J. Anim. Breed. Genet. ISSN 0931-2668

ORIGINAL ARTICLE

Analysis of the mouse high-growth region in pigs

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Keywords
Growth; pig; QTL; SSC5.

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Received: 4 July 2008;
accepted: 18 January 2009

Summary

In the mouse, homozygous animals for the high growth mutation show a 30–50% increase in growth without becoming obese. This region is homologous to the distal part of pig chromosome 5 (SSC5). A previous genome scan detected several quantitative trait loci (QTL) in this region for body composition and meat quality using a three generation Berkshire × Yorkshire resource family. In this study, the effects on swine growth, fat and meat quality traits of three genes previously identified within the mouse high growth region were analysed. The genes studied were CASP2 and RIPKI domain containing adaptor with death domain (*CRADD*), suppressor of cytokine signalling 2 (*SOCS2*) and plexinC1 (*PLXNC1*). In addition, the influence of two other genes located very close to this region, namely the plasma membrane calcium-transporting ATPase 1 (*ATP2B1*) and dual specificity phosphatase 6 (*DUSP6*) genes, was also investigated. Single nucleotide polymorphisms were identified and used to map these genes to the QTL region on SSC5. Results indicate significant associations between these genes and several phenotypic traits, including fat deposition and growth in pigs. The present study suggests associations of these genes with swine fat and growth related traits, but further studies are needed in order to clearly identify the genes involved in the regulation of the QTL located on SSC5.

Introduction

The mouse high growth mutation is a deletion on chromosome 10 which causes a 30–50% increase in growth in the homozygous animal (Bradford & Famula 1984). High-growth mice have increased levels of plasma insulin-like growth factor I (IGF-I) and decreased levels of growth hormone (GH), suggesting that the causal mutation influences growth by deregulating the GH/IGF1 system (Horvat & Medrano 2001). Studies with mice have identified several genes within this high growth region, including *CRADD*, *SOCS2* and *PLXNC1* (Wong *et al.* 2002). The high growth mouse deletion comprises 486, 178 bp, with one breakpoint at 633 bp downstream of *SOCS2* exon 2, and another 8589 bp upstream to *PLXNC1* exon 3. This results in the fusion of the two genes, *SOCS2* exons 1–2 and *PLXNC1* exons 3–20, and in the deletion of the entire *CRADD* gene in the high growth animal genome (Wong *et al.* 2002).

The mouse *PLXNC1* protein is a member of the semaphorin family. This is a large family of secreted and transmembrane proteins best known for being related to neural development and the immune system (Comeau *et al.* 1998). CRADD is an adapter molecule that contains an aminoterminal caspase recruitment domain region and a carboxy-terminal 'death domain'. It mediates the action of cysteine proteases involved in the apoptosis pathway (Duan & Dixit 1997). Therefore, the increase in cell number

doi:10.1111/j.1439-0388.2009.00801.x

observed in the high growth phenotype is possibly the result of alterations in the apoptosis pathway (Horvat & Medrano 1998). *SOCS2* is a member of the suppressor of cytokine signalling family, a group of related proteins implicated in the negative regulation of cytokine action through inhibition of the Janus kinase signal transducers and activators of transcription signal-transduction pathway (Greenhalgh *et al.* 2002). *SOCS2* is an essential negative regulator of GH signalling *in vivo*, and its absence leads to increased growth through increased production of IGF-1 (Metcalf *et al.* 2000). This gene was previously mapped to SSC5 using radiation hybrids (Piper *et al.* 2005).

The high growth region on mouse chromosome 10 (MMU10) is homologous to human chromosome 12 (HSA12) (Horvat & Medrano 1995). Comparative mapping indicated that the SSC5 distal region, where several quantitative trait loci (QTL) were detected, is homologous to the high growth region on MMU10 and to the correspondent region on HSA12. Two additional genes (*ATP2B1* and *DUSP6*) anticipated to map to the SSC5 QTL region were also analysed in this study.

