

Candidate Genes Associated with Sow Longevity

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Introduction

The economic efficiency of swine operations is always a topic of discussion for pork producers and allied industries especially now when feed grain prices are being pushed higher as the demand for bio-fuels increases. However, many factors outside of feed prices influence the breakeven costs and thus economic efficiency for swine operations. Of those additional factors, sow herd performance is typically one of the most important categories. When producers talk about sow herd performance, most producers think about farrowing rate, pigs weaned per litter, or generally the number of pigs weaned per sow per year. We suggest that when talking about sow herd performance we need to take a more holistic view of the sow herd and incorporate sow longevity, more accurately called sow productive life (SPL) into the profit equation. The growing percentage of sows leaving the farm before they recuperate their investment cost has been increasing as of late. These sows are being involuntarily removed from the farm for reasons such as reproductive failure, locomotion failure, and death. This early removal or premature death increases sow replacement rates and has both economic and welfare consequences to the swine industry.

PigCHAMP™ records from 1998 through 2005 show an increasing trend in the death rate from 5.9% in 1998 to 8.94% in 2005 (see figure 1). The same records show that the culling rate is more variable but was at an unprecedented 51% in the most recent data available (see figure 2) (PigCHAMP™, 2006). The high culling rate seen in 2005 could be generated in part by producers taking advantage of profits and restocking their herds. High replacement rates driven by involuntary culling infer that producers are required to lower their selection intensity to maintain herd size. High replacement rates can cause a downward spiral in herd performance in systems with undersized multiplication efforts, since a heavy demand for replacement gilts may result in sub-standard gilts or gilts not properly developed entering the breeding herd. Improving SPL would help alleviate the pressures placed on multiplication herds allow for gilts to be selected more on quality than simply on quantity.

Using standard net present value calculations for a farrow to finish operation such as a purchase price of \$200 per gilt, an average number born alive/litter of 10.2, 8.5 pigs sold per litter, and an average price of 44 \$/CWT for market hogs, an increase in net present value of \$77.38 per sow could be realized if an operation could increase litters per sow from three to four (Stalder *et al.*, 2000). Thus an increase in average parity of just one tenth would increase the profit by \$0.23 for every market hog sold from the operation. For a farrow to wean operation, using the same purchase price, number born alive/litter with an average price per head of \$28 for segregated early weaned (SEW) pigs, and marketing 9 pigs per litter, the net present value per sow would increase by \$45.59 if a sow would have four parities instead of three (Stalder *et al.*, 2003). An increase in the average parity of one tenth would increase the profit of a farrow to wean

operation by \$0.13 per pig sold. Taken as a whole, a one tenth increase in average parity would raise the profit by approximately \$15,000,000 per year in the U.S. alone.

Limited studies have been performed researching productive life in pigs. Most studies were only conducted up to either sow parity three (Rozeboom *et al.*, 1996) or four (Moeller *et al.*, 2004) allowing for some understanding as to why sows leave the herd in early parities, but never accounting for reasons why other sows can thrive well beyond four parities. These previous studies revealed significant line interactions on sow longevity and noted that further studies should be conducted to identify the genetic mechanisms associated with sows having increased numbers of parities. Scientists have begun identifying genes in model organisms that play a role in the aging process and longevity itself (Hasty *et al.*, 2003; Hekimi and Guarente, 2003; Longo and Finch, 2003; Simon *et al.*, 2003; and Tatar *et al.*, 2003). Research has shown that yeast and *C. elegans* (nematode) share a number of homologous genes in the so called “longevity pathways” and that increased longevity is often the result of inactivation of the pathways that promote growth and a reduction in oxidative damage and other forms of stress (Longo and Finch, 2003). Similar results have also been shown in the fruit fly such as mutations in the insulin / IGF-1 pathways extending lifespan. The overriding theme gathered from studying these genes is their role in reduction of caloric intake that enables animals to live longer as well as reducing susceptibility to disease in the aging process. However, some research has indicated that leaner gilts have the tendency to be removed from the herd earlier (Stalder *et al.*, 2005).

