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# Effect of polymorphisms in candidate genes on reproduction traits in Finnish pig populations

## Abstract

Reproduction traits play an important role in economically viable piglet production and are closely related to the quality and length of the productive life of the sow. A increased removal rate of young sows is undesirable not only because of the associated financial penalties incurred, but also because of ethical concerns. Candidate genes and gene pathways have been identified for fertility in model species, and recent studies have provided evidence that polymorphisms within these genes are associated with reproduction traits in American Yorkshire/Large White and Landrace populations. In this study we evaluated the impact of single polymorphisms ( $n = 7$ ) in 7 candidate genes on reproductive efficiency in Finnish Yorkshire ( $n = 280$ ) and Landrace ( $n = 271$ ) populations: *IGFBP1*, *IGFBP2*, *IGFBP3*, *IGFBP5*, *CPT1A* (carnitine *O*-palmitoyltransferase I), *COX2* (PG-endoperoxide synthase 2, also known as cyclooxygenase-2), and *SLC22A5* [organic cation/carnitine transporter 2 (solute carrier family member I), *OCTN2*]. In the Finnish Yorkshire population, only 4 of the analyzed markers were polymorphic. Significant effects on farrowing time were detected from the Yorkshire data, with polymorphisms within the genes *CPT1A* [a (allele substitution effect of allele A) = 2.97 d for age at first farrowing)], *IGFBP3* ( $a = 0.54$  d for farrowing interval of parities  $>1$ ), and *IGFBP5* ( $a = 3.22, 1.27, \text{ and } 0.85$  d for age at first farrowing and farrowing interval in the first and later parities, respectively). For the Landrace population, 6 markers were polymorphic, and significant effects were detected for traits affecting litter size. The polymorphism within the *COX2* gene had an additive effect of 0.3 piglets for litter size in parities  $>1$ , and the *IGFBP1* gene had an additive effect of 0.21, 0.26, and 0.11 piglets for litter size in the first parity, parities  $>1$ , and stillborn in parities  $>1$ , respectively. The additive effect of the SNP within the *IGFBP2* gene was 0.16, 0.09, and 0.09 piglets for litter size in parities  $>1$  and stillborn in the first and later parities, respectively. Finally, the *IGFBP5* gene had an additive effect of 0.18, 0.07, and 0.07 piglets for litter size in the first parity, stillborn in parities  $>1$ , and mortality between farrowing and weaning in the first parity, respectively. These results support the suitability of the candidate gene approach for identification of markers to improve the reproductive performance of sows and to provide potential markers for marker-assisted selection.

## Keywords

candidate gene, pig, reproduction, sow productive life

## Disciplines

Agriculture | Animal Sciences | Genetics and Genomics

## Comments

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# Effect of polymorphisms in candidate genes on reproduction traits in Finnish pig populations<sup>1</sup>

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**ABSTRACT:** Reproduction traits play an important role in economically viable piglet production and are closely related to the quality and length of the productive life of the sow. An increased removal rate of young sows is undesirable not only because of the associated financial penalties incurred, but also because of ethical concerns. Candidate genes and gene pathways have been identified for fertility in model species, and recent studies have provided evidence that polymorphisms within these genes are associated with reproduction traits in American Yorkshire/Large White and Landrace populations. In this study we evaluated the impact of single polymorphisms ( $n = 7$ ) in 7 candidate genes on reproductive efficiency in Finnish Yorkshire ( $n = 280$ ) and Landrace ( $n = 271$ ) populations: *IGFBP1*, *IGFBP2*, *IGFBP3*, *IGFBP5*, *CPT1A* (carnitine *O*-palmitoyltransferase I), *COX2* (PG-endoperoxide synthase 2, also known as cyclooxygenase-2), and *SLC22A5* [organic cation/carnitine transporter 2 (solute carrier family member I), *OCTN2*]. In the Finnish Yorkshire population, only 4 of the analyzed markers were polymorphic. Significant effects on farrowing time were detected from the Yorkshire data, with polymorphisms within the genes *CPT1A* [a (allele substitution

