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Effect of DNA Markers in Nebraska Selection Lines

Rodger Johnson¹

Summary

DNA from 57 generation-28 boars that had sired progeny in the NE selection and control lines was submitted to GeneSeek Inc., where genotypes for eight Single Nucleotide Polymorphic Markers (SNPs) affecting economic traits in pigs were determined. Three markers are reported to be associated with growth and composition of growth, three with meat quality, and two with number of live pigs per litter. Frequencies of marker alleles were estimated in two selection lines and in their respective controls to determine whether selection had increased the frequencies of alleles associated with increased performance. Relationships of boar marker genotype with growth, backfat, and loin eye area were studied by regressing both boar phenotype and progeny phenotype on the number of favorable alleles in the boar's genotype. Frequencies of markers affecting reproduction (ESR and EPOR) were inconsistent with the selection background of the lines. Frequencies of alleles of CCKAR and MC4R, markers that affect growth and composition of growth, in selection and control lines are consistent with observed selection responses, suggesting that the allele that decreased backfat was being selected for. Regression analyses were consistent with that result. There was little evidence there had been selection for meat quality markers in these lines. The study demonstrated that selection for markers in some populations may not produce desired responses.

Introduction

A large number of genetic markers associated with economic traits in pigs have been identified. But for several reasons, relatively few of them are being used to enhance response to selection in commercial populations. Genes are DNA sequences within

chromosomes that contain the code (order of nucleotides) to produce a specific protein. Markers are not the entire gene but rather are very small segments of the chromosome where differences among individuals can be identified. There are many different types of markers, but most markers used today are **single-nucleotide polymorphism (SNP, pronounced snip)** which is a DNA sequence variation occurring when a single nucleotide – A, T, C, or G – differs among individuals or between the paired chromosomes of an individual. For example, two sequenced DNA fragments from different individuals, AAGCCTA to AAGCTTA, contain a difference in a single nucleotide. Thus, there are two alleles (C and T) for this marker.

Some markers are within the coding region of a gene with a causative effect on an economic trait. But most markers are not in coding regions of causative genes but are on the same chromosome positioned close to a causative gene. In those cases, the gene and the marker are linked and they tend to be inherited together. Then, marker genotype tells us something about whether the individual contains a desirable copy of the causative gene. Thus, the value of a marker depends on the linkage relationship between the causative gene and the marker. Markers loosely linked with causative genes are of limited value. Even when closely linked, which marker allele is linked with the desirable allele of the causative gene may differ among populations. As a result, selection for a particular marker allele to enhance response in an economic trait may be effective in one population, but ineffective in another.

Even if markers are within causative genes, the effectiveness of selecting on them may differ among populations because average gene effects in the population are frequency dependent. Genes have their greatest average effect and selection for desirable alleles produces the greatest response when alternative alleles

(different forms of the gene) have intermediate frequencies, between 0.25 and 0.75. If the better allele is at high frequency, then little extra increase in performance from pushing its frequency even closer to one is available. When the better allele has low frequency, it is rare and variation at that gene locus may explain very little of the genetic variation in the trait. However, long-term selection opportunities are greatest when initial frequency of desirable alleles is low. Even when alleles of causative genes have intermediate frequencies, their effects may be relatively small in proportion to the total genetic variation for the trait, and selecting on these markers may cause only small changes in performance. Thus, many questions about which markers to use and their value in selection programs still exist.

Long-term selection in pigs at the University of Nebraska for increased reproduction, increased growth, and decreased backfat has produced lines that differ from randomly selected control lines by more than 50% in litter size and 12 to 15% in rate of growth and backfat thickness. Frequencies of marker alleles are expected to differ between selection and control lines if genetic markers are associated with these traits. Previous research identified more than 30 regions of the chromosomes that harbor genes affecting both reproduction and growth traits in these lines, but positions of causative genes were not identified precisely enough (close linkage was not established) to use these markers in selection.