The hypothesis that guides this comparative genomics research is that the similarity between functions of certain genes in the various species studied suggests that the same genes may be associated with SPL in the pig. It is possible that genes associated with increasing simple lifespan in model organisms might not be correlated with SPL since it is more than a measure of longevity. It is also plausible that alleles associated with increased fatness could be more beneficial to SPL as sows with more backfat have shown the tendency for having a longer SPL or remain in the breeding herd for a longer period of time. Additionally, other genes more specific to swine may need to be isolated and examined. Genes studied include those that function as antioxidants, are involved in reproduction, and are components of the insulin pathway that regulate food intake. The identification of molecular markers associated with the length of a sow’s productive life would allow breeders to use marker assisted selection to select individuals, based on the animal’s genotype, at early ages that would have the best opportunity to remain in the herd far beyond the current average sow.

Animal Populations

We have used several distinctly different populations throughout this study. The first population that was analyzed consisted of approximately 1000 commercial sows where half were younger than parity four and the remaining were parity six or greater. The only phenotypic data collected on these animals was the number of parities each sow generated. The second population consisted of approximately 200 sires. The information collected and used in the analysis of this population was the EBVs based on phenotypes from a minimum of ten daughters per sire. The third population consisted of commercial females from varying parities and was primarily used to evaluate reproduction performance and thus contained reproductive data. The previous three populations were primarily mid 1990s genetics and no one population contained all the

phenotypic records necessary to completely evaluate the candidate genes for SPL. Therefore, we felt it necessary to sample current genetics where all phenotypic records were collected from one population which would enable accurate analysis of the current state of commercial sow industry. The fourth population used here to validate the earlier results of Mote *et al.*, 2005, consisted of 2,000 commercial crossbred females composed of two parent lines where heterosis is maximized. Commercial crossbred females were selected for this study, since these females are the objective of an effective breeding program seeking to improve maternal line traits and are where traits like SPL should be evaluated. Equal numbers of sows were randomly sampled from each of the two crossbred lines utilized in this study. The experimental sows were randomly sampled from three farms that contained a total of 11,400 sows in their production system. Half (1000 animals) of the sampled sows have had greater than 5 parities and serve as the selected group and the remaining half (1000 animals) are replacement gilts and served as the unselected group. Equal numbers of selected and unselected females were sampled from each of three farms. Two of the farms utilized one sow commercial line (Line A) and the other farm utilized a second commercial line (Line B). At the time of the last data sampling (June 1, 2006), 201 of the young females had already been removed from the herd with 75 females failing to produce 1 litter, 112 failing after their first litter, and 14 failing after their second litter (at this time point, not all females had sufficient time to produce their second litter).

Data Collection

Ear tissue was sampled from all sows using the TypiFix™ ear tag from Agrobiogen. This system allows simultaneous identification and tissue collection to prevent sample misidentification. DNA was isolated from tissue samples using the Nexttec™ DNA isolation system (Nexttec GmbH Biotechnologie) adhering to the manufacture's protocol. PigCHAMP™ records were obtained for all sows at time of tissue collection. The litter records will be resampled approximately every six months so that gilts in the unselected group have sufficient time to farrow additional litters and / or be culled from the breeding herd.

Statistical analysis

Sows' genotypes were analyzed using Fisher's exact test to identify if there was a significant deviation in frequency for the gene markers between the select and unselected sow groups for sows remaining in the herd until the fifth parity. Contrast statements were used to identify the differences between genotypes and to determine if the gene had an additive or dominant effect. The PROC MIXED procedure of SAS was used to determine genotype effects on the total number of pigs born alive for the sows using line, farm, group (select vs. unselect) or number of parities, and the sow's genotype as fixed effects. Additive and dominance effects were estimated for the total number of pigs born alive.

Results and Discussion

To date, nineteen genes have been studied throughout this research project. At the onset of this project, gene markers were first tested for association in populations 1 and 2 before they were allowed to be tested in populations 3 and 4 for genes believed to be involved in reproduction or in population 4 only if the gene marker did not show association for reproduction but did show

association for other SPL traits. Eight genes showed no association with any SPL trait and have been dropped from the study. Seven genes have been tested for association in all pertinent populations while complete analysis has yet to be completed on four gene markers. The seven gene markers that have been fully analyzed in all pertinent populations are: *insulin-like growth factor binding protein 1 (IGFBP1)*, *insulin-like growth factor binding protein 2 (IGFBP2)*, *insulin-like growth factor binding protein 3 (IGFBP3)*, *insulin-like growth factor binding protein 5 (IGFBP5)*, *carnitine O-palmitoyltransferase I (CPT1A)*, *organic cation/carnitine transporter 2 (Solute carrier family 22 member 5; SLC22A5)*, and *cyclooxygenase-2 (COX2)*. These genes were targeted due to their role in the insulin/IGF-1 pathways which has been implicated in model organisms for regulating feed intake and increasing lifespan, their known function in reproduction, or because they are implicated in both roles.