effect of allele A) = 2.97 d for age at first farrowing)], *IGFBP3* ( $a = 0.54$  d for farrowing interval of parities  $>1$ ), and *IGFBP5* ( $a = 3.22, 1.27,$  and  $0.85$  d for age at first farrowing and farrowing interval in the first and later parities, respectively). For the Landrace population, 6 markers were polymorphic, and significant effects were detected for traits affecting litter size. The polymorphism within the *COX2* gene had an additive effect of 0.3 piglets for litter size in parities  $>1$ , and the *IGFBP1* gene had an additive effect of 0.21, 0.26, and 0.11 piglets for litter size in the first parity, parities  $>1$ , and stillborn in parities  $>1$ , respectively. The additive effect of the SNP within the *IGFBP2* gene was 0.16, 0.09, and 0.09 piglets for litter size in parities  $>1$  and stillborn in the first and later parities, respectively. Finally, the *IGFBP5* gene had an additive effect of 0.18, 0.07, and 0.07 piglets for litter size in the first parity, stillborn in parities  $>1$ , and mortality between farrowing and weaning in the first parity, respectively. These results support the suitability of the candidate gene approach for identification of markers to improve the reproductive performance of sows and to provide potential markers for marker-assisted selection.

**Key words:** candidate gene, pig, reproduction, sow productive life

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## INTRODUCTION

Sow productive life (SPL) is an important trait in modern pork production. Sow productive life is a mea-

sure of the longevity and reproductive performance of a sow and is directly related to the number of viable piglets produced during its lifespan. Sows with reduced piglet production are removed early in their productive lifetime. Approximately 15 to 20% of the sows removed have produced only 1 litter, and more than 50% are removed before their fifth parity (Lucia et al., 2002; Engblom et al., 2007, 2008). The increased removal rate of young animals is of considerable concern. Reproductive traits are known to be of poor heritability (Roehe and Kennedy, 1995; Ehlers et al., 2005; Holm et al., 2005); however, these traits are correlated with the length of SPL (Serenius and Stalder, 2004, 2006; Serenius et al., 2008). The economic cost and ethical issues associated

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**Table 1.** Genetic markers tested for associations with reproduction traits in the Finnish Yorkshire and Landrace populations

Gene <sup>1</sup>	Forward/reverse primer (5' to 3')	PCR size	Chromosome: position <sup>2</sup>	Location <sup>3</sup>	SNP <sup>4</sup> : position <sup>5</sup>	Enzyme	Allele 1 <sup>6</sup>	Allele 2 <sup>6</sup>
<i>CPT1A</i>	AGCTCTAGTTGGTTGTGGAATC/ ACCTACGGGTAAGCGGGAAC	350	2: 2.5	Intron 11	T/C: 87	<i>Bst</i> NI	299, 51	212, 87, 51
<i>IGFBP1</i>	AAAATCAGGGTATCGGTCTTCA/ TCGTTCTGTGCCATCTACA	402/393	18: 48.7	Intron 2	CATCCCCAGG <sup>7</sup> : 252	<i>Bts</i> CI	302, 91	160, 125, 91, 26
<i>IGFBP3</i>	CAAGTCTCAAGCACGGACAC/ GCCAGGGCTCTCTCTTTT	438	18: 48.8	Intron 2	A/G: 114	<i>Bsa</i> HI	438	326, 112
<i>SLC22A5</i>	CCTGCCCTACATTTCTCATGG/ CACTCTGGGGCTTTCTTCAC	539	2: 12.2	Intron 9	C/G: 235	<i>Hae</i> III	374, 165	304, 165, 70
<i>COX2</i>	TCAATCGACCAGAGCAGAGA/ CGAGCTGTGGATCTTGAACA	555	9: 120	Intron 9	A/G: 172	<i>Bsr</i> BI	555	386, 169
<i>IGFBP2</i>	GGAACCTTGCTCACCCCTTGTC/ CAGGAAGAAGCCCAAGGTATG	361	6: 49	Intron 2	A/T: 135	<i>Mbo</i> II	346, 15	200, 146, 15
<i>IGFBP5</i>	CGCCTGAGATGAGACAGGA/ GGACAGGAGGGGTGAGAGG	312	14: 138.5	Intron 2	C/A: 107	<i>Ava</i> I	252, 60	147, 105, 60

<sup>1</sup>*CPT1A* = carnitine *O*-palmitoyltransferase I; *SLC22A5* = organic cation/carnitine transporter 2 (solite carrier family member 1), *OCTN2*; *COX2* = PG-endoperoxide synthase 2.

<sup>2</sup>The position (Mbp) of the gene from the beginning of the chromosome.

