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Variants in BMP7 and BMP15 3’-UTRs Associated with Reproductive Traits in a Large White Pig Population

Hang Yin †, Xing Du †, Qiqi Li, Zengxiang Pan, Wangjun Wu, Honglin Liu and Qifa Li *

College of Animal Science and Technology, Nanjing Agricultural University, Nanjing 210095, China; 18151665587@163.com (H.Y.); duxing@njau.edu.cn (X.D.); 2015105012@njau.edu.cn (Q.L.); owwa@njau.edu.cn (Z.P.); wuwangjun2012@njau.edu.cn (W.W.); liuhonglin@njau.edu.cn (H.L.)

* Correspondence: liqifa@njau.edu.cn; Tel.: +86-025-8439-5046; Fax: +86-025-8439-5314
† These authors contributed equally to this work.

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Abstract: Bone morphogenetic protein 7 (BMP7) and BMP15, which encode members of the BMP family, have been identified by whole-genome resequencing as breeding-related genes that overlap with a known quantitative trait locus for reproductive traits. In this study, we investigated the effects of variants at the BMP7 and BMP15 gene loci on sow reproductive traits. We isolated 669 and 1213 bp sequences of the 3’-untranslated region (3’-UTR) of the porcine BMP7 and BMP15 genes, respectively, and detected several RNA regulatory elements, such as miRNA response elements and AU-rich elements. Pooled DNA sequencing identified two novel point mutations (viz., BMP7 c.1569A>G and BMP15 c.2366G>A) in the 3’-UTR. Association analysis showed that the c.1569A>G polymorphism was associated with the litter weight trait in a Large White pig population. Furthermore, analysis of the combined genetic effects revealed that AA/GA and AG/GG were the favorable combined genotypes for the total number of piglets born (TNB) and the total number of piglets born alive (NBA), whereas. Together, our findings confirm that BMP7 and BMP15 are candidate genes for porcine reproductive performance.

Keywords: BMP7; BMP15; reproductive trait; variant; Large White pig

1. Introduction

Bone morphogenetic proteins (BMPs) are a group of multifunctional cytokines that belong to the BMP subfamily of the transforming growth factor beta (TGF-β) superfamily. As secreted signaling molecules and ligands, BMPs often exert their biological functions (e.g., ovarian functions) by forming the BMP/SMAD signaling pathway with receptors such as bone morphogenetic protein receptor type 1A (BMPR1A), BMPR1B, and BMPR2, and SMAD proteins (including SMAD1, SMAD5, SMAD8, and SMAD4) [1,2]. In the ovary, BMPs first interact with their heterotetrameric receptor complexes on the surface of granulosa cells (GCs). As an oocyte-secreted growth factor, BMP15 usually forms a homodimer or heterodimer with another oocyte-secreted growth factor, growth differentiation factor 9 (GDF9), before interacting with its receptors [3]. In the cytoplasm, these receptors activate SMAD1, SMAD5, and SMAD8 by mediating their phosphorylation, and the activated SMADs then form complexes with SMAD4. These SMAD complexes subsequently enter the nucleus where they control several key genes for follicular development, oocyte maturation and ovulation, and luteal formation by acting as a transcription factor [4–6].

In mammals, the BMPs are known to be essential for female fertility. Increasing evidence suggests that the dysregulation and dysfunction of the BMPs can cause follicular development arrest, ovulation...
disorders, decreased ovulation rate and litter size, and even infertility and other ovarian diseases [7,8]. Notably, in domestic animals, the BMPs are either major genes for high fecundity or candidate genes for reproductive traits [9–13]. In sheep, BMP15 and BMPR1B are the major genes for high fecundity traits, where the FecB mutation of BMPR1B, in particular, has been widely used in sheep breeding [9–11]. In Large White and Taihu sows, BMP7 and BMP15 have been identified through whole-genome resequencing to be breeding-related genes that overlap with a known quantitative trait locus for reproductive traits, respectively [12,13]. However, variants that affect reproductive performance have not been found in the 3'-untranslated region (3’-UTR) of the porcine BMP7 and BMP15 genes. Therefore, we aimed to characterize the 3’-UTR of these two porcine genes in this study. We also aimed to screen mutations in these regions, and to understand the relationship between the mutations and reproductive performance in a Large White pig population.

