



Review

PROLACTIN RECEPTOR GENE (PRLR) ROLE IN SWINE REPRODUCTION

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ABSTRACT

PRLR gene has been studied as a candidate gene for litter size in swine because of prolactin biological functions and their association with reproduction. Prolactin receptor gene is mapped on porcine chromosome 16. The established PCR-RFLP polymorphism at PRLR locus demonstrated the presence of two alleles, A and B and three genotypes AA, AB and BB. There were found different allele and genotype frequencies in different pig populations with variation of the effects of PRLR genotypes on litter traits. Additional studies should be done in specific breeds and populations to evaluate the association of existing PRLR locus polymorphism with reproductive traits before application of marker-assisted selection in these populations.

Key words: PRLR gene, polymorphism, genetic marker, litter size

Intensive and efficient pork production implies improved production traits - growth traits, carcass and meat quality traits, but also needs sows with high reproductive potential and substantial survival rates of pigs (1, 2).

Because of low heritability of litter size traits in swine, efficient approach in genetic improvement of these traits is application of marker-assisted selection (MAS) alongside with classical selective breeding, (3).

Ernst and Steibel affirmed that a candidate gene is a gene, identified on the basis of its physiological function or genome location, that potentially controls part of variation of a specific trait (4). The advances in genome studies in swine allowed for identification of quantitative trait loci (QTL) and genes involved in the genetic control of meat production and reproduction traits (5 - 12).

Biochemical functions of prolactin and the PRLR gene and mapping in pigs

Prolactin (PRL) is a peptide hormone

discovered a century ago (13, 14). The synthesis and release of the hormone from the anterior pituitary is under negative control by dopamine (15), which binds to surface prolactin receptors in target tissues. Prolactin is detected in different tissues and cells and its concentrations vary during the estrus, pregnancy and lactation (16-18). It is essential for the formation and differentiation of mammary epithelial cells during the gestation (19). Blood prolactin levels in pregnant sows are usually low but become increased in the per parturient period and lactation (20). Active prolactin binds to specific surface prolactin receptors (PRLRs) encoded by the prolactin receptor gene (PRLR) and controls intracellular protein activity (21, 22). Prolactin becomes active after binding to PRLRs, and the latter are essential for various events connected with reproduction as mammary gland development, lactation and maternal behavior (23).

Bole-Feysot et al., reported that prolactin is involved in hundreds biochemical reactions with direct relationships with estrogens in prepubertal swine and with PRLR-mediated changes in ovaries and the uterus. This hormone regulates luteal and follicular estrus

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stages in sows and plays a primary role in maintaining the functions of yellow body. By the end of lactation in sows or after piglets weaning, prolactin influences the cyclic ovarian activity and the estrus onset (24). Furthermore it has an influence on progesterone and relaxin hormones production in the presence of prolactin receptors in endometrial cells of sows, and this effect is associated to gestational age (25, 26). This presumes a possible prolactin role in the

preparation and maintenance of gestation in sows. Based on physiological effects expressed at fertilization and gestation and its complex role in a number of reproductive events, the PRLR gene is accepted as a candidate gene associated with litter size traits in sows (28 - 30). The PRLR gene is mapped on chromosome 16 in swine 16q 1.4 or 16q 2.2-2.3 (31). The location of PRLR gene is presented on region of the physical map of the porcine chromosome 16 (**Figure 1**).