<sup>3</sup>The position of the SNP within the gene.

<sup>4</sup>The first base by convention is allele 1 and the second SNP is allele 2.

<sup>5</sup>The position (bp) of the SNP from the beginning of the PCR fragment.

<sup>6</sup>Allele descriptions correspond to detected band lengths (bp) on agarose gel.

<sup>7</sup>The CATCCCCAGG is a 10-bp insertion/deletion.

with a short SPL has increased the interest in selecting for traits affecting the SPL in pig breeding programs.

Polymorphisms within genes that lead to a longer lifespan and reproduction defects in model organisms have been tested for associations with survival and prolificacy traits in American Yorkshire and Landrace populations (Mote et al., 2009). Significant correlations with litter size have been detected using SNP within the genes *IGFBP1*, *SLC22A5* [organic cation/carnitine transporter 2 (solute carrier family member I), *OCTN2*], and *CPT1A* (carnitine *O*-palmitoyltransferase I). Furthermore, polymorphisms within the *CP-T1A* and *IGFBP3* genes were found to be associated with sow survival. These genes play an important biological role in female fertility: *IGFBP* modulates the action of IGF, which is involved in regulation of follicular function; *SLC22A5* plays an important role in placental carnitine transport; and *CPT1A* is essential to the production of ATP. We also studied the association of an SNP within the *COX2* (PG-endoperoxide synthase 2, also known as cyclooxygenase-2) gene, which catalyzes the initial steps in PG synthesis. This study reports the association of markers within 7 candidate genes with reproduction traits in the Finnish Yorkshire and Landrace pig populations.

## MATERIALS AND METHODS

Institutional Animal Care and Use Committee was not obtained for this study because already existing hair samples were used for genotyping. Only hair samples were collected from animals.

### Animal Material and DNA Samples

Hair samples of 280 Finnish Yorkshire and 271 Landrace boars were collected for DNA extraction. Boars were selected based on the number of tested daughters, with the minimum being 30 for Yorkshire and 47 for Landrace. The average number of daughters for Landrace boars was 143 and the average number was 141

for the Yorkshire boars. The roots of 1 to 2 hairs were lysed in lysis buffer [0.5 mg/mL of proteinase K and 2  $\mu$ L Mg-free PCR buffer (Dynazyme DNA polymerase, Finnzymes, Espoo, Finland) in distilled H<sub>2</sub>O] at 55°C for 60 min after proteinase K inactivation at 98°C for 10 min. For the genotyping of individual samples, 5  $\mu$ L of the lysate was added to the PCR reaction mixture [containing 1 unit of Dynazyme DNA polymerase (Finnzymes), 1.5 mM MgCl<sub>2</sub>, 0.2 mM deoxynucleotide 5'-triphosphate, and 10 pmol of each primer in a final concentration of 30  $\mu$ L] and subjected to 30 amplification cycles (94°C, 1 min; 58°C, 1 min; 72°C, 1 min) with some marker-specific changes in annealing temperature. Thereafter, PCR products were digested with 5 units of the appropriate restriction enzyme and incubated overnight at 37°C. Digested samples were analyzed on 5% agarose gels.

### Genetic Markers and Analyzed Traits

Intronic SNP within 7 candidate genes were analyzed: *IGFBP1*, *IGFBP2*, *IGFBP3*, *IGFBP5*, *CPT1A*, *COX2*, and *SLC22A5*. Detailed information on the SNP (positions, specific primers, and allele nominations) is given in Table 1. The analyzed traits for both breeds were age at first farrowing, first farrowing interval, second farrowing interval, total number of piglets born (litter size) in the first and later parities, number of stillborn piglets in the first and later parities, and piglet mortality between farrowing and weaning in the first and later parities. The sire phenotypes (EBV) were estimated based on their daughter evaluations ( $n > 30$ ). The mean EBV, minimum and maximum of the EBV, and SD are shown in Table 2.