ATP2B1 is an integral membrane protein that removes bivalent calcium ions from eukaryotic cells and catalyses the hydrolysis of ATP coupled with the transport of calcium. In swine, *ATP2B1* has been mapped by fluorescence in-situ hybridization to SSC5q23 (Zambonelli *et al.* 2001). *DUSP6* is a member of the dual specificity protein phosphatase subfamily and it negatively regulates members of the mitogen-activated protein kinase superfamily, which are associated with cellular proliferation, differentiation and apoptosis. Previously, radiation hybrid and linkage mapping were used to map DUSP6 to SSC5 (Farber *et al.* 2003).

The objectives of this study were to linkage map the *PLXNC1*, *CRADD*, *SOCS2*, *ATP2B1* and *DUSP6* genes in the pig genome and evaluate their roles in porcine growth, fat and meat quality phenotypes.

Materials and methods

Animals and phenotypic data

Phenotypic data and DNA samples were obtained from a Berkshire by Yorkshire (B×Y) intercross pig reference family developed at Iowa State University. The B×Y reference family was created by crossing nine Yorkshire dams and two Berkshire boars to yield nine F1 litters. From the F1 litters, eight boars and 26 sows were mated to produce a total of 515 F2 animals. This pedigree was originally utilized to map QTL for meat quality and growth and body composition traits using microsatellite markers (Malek *et al.* 2001a,b). The traits available included several backfat measurements, growth, including early growth data collected approximately at weaning (16 day weight) and various meat quality traits, including pH, meat colour, tenderness, flavour and off-flavour, water holding capacity, among others. Details on the management of pigs as well as detailed information regarding the phenotype measurement were previously described (Malek *et al.* 2001a,b).

Molecular genetic marker evaluation

Initially, primer sets were designed in order to amplify several PCR fragments from each gene. After optimization, the PCR products were directly sequenced to identify polymorphisms. Pooled PCR products from different pig breeds were sequenced and the sequences compared using Sequencher software version 3.0 (Gene Codes, Ann Arbor, MI, USA) to identify single nucleotide polymorphisms (SNPs). One polymorphism in each gene was used to develop PCR-RFLP tests that were then used to genotype the entire B×Y pedigree. Polymorphisms located on coding or regulatory regions were selected, whenever possible, otherwise intronic SNPs were used. The sequences of these primer sets are indicated in Table 1. Amplifications were performed using standard PCR conditions. Digestion with specific restriction enzymes was performed following the recommendations of the manufacturer. The locations of the SNPs within the genes, as well as the fragment sizes for each allele, are also presented in Table 1.

Linkage mapping, QTL and association analyses

All genes were mapped to the B×Y SSC5 linkage map using the CRIMAP (version 2.4, St Louis, MO, USA) mapping program (Green *et al.* 1990). Two-point and multipoint linkage analyses were performed in order to place genes into linkage groups and determine the best map. The linkage map contained a total of 16 markers, including the microsatellite markers described previously (Malek *et al.* 2001a,b) and the perosixome proliferator activated receptor alpha gene, that was also assigned to SSC5 (Pita *et al.* 2003).

Quantitative trait loci analyses were carried out with QTL Express (Seaton *et al.* 2002) using the linkage map previously determined. The model used for QTL analysis included the fixed effects of sex and

Table 1 Information regarding the genes analysed, primers designed, position of SNPs, restriction enzymes used and PCR-RFLP fragment sizes