2. Materials and Methods

2.1. Samples

Ear samples of Large White sows (n = 227) were randomly collected from Jiangsu Kangle Farming Co. (Changzhou, China). Their reproductive traits are listed in Supplementary Table S1. All animal-related experiments were approved by the Animal Ethics Committee at Nanjing Agricultural University, China (SYXK 2017-0027).

2.2. Genomic DNA Extraction

DNA was extracted from the ear samples using the conventional phenol–chloroform method. In brief, the ear tissues from Large White sows were lysed by DNA lysis buffer and proteinase K for 12 h and the impurities were separated by using Tris saturated phenol, chloroform or isoamyl alcohol in sequence. Finally, the genomic DNA was extracted and stored at −20 °C for further analysis.

2.3. Primer Design

The specific primers used to isolate the 3’-UTR sequences of the Large White pig BMP7 and BMP15 genes were designed using Primer Premier v5.0 software (PREMIER Biosoft, Palo Alto, CA, USA), according to the sequences of the porcine BMP7 and BMP15 genes provided by the NCBI database (https://www.ncbi.nlm.nih.gov). The primers (listed in Table 1) were synthesized by Tsingke Biological Technology (Tsingke, Beijing, China).

| Gene | Primer Sequences (5'-3') | Annealing Temp (°C) | Product Size (bp) | Accession No. |
|------|--------------------------|---------------------|------------------|---------------|
| P1   | BMP7                     | F: GTGTTCCAGGTCCACCTCAT R: CCCAACTCCAAAGCAAAAA | 54 °C | 822 | XM_005673044.3 |
| P2   | BMP15                    | F: GTGCCTATAGCATCCCTCC R: CTAACTGAAGCGCTCTACCC | 54 °C | 1063 | NM_001005155.2 |
| P3   | BMP15                    | F: TTTGAGGGAAACAGAAGG R: GTGGCTAAGAGGAACAAA | 54 °C | 723 | NM_001005155.2 |

2.4. PCR Amplification and Sequencing

Polymerase chain reactions (PCRs) were performed in a 20 μL volume containing 10 μL of 2× VazymelAmp® Master Mix, 7 μL of ddH2O, 1 μL of forward primer, 1 μL of reverse primer, and 1 μL of DNA. The PCR cycles were as follows: 5 min at 94 °C, then 35 cycles of 30 s at 94 °C, 30 s at the annealing temperature (Table 1), 1 min at 72 °C, and finally, 7 min at 72 °C. PCR products were identified by 1.5% agarose gel electrophoresis and only the single and clear bands that fit for the expected length were selected for sanger sequencing (Tsingke, Beijing, China).
2.5. Sequence Analysis

DNAStar v5.22 software (DNASTAR, Madison, WI, USA) was used to analyze the nucleotide sequences of the 3’-UTR. The miRBase and miRTarBase websites were used to predict the microRNA (miRNA) response elements (MREs) within the BMP7 and BMP15 3’-UTR sequences.

2.6. Genotyping

The point mutations in the 3’-UTR of the porcine BMP7 and BMP15 genes were genotyped by direct sequencing; the specific primers used are listed in Table 1.