### Statistical Analyses

For all genotyped boars, standardized BLUP breeding values of the studied traits were obtained from Faba Breeding (Vantaa, Finland) to determine the associations between genetic markers and prolificacy-related

**Table 2.** Traits analyzed in the Finnish Yorkshire and Landrace populations

Trait	Yorkshire			Landrace		
	Mean <sup>1</sup>	Minimum to maximum <sup>2</sup>	SD (SD population) <sup>3</sup>	Mean <sup>1</sup>	Minimum to maximum <sup>2</sup>	SD (SD population) <sup>3</sup>
Litter size, first parity	10.3	-2.4 to 1.7	0.69 (0.43)	10.7	-2.3 to 1.7	0.77 (0.49)
Litter size, later parities	11.9	-2.5 to 1.7	0.73 (0.43)	12.2	-2.5 to 1.7	0.78 (0.52)
No. of stillborn, first parity	1.2	-0.6 to 1.3	0.31 (0.18)	1.1	-0.6 to 1.3	0.28 (0.21)
No. of stillborn, later parities	1.2	-0.6 to 0.9	0.31 (0.17)	1.1	-0.6 to 1.0	0.27 (0.21)
Mortality between farrowing and weaning, first parity	1.0	-0.5 to 1.2	0.26 (0.18)	1.5	-0.8 to 1.5	0.33 (0.19)
Mortality between farrowing and weaning, later parities	1.5	-0.6 to 1.3	0.29 (0.16)	1.8	-0.9 to 1.4	0.34 (0.21)
Farrowing interval, first parity, d	176	-5 to 9	3.31 (2.58)	177	-7 to 13	4.17 (2.76)
Farrowing interval, later parities, d	168	-4 to 7	2.20 (1.63)	169	-6 to 9	2.71 (1.63)
Age at first farrowing, d	378	-18 to 30	9.32 (7.69)	369	-20 to 27	8.93 (8.21)

<sup>1</sup>Population phenotypic mean.

<sup>2</sup>Minimum and maximum values of the EBV expressed as a deviation from the population mean.

<sup>3</sup>SD of the EBV in the data. Values in parentheses indicate SD of the EBV of the total population.

traits. Associations with gene variants (SNP) and fertility traits were tested using the GLM procedure (SAS Inst. Inc., Cary, NC). The model included sire of the boar as a fixed effect and genotype as a covariate (AA = 2, AB = 1, BB = 0), where A (allele 1 in Table 1) and B (allele 2 in Table 1) are 2 alleles of each SNP. This modeling allows estimation of the allele substitution effect of allele A (later marked as “a”). Results with  $P < 0.05$  were considered significant. This method does not allow for multiple testing, but the focus of this article was to validate the previous positive findings (Mote et al., 2009), rather than to test a random set of SNP.

## RESULTS

Genotyping of Yorkshire and Landrace boars over all the tested markers revealed greater variation within the Finnish Landrace population than within the Finnish Yorkshire population for the studied markers (Table 3). Only 4 out of 7 markers within the studied genes were polymorphic (allele frequency  $>0.05$ ) in the Finnish Yorkshire population (Table 3). In the Finnish Landrace population, 6 out of 7 markers had a minor allele frequency greater than 0.05. Overall, these 2 breeds were considerably different in allele frequencies in all 7 markers. All SNP were in Hardy-Weinberg equilibrium.

### Marker Associations in the Finnish Yorkshire

In the Yorkshire population, the SNP in the *CPT1A* gene was associated with age at first farrowing. The substitution effect of allele 1 in *CPT1A* was  $-2.97$  d ( $P < 0.05$ ). Thus, the homozygote 22 sows were on average 5.94 d older at first farrowing than the homozygote 11 sows (Table 4). The frequency of the favorable allele 1 was 0.78.

The SNP in the *IGFBP3* and *IGFBP5* genes also showed a tentative association ( $P < 0.1$ ) with the farrowing intervals. There was an association of *IGFBP5* with the age at first farrowing and with farrowing intervals in the first and later parities. The beneficial allele for all associated traits with this marker was allele 2, with substitution effects of  $-3.22$ ,  $-1.27$ , and  $-0.85$  d ( $P < 0.1$ ), respectively (Table 4). The SNP within *IGFBP3* was associated with the farrowing interval in later parities. The substitution effect of allele 1 was  $-0.54$  d ( $P < 0.1$ ). Frequencies of the favorable alleles for *IGFBP3* and *IGFBP5* were 0.30 and 0.79, respectively (Table 3).

