81274366      | 10  | 57593745   | G      | intron_variant       | PARD3  | TNB   | Erhualian   | [28]      |
Table 2. Cont.

| No  | SNP        | SSC | Location   | Allele | Consequence                  | SYMBOL | Trait | Breed           | Reference |
|-----|------------|-----|------------|--------|-------------------------------|--------|-------|-----------------|-----------|
| 142 | rs81426281 | 10  | 57913635   | T      | upstream_gene_variant         | -      | TNB   | Erhualian       | [8]       |
| 143 | rs81314128 | 10  | 59665035   | T      | intergenic_variant            | -      | TNB   | Erhualian       | [8]       |
| 144 | rs80941850 | 11  | 8940153    | T      | intron_variant                | -      | TNB   | Erhualian       | [8]       |
| 145 | rs81477765 | 11  | 19542650   | G      | intergenic_variant            | -      | TNB   | Erhualian       | [8]       |
| 146 | rs81332839 | 11  | 19542846   | T      | intergenic_variant            | -      | TNB   | Erhualian       | [8]       |
| 147 | rs81285980 | 11  | 19544324   | A      | intergenic_variant            | -      | TNB   | Erhualian       | [8]       |
| 148 | rs81237348 | 11  | 22281193   | C      | intron_variant                | NUFIP1 | TNB   | Erhualian       | [8]       |
| 149 | rs80989787 | 11  | 23362846   | T      | intron_variant                | ENOX1  | TNB   | Large White     | [30]      |
| 150 | rs81289355 | 11  | 23410214   | C      | intron_variant                | ENOX1  | TNB   | Large White     | [30]      |
| 151 | rs81293918 | 11  | 27751988   | A      | intergenic_variant            | -      | TNB   | Erhualian       | [8]       |
| 152 | rs80813604 | 11  | 48641897   | C      | intergenic_variant            | -      | TNB   | Erhualian       | [8]       |
| 153 | rs80950312 | 11  | 48749391   | T      | intergenic_variant            | -      | TNB   | Erhualian       | [8]       |
| 154 | rs80869156 | 11  | 64316157   | G      | intergenic_variant            | -      | TNB   | Erhualian       | [8]       |
| 155 | rs81329621 | 11  | 66354904   | G      | intergenic_variant            | -      | TNB   | Erhualian       | [8]       |
| 156 | rs81343376 | 12  | 6971812    | G      | intergenic_variant            | -      | TNB   | Erhualian       | [8]       |
| 157 | rs81332319 | 12  | 7414272    | C      | intergenic_variant            | -      | TNB   | Erhualian       | [8]       |
| 158 | rs81439394 | 12  | 9810809    | G      | intergenic_variant            | -      | TNB   | Duroc           | [29]      |
| 159 | rs81433045 | 12  | 26992374   | G      | intron_variant                | ANKRD40| TNB   | Erhualian       | [8]       |
| 160 | rs81433877 | 12  | 33577229   | G      | intron_variant                | MSI2   | TNB   | Erhualian       | [8]       |
| 161 | rs81434044 | 12  | 33799100   | C      | intron_variant                | MSI2   | TNB   | Erhualian       | [8]       |
| 162 | rs81434064 | 12  | 33903675   | A      | intron_variant                | MSI2   | TNB   | Erhualian       | [8]       |
| 163 | rs81434489 | 12  | 35993482   | G      | intron_variant                | VMP1   | TNB   | Erhualian       | [8]       |
| 164 | rs81434499 | 12  | 36207006   | G      | intergenic_variant            | -      | TNB   | Erhualian       | [8]       |
| No  | SNP            | SSC | Location     | Allele | Consequence             | SYMBOL | Trait | Breed       | Reference |
|-----|----------------|-----|--------------|--------|-------------------------|--------|-------|-------------|-----------|
| 165 | rs81309004     | 12  | 40519573     | T      | intergenic_variant      | -      | TNB   | Erhualian   | [8]       |
| 166 | rs81434931     | 12  | 40974978     | A      | intron_variant          | ASIC2  | TNB   | Erhualian   | [8]       |
| 167 | rs81435036     | 12  | 41338150     | C      | intron_variant          | ASIC2  | TNB   | Erhualian   | [8]       |
| 168 | rs81477883     | 12  | 43427846     | T      | intron_variant          | RAB11FIP4 | TNB | Erhualian   | [8]       |
| 169 | rs81447979     | 13  | 11362350     | A      | upstream_gene_variant   | THR8   | TNB   | Erhualian   | [8]       |
| 170 | rs80837222     | 13  | 13802573     | T      | intron_variant          | NEK10  | TNB   | Erhualian   | [8]       |
| 171 | rs81445072     | 13  | 38880472     | C      | intron_variant          | ARHGEF3 | TNB | Erhualian   | [8]       |
| 172 | rs80964445     | 13  | 75637294     | G      | intron_variant          | CEP63  | TNB   | Erhualian   | [8]       |
| 173 | rs81447100     | 13  | 80866929     | A      | intron_variant          | CLSTN2 | TNB   | Erhualian   | [8]       |
| 174 | rs81441751     | 13  | 182451198    | C      | intron_variant          | CHODL  | TNB   | Large White | [30]      |
| 175 | rs81442196     | 13  | 190614395    | G      | intergenic_variant      | -      | TNB   | Erhualian   | [8]       |
| 176 | rs80961068     | 13  | 200778735    | T      | intron_variant          | TTC3   | TNB   | Large White | [23]      |
| 177 | rs80841768     | 14  | 12118215     | T      | intron_variant          | PNOC   | TNB   | Erhualian   | [8]       |
| 178 | rs330621374    | 14  | 15126027     | A      | intergenic_variant      | -      | TNB   | Landrace/Yorkshire | [14] |
| 179 | rs339777110    | 14  | 25374812     | G      | intron_variant          | TMEM132D | TNB | Duroc       | [29]      |
| 180 | rs334650508    | 14  | 26675179     | A      | intergenic_variant      | -      | TNB   | Erhualian   | [8]       |
| 181 | rs318344052    | 14  | 26907303     | T      | intergenic_variant      | -      | TNB   | Erhualian   | [8]       |
| 182 | rs80979042     | 14  | 62040147     | T      | intron_variant          | BICC1  | TNB   | Duroc       | [29]      |
| 183 | rs808251112    | 14  | 62071531     | A      | intron_variant          | BICC1  | TNB   | Duroc       | [29]      |
| 184 | rs80892145     | 14  | 73289391     | T      | intron_variant          | LRRC20 | TNB | Erhualian   | [8]       |
| 185 | rs80960182     | 14  | 84555165     | A      | intergenic_variant      | -      | TNB   | Erhualian   | [8]       |
| 186 | rs80873788     | 14  | 85481113     | A      | upstream_gene_variant   | RGR    | TNB   | Erhualian   | [8]       |
| 187 | rs80799654     | 14  | 98901034     | T      | intergenic_variant      | -      | TNB   | Erhualian   | [8]       |
| 188 | rs80800806     | 14  | 104041994    | T      | intron_variant          | IDE    | TNB   | Erhualian   | [8]       |
Table 2. Cont.