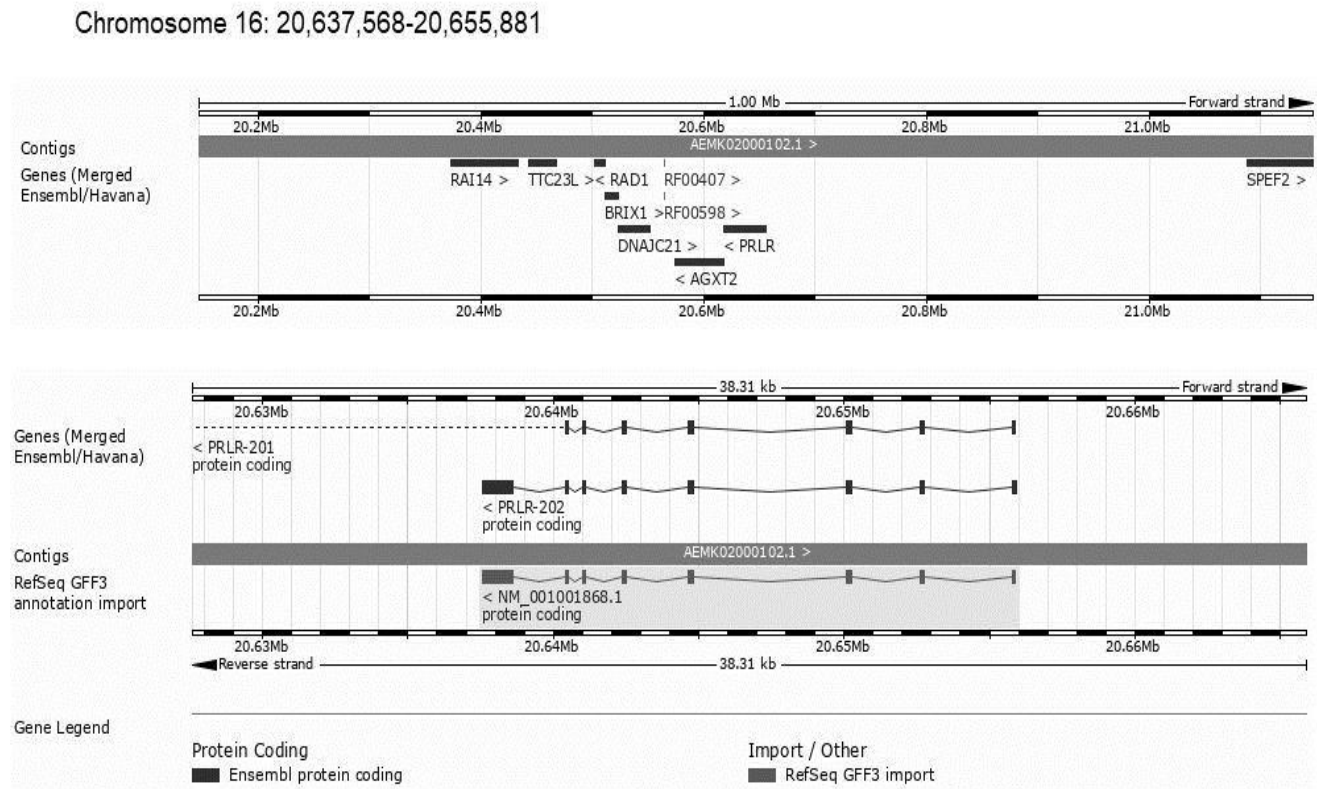


Figure 1. Physical map of porcine chromosome 16 region with the PRLR locus. (http://www.ensembl.org/Sus_scrofa/Gene/Summary?db=otherfeatures;g=414916;r=16:20637568-20655881;t=NM_001001868.1).

Polymorphism at the porcine PRLR locus

The *AluI* polymorphism in the porcine PRLR gene and its effects on litter size were studied first by Vincent et al. and Rothschild et al. (31, 32). This established PCR-RFLP genetic polymorphism at the PRLR locus demonstrated the presence of two alleles A and B and three genotypes (AA, AB and BB) with varying frequencies in the different swine populations (27, 33). In Large White, Landrace and crossbred sows, Mihailov et al., found PRLR allele frequencies of 0.33, 0.58 and 0.52 respectively for allele A and 0.66, 0.41 and 0.47 for allele B (34). In another study, allele A frequencies were found to be relatively similar in Large White and Landrace sows, with genotype frequencies of 0.24 and 0.18 for