### Marker Associations in the Finnish Landrace

Four of the analyzed markers showed associations with reproduction traits in the Finnish Landrace population (Table 5). The most significant effect was detected with the SNP within *IGFBP2*: allele 1 was as-

**Table 3.** Genotype frequencies of SNP within the genes *IGFBP1*, *IGFBP2*, *IGFBP3*, *IGFBP5*, *SLC22A5*, *CPT1A*, and *COX2*<sup>1</sup> in the Landrace (LAN) and Yorkshire (Y) data

Genotype	<i>IGFBP1</i>		<i>IGFBP2</i>		<i>IGFBP3</i>		<i>IGFBP5</i>		<i>SLC22A5</i>		<i>CPT1A</i>		<i>COX2</i>	
	LAN	Y	LAN	Y	LAN	Y	LAN	Y	LAN	Y	LAN	Y	LAN	Y
11	196	40	115	61	134	21	7	4	68	0	176	119	16	0
12	66	98	117	2	80	81	66	45	111	2	9	60	68	3
22	4	79	22	0	6	100	186	80	56	56	0	12	90	73
Total	266	217	254	63	220	202	259	129	235	58	185	191	174	76
Minor allele frequency	0.14	0.41	0.32	0.02	0.21	0.30	0.15	0.21	0.47	0.02	0.02	0.22	0.29	0.02

<sup>1</sup>*SLC22A5* = organic cation/carnitine transporter 2 (solute carrier family member 1), *OCTN2*; *CPT1A* = carnitine *O*-palmitoyltransferase 1; *COX2* = PG-endoperoxide synthase 2, also known as cyclooxygenase-2.

sociated with a smaller number of stillborn piglets in the first and later parities than was allele 2 ( $a = -0.09$  piglets;  $P < 0.01$  in the first and later parities). Allele 1 of *IGFBP2* also had a trend toward a smaller litter size in later parities ( $a = -0.16$ ;  $P < 0.1$ ). A more significant effect on the litter size for later parities was detected with an SNP within the gene *COX2*. The additive effect of allele 1 was 0.30 ( $P < 0.05$ ), indicating a 0.6-piglet larger litter size for 11 homozygote sows compared with 22 sows. Allele 1 of *IGFBP1* also had a significant effect on litter size ( $a = -0.26$ ;  $P < 0.05$ ) and the number of stillborn piglets ( $a = -0.11$ ;  $P = 0.038$ ) in later parities and had tentative significance for an effect in litter size in the first parity ( $-0.21$ ;  $P < 0.1$ ). Furthermore, the polymorphism within *IGFBP5* indicated a trend toward significance for an effect in litter size (Table 5). The beneficial allele for litter size in the genes *IGFBP1*, *IGFBP2*, and *IGFBP5* was allele 2, with frequencies of 0.14, 0.32, and 0.85, respectively, and beneficial allele for litter size in *COX2* was allele 1, with a frequency of 0.29 (Table 5). The favorable allele of these genes for litter size had a negative effect on the number of stillborn piglets. However, the favorable effect on litter size seemed to be twice as large as the unfavorable effect on the number of stillborn piglets; thus, the number of weaned piglets increased.

## DISCUSSION

Even though SPL is not very heritable (Serenius and Stalder, 2004), its economic importance in pig production highlights the potential benefits of identifying markers for the selection of high-performance sows. Initial analysis of American Yorkshire and Landrace populations indicated that several markers were significantly associated with either sow survival or reproductive traits (Mote et al., 2009). Markers selected from these preliminary data were evaluated in 2 Finnish pig populations. Our data included AI boars with relatively reliable EBV for reproduction traits based on their daughter records. The reliability of the results was ensured by applying the 30-daughter limit for boar selection. However, the limited number of boars tested and the low variance in some of the analyzed SNP diminished the power of the analysis and restricted the amount of information that could be generated from the data. Irrespective of these constraints and limita-

tions, it was possible to detect significant effects of specific gene variants on reproduction traits.

In a recent association analysis (Mote et al., 2009), the most promising markers for sow survival were within genes C-C chemokine receptor 7 (*CCR7*) and *CP-T1A*. The *CPT1A* gene codes for an enzyme involved in the transport of certain long-chain fatty acids into mitochondria, a process essential to the production of ATP. Tissue energy balance is one of the most important factors influencing reproduction efficiency in the sow, and it is possible that energy status is associated with variation in *CPT1A* activity. Our results support the potential of the *CPT1A* gene as a possible marker for farrowing age. This study demonstrated that Finnish Yorkshire gilts carrying allele 1 of this gene were 3 d younger at first farrowing than gilts carrying the other allele. However, the beneficial allele 1 was already the major allele in this population, diminishing the entire value of this marker in marker-assisted selection.