2.7. Association Analysis

The general linear model of the SAS v9.2 software package (SAS Institute Inc., Cary, NC, USA) was applied for analysis of the effects of different parities and genotypes on various reproductive traits of Large White pigs; namely, the total number of piglets born (TNB), the total number of piglets born alive (NBA), number of stillborns (NSB), and litter weight (LW). The statistical model was 

\[ y_{iklmn} = \mu + HYS_i + P_k + A_l + G_m + e_{iklmn} \]

where \( y_{iklmn} \) is the individual observation for the traits, \( \mu \) is the overall population mean, \( HYS_i \) is the effect of hoggy-year-season, \( P_k \) is the effect of parity, \( A_l \) is the effect of age (days), \( G_m \) is the effect of the gene, and \( e_{iklmn} \) is the random residual effect.

3. Results

3.1. Isolation and Characterization of the 3’-UTR of the Porcine BMP7 Gene

The partial sequence of the 3’-UTR of BMP7 was isolated by PCR amplification and sequencing (Figure 1). Several classic regulatory elements, such as the poly(A) signal (PAS; AAUAAA) and AU-rich element (ARE; AUUUA), were identified within this region; that is, at c.1714—1719, and c.1769—1773 (the transcription start codon of the porcine BMP7 was assumed as +1). In addition, the putative response elements for miR-6720-3p, miR-1342-3p, miR-1304-3p, miR-11978, miR-9340, and miR-3170 were predicted at c.1479—1497, c.1676—1698, c.1679—1699, c.1818—1836, c.1838—1858, and c.1859—1880, respectively.

Figure 1. Characterization of the partial sequence of the 3’-untranslated region of the Large White pig bone morphogenetic protein 7 (BMP7) gene. (A) Sequence of different genotypes at the mutation c.1569A>G. The arrow indicates the substitution.

3.2. Polymorphism of the 3’-UTR of the Porcine BMP7 Gene

An A/G point mutation site was detected in this region and designated as c.1569A>G (Figure 2A). Three genotypes, AA, AG, and GG were discovered in the Large White pig population (Figure 2A,B). A was the dominant allele with a frequency of 0.600, and AG was the dominant genotype with a
frequency of 0.449 (Figure 2C). The Chi-square test indicated that this single nucleotide polymorphism fitted the Hardy–Weinberg equilibrium ($p > 0.05$).

![Figure 1.](image1)

**Figure 1.** Characterization of the partial sequence of the 3'-untranslated region of the Large White pig bone morphogenetic protein 7 (BMP7) gene. The transcription start codon was assumed as +1 (GenBank ID: XM_005673044.3). The underline indicates the regulatory elements. Red arrows indicate the mutation c.1569A>G.

### 3.2. Polymorphism of the 3'-UTR of the Porcine BMP7 Gene

An A/G point mutation site was detected in this region and designated as c.1569A>G (Figure 2A). Three genotypes, AA, AG, and GG were discovered in the Large White pig population (Figure 2A–B). A was the dominant allele with a frequency of 0.600, and AG was the dominant genotype with a frequency of 0.449 (Figure 2C). The Chi-square test indicated that this single nucleotide polymorphism fitted the Hardy–Weinberg equilibrium ($p > 0.05$).

![Figure 2A](image2)

**Figure 2.** Mutation c.1569A>G in the 3'-untranslated region of the Large White pig BMP7 gene. (A) Sequence of different genotypes at the mutation c.1569A>G. The arrow indicates the substitution position. (B) Genotype frequency of the mutation c.1569A>G. (C) Allele frequency of the mutation c.1569A>G. $n = 227$.

### 3.3. Association Analysis between the BMP7 c.1569A>G Polymorphism and Reproductive Traits

The effects of the point mutation c.1569A>G on the TNB, NBA, NSB, and LW traits of Large White pigs were determined using a mixed model. The results showed that the LW of sows with the AG genotype was significantly higher than that of sows with genotype GG ($p < 0.05$) or AA ($p < 0.01$) (Table 2, and Supplementary Table S2). Although the effects of AA genotype and GG genotype on TNB and NBA have no significant difference in statistics, it is worth noting that the TNB and NBA of sows with the AA genotype are 0.61 and 0.47 per parity are higher than that of sows with the GG genotype, respectively (Table 2).