A few markers in the pig genome have been researched in great depth, and there is a high degree of confidence in their effects on the discovery populations. These markers are either within the DNA sequence of causative genes or very tightly linked with causative genes. GeneSeek Inc., Lincoln, Neb., provides genotyping services for eight markers whose effects on reproduction, growth, or pork quality are estimated quite precisely. None

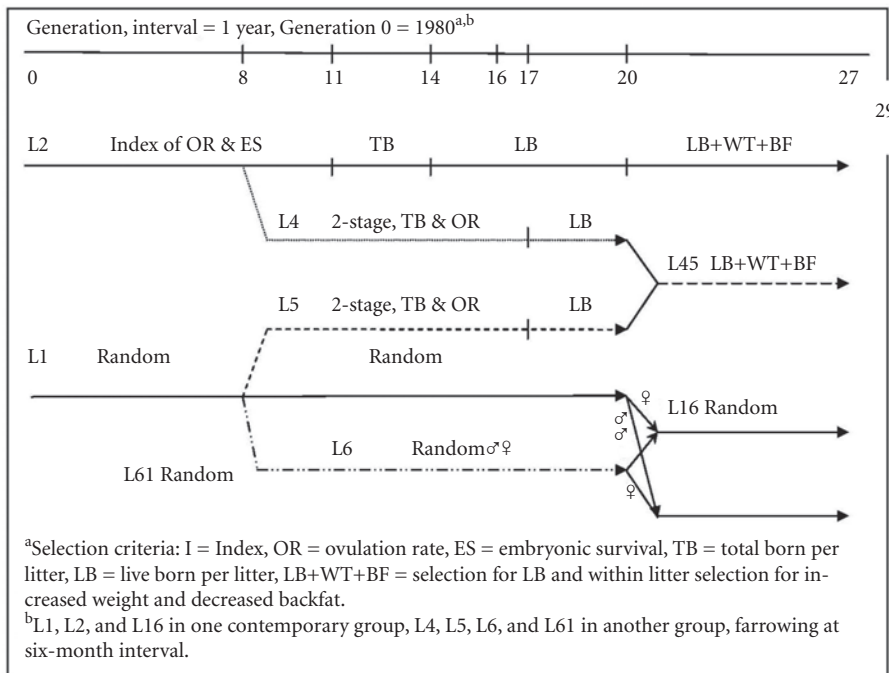


Figure 1. Evolution of the Nebraska selection lines.

of these markers were identified in Nebraska selection lines. The purpose of this report is to estimate allele frequency and marker effects in the Nebraska selection lines for the panel of genes for which GeneSeek Inc. provides commercial genotyping services.

Methods

The Nebraska lines include a selection and control line in each of a summer (Lines 2 and 16) and winter (Lines 45 and 61) farrowing group. All lines derived from the same base population, a Large White x Landrace cross made in 1979. Evolution of the lines is illustrated in Figure 1. Line 2 was selected 11 generations for an index of ovulation rate and embryonic survival, nine generations for increased total born or live born per litter, and nine generations for increased live born per litter, increased 180-day weight, and decreased backfat thickness. Line 1, the control line in the summer group through generation 20, was selected randomly. Three additional lines (Lines 4, 5, and 6), derived from Lines 1 and 2, were formed in Generation 8 and made up the winter group. Line 4, derived from Line 2, and Line 5, derived from Line 1, were se-

lected eight generations for ovulation rate and total born per litter and then three generations for live born per litter. Lines 4 and 5 were then crossed to form Line 45 which has been selected for nine additional generations for increased live born per litter, increased 180-day weight, and decreased backfat thickness in the same way as Line 2 was selected during that time. Line 6 was selected randomly from Generations 8 to 20. At Generation 20, control Lines 1 and 6 were crossed to from Lines 16 and 61, which were each continued with random selection. Thus, Lines 2 and 45 have undergone 29 generations of selection for increased litter size with added selection for increased growth and decreased backfat in the last nine generations.

Generation interval for all lines has been one year as only gilts were farrowed. Line sizes were 40 to 80 litters per generation by 14 to 20 sires. Selection rates during all generations have been 1/4 to 1/3 for females and 1/6 to 1/4, depending on the selection criteria, for males.

Tissue samples collected from all breeding boars of generation 29 were submitted to GeneSeek, Inc. and their genotypes for eight markers were determined. The boars were considered

to adequately represent the population. They contribute one-half of the genes to the progeny generation, and most of them also have full and half sibs that were selected. Gene frequencies of female parents in this generation are expected to be similar to that of the boars.