Quantitatively, the most relevant effect was detected within the Landrace population: the sows carrying allele 1 of the *COX2* gene had 0.3 piglets more in later parities than sows carrying the other allele. The beneficial allele was also the minor allele (frequency of 0.29) in the Finnish Landrace population. The metabolism of cyclooxygenase is the initial step in PG synthesis. It is generally considered that COX1 has more of a housekeeping function, whereas COX2 is induced by a variety of stimuli (Breyer et al., 2000; Smith et al., 2000). The synthesis of PG via the activity of COX2 plays an important role in embryo hatching (Huang et al., 2003, 2004), blastocyst development (Pakrasi and Jain, 2007), and implantation (Huang et al., 2007; Pakrasi and Jain, 2008). In the pig, polymorphisms within the *COX2* gene may influence litter size via the effects on PG production that affect early embryonic development.

The minor alleles (allele 2) of the SNP within the genes *IGFBP1* and *IGFBP2* had positive effects on litter size in later parities of Finnish Landrace sows. This allele also increased the number of stillborn piglets, probably because of the larger litter size, but the beneficial effect on litter size was greater than the negative effect on the number of stillborn piglets. Thus, these markers can be seen as useful candidates for marker-assisted selection to increase litter size in the Finnish Landrace population. In addition, the marker within

**Table 4.** Estimates of additive genetic effects (a) of reproduction traits for Finnish Yorkshire<sup>1</sup>

Trait	<i>CPT1A</i> (n = 191)			<i>IGFBP3</i> (n = 202)			<i>IGFBP5</i> (n = 129)		
	a	SE	P-value	a	SE	P-value	a	SE	P-value
Age at first farrowing, d	-2.97	1.33	0.03	NS	NS	NS	3.22	1.79	0.08
Farrowing interval, first parity, d	NS	NS	NS	NS	NS	NS	1.27	0.68	0.05
Farrowing interval, later parities, d	NS	NS	NS	-0.54	0.31	0.08	0.85	0.44	0.06

<sup>1</sup>*CPT1A* = carnitine *O*-palmitoyltransferase I; n = number of animals; a = additive effects represent the effect of allele 1; NS = not significant.

**Table 5.** Estimates of the additive effects (a) of reproduction traits for Finnish Landrace<sup>1</sup>

Trait	<i>COX2</i> (n = 174)			<i>IGFBP1</i> (n = 266)			<i>IGFBP2</i> (n = 254)			<i>IGFBP5</i> (n = 259)		
	a	SE	P-value	a	SE	P-value	a	SE	P-value	a	SE	P-value
Litter size, first parity	NS	NS	NS	-0.21	0.12	0.09	NS	NS	NS	-0.18	0.10	0.07
Litter size, later parities	0.30	0.15	0.05	-0.26	0.13	0.04	-0.16	0.09	0.09	NS	NS	NS
No. of stillborn, first parity	NS	NS	NS	NS	NS	NS	-0.09	0.03	0.01	NS	NS	NS
No. of stillborn, later parities	NS	NS	NS	-0.11	0.05	0.04	-0.09	0.03	0.01	-0.07	0.04	0.05
Mortality between farrowing and weaning, first parity	NS	NS	NS	NS	NS	NS	NS	NS	NS	-0.07	0.04	0.10

<sup>1</sup>*COX2* = PG-endoperoxide synthase 2; n = number of animals; a = additive effects represent the effect of allele 1; NS = not significant.

the *IGFBP5* gene showed associations with traits affecting the litter size. However, the beneficial allele 2 is already common (frequency of 0.85) in the Finnish Landrace population. The *IGFBP5* gene was also associated with farrowing intervals in the Finnish Yorkshire. As in the Landrace population, the beneficial allele 2 was also the major allele in this population (frequency of 0.79); therefore, selection for this marker would not have a major impact on these populations. Another *IGFBP* marker demonstrating a moderate association with sow survival was recently detected in the *IGFBP3* gene (Mote et al., 2009). In the Finnish Yorkshire population, this marker was moderately associated with farrowing interval in later parities (0.5-d shorter interval for sows carrying allele 1).