Gene	Primer sequence (5′–3′)	SNP position	Restriction enzyme	Fragment sizes
PLXNC1	F: GCACAAGTTCAAAGTAAAAGAAATG	Intron 26	*Msc*I	1158 and 65 (allele 1)
	R: GGGCATCCAAAAAGTCAAAA			617, 541, 65 (allele 2)
CRADD	F: TTCCCAGCACTCCCTTTTTAG	5′UTR	*Bsr*GI	635 (allele 1)
	R: ACCCCATCACGGCAGAAA			470, 165 (allele 2)
SOCS2	F: ACCCAACCCTCCACTTTCTC	Intron 1	*Sac*II	635, 262 (allele 1)
	R: GCAACCCTCCTCCTTTCC			439, 262, 196 (allele 2)
ATP2B1	F: AATAAGCCTCTCATCTCACGCA	Intron 17	*Afl*III	400, 330 (allele 1)
	R: AAAGTGCCTAAAACAATTGTGC			400, 166, 164 (allele 2)
DUSP6	F: TGCAGGTCTCTACGTTCCAA	Exon 3	*Pst*I	820, 170 (allele 1)
	R: GCCAAGCAATGCACCAAG			723, 170, 97 (allele 2)

SNP, single nucleotide polymorphisms; PCR-RFLP, polymersae chain reaction-restriction fragment length polymorphism.

year-season for all traits, along with additive and dominance coefficients for the putative QTL. In addition, the model for the carcass composition traits included live weight as a covariate. Chromosome-wise significance thresholds were derived by the permutation test of Churchill & Doerge (1994) implemented in QTL Express. A total of 10 000 random permutations of the data were performed.

An analysis of variance procedure was used to test associations between all genes with the available phenotypic traits using the MIXED procedure of SAS (SAS 1996). For *PLXNC1*, *CRADD* and *ATP2B1*, genotypes with a very low number of observations were removed from the analysis. The associations were tested using a mixed-model that included sex, slaughter date and all five genes as fixed effects (all genes were included in the model simultaneously), while dam was included as a random effect. In addition, live weight at slaughter was included as a covariate in the model for carcass traits while the model for the traits related with glycogen metabolism (average lactate, average glycogen and average glycolytic potential) included the genotype for the *PRKAG3* (protein kinase, AMP-activated, gamma 3 non-catalytic subunit) Ile199Val mutation described by Ciobanu *et al.* (2001) as a fixed effect.

Results

Linkage mapping and QTL analysis

All genes were found to be significantly linked to several markers on the SSC5 linkage map. The best map order produced by multi-point analysis with other linked markers was (position in cM): *SW995* (117.9) – *PLXNC1* (121.9) – *SW1954* (129) – *CRADD* (129.0) – *SOCS2* (129.0) – *SW378* (132.5) – *ATP2B1* (133.1) – *DUSP6* (141.7).

Previous QTL analyses by Malek *et al.* (2001a,b) detected several significant QTL in the distal region of SSC5. These included QTL for body composition (average backfat, last rib backfat and lumbar backfat)

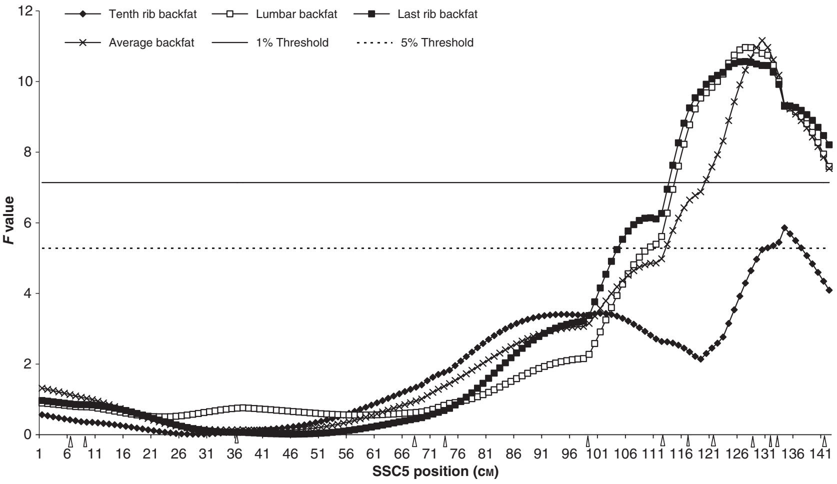

Figure 1 *F*-statistic curves from an univariate F2 quantitative trait loci (QTL) analysis using QTL Express, indicating QTL position estimates for average backfat, last rib backfat, lumbar backfat and tenth rib backfat. The SSC5 relative position (in cM) is indicated on the *x*-axis. The *y*-axis indicates the *F*-statistic values. The chromosome-wise 5% and 1% significance thresholds are represented by a solid and a dashed line, respectively. The 1% and 5% chromosome-wise significance levels were estimated to be 7.14 (solid line) and 5.28 (dashed line), respectively. The triangles in the *x*-axis represent the approximate location of the markers on the SSC5 linkage map.