The results for Fisher's exact test concluded that there were significant genotype differences ($P < .01$) for the gene markers of *IGFBP1* (figure 3), *IGFBP3* (figure 4), *CPT1A* (figure 5), and *SLC22A5* (figure 6) between the select and unselected groups indicating that there are significant genotypic effects for remaining in the herd until the fifth parity. Additionally for *IGFBP1*, the same genotype favored for greater longevity also had a significant association with the total number of pigs born alive over the sow's lifetime ($P < .04$) (figure 7). Therefore a sow with the beneficial genotype for *IGFBP1* will not only have a greater probability of staying in the herd until parity 5, but will also produce an additional 1.5 pigs while doing so. The frequency for *IGFBP1* was 0.3 for the 11 genotype and 0.18 for the 22 genotype (favored genotype) in the select group and 0.36 for the 11 genotype and 0.14 for the 22 genotype in the unselected group which also demonstrates that selection is possible on this gene marker. *CPT1A* was significantly associated ($P < .05$) with the number of pigs born alive (NBA) but only after the third parity with effects as large as 0.7 of a live pig per litter. The favored genotype for pigs born alive is also the favored genotype for sows remaining in the herd until the fifth parity. *IGFBP2* showed a significant association with NBA (figure 8). The genotype that is favored for remaining in the herd shows larger litters in the first two parities with no significant advantage in the third parity, but is then the unfavorable genotype from parity four on. Production goals for the pig production company and genetic company must be evaluated before the use of this genetic marker is implemented into marker-assisted selection (MAS).

Sampling of pigs was from large synthetic lines, so it is unlikely that a founder effect exists but it cannot be completely excluded as a cause for the differences in genotypic frequencies between the select and unselected group. In addition, because sampling consisted of animals from two distinct lines, from three farms, and because a large number of sires are used in traditional multiplication systems, a discrepancy in genotypic frequency caused by a founder effect should be minimized if it exists at all.

Conclusions

Genetic markers associated with components of SPL have been demonstrated using parent animals recently sampled from commercial operations directly addressing the problem of SPL seen in the swine industry today. Four genes (of the completely analyzed 15 genes) (*IGFBP1*, *IGFBP3*, *CPT1A*, and *SLC22A5*) showed significant association with a sows ability to remain in the herd until her fifth parity. Three genes (*IGFBP1*, *IGFBP2*, and *CPT1A*) showed

significant associations with reproductive traits during the sow's productive lifetime. All significant genes have allele frequencies that are favorable for use in MAS. These results are evidence that there are genes causing variation in sow productive life and give promise to the use of marker assisted selection to improve sow productive life.

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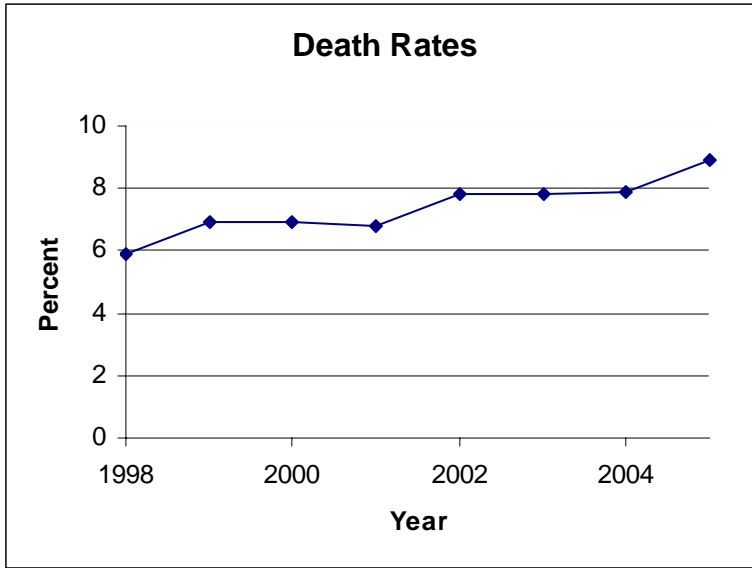


Figure 1.
This figure shows the increasing death rates in commercial swine operations using PigCHAMP™ since 1998.