Gene Marker Descriptions and Favorable Alleles

Information about the gene markers evaluated was obtained from the GeneSeek, Inc. Web site (www.gene-seek.com/prod_pigs.php). Two of the gene markers (**ESR** and **EPOR**) have been reported to have significant effects on litter size, operating primarily on uterine capacity or embryonic survival. If these genes have contributed significantly to variation in litter size, then frequencies of favorable alleles are expected to be higher in selection lines than in controls. Three of the gene markers (**CCKAR**, **HMGAI1**, and **MC4R**) affect growth and/or composition of growth and selection during the last nine generations is expected to have changed frequencies of their alleles. Three of the gene markers (**CAST249**, **CAST 638**, and **PRKAG3**) affect meat quality and are not known to affect any of the traits selected for in Lines 2 and 45. More information regarding these markers is presented in the appendix of this paper.

Estimation of Marker Effects

Frequencies of marker alleles were determined from the distributions of genotypes in each line. Effects of the genes for growth and meat quality were estimated with regression. First, the boar's own phenotype was regressed on the number of favorable alleles in the boar's genotype, which estimates the average increase or decrease in boar performance per copy of the favorable allele. A total of 57 boars were selected as breeders, 11 to 16 per line, too few for highly reliable estimates of marker effects; thus, these regressions have quite large standard errors. The relationship between sire marker genotype and progeny phenotype was also estimated by regressing

(Continued on next page)



sire's progeny phenotype on the number of copies of the favorable allele in sire's genotype. Sire progeny phenotype provides an estimate of one-half of the sire's breeding value. Each boar had between 10 and 25 progeny, so these regressions are somewhat analogous to regressing 1/2 sires breeding value on his marker genotype. The number of progeny was insufficient for a highly accurate estimate of each boar's breeding value, but averaged across all boars, this method provides quite reliable estimates of marker effects. Regression analyses could not be done for the reproduction markers, **ESR** and **EPOR**, as daughters of these boars have not yet produced litters.

Results

Litter size means for Generation 29 dams and growth trait means for Generation 30 progeny are in Table 1. The two selection lines (Lines 2 and 45) differ from respective controls by 37 to 48% in live pigs per litter, 11 to 12% in 180-day bodyweight, and -12 to -14% in backfat thickness. Selection has not caused change in longissimus muscle area.

Genotypic distributions and allele frequencies of Generation 29 sires are in Table 2. Frequencies of alleles are presented as the probability of the favorable allele (e.g., Pr (A)) for each gene.

Reproductive Genes. The **ESR** gene marker was not segregating in either of the selection lines — the frequency of the favorable allele was zero. Only one copy of the favorable **ESR** allele existed in this sample of boars and it was in a control, Line 16 boar. This same **ESR** polymorphism was genotyped in Lines 4, 5, and 6 at Generation 16. At that time, the frequency of the favorable **G** allele was .06 in Line 4 and 0 in Lines 5 and 6. Thus, the **ESR** polymorphism was segregating in the base population but probably at low frequency. It is a marker for litter size, not a causative gene, and linkage relationships were different in this population from the ones in which the marker allele was discovered and had an effect. There clearly has not been selection on the **ESR** marker in the selection lines.

Table 1. Means for generations 29 (litter traits) and 30 (growth traits).

Trait	Line 2		Line 16		Line 45		Line 61	
	n	Mean	n	Mean	n	Mean	n	Mean
Total Born	32	13.3	41	8.9	36	16.1	37	10.1
Live Born	32	11.5	41	8.4	36	14.1	37	9.5
180-day Wt, kg	195	103.2	94	92.2	219	104.8	87	94.5
10 rib backfat, cm	195	2.05	94	2.38	219	2.12	87	2.42
Longissimus area, cm ²	195	28.2	94	28.6	219	28.7	87	28.2

The other gene with reported effects on litter size, **EPOR**, was segregating in all lines, but the frequency of the favorable **T** allele was very low in both Lines 2 and 45 compared with Control Lines 16 and 61. It has been reported that females with two copies of the **T** allele (genotype **TT**) have approximately one more pig per litter than those homozygous for the **C** allele (genotype **CC**). If that relationship existed in these populations, it is highly likely that the frequency of the **T** allele would be much greater in both selection lines, especially as compared with the control lines. Either the **EPOR** polymorphism is not a causative gene, but is linked with another gene affecting litter size, or its effect is less in this population than in others so that it explains only a small proportion of the variation in litter size. Whichever the case, it is unlikely that selection on the **EPOR** polymorphism will enhance response to selection in these lines.