and meat quality (24-h loin pH, 24-h loin Minolta *L*-score, 48-h loin pH, 48-h loin Minolta *L*-score and 48-h loin Hunter *L*-score) traits. In this study, new QTL analyses were performed using the new SSC5 linkage map including the five genes mentioned above and all other markers available on the SSC5 linkage map, for a total of 16 markers. The profiles for the significant QTL traits are in Figures 1, 2 and 3.

The QTL analyses performed detected new QTL for tenth rib backfat, average drip loss and water holding capacity. In addition, the significance of several of the QTL detected by Malek *et al.* (2001a,b) was higher. This was because the *F*-values for average backfat, last rib backfat, lumbar backfat and 48-h loin pH increased, when compared with the previous analyses by Malek *et al.* (2001a,b). In particular, *F*-values increased from 7.35 to 11.16 for average backfat, from 9.51 to 10.56 for last rib backfat, from 7.25 to 10.96 for lumbar backfat, and from 6.20 to 6.55 for 48-h loin pH. The QTL for last rib backfat, lumbar backfat and average backfat were significant at the 1% chromosome-wise level (7.14), while the other QTL were significant at the 5% chromosome-wise threshold (5.28). Most of these QTL were located in the same region where the five candidate genes were mapped. The QTL peak for average backfat was located at position 129 cM, while the peaks for lumbar and last rib backfat were both located at position 126 cM. An additional significant fat QTL peak for tenth rib backfat was located at 133 cM, a position where QTL peaks for 48-h loin Minolta and Hunter *L*-score were also found and where the *ATP2B1* gene was mapped. Significant QTL for other meat quality traits were located at positions 141 cM (24-h loin Minolta *L*-score), 123 cM (water holding capacity) and 41 cM (average drip loss). The QTL for 24-h loin pH detected by Malek *et al.* (2001b) was no longer significant in this study, despite presenting an *F*-value (5.02) that approached the 5% chromosome-wise significance level.

Association analyses

The results of the association analyses for growth and carcass composition and meat quality traits are presented in Tables 2 and 3, respectively. The *PLXNC1 Msc*I polymorphism showed significant effects on average daily gain on test and carcass weight, with animals carrying genotype 12 being associated with faster growth and heavier carcasses. However, animals carrying this genotype also displayed lower ham pH values and suggestive higher chew score, potentially indicating poorer meat quality.

Significant effects of the *CRADD BrsG*I polymorphism were detected for fat related traits, as animals with genotype 12 presented higher total lipid percentage and marbling. This genotype was also significantly associated with higher values for average daily gain on test.

The *SOCS2 Sac*II polymorphism was significantly associated with early growth traits, as well as with carcass weight. Individuals displaying genotype 22 for this marker were associated with significant effects for weaning weight and average daily gain from birth to weaning. In addition, this genotype was also associated with less back fat. Considering