| No  | SNP               | SSC | Location      | Allele | Consequence        | SYMBOL  | Trait | Breed       | Reference   |
|-----|-------------------|-----|---------------|--------|-------------------|---------|-------|-------------|-------------|
| 189 | rs80968475        | 14  | 107031142     | T      | intron_variant    | SORBS1  | TNB   | Erhualian   | [8]         |
| 190 | rs80959797        | 14  | 107336340     | G      | intron_variant    | ENTPD1  | TNB   | Erhualian   | [8]         |
| 191 | rs80938898        | 14  | 107377294     | C      | intron_variant    | ENTPD1  | TNB   | Erhualian   | [8]         |
| 192 | rs80971725        | 14  | 107584405     | C      | intergenic_variant| -       | TNB   | Erhualian   | [8]         |
| 193 | rs80843720        | 14  | 107597908     | T      | intron_variant    | ZNF518A | TNB   | Erhualian   | [8]         |
| 194 | rs80987149        | 14  | 107725686     | T      | intergenic_variant| -       | TNB   | Erhualian   | [8]         |
| 195 | rs81449479        | 14  | 107794160     | G      | 3_prime_UTR_variant| OPALIN  | TNB   | Erhualian   | [8]         |
| 196 | rs80867623        | 14  | 129792523     | G      | intron_variant    | SEC23IP | TNB   | Large White | [22]        |
| 197 | rs80983641        | 14  | 137193623     | G      | intron_variant    | PTPRE   | TNB   | Erhualian   | [8]         |
| 198 | rs80892643        | 14  | NA            |        |                   |         | TNB   | Erhualian   | [8]         |
| 199 | rs80782668        | 14  | NA            |        |                   |         | TNB   | Erhualian   | [8]         |
| 200 | rs80947288        | 14  | NA            |        |                   |         | TNB   | Duroc       | [29]        |
| 201 | rs80868389        | 15  | 9150979       | A      | intergenic_variant| -       | TNB   | Erhualian   | [8]         |
| 202 | rs81452018        | 15  | 26337909      | G      | intergenic_variant| -       | TNB   | Landace/Large White | [31]         |
| 203 | rs80893476        | 15  | 82075550      | C      | intron_variant    | MTX2    | TNB   | Erhualian   | [8]         |
| 204 | rs45435330        | 15  | 118847390     | A      | intron_variant    | IGFBP2  | TNB   | Berkshire   | [24]        |
| 205 | rs324003968       | 15  | NA            |        |                   |         | TNB   | Commercia   | [25]        |
| 206 | rs81459026        | 16  | 41470716      | G      | intron_variant    | IPO11   | TNB   | Erhualian   | [8]         |
| 207 | rs81289648        | 16  | 74903886      | A      | intergenic_variant| -       | TNB   | Erhualian   | [28]        |
| 208 | rs81463092        | 16  | 74971494      | G      | intergenic_variant| -       | TNB   | Erhualian   | [8]         |
| 209 | rs81463053        | 16  | NA            |        |                   |         | TNB   | Erhualian   | [8]         |
| 210 | rs331119584       | 17  | 1486143       | T      | intron_variant    | DLC1    | TNB   | Erhualian   | [8]         |
| No | SNP           | SSC | Location   | Allele | Consequence         | SYMBOL | Trait | Breed          | Reference |
|----|---------------|-----|------------|--------|---------------------|--------|-------|----------------|-----------|
| 211 | rs328230332   | 17  | 34329730   | T      | intergenic_variant  | -      | TNB   | Duroc          | [29]      |
| 212 | rs81472303    | 18  | 18253338   | C      | intron_variant      | COPG2  | TNB   | Large White    | [22]      |
| 213 | rs81471172    | 18  | 51640938   | T      | intron_variant      | HECW1  | TNB   | Large White    | [23]      |
| 214 | rs81471381    | 18  | 53672799   | G      | intron_variant      | SUGCT  | TNB   | Large White    | [30]      |
| 215 | rs332595701   | 18  | 53697787   | G      | intron_variant      | SUGCT  | TNB   | Large White    | [30]      |
| 216 | rs1225238     | X   | 15335129   | T      | intron_variant      | PHKA2  | TNB   | Erhualian      | [8]       |
| 217 | rs80891661    | X   | 101710962  | C      | intergenic_variant  | -      | TNB   | Erhualian      | [8]       |
| 218 | rs322114058   | X   | 101975674  | A      | intron_variant      | TENM1  | TNB   | Erhualian      | [8]       |
4. Potential Candidate Genes for Litter Traits of Pig