Growth and Carcass Genes. The **CCKAR** marker is associated with feed intake and growth. The frequency of the favorable **G** allele was low in Line 2 relative to Line 16 (.23 vs. .91), and high in both Lines 45 and 61 (.72 vs. .90). Although it is not reported that the gene affects backfat, greater feed intake often causes increased backfat. The lower frequencies in both selection lines, relative to respective controls, may be the result of selection for leanness. Results for the **MC4R** polymorphism are consistent with that relationship. The **A** allele of **MC4R** causes pigs to grow faster and the **G** allele causes them to be leaner. The frequency of the **A** allele was intermediate in both control lines (Lines 16 and 61) and low in selection lines (Lines 2 and 45). There was selection for both

growth and leanness in the selection lines. Increased frequency of the allele conferring leanness rather than the one for growth indicates that selection for lean placed more weight on this locus than did selection for growth if the marker associations are the same in the Nebraska lines as in the discovery populations. Allele frequencies for **HMGA** are intermediate in all lines and appear to not have been affected greatly by selection.

Meat Quality Genes. There is no reason to believe that frequencies of alleles for the three markers with effects on meat quality (**CAST249**, **CAST 638**, and **PRKAG3**) should have been changed by selection as none of these markers have been reported to affect reproduction, growth, or carcass traits. The frequencies in these lines are of interest simply to characterize changes not expected to be related to selection. All lines had intermediate frequencies of **Cast 249** and are not greatly differentiated. Line differences could easily be the result of random genetic drift. All lines, except Control Line 61, had high frequencies of the favorable **A** allele of **CAST 638**. It is likely that the frequency of this allele was relatively high in the base generation and has drifted down in Control Line 61, or it was at intermediate frequency in the base generation and drifted up in Lines 2, 45, and 16. In either case, there is some opportunity to improve meat quality in the selection lines by selecting for the **AA** genotype of **CAST 249**. Because there is already a high frequency of the **AA** genotype for **CAST 638**, little additional response is expected from selecting for the **AA/AA** haplotype of the two markers.

The **PRKAG3** marker was not segregating in Line 2, for which the



Table 2. Genotypes of Generation 29 sires in lines selected for litter size, growth and backfat (Lines 2 and 45) and respective controls (Lines 16 & 61). See text for description of genes and favorable allele.^a

CAST_249		CAST_638		CCKAR		EPOR		HMGA		MC4R		ESR		PRKAG3	
Genotype	N	Genotype	N	Genotype	N	Genotype	N	Genotype	N	Genotype	N	Genotype	N	Genotype	N
Line 2															
AA	4	AA	15	AA	8	CC	13	CC	3	AA	0	AA	15	AA	0
AG	8	AC	0	AG	7	CT	2	CT	8	AG	0	AG	0	AG	0
GG	3	CC	0	GG	0	TT	0	TT	4	GG	15	GG	0	GG	15
Pr(A)	0.53	Pr(A)	1.00	Pr(G)	0.23	Pr(T)	0.07	Pr(T)	0.53	Pr(A)	0.00	Pr(G)	0.00	Pr(A)	0.00
Line 16															
AA	1	AA	8	AA	0	CC	6	CC	2	AA	3	AA	10	AA	3
AG	7	AC	3	AG	2	CT	4	CT	7	AG	6	AG	1	AG	4
GG	3	CC	0	GG	9	TT	1	TT	2	GG	2	GG	0	GG	4
Pr(A)	0.41	Pr(A)	0.86	Pr(G)	0.91	Pr(T)	0.27	Pr(T)	0.50	Pr(A)	0.55	Pr(G)	0.05	Pr(A)	0.45
Line 45															
AA	1	AA	13	AA	0	CC	10	CC	5	AA	0	AA	16	AA	4
AG	6	AC	3	AG	9	CT	6	CT	10	AG	4	AG	0	AG	8
GG	9	CC	0	GG	7	TT	0	TT	1	GG	12	GG	0	GG	4
Pr(A)	0.25	Pr(A)	0.91	Pr(G)	0.72	Pr(T)	0.19	Pr(T)	0.37	Pr(A)	0.13	Pr(G)	0.00	Pr(A)	0.50
Line 61															
AA	2	AA	4	AA	0	CC	6	CC	9	AA	1	AA	15	AA	3
AG	5	AC	6	AG	3	CT	6	CT	5	AG	8	AG		AG	6
GG	8	CC	5	GG	12	TT	3	TT	1	GG	6	GG	0	GG	6
Pr(A)	0.30	Pr(A)	0.47	Pr(G)	0.90	Pr(T)	0.40	Pr(T)	0.23	Pr(A)	0.33	Pr(G)	0.00	Pr(A)	0.40