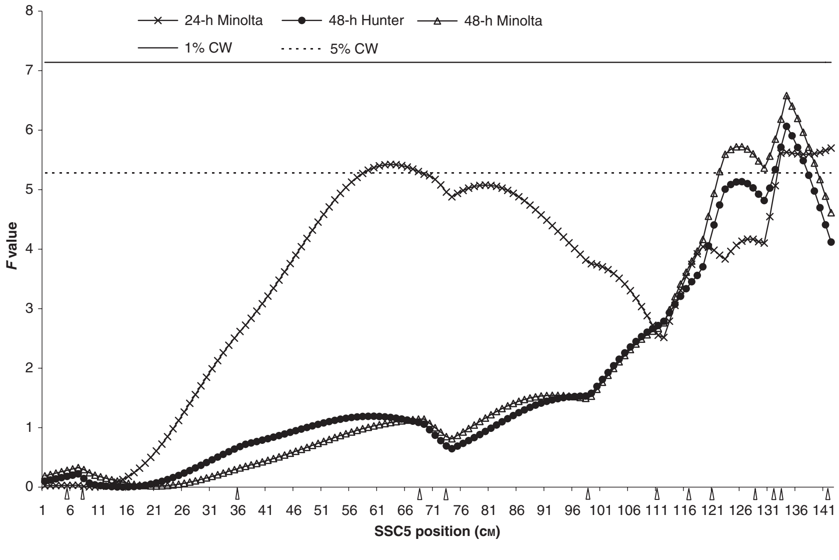

Figure 2 *F*-statistic curves from an univariate F2 quantitative trait loci (QTL) analysis using QTL Express, indicating QTL position estimates for 24-h Minolta *L*-value,48-h Hunter *L*-value and 48-h Minolta *L*-value. The SSC5 relative position (in cM) is indicated on the *x*-axis. The *y*-axis indicates the *F*-statistic values. The chromosome-wise 5% and 1% significance thresholds are represented by a solid and a dashed line, respectively. The 1% and 5% chromosome-wise significance levels were estimated to be 7.14 (solid line) and 5.28 (dashed line), respectively. The triangles in the *x*-axis represent the approximate location of the markers on the SSC5 linkage map.

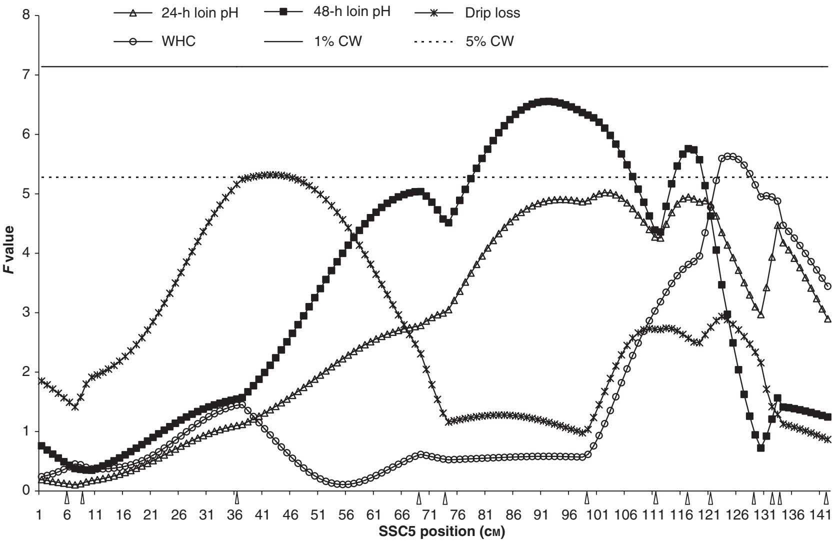

Figure 3 *F*-statistic curves from an univariate F2 quantitative trait loci (QTL) analysis using QTL Express, indicating QTL position estimates for 24-h loin pH, 48-h loin pH, drip loss percentage and water holding capacity (WHC). The SSC5 relative position (in cM) is indicated on the *x*-axis. The *y*-axis indicates the *F*-statistic values. The chromosome-wise 5% and 1% significance thresholds are represented by a solid and a dashed line, respectively. The 1% and 5% chromosome-wise significance levels were estimated to be 7.14 (solid line) and 5.28 (dashed line), respectively. The triangles in the *x*-axis represent the approximate location of the markers on the SSC5 linkage map.

carcass weight, animals with genotype 12 were associated with heavier carcasses.