| Genotypes ($n$) | Traits (LSM ± SE) | 
|-----------------|-------------------|
|                 | TNB               | NBA               | NSB               | LW                |
| AA (83)         | 12.26(±0.53) a    | 12.07(±0.52) a    | 0.18(±0.15) a    | 17.00(±0.70) b    |
| AG (99)         | 12.10(±0.54) a    | 11.87(±0.54) a    | 0.23(±0.16) a    | 18.03(±0.72) a    |
| GG (45)         | 11.65(±0.63) a    | 11.60(±0.62) a    | 0.16(±0.17) a    | 17.40(±0.82) ab   |

Data represent the least squares means ± SE. $n = 227$. TNB = the total number of piglets born; NBA = the total number of piglets born alive; NSB = number of stillborn; LW = litter weight. Values in each line with different lowercase superscripts are at $p < 0.05$; those with same lowercase superscripts mean that there were no differences ($p > 0.05$).
3.4. Isolation and Characterization of the 3'-UTR of the Porcine BMP15 Gene

We next isolated a 1213-bp sequence of the 3'-UTR of BMP15 gene from the Large White pig (Figure 3) and found that this was also a gene containing a PAS motif. The partial sequence contained three classic GU-rich element (GRE; UUGUU) motifs located at c.1337/1341 (GRE1), c.2018/2022 (GRE2), and c.2246/2250 (GRE3), and a PAS motif located at c.2402/2407 (the transcription start codon of the porcine BMP15 was assumed as +1), but ARE motifs were not detected. Furthermore, ten target sites of miRNAs were detected in the partial 3'-UTR sequence, such as miR-21-3p (c.1322/1342), miR-17-3p (c.2154/2175), miR-132-5p (c.2204/2225), and miR-29a-5p (c.2391/2412).

Figure 3. Characterization of the partial sequence of the 3'-untranslated region of the Large White pig BMP15 gene. The transcription start codon was assumed as +1 (GenBank ID: NM_001005155.2). The underline indicates the regulatory elements. Red arrows indicate the mutation c.2366G>A.

3.5. Detection of a G/A Point Mutation Site in the 3'-UTR of the BMP15 Gene

A G/A point mutation site was identified in the 3'-UTR of the BMP15 gene and designated as c.2366G>A (Figure 4A). Only two genotypes, GG and GA, were discovered in the Large White pig population (n = 227) (Figure 4B). G was the dominant allele with a frequency of 0.866, and GG was the dominant genotype with a frequency of 0.732 (Figure 4C). The Chi-square test showed that this point mutation fitted the Hardy–Weinberg equilibrium (p > 0.05).
Figure 3. Characterization of the partial sequence of the 3'-untranslated region of the Large White pig BMP15 gene. The transcription start codon was assumed as +1 (GenBank ID: NM_001005155.2). The underline indicates the regulatory elements. Red arrows indicate the mutation c.2366G>A.

3.5. Detection of a G/A Point Mutation Site in the 3'-UTR of the BMP15 Gene

A G/A point mutation site was identified in the 3'-UTR of the BMP15 gene and designated as c.2366G>A (Figure 4A). Only two genotypes, GG and GA, were discovered in the Large White pig population (n = 227) (Figure 4B). G was the dominant allele with a frequency of 0.866, and GG was the dominant genotype with a frequency of 0.732 (Figure 4C). The Chi-square test showed that this point mutation fitted the Hardy–Weinberg equilibrium (P > 0.05).

Figure 4. Mutation c.2366G>A in the 3'-untranslated region of the Large White pig BMP15 gene. (A) Sequence of different genotypes at the mutation c.2366G>A. The arrow indicates the substitution position. (B) Genotype frequency of the mutation c.2366G>A. (C) Allele frequency of the mutation c.2366G>A. n = 227.