It is conceivable that the *IGFBP* gene could affect the litter size and survival of sows through IGF-I and IGF-II, which are local regulators of follicular function with a possible role in the regulation of follicular development and intraovarian sex steroid production (Adashi et al., 1985; Stadtmauer et al., 1998). The *IGFBP1* protein is involved in regulating the menstrual cycle, ovulation, implantation, and fetal growth (Fowler et al., 2000). In humans, *IGFBP1* serum concentrations are decreased in polycystic ovarian syndrome, which causes menstrual disturbance and anovulatory infertility (Fowler et al., 2000). Conversely, elevated concentrations of *IGFBP1* cause poor implantation, uterine receptivity, and subsequent miscarriage (Fowler et al., 2000). The concentrations of *IGFBP3* have been shown to be reduced in women experiencing abnormal menstrual cycles (de Boer et al., 1997).

The effect of the *IGFBP2* gene on the number of stillborn piglets found in the Landrace population may be derived from the function of *IGFBP2* in fetal development. The *IGFBP2* gene is expressed at increased concentrations (Han et al., 1996; van Kleffens et al., 1999) and is known to play an important role in prenatal development and cell movement (Wang et al., 2006). Knockdown of *IGFBP2* results in developmental delay, growth retardation, and cardiovascular disruption in Zebrafish embryos (Wood et al., 2005). Based on previously reported evidence, the *IGFBP* genes appear to be good candidate markers for reproductive performance and may affect sow survival via their actions in the female reproductive system.

In conclusion, the current data suggest that the selection of markers within candidate genes could be used to improve SPL. In the Finnish Landrace population, markers within the *IGFBP1*, *IGFBP2*, *IGFBP5*, and *COX2* genes are potentially useful in marker-assisted selection for litter size. In the Finnish Yorkshire population, markers within the *CPT1A*, *IGFBP3*, and *IGFBP5* genes are potentially useful for reducing farrowing intervals. The *CPT1A* gene appears to be a particularly promising candidate marker for sow survival because it was also found in the American pig populations (Mote et al., 2009). Similarities in associations between this and previous evaluations suggest that, at least to some



extent, marker information for different pig populations could possibly be used across breeds. However, identification of polymorphisms and their impact on desirable traits need to be validated for each population.