Accordingly, Pig QTLdb presents 306 SNPs associated with TNB (218 SNPs) and NBA (88 SNPs) in pigs of various breeds. We should note that 12 SNPs out of 306 SNPs provided in PigQTLdb as a Genome map association with TNB and NBA, are presented twice (add file 1). Perhaps this is due to the fact that the connection of SNPs with TNB and NBA was established in one study, for example, as for SNPs rs81348779 on SSC1 and rs81356698 on SSC2 [23]. These SNPs are localized in the intron of the UBE3A (SSC1) and EIF3M (SSC2) genes. The UBE3A gene encodes ubiquitin protein ligase E3A, which plays an essential role in the normal development and functioning of the nervous system, and helps regulate the balance between proteostasis synthesis and degradation in the joints between synapses. Human and mouse UBE3A is maternal imprinted [34]. However, there is no precise information regarding imprinting of pig UBE3A. According to the study performed by Wang et al. [35] UBE3A was not imprinted in the skeletal muscle of neonate pigs of Landrace boars and Laiwu sows cross. Further research will probably provide more information to clarify the effects of the UBE3A gene and its and its relation to pig fecundity. The EIF3M gene (the eukaryotic translation initiation factor 3 subunit M) is a complex translation initiation factor consisting of 13 subunits (EIF3A-EIF3M) and which is involved in mRNA modulation [36]. The EIF3 complex is necessary for the key stages of protein synthesis initiation [37]. Previous studies have shown that EIF3M encodes a protein that is critical for mouse embryonic development [38].