3.6. Association Analysis between the BMP15 c.2366G>A Polymorphism and Reproductive Traits

Analyses of the effect of the point mutation c.2366G>A on the various reproductive traits revealed that this polymorphism was not significantly effective on any of the traits in the Large White pig population (p > 0.05) (Table 3).

Table 3. Effect of the c.2366 G>A polymorphism on reproductive traits of a Large White pig population.

| Genotypes (n) | Traits (LSM ± SE) |
|--------------|-------------------|
|              | TNB       | NBA       | NSB       | LW        |
| GA(56)       | 12.56±0.44  | 12.24±0.42| 0.21±0.15 | 17.20±0.72|
| GG(171)      | 12.63±0.43  | 12.34±0.42| 0.20±0.15 | 17.57±0.71|

Data represent the least squares means ± SE. n = 227. TNB = the total number of piglets born; NBA = the total number of piglets born alive; NSB = number of stillborn; LW = litter weight. No markers means that there were no differences (p > 0.05).

3.7. Association Analysis between the Combined Genotypes of BMP7 c.1569A>G and BMP15 c.2366G>A and Reproductive Traits

BMP7 c.1569A>G and BMP15 c.2366G>A formed six combined genotypes (viz., AA/GA, AA/GG, AG/AG, AG/GG, GG/GA, and GG/GG) in the Large White pig population (n = 227) (Figure 5). Of these, the frequency of genotype AG/GG was the highest (0.348), whereas that of genotype GG/GA was the lowest (0.048). The effects of the combined genotypes on the various reproductive traits in this pig population are shown in Table 4. For the TNB and NBA traits, sows with the AA/GA and AG/GG genotypes had significantly higher numbers than sows with the genotype AG/GA (p < 0.05).
BMP7 c.1569A>G and BMP15 c.2366G>A in Large White pig population. $n = 227$.

### Table 4. Combination effect of the genotypes formed by BMP7 c.1569A>G and BMP15 c.2366G>A on reproductive traits.

| Genotypes (n) | TNB (LSM ± SE) | NBA (LSM ± SE) | NSB (LSM ± SE) | LW (LSM ± SE) |
|---------------|----------------|----------------|----------------|--------------|
| AA/GA(25)     | 12.44(±0.60)$^{a}$ | 12.21(±0.59)$^{a}$ | 0.03(±0.20)$^{a}$ | 17.08(±0.95)$^{a}$ |
| AA/GG(58)     | 12.02(±0.59)$^{ab}$ | 11.91(±0.58)$^{ab}$ | 0.07(±0.20)$^{a}$ | 17.06(±0.93)$^{a}$ |
| AG/GA(20)     | 11.17(±0.67)$^{b}$ | 11.04(±0.66)$^{b}$ | 0.04(±0.22)$^{a}$ | 17.04(±1.09)$^{a}$ |
| AG/GG(79)     | 12.31(±0.56)$^{a}$ | 12.08(±0.56)$^{a}$ | 0.14(±0.19)$^{a}$ | 18.25(±0.90)$^{a}$ |
| GG/GA(11)     | 11.81(±0.80)$^{ab}$ | 11.78(±0.80)$^{ab}$ | 0.01(±0.26)$^{a}$ | 17.36(±1.32)$^{a}$ |
| GG/GG(34)     | 11.49(±0.69)$^{ab}$ | 11.48(±0.68)$^{ab}$ | 0.04(±0.23)$^{a}$ | 16.97(±1.09)$^{a}$ |

Data represent the least squares means ± SE. $n = 227$. TNB = the total number of piglets born; NBA = the total number of piglets born alive; NSB = number of stillborn; LW = litter weight. Values in each line with different lowercase superscripts are at $p < 0.05$. Same lowercase superscripts means that there were no differences ($p > 0.05$).

