

# The Prolactin Receptor Gene is Associated with Increased Litter Size In Pigs

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## Summary and Implications

The prolactin receptor gene was investigated as a candidate gene for reproduction traits in five PIC lines consisting of Large White (2), Landrace, Duroc, and Large White/Meishan origin. Least squares means for total number born (TNB) and number born alive (NBA) were calculated for each genotype in addition to an analysis of additive and dominance effects by line. The *PRLR* gene was significantly associated with TNB and/or NBA in three of the lines tested. The effect was greater than one pig for NBA in one line, although the effect clearly varied depending on the background genetics of the line. Additional data is needed to confirm the significant effects seen in these three lines. However, the effects observed to date suggest that this gene test has the potential to be a powerful tool when used in conjunction with traditional selection methods for some lines.

## Introduction

Improvement of reproductive traits in livestock species has become of increasing interest, especially in swine where moderate increases in litter size can equal large gains in profit. The use of molecular genetic markers in Marker Assisted Selection (MAS) could potentially be employed in conjunction with traditional selection methods to accelerate the rate of change in economically important traits. The candidate gene approach was used to identify a significant association between the estrogen receptor gene (*ESR*) and litter size. The *ESR* gene has been demonstrated to have large allelic effects ranging from a 0.4 to 1.15 pigs per litter increase in the pig (2, 3). Other hormone receptors are presumed to be good candidate genes for quantitative traits because they are the limiting factor in many reproductive pathways.

The prolactin receptor (*PRLR*) is the specific receptor for prolactin (PRL), an anterior pituitary peptide hormone

essential for reproductive success. Mice with null mutations in *PRLR*, eliminating functional receptors, are sterile due to a failure of embryonic implantation and also demonstrate irregular cycles, reduced fertilization rates, and defective embryonic development (1). *PRLR* is a strong candidate gene for reproductive traits in the pig due to its role in reproduction. The *PRLR* gene has been recently linkage and physically mapped to pig chromosome 16 (4).

## Materials and Methods

A total of 2,714 litter records from 1,077 sows was included in the litter size analyses. Traits included TNB and NBA from five different PIC lines. The five lines examined were of Large White (two different origins) and Landrace origin, as well as synthetic lines consisting of Duroc, Large White, and Large White/Meishan origin. These lines were all housed in genetic nucleus farms owned by PIC UK or PIC USA and were raised in accordance with approved farm management practices. Animals were genotyped for the *PRLR* marker at Dalgety Food Technology Center (Cambridge, UK), PIC's Genetic Diagnostic Laboratory (Franklin, KY), or Iowa State University by using previously described methods (4).

The TNB and NBA traits were analyzed with a sire model, including fixed effects of herd-season, service type (natural or AI), *PRLR* genotype, and parity. Sire was included as a random effect. Interactions among herd, *ESR*, and *PRLR* were tested for significance. Heritability for the litter traits was assumed as .10 and repeatability as .21. Allele substitution effects were estimated by substituting for *PRLR* genotype a covariate that included the number of A alleles present. Dominance effects were estimated as the deviation of the heterozygotes from the average of the homozygotes.

## Results and Discussion

The *PRLR* genotype was shown to explain a significant amount of variation in litter size in three of the lines tested. Two of the lines did not show any significant effect ( $P > 0.1$ , results not shown). The least squares means for TNB and NBA for each of the three significant lines are summarized in Table 1. The Large White based line sample consisted of 400 sows with 1,197 litter records. The AA animals have a 0.66 pig per litter advantage in NBA over the AB and BB animals ( $P < 0.05$ ). There are indications of a dominance effect with the B allele. The Meishan based line sample consisted of 261 sows with 832 litter records. An additive effect for TNB ( $P < 0.05$ ) and NBA ( $P < 0.05$ ) and an overdominance effect for NBA ( $P < 0.01$ ) were observed in this line. The largest effect was detected in the Landrace based line sample, composed of 416 sows and 685 litter records. A greater than one pig per litter difference between the two homozygous genotypes was detected for both TNB

( $P < 0.08$ ) and NBA ( $P < 0.1$ ), with the A allele being favorable.

*PRLR* was investigated as a candidate gene for litter size due to its integral role in several reproductive pathways. The results of this initial study indicate that *PRLR* has a significant effect on litter size as measured by TNB and NBA in three commercial lines. The background genetics of each different line may play a part in the manner and the magnitude of the effect on the trait. Further analysis must be done to ensure that the increase in litter size associated with *PRLR* does not negatively affect traits such as birth weight. Gains made by increased litter size may be outweighed by losses due to smaller birth weights because smaller birth weights are correlated with decreased survivability. Although no difference has been shown for average birth weight, the use of the *PRLR* marker must proceed with caution until further data can be collected and analyzed to assure no negative effects for birth weight or other traits will be inherited in conjunction with the favorable allele of *PRLR*.

It is not clear at this time whether *PRLR* is a major gene responsible for the effect seen in this study or if it is linked to the gene having the effect. *PRLR* is mapped to chromosome 16 in the pig, which has a relatively few number of genes mapped to it, making it difficult to identify other possible genes that may be truly causing the effect. Further mapping and investigation of genes or markers near *PRLR* are required to resolve this issue. Increasing the numbers of animals and records for each line also will be required to confirm the effect. In analysis of the ESR gene, at least 1,000 sow records were necessary to reach a stable litter size effect of 0.4 pigs per litter (3).

Incorporating reliable markers into a MAS program has potential for large financial returns in a shorter time frame than traditional selection alone because environmental factors play a large role in litter size and the traits can only be directly measured in female animals. Selection also can be done before animals reach reproductive maturity. The early *PRLR* results indicate a sizable increase in NBA in both the white dam lines. The existence of the association with litter size in the Landrace based line may be especially useful as the favorable ESR B allele was present in a low frequency in this line.

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**Table 1. Least squares means for each *PRLR* genotype across all parities for TNB and NBA for three commercial lines of pigs.**

Commercial line	<i>PRLR</i> genotype	TNB	NBA
Large White Synthetic	AA	12.51	12.39
	AB	12.35	11.73
	BB	12.71	11.73
			$P < 0.05$
Effects	a	-0.10	0.33 <sup>b</sup>
	d	-0.26	-0.33 <sup>a</sup>
Meishan Synthetic	AA	13.64	12.95
	AB	14.35	13.74
	BB	13.96	13.27
		$P < 0.05$	$P < 0.05$
Effects	a	0.16 <sup>b</sup>	0.16 <sup>b</sup>
	d	0.55 <sup>b</sup>	0.63 <sup>c</sup>
Landrace Synthetic	AA	12.13	11.33
	AB	11.72	10.92
	BB	10.98	10.31
		$P < 0.08$	$P < 0.10$
Effects	a	0.51 <sup>b</sup>	0.47 <sup>b</sup>
	d	0.17	0.10

a=additive effect; d=dominance effect; effects are significant at <sup>a</sup> $P < 0.1$ , <sup>b</sup> $P < 0.05$ , <sup>c</sup> $P < 0.01$ .