In studies performed by Wang et al. [22] a relationship with TNB and NBA was defined for SNPs rs334867206 (intergenic variant) and rs319494663 (upstream gene variant ssc-let-7a-2) on SSC3 and rs81471172 (intron variant HECW1) on SSC18. Sus scrofa let-7a-2 stem-loop (ssc-let-7a-2) belongs to miRNAs, a class of small non-coding RNAs (~21 nt) that regulate the mRNAs translation on the post-transcriptional level, mainly by binding their targets with the three prime untranslated region (3'-UTR) [39]. A variety of studies have shown that miRNAs can play a potential regulatory role in porcine ovary, testis and spermatogenesis [40–42].

The HECW1 gene, also known as NEDD4-like ubiquitin protein ligase 1 (NEDL1), is expressed in human neuronal tissues and enhances p53-mediated apoptotic cell death [43]. Supposedly, it regulates the bone morphogenetic protein signaling pathway during embryonic development and bone remodeling [44]. In the work of Li et al. [25] associations with TNB and NBA are defined for SNP rs342908929, which is localized on SSC6 in the intron of the ZFYVE9 gene (zinc finger FYVE-type containing 9 domain). The protein encoded by ZFYVE9 is involved in the signaling pathway of transforming growth factor-beta (TGFβ) and directly interacts with SMAD2 and SMAD3, needed for normal follicular development and ovulation [45].

In the studies performed by Ma et al. [28] a relation with TNB and NBA was defined for SNPs rs80882306 (intergenic variant) on SSC7 and rs319494663 (intron variant PARD3) on SSC10. PARD3 (PAR-3) is a scaffold-like PDZ-containing protein. PAR-3 forms a complex with PAR-6 and atypical protein kinase C (PAR-3-atypical protein kinase C-PAR-6 complex) and is associated with the establishment of cell polarization [46–48]. McCole [49] argued that mutations in PARD3 can also influence the recovery of wounds by weakening the response of the epithelial barrier to a damage or inflammation. Concerning its significant role in the regulation of various stages of ovarian development and the control of steroidogenesis in a ripening follicle An et al. [24] studied the IGFBP-2 gene (SSC15) and defined SNP rs45435330 associated with TNB and NBA [50].

But more interesting are the variants repeated in two independent studies. Thus, rs80927364 (intron variant DDAH1) on SSC4, rs81434499 (intergenic variant) on SSC12, rs81447100 (intron variant CLSTN2) on SSC13 showed significant associations with TNB and NBA in the studies of He et al. [8] and Ma et al. [28] respectively.

The DDAH1 gene (dimethylarginine dimethylaminohydrolase 1), along with other DDAH genes, is involved in the metabolic control of asymmetric dimethylarginine (ADMA), contributes to the maintenance of vascular homeostasis due to the expansion of blood vessels, suppression of inflammation and inhibiting vascular smooth muscle cells, adhesion and aggregation of platelets [51–53]. Data on
the metabolic control of ADMA by DDAH genes and their effect on endothelial cells were obtained in animal studies. Transgenic mice with overexpression of DDAH1 showed a twofold decrease of ADMA in plasma, associated with a twofold increase of NOS activity in tissue [54]. Conversely, the DDAH1 Knock Out Mice exhibited increased pulmonary endothelial permeability as a result of increased ADMA, which was prevented by over-expression of DDAH1 and DDAH2 in endothelial cells [55].