## LITERATURE CITED

- Adashi, E. Y., C. E. Resnick, A. J. D'Ercole, M. E. Svoboda, and J. J. Van Wyk. 1985. Insulin-like growth factors as intraovarian regulators of granulosa cell growth and function. *Endocr. Rev.* 6:400–420.
- Breyer, R. M., C. R. Kennedy, Y. Zhang, and M. D. Breyer. 2000. Structure-function analyses of eicosanoid receptors. Physiologic and therapeutic implications. *Ann. N. Y. Acad. Sci.* 905:221–231.
- de Boer, J. A., J. Schoemaker, and E. A. van der Veen. 1997. Impaired reproductive function in women treated for growth hormone deficiency during childhood. *Clin. Endocrinol. (Oxford)* 46:681–689.
- Ehlers, M. J., J. W. Mabry, J. K. Bertrand, and K. J. Stalder. 2005. Variance components and heritabilities for sow productivity traits estimated from purebred versus crossbred sows. *J. Anim. Breed. Genet.* 122:318–324.
- Engblom, L., N. Lundeheim, A. M. Dalin, and K. Andersson. 2007. Sow removal in Swedish commercial herds. *Livest. Sci.* 106:76–86.
- Engblom, L., N. Lundeheim, E. Strandberg, M. del P. Schneider, A. M. Dalin, and K. Andersson. 2008. Factors affecting length of productive life in Swedish commercial sows. *J. Anim. Sci.* 86:432–441.
- Fowler, D. J., K. H. Nicolaidis, and J. P. Miell. 2000. Insulin-like growth factor binding protein-1 (IGFBP-1): A multifunctional role in the human female reproductive tract. *Hum. Reprod. Update* 6:495–504.
- Han, V. K., D. G. Matsell, P. J. Delhanty, D. J. Hill, S. Shimasaki, and K. Nygard. 1996. IGF-binding protein mRNAs in the human fetus: Tissue and cellular distribution of developmental expression. *Horm. Res.* 45:160–166.
- Holm, B., M. Bakken, O. Vangen, and R. Rekaya. 2005. Genetic analysis of age at first service, return rate, litter size, and weaning-to-first service interval of gilts and sows. *J. Anim. Sci.* 83:41–48.
- Huang, J. C., J. S. Goldsby, and W. S. Wun. 2004. Prostacyclin enhances the implantation and live birth potentials of mouse embryos. *Hum. Reprod.* 19:1856–1860.
- Huang, J. C., W. S. Wun, J. S. Goldsby, I. C. Wun, S. M. Falconi, and K. K. Wu. 2003. Prostacyclin enhances embryo hatching but not sperm motility. *Hum. Reprod.* 18:2582–2589.
- Huang, J. C., W. S. Wun, J. S. Goldsby, I. C. Wun, D. Noorhasan, and K. K. Wu. 2007. Stimulation of embryo hatching and implantation by prostacyclin and peroxisome proliferator-activated receptor  $\delta$  activation: Implication in IVF. *Hum. Reprod.* 22:807–814.
- Lucia, T. Jr., M. N. Corrêa, J. C. Deschamps, I. Bianchi, M. A. Donin, A. C. Machado, W. Meincke, and J. E. M. Matheus. 2002. Risk factors for stillbirths in two swine farms in the south of Brazil. *Prev. Vet. Med.* 53:285–292.
- Mote, B. E., K. J. Koehler, J. W. Mabry, K. J. Stalder, and M. F. Rothschild. 2009. Identification of genetic markers for productive life in commercial sows. *J. Anim. Sci.* 87:2187–2195.
- Pakrasi, P. L., and A. K. Jain. 2007. Evaluation of cyclooxygenase 2 derived endogenous prostacyclin in mouse preimplantation embryo development in vitro. *Life Sci.* 80:1503–1507.
- Pakrasi, P. L., and A. K. Jain. 2008. Cyclooxygenase-2-derived endogenous prostacyclin reduces apoptosis and enhances embryo viability in mouse. *Prostaglandins Leukot. Essent. Fatty Acids* 79:27–33.
- Roehe, R., and B. W. Kennedy. 1995. Estimation of genetic parameters for litter size in Canadian Yorkshire and Landrace swine with each parity of farrowing treated as a different trait. *J. Anim. Sci.* 73:2959–2970.
- Serenius, T., and K. J. Stalder. 2004. Genetics of length of productive life and lifetime prolificacy in the Finnish Landrace and Large White pig populations. *J. Anim. Sci.* 82:3111–3117.
- Serenius, T., and K. J. Stalder. 2006. Selection for sow longevity. *J. Anim. Sci.* 84(Suppl):E166–E171.
- Serenius, T., K. J. Stalder, and R. L. Fernando. 2008. Genetic associations of sow longevity with age at first farrowing, number of piglets weaned, and wean to insemination interval in the Finnish Landrace swine population. *J. Anim. Sci.* 86:3324–3329.
- Smith, W. L., D. L. DeWitt, and R. M. Garavito. 2000. Cyclooxygenases: Structural, cellular, and molecular biology. *Annu. Rev. Biochem.* 69:145–182.
- Stadtmaier, L., A. Vidali, S. R. Lindheim, and M. V. Sauer. 1998. Follicular fluid insulin-like growth factor-I and insulin-like growth factor-binding protein-1 and -3 vary as a function of ovarian reserve and ovarian stimulation. *J. Assist. Reprod. Genet.* 15:587–593.
- van Kleffens, M., C. A. H. Groffen, N. F. J. Dits, D. J. Lindenbergh-Kortleve, A. G. P. Schuller, S. L. Bradshaw, J. E. Pintar, E. C. Zwarthoff, S. L. S. Drop, and J. W. van Neck. 1999. Generation of antisera to mouse insulin-like growth factor binding proteins (IGFBP)-1 to -6: Comparison of IGFBP protein and messenger ribonucleic acid localization in the mouse embryo. *Endocrinology* 140:5944–5952.
- Wang, G. K., L. Hu, G. N. Fuller, and W. Zhang. 2006. An interaction between insulin-like growth factor-binding protein 2 (IGFBP2) and integrin  $\alpha 5$  is essential for IGFBP2-induced cell mobility. *J. Biol. Chem.* 281:14085–14091.
- Wood, A. W., P. J. Schlueter, and C. Duan. 2005. Targeted knock-down of insulin-like growth factor binding protein-2 disrupts cardiovascular development in Zebrafish embryos. *Mol. Endocrinol.* 19:1024–1034.