### 4. Discussion

The 3′-UTRs are the multi-functional components of mRNAs, representing a central regulatory hub that recruits RNA-binding proteins (RBPs) and non-coding RNAs (ncRNAs) to control mRNA translation, localization, stability, and the polyadenylation status [14,15]. Recognition sites for RBPs and ncRNAs (also known as RNA regulatory elements) have been shown to mediate the 3′-UTR-determined gene expression level in various tissues and cells [15,16]. In this study, we isolated and characterized partial sequences of the 3′-UTRs of the porcine BMP7 and BMP15 genes, and multiple RNA regulatory elements such as miRNA response elements (MREs), GREs, and AREs were detected. MREs are sequences in the 3′-UTR of mRNAs that recognize the seed region on the miRNA, thereby mediating direct interactions between the miRNA and its target mRNA [16,17]. Importantly, several putative BMP7- or BMP15-targeted miRNAs, such as miR-17-3p [18], miR-21-3p [19], miR-29a-5p [20], and miR-132-5p [21], have been demonstrated to be related to reproduction [22,23]. The ARE motif, an important cis-element for RNA regulation, is involved in RNA processing, transport, and translation through its interaction with ARE-binding proteins, such as the tristetraprolin (TTP), heterogeneous nuclear ribonucleoprotein D (HNRPD; also AUF1), ELAV-like RNA-binding protein 1 (ELAV1; also HuR), and KH-type splicing regulatory protein (KSRPH) [24,25]. The GRE motif, a conserved sequence enriched in the 3′-UTR of mRNAs, which mediated regulation of GRE-binding proteins (e.g., nucleolin and fragile X mental retardation protein) on mRNA stability [26,27]. However, the regulation of porcine BMP7 and BMP15 genes by these RNA regulatory elements has not been experimentally verified and needs further investigation.

BMP7 is an important ligand of the BMP/SMAD signaling pathway, which plays a critical role in steroidogenesis, follicular development, and female fertility [13,28]. In the mammalian ovary, BMP7 is
highly expressed in the GCs and theca cells (TCs) of dominant follicles [28]. In follicular cells cultured in vitro, the inhibition of BMP7 induced the suppression of androgen secretion by bovine ovarian TCs [29], whereas the addition of recombinant BMP7 stimulated estrogen (E2) release by buffalo ovarian GCs [28], as well as progesterone (P4) production by human ovarian granulosa lutein cells [30], and buffalo ovarian luteal cells [31]. BMP7 also promoted GC survival in the buffalo ovary [28] and GC proliferation in the rat ovary [32]. Injections of BMP7 into the ovarian bursa of rats increased the numbers of primordial, primary, preantral, and antral follicles, and decreased the ovulation rate and serum P4 levels [32]. Furthermore, both ovarian BMP7 levels and BMP7 polymorphisms have been shown to be associated with fertility in domestic animals [13,33]. In sheep, the BMP7 mRNA levels were significantly higher in the ovarian follicles of FecB-carrying ewes with high fecundity [33].

High-throughput technology showed that BMP7 was a candidate gene for reproductive traits in Large White pigs [13] and for the high prolificacy of Hu sheep [34]. In this study, we identified the novel point mutation c.1569A>G in the 3'-UTR of the porcine BMP7 gene and found that its polymorphism was associated with the LW trait in a Large White pig population. In three pig populations (Landrace, Yorkshire, and Duroc), the g.35161T>C polymorphism was shown to be significantly associated with the NBA and LW traits (p < 0.05), and the LW at 21 days (p < 0.01) [35]. Our findings further demonstrated that BMP7 is a candidate gene for the reproductive traits of sow, and would be a novel marker for marker-assisted selection in pig breeding.

BMP15 is an important cytokine that is expressed specifically in the ovaries of mammals [3]. As an oocyte-secreted growth factor, BMP15 plays paracrine/autocrine roles in regulating the functions of GCs (e.g., proliferation, differentiation, and apoptosis) and in stimulating the action of follicle-stimulating hormone (FSH), the expansion of cumulus cells, and ovulation [36–38]. Importantly, BMP15 has been shown to be essential for female fertility in most mammalian species; in particular, homozygosity for BMP15 mutations leads to subfertility in mice and sterility in sheep [39,40]. In addition, the BMP15 levels and GDF9:BMP15 ratio have been demonstrated to be directly correlated with the litter size in mammals [36,41].