CLSTN2 (calsintenin 2) is associated with obesity in mammals, especially in the process of increasing adipocytes in visceral tissues and in subcutaneous fat [56]. Santana et al. [57] defined CLSTN2 as a candidate gene associated with ultrasound-derived measurements of the rib-eye area, backfat thickness and rumpfat thickness in Nellore cattle. Adipose tissue is an active endocrine organ and proteins involved in forming adipose tissue is increasingly attracting attention as mammalian reproduction markers [58,59].

We can also note SNPs rs81463092 (intergenic variant) and rs81289648 (intergenic variant) defined in the works of He et al. [8] and Ma et al. [28], localized on SSC16 and lying in close proximity to each other (68 kb). The table shows the intervals between neighboring SNPs (add file 1). Hence, we can note a number of closely related SNPs identified in various studies. For example, rs55618224 (3 prime UTR variant) and rs81388947 (intergenic variant) on SSC6 are defined by Liu et al. [53] and Chen et al. [27] and the interval between them is 140 kb. SNP rs336670754 (synonymous variant ARID1A) and SNP rs329711941 (intronic variant ZDHHC18) are located at a distance of about 39 kb from each other, defined on SSC6 by Chen et al., (2019) and Zhang et al. [29] respectively.

On the whole, we can note that SNPs presented in PigQTLdb as associations with TNB and NBA are more localized in genes (intron variant 60%). Wherein that, 15% are intergenic variants and this can be considered as an evidence of significance for intergenic variants in the genetic architecture of reproductive traits (add file 2).

In conclusion, we wanted to estimate the gene-based protein-protein interactions obtained with the studied SNPs being localized. The total number of genes was 127, but only 40 genes formed some pairs or chains (Figure 1). It is interesting that some chains are composed of genes (SNPs) identified in only one study (add file 3). For example, RBP7, LRRK1,UBE4B,TRPC5,LHFPL1 genes were identified by Suwannasing et al. [26]; DLC1, SEMA3A, DPYSL3, NRPI by He et al. [8] similarly. However, the other chains includes genes identified in various studies such as GRIA4 [8], CLSTN2 [8], GRIP1 [28], GABRA5 [22], UBE3A [22], COPG2 [22], ANKRD40 [8], MYO10 [7], SHISA9 [8].

The presented review shows that most SNPs annotated from genome-wide studies are found in chromosome regions where candidate genes or QTLs have already been identified. Future research will be aimed at annotating sequences and analyzing these data, which can contribute to better understanding the mechanisms of reproductive traits formation.

However, the main problem in summarizing the results is the design of the experiment (consideration of traits, features of the studied populations, etc.). Some of the factors affecting the result are not controlled by the researcher (such as the trait inheritance level, the genetic architecture of the population, linkage disequilibrium, etc.). On the other hand, control over the reference data design (the choice of markers, the model for evaluating effects, etc.) that affects the accuracy of the results is controlled by the researcher. In the analyzed studies the majority of genotyping works were done by using Illumina PorcineSNP60 BeadChip or GeneSeek PorcineSNP80 BeadChip. There are numerous statistical approaches to conducting GWAS. However, the mixed model is more preferable, being implemented in various software packages (GEMMA, ASREML, GenABEL, etc.). There is still no consensus on the best method. Many researchers emphasize that the defined associations and their significance depend on the methodologies and details of data analysis, and we need to develop statistical approaches in order to improve the accuracy of the obtained information [16,19].
Figure 1. Protein-protein interactions obtained with the studied SNPs (STRING db).

5. Conclusions

The results of genome studies show the prospects of this approach to studying the genetic architecture of reproductive indicators in pigs. The material presented in this overview can be used in developing local test systems for a limited number of SNPs to estimate their effect on the own livestock. In addition, gene networks can be built on the basis of the presented SNPs to find potential candidate genes for reproductive signs. On the whole, these results help us to understand the genetic basis of pig reproductive traits and can be used in further studies. Further research in this direction will provide new data that will be a powerful impetus for creating breakthrough breeding technologies and improving the efficiency of breeding production in pig farming.

Supplementary Materials: The datasets produced and/or analyzed during the current study are available from the addition files. The following are available online at http://www.mdpi.com/2073-4425/11/5/491/s1, file 1: List of SNPs, file 2: Consequences of SNPs, file 3: List of genes in which SNP is defined.

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