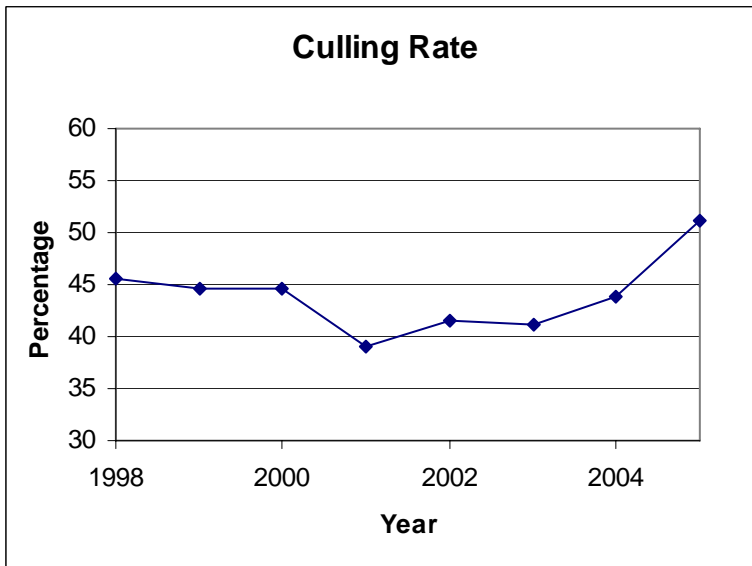


Figure 2.
This figure shows the variable culling rate in commercial swine units since 1998.

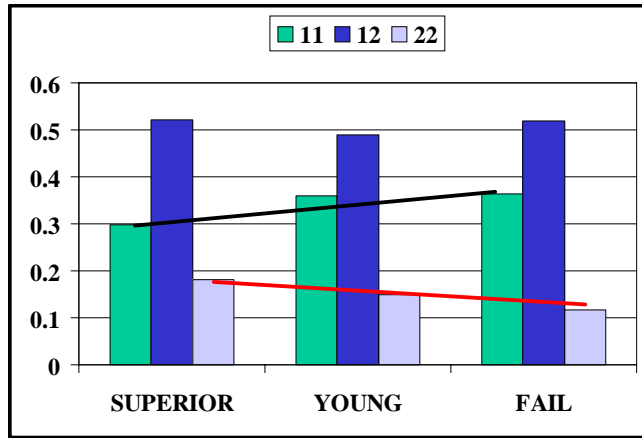


Figure 3.

This figure shows the genotypic frequencies for *IGFBP1* of the sows that had 5+ parities (superior), the gilts (young), and the gilts that have been removed from the herd (fail). The trend lines are to illustrate the decreasing frequency of the 22 genotype in the young and fail groups.

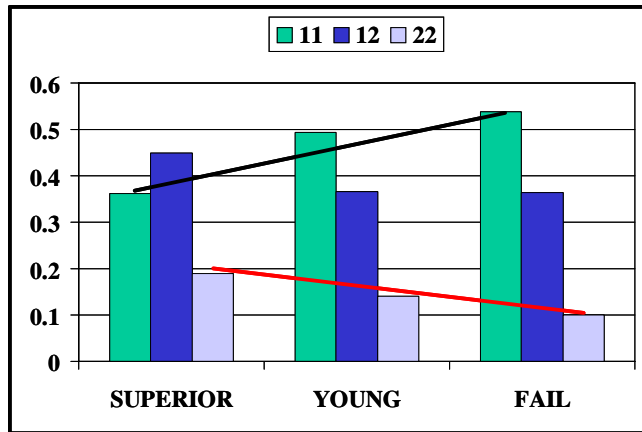


Figure 4.

This figure shows the genotypic frequencies for *IGFBP3* of the sows that had 5+ parities (superior), the gilts (young), and the gilts that have been removed from the herd (fail). The trend lines are to illustrate the decreasing frequency of the 22 genotype in the young and fail groups.