^aPr = probability of the favorable allele.

frequency of the favorable allele was 0, and alleles had intermediate frequencies in other lines. It is likely that allele frequencies were intermediate in the base population and random drift, not selection, caused the favorable allele to be removed from Line 2, assuming the frequency was zero in dams as well.

Regressions. Regression coefficients are in Table 3. The most reliable ones are for progeny phenotype on sire genotype. The G allele of **CCKAR** is associated with increased feed intake and growth. Its effects in this sample were inconsistent, being positive for boar 180-day weight (4.87 ± 2.06 kg per copy), but negative for progeny weight (-1.88 ± 1.00 kg per copy). It was significantly associated with decreased LEA in progeny, but not boar LEA, and did not affect backfat.

Estimates of the effects of the T allele of **HMGA** were consistent in both boar and progeny. Each additional copy was associated with increased 180-day weight, (1.97 ± 1.57 and $1.23 \pm .75$ kg), decreased backfat ($-.13 \pm .065$ and $-.056 \pm .026$ cm per copy) and decreased LEA, (-1.57 ± 0.56 and

$-.64 \pm .23$ cm² per copy in boars and progeny, respectively).

The **MC4R** marker is known to be within the causative gene as the effect of this marker is consistent across many populations and results here are in agreement. Each copy of the A allele was associated with increased boar 180-day weight (4.05 ± 1.96 kg) and increased progeny weight (4.07 ± 1.03 kg). The A allele also significantly increased progeny backfat (0.08 ± 0.036 cm per copy). These results are consistent with changes in allele frequencies in which selection in Lines 2 and 45 was for the allele that conferred greater leanness.

There was some evidence that the meat quality genes (**CAST249**, **CAST638**, and **PRKAG3**) also affected growth and leanness. Regressions of progeny phenotype on number of copies of the favorable allele were significant for **CAST 249** (backfat), **CAST 638** (LEA), and **PRKAG3** (backfat). Progeny 180-day weight increased 2.65 ± 0.72 kg with each copy of the **CAST 249** A allele in sire's genotype. Progeny LEA increased 0.72 ± 0.35 cm² for

each copy of the A allele of **CAST 638**, and progeny backfat decreased 0.068 ± 0.027 cm with each copy of the A allele of **PRKAG3**. In each case, regressions of boar's phenotype on number of copies of the favorable allele in the boar's genotype produced regressions with the same sign, although they were not significant, lending additional evidence that these genes affected these performance traits. However, these genes probably explain only a small percentage of the variation in these traits and were under weak selection as changes in allele frequencies (Table 2) are either small or inconsistent with regression results.

Discussion

This study demonstrates why analyzing marker genotypes in small selection lines may not tell much about whether significant selection has been applied to individual loci. Results are often inconsistent with expectations. Part of the explanation is that studies to identify important candidate genes

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Table 3. Regressions of phenotype on number of favorable alleles (b), standard errors of regressions (se), and probability regressions differ from zero (p).

Trait	Regressions of boar's own phenotype on number of favorable alleles in boar's genotype			Regressions of boar's progeny phenotype on number of favorable alleles in sire's genotype		
	b	se	p	b	se	p
CCKAR						
WT, kg	4.87	2.06	0.02	-1.88	1.00	0.06
BF, cm	0.076	0.094	0.42	-0.006	0.035	0.86
LEA, cm ²	-0.098	0.83	0.91	-0.82	0.31	0.008
HMG4						
WT, kg	1.97	1.57	0.21	1.23	0.75	0.1
BF, cm	-0.13	0.065	0.04	-0.046	0.026	0.07
LEA, cm ²	-1.57	0.56	0.007	-0.64	0.23	0.005
MC4R						
WT, kg	4.05	1.96	0.04	4.07	1.03	0.0001
BF, cm	-0.007	0.09	0.93	0.08	0.036	0.03
LEA, cm ²	-0.13	0.78	0.87	0.26	0.32	0.42
CAST249						
WT, kg	1.84	1.51	0.23	2.65	0.72	0.0003
BF, cm	-0.096	0.062	0.13	0.012	0.026	0.64
LEA, cm ²	-0.305	0.56	0.59	-0.23	0.23	0.31
CAST638						
WT, kg	-1.48	2.01	0.47	-1.53	1.14	0.18
BF, cm	-0.22	0.08	0.01	-0.026	0.04	0.51
LEA, cm ²	0.46	0.76	0.55	0.72	0.35	0.04
PRKAG3						
WT, kg	2.97	1.49	0.05	0.23	0.78	0.76
BF, cm	-0.035	0.066	0.59	-0.068	0.027	0.01
LEA, cm ²	0.26	0.58	0.65	-0.41	0.24	0.08