the homozygous genotype AA; 0.48 and 0.57 for the heterozygous genotype AB; 0.28 and 0.25 for the homozygous genotype BB (2). In Mangalica×Duroc crosses, similar frequencies of alleles A and B were found (0.52 and 0.48), with relatively lower frequencies of homozygous AA and BB genotypes (0.18; 0.15) and comparatively higher frequency of the heterozygous AB genotype – 0.67 (35). In Large White sows, Liu et al., estimated allele B frequency of 0.54 that was higher than that of allele A – 0.46 (36). Close results were found for the wild boar and Large White crosses, with lower frequency of allele A (0.44) versus that of allele B (0.56) and predominance of the frequency of the heterozygous PRLR AB genotype: 0.51, as

compared to those of both homozygous genotypes - 0.19 for PRLR AA and 0.30 for PRLR BB (37). Another study in different pig breeds established higher frequency for allele A in Hungarian Large White and Pietrain breeds (0.63 and 0.59 respectively) than for allele B frequency (0.37 and 0.41). In the same study Duroc sows, allele A frequency was lower than that of allele B (0.17 vs 0.83) (38).

Association of porcine PRLR gene polymorphism with reproduction traits

Vincent et al., reported the PRLR-*AluI* gene polymorphism (allele A) association with bigger litter size at birth in Large White, Landrace, Duroc×Large White and Large White × Meishan crosses (39). PRLR gene allele A additive genetic effects on sows litter traits were found in six PIC lines (22, 32), in Large White, Landrace, Meishan (40) and Duroc breeds (30). Sows, F2 crosses of Large White × Meishan, with PRLR AA genotype, were significantly better for number of total born and live born piglets compared to sows from the other two PRLR genotypes (22). Similar results were found in study of crossbred sows Polish Large White × Landrace (28). The PRLR *AluI* polymorphism was found to be associated with first parity litter size at birth in sows from the Landrace breed whereas the PRLR *HpaII* polymorphism – with the litter size at weaning in both Landrace and Large White lines (41). Results of Wang et al., pointed that first parity Beijing Black sows with PRLR AA genotype were slightly better with respect to the total number born and live-born pigs, but not significant to the other two genotypes (42). The authors however, reported significantly higher total number born and number of live-born pigs for next parities.

Another studies on the problem showed that the PRLR genotype favorably associated with litter size traits could be different for sows from different breeds and lines (43, 44).

In addition, to the studies on the effects of polymorphism at the PRLR gene on litter traits in sows, many studies have been focused on its influence on reproductive traits in boars. Kmiec and Terman found that the genotype PRLR AB boars were with significantly greater ejaculate volume, higher spermatozoa concentrations, live spermatozoa percentages and number in ejaculate compared to boars from the homozygous PRLR AA and PRLR BB genotypes (46). Similarly, Huang et al. reported similar effect on semen quality, ejaculate volume, spermatozoa concentrations,

and number/percentage of live spermatozoa in the ejaculate (46), but in another study (47) results did not pointed for the presence of any significant effects of PRLR genotypes on semen quality and fertility traits in boars.

Association of porcine PRLR gene polymorphism with meat production traits

The primary breeding goals in pig breeding programs are meat production traits – growth, carcass and meat quality traits. The proper application of genetic markers with regard to improvement of reproductive traits of swine, their associations with meat production traits should be also considered. This is especially important to avoid potential contradictory effects of genetic markers associated with reproduction on pork production traits. In this sense, a beneficial effect of PRLR allele A was found in terms of lower backfat thickness, less days to 90 kg weight and increased average daily weight gain in Berkshire pigs (48). Similar results found by Mihailov et al., confirmed that PRLR genotype AA had better meat production traits in crossbred pigs (34). In a study on Mangalica×Duroc crosses, no pleiotropic effects of PRLR genotypes on production traits were demonstrated (35).

In conclusion, presented results provide evidence for a substantial variation of PRLR allele and genotype frequencies in populations of various pig breeds and lines. Along with the variable effect of PRLR genotypes on litter traits in different pig populations and the lack of antagonistic effect on primary production traits in pig populations, the PRLR gene seems promising as genetic marker of reproductive traits. Additional studies should be done in specific breeds and populations to evaluate the association of existing polymorphism at PRLR locus with reproduction traits before application of marker-assisted selection in these populations.

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