BMP15 has been identified as a major gene for high fecundity traits, including the litter size and ovulation rate in sheep, and multiple mutations (e.g., FecX<sup>B</sup>, FecX<sup>Bar</sup>, FecX<sup>G</sup>, FecX<sup>Grs</sup>, FecX<sup>H</sup>, FecX<sup>L</sup>, FecX<sup>O</sup>, and FecX<sup>R</sup>) have been proven to significantly improve fecundity [9,11,42].

Recently, the novel haplotype variant FecX<sup>Bfr</sup> that consists of three polymorphisms (viz., c.301G>T, c.302_304delCTA, and c.310insC) was observed in exon 1 of the BMP15 gene of the W flock (a strain line originally created using prolific Barbarine ewes), and this allele increased the ovulation rate by 0.7 and the litter size by 0.3 lambs [43]. In Taihu pigs, BMP15 has been identified through whole-genome resequencing to be a breeding-related gene that overlaps with a known quantitative trait locus for reproductive traits [12]. Therefore, the selection of a single locus or a single gene is insufficient to improve the reproductive performance of sows in the pig breeding industry. Therefore, the analysis of the combined genetic effects of multiple genes or multiple loci on reproductive traits has attracted increasing attention [45,46]. For instance, in Hirschmann hybrid-line sows, two point mutations (657C>T and 749G>C) in intron 6 of the porcine pregnancy-associated glycoprotein 2-like subfamily (pPAG2-Ls) gene were combined into a diplotype; subsequently, significant associations of the NBA trait with the combined genotype 657C/749GC (12.71 ± 0.47) were shown compared with 657CT/749GG (11.39 ± 0.22) [45]. A recent report described 26 putative lethal haplotypes in a Finnish Yorkshire population (observed using genome-wide association analysis), where haplotype 8-2026 on chromosome 8 (position 107.0–113.3 Mb, 135 marker) was significantly associated with the NSP trait [47]. In this study, we showed that BMP7 c.1569A>G and BMP15 c.2366G>A formed six combined genotypes, of which AA/GA and AG/GG were preferable for sows, being associated with higher TNB and NBA.
Similarly, six combined genotypes that were favorable for reproductive traits (viz., estrogen receptor (ESR)AA/FSHbBB, ESRAA/catenin alpha-like 1 (CTNNAL1)CG, ESRAA/miR-27aAA, FSHbBB/CTNNAL1CC, FSHbBB/miR-27aAA, and CTNNAL1CG/miR-27aAB) were identified in another study of a Large White pig population [46]. Together, our findings provide the optimal genotype combinations between the BMP7 and BMP15 genes for the polygene pyramiding breeding of reproductive traits in Large White pig populations.

5. Conclusions

In summary, for the first time, the 3'-UTR of the porcine BMP7 and BMP15 genes was isolated and characterized. Furthermore, two point mutations (c.1569A>G in BMP7 and c.2366G>A in BMP15) were identified, where c.1569A>G was found to be significantly effective on some of the sow reproductive traits in a Large White pig population. For the BMP7 and BMP15 genes, the AA/GA combined genotype could be the ideal model for further breeding selection. Our findings not only confirm that BMP7 and BMP15 are candidate genes for porcine reproductive capacity, but that they are also potentially novel genetic markers for marker-assisted selection and genome selection in pig breeding.

Supplementary Materials: The following are available online at http://www.mdpi.com/2076-2615/9/11/905/s1, Supplementary Table S1: Statistical description of reproductive traits, Supplementary Table S2: Additive and dominant effect of BMP7 on the reproductive traits in a Large White pig population.

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