usually report differences between extremes. If the marker is an A/G polymorphism, mean phenotypes for individuals with AA and GG genotypes are estimated (AA – GG) or the mean phenotype for heterozygotes compared with the mean of the homozygotes (AG – ½ (AA + GG)) is estimated. For example, the difference between TT and CC genotypes at **EPOR** has been estimated at one pig per litter. But the effect of the T allele in a selection line and the selection applied to it, relative to other genes affecting litter size, are frequency dependent. In fact, they are approximately equal to the ratio of genetic variance at that locus relative to total genetic variance for the trait. That ratio decreases as frequency of T increases. Thus, when frequency of an allele with big effects, as estimated by difference between homozygotes gets up to .5 or greater, there is increasingly less selection on it. In fact there may be very little selection applied at that

locus relative to all the other genes influencing the trait. Then, genetic drift is the most powerful force influencing allele frequencies.

Genotyping for a small number of markers and then practicing selecting mainly or only on marker genotypes can be a large mistake. A better approach is to include the markers in estimating breeding values because that method accounts for marker frequencies if marker genotypes are known for all selection candidates and produces the most accurate estimates of breeding values. When allele frequencies get to intermediate values, there may be little change in frequency of a gene with fairly large effect. In larger commercial populations, allele frequencies are expected to be at values that optimize response to selection. If drift moves the frequency of the desired allele down, then in the next generation there will be a bit more pressure on that allele and it will

move back up. If by chance, in some generation both drift and selection move the frequency higher, then in the next generation there will be even less selection on that locus. After a very large number of generations and without mutation, fixation of favorable alleles can occur. But if populations are small, fixation of the undesirable allele also can occur. Because many of the reported markers with effects on economic traits are really linked markers and linkage relationships are different across populations, there can be considerable variation in marker effects across populations. Breeders are advised to not select on individual marker genotypes, but if genotypes are known on all candidates for selection, include the data in the EBV process.

¹Rodger Johnson, professor, Animal Science Department, University of Nebraska–Lincoln.



Appendix

Description of Gene Markers (www.geneseek.com/prod_pigs.php)

CAST* (U.S. Patent Application #20,070,172,848): Calpastatin (CAST) is a specific inhibitor of μ - and m-calpain proteases. There is evidence indicating that in different species, including the pig, calpastatin activity post-mortem is highly related to meat tenderness. Two missense mutations (**CAST Hpy188I** or **Arg249Lys** and **CAST PvuII** or **Arg638Ser**) were identified and when used in tandem, are significantly associated with firmness, juiciness, Instron force, chewiness, and tenderness scores. Both mutations can be genotyped and used individually. The A allele is the favorable allele for the first mutation (**CAST 249Arg (SNP=A)**) and is associated with higher tenderness, lower cooking loss, and Instron force.

Similar effects were observed with the second **CAST** mutation: **CAST Arg638Ser**. This mutation was also found to be a significant source of variation for cured ham moisture content. The A allele of **CAST 638Arg (SNP=A)** is again the favorable allele and is associated with higher moisture in the cured ham than **CAST 638Ser (C allele)**.

Both mutations can be used together as a haplotype maximizing the accuracy of selection for tenderness, cooking loss, and related traits. Haplotype **249Lys/Arg638** is the favorable haplotype (SNP's A/A).

(Ciobanu et al., J Anim Sci. 2004 Oct;82(10):2829-39.)