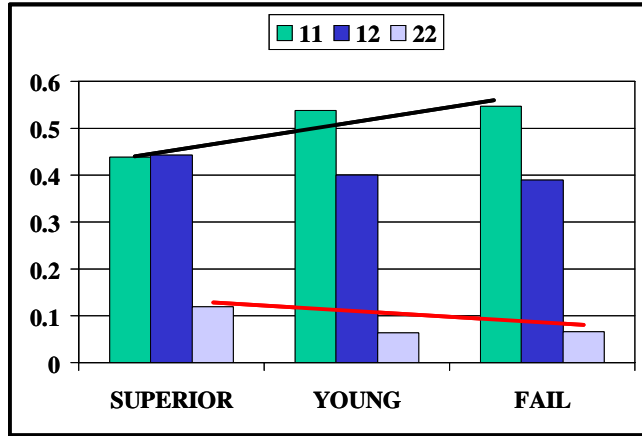


Figure 5.

This figure shows the genotypic frequencies for *CPT1A* of the sows that had 5+ parities (superior), the gilts (young), and the gilts that have been removed from the herd (fail). The trend lines are to illustrate the decreasing frequency of the 22 genotype in the young and fail groups.

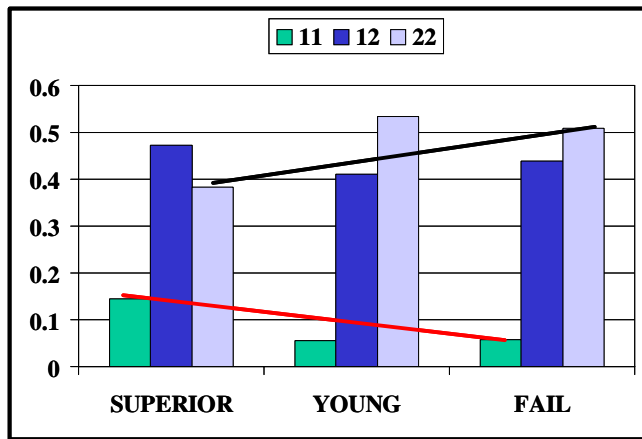


Figure 6.

This figure shows the genotypic frequencies for *SLC22A5* of the sows that had 5+ parities (superior), the gilts (young), and the gilts that have been removed from the herd (fail). The trend lines are to illustrate the decreasing frequency of the 11 genotype in the young and fail groups.

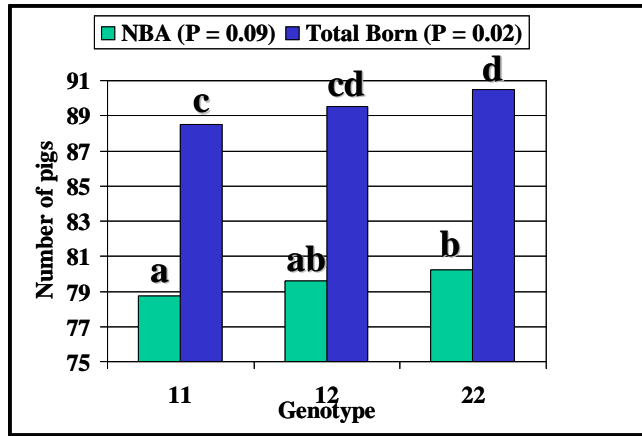


Figure 7.

This figure shows LS Means for the three genotype classes of IGFBP1 for both the number born alive (NBA) and the total pigs born.

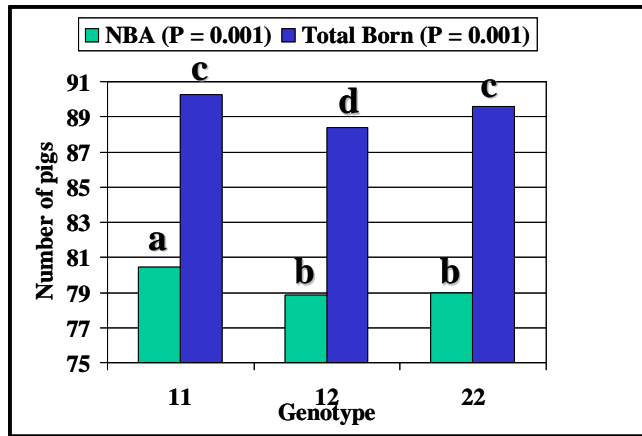


Figure 8.

This figure shows LS Means for the three genotype classes of IGFBP2 for both the number born alive (NBA) and the total pigs born.