CCKAR: The cholecystokinin type A receptor (CCKAR) genetic test is associated with physiological control of feed intake, hunger fulfillment, and obesity. Animals with at least one copy of the dominant G-variant have, on average, ~5% greater daily feed intake, 3% greater daily gain, and 3% fewer days to reach 180 kg, when compared to homozygotes for the A-variant.

SNP G = Favorable allele for growth

(Houston et. at., Genetics. 2006 Nov; 174(3):1555-63.)

Erythropoietin (EPOR): A genetic variant in the swine erythropoietin receptor gene is associated with uterine capacity and litter size. The favorable genetic variate (T allele) has demonstrated an increase in uterine capacity as well as an increase in live births in two different swine populations at USDA-MARC. In a commercial herd, an extra pig per litter was observed when comparing boars that have two copies of the favorable **EPOR** marker (TT) versus boars with zero copies (CC). The T allele is the favorable allele.

(Vallet, J.L., et. al., Animal Genetics. 2005 36(2): 97-103).

HMGA1* (U.S. Patent No. 20,040,029,145) : The high mobility group AT-hook protein 1 (HMGA1) genetic test is associated with lean mass percentage, growth and backfat in several swine breeds. The T allele is favorable (T-variant at position 576) and pigs with that allele are likely to be leaner and produce offspring that are leaner than those with the C allele.

(Kim et. al., Obes Res. 2004 Dec;12(12):1981-94.)

MC4R* (U.S. Patent #6,803,190): The melanocortin-4 receptor (**MC4R**) is expressed in virtually all brain regions of mammals and plays an important role in energy homeostasis. **MC4R** has been described in several studies as a functional gene controlling several growth and performance traits in pigs. Allele frequencies of a polymorphism (Asp298Asn) were quite different among commercial pig breeds where divergent selection has been practiced intensively. In general, Asn298 allele (SNP=A) is associated with higher average daily gain and backfat thickness. Conversely, the Asp298 allele (SNP=G) is associated with lean growth with high feed conversion rate.

Allele (SNP) A = (Asn298-ASPARAGINE): Pigs with genotype A/A grow significantly faster (37 g/day) and consume more daily feed (~8%) than pigs that are G/G. Allele (SNP) G = (Asp298-ASPARTIC ACID): Pigs that are G/G have 9% less backfat and lower feed intake than pigs that are A/A. The allele effects appear to be additive. The heterozygotes fall between the two homozygotes.

(Kim et. al., Mamm Genome. 2000 Feb;11(2):131-5.)



Estrogen Receptor (ESR) U.S. Patent #5,550,024: Estrogen plays an essential role in several reproductive functions, including expression of estrus, fertility, embryo and fetal development, and maintenance of pregnancy. A genetic variant of the ESR gene (allele G) is associated with increased litter size. Females that carry one copy of the favorable variation of the gene (G-SNP) will, on average, yield 0.4 pigs per litter increase. Homozygotes (2 copies, GG) for this genetic variation yield 0.8 pigs per litter increase (average) compared with those homozygous for the A allele (AA). This test is reported to be effective in Large White or Yorkshire breeds or crosses that involve them. The G allele is favorable.

Rothschild, et. al., Proc. Natl. Acad. Sci. 1996 Jan; Vol. 93: 201-205

PRKAG3* (U.S. Patent #6,919,177): PRKAG3 is a regulatory subunit of AMP-activated protein kinase, which is involved in the regulation of energy homeostasis in eukaryotes. The *PRKAG3* gene is well known for one of its alleles called RN- (200Q), present only in Hampshire pigs. This mutation affects glycogen content in muscle and, in general, meat quality traits of pigs that include ultimate pH and color measures which are correlated with other characteristics like drip loss, water holding capacity, tenderness, and cooking loss. Another mutation, I199V, which is nearby and causative as well, affects also glycogen content, ultimate pH and color, but this mutation is present in all breeds. The favorable allele is 199I (SNP=A) and is associated with lower glycogen, higher ultimate pH and favorable color. The differences between homozygotes account for .1 ultimate pH between I/I (SNP= A/A) and V/V (SNP G/G) animals with the heterozygotes being intermediate. In addition, the I/I animals are significantly better for lower glycolytic potential, better color and Minolta reflectance scores. SNP A = Isoleucine (I), the favorable allele SNP G = Valine (V) = unfavorable allele

(Ciobanu et.al., Genetics. 2001 Nov; 159(3):1151-62.).