The *AT2B1 Pst*I polymorphism had significant and suggestive effects on several meat quality and fat traits. Genotype 22 for this marker was the preferred genotype for average glycogen, 24-h loin Hunter *L*-score and marbling, but not for carcass length, a trait for which the 12 animals presented higher values, indicating longer carcasses. Suggestive associations were found for tenderness score, percent of cooking loss, tenth rib back fat and 24-h loin pH.

The *DUSP6 Afl*III polymorphism displayed significant associations with several fat related traits, including average, last rib, lumbar and tenth rib backfat. For these four traits, animals carrying genotype 11 presented lower values of backfat thickness when compared to individuals carrying genotypes 12 and 22. In addition, animals with *DUSP6* genotype 11 were also associated with increased early growth and better meat quality parameters, as indicated by the associations detected between this marker and average daily gain from birth to weaning, weaning weight, average lactate and average glycolytic potential. For carcass weight, animals carrying the 22 genotype presented the highest values.

Discussion

Linkage analysis was used to map the *PLXNC1*, *CRADD*, *SOCS2*, *ATP2B1* and *DUSP6* genes to SSC5. The results of this study confirmed the synteny between SSC5, HSA12 and MMU10, which is in accordance with the results obtained by chromosomal painting between humans and pigs (Goureau *et al.* 1996).

The SSC5 QTL described previously by Malek *et al.* (2001a,b) were confirmed in this study, with relatively few changes observed regarding their position. Overall, most of these QTL were located in a region spanning 10 cM, from positions 123 to 133 cM in the linkage map, a region where three of the genes analysed in this study were mapped. However, several differences were observed for the F-profiles of the significant QTL traits. Several QTL became more significant after the addition of the five genetic markers mapped in the present study. Previously, QTL for fat related traits had also been mapped to SSC5 (Knott *et al.* 1998; Rohrer & Keele 1998; Bidanel *et al.* 2001; de Koning *et al.* 2001; Milan *et al.* 2002; Lee *et al.* 2003; Nii *et al.* 2006). The comparison of QTL positions across studies is not straightforward since those positions depend on the length of the linkage maps used, that in turn are affected by the populations used for QTL mapping, the size of those populations and the number of markers used. Nevertheless, the only QTL that were mapped approximately to the same distal SSC5 region included QTL for ham weight and the percentage of the combined ham and loin weight (Milan *et al.* 2002) and also a reproduction QTL for the number of stillborn pigs (Cassady *et al.* 2001). From the QTL results obtained so far, it is clear that SSC5 plays an important role in the regulation of fat deposition in pigs, and that genes located in more than one SSC5 region are involved.

All three genes involved in the mouse high growth mutation (*PLXNC1, CRADD* and *SOCS2*) were significantly associated with growth traits in the pig. While in the mouse high growth phenotype the *CRADD*

Table 2 Least squares means and standard errors for the association analysis of *CRADD*, *PLXNC1*, *ATP2B1* and *DUSP6* with growth and carcass composition phenotypes in an F2 Berkshire × Yorkshire pig population

	Genotypic least squares means		
Gene/trait	11	12	22
PLXNC1	n = 398	n = 95	
Carcass weight (kg)	86.81 ± 0.19^{c}	87.52 ± 0.29^{d}	
Average daily gain on test (kg/day)	0.67 ± 0.01^{e}	0.69 ± 0.01^{f}	
CRADD	n = 271	n = 229	
Marbling (1–5)	3.57 ± 0.08^{c}	3.77 ± 0.09^{d}	
Total lipid (%)	2.89 ± 0.17^{e}	3.61 ± 0.18^{f}	
Average daily gain on test (kg/day)	0.67 ± 0.01^{c}	0.69 ± 0.01^{d}	
SOCS2	n = 162	n = 256	n = 82
Carcass weight (kg)	87.00 ± 0.27^{c}	87.66 ± 0.21^{d}	86.84 ± 0.31^{c}
Average back fat (cm)	3.31 ± 0.07^{a}	3.32 ± 0.06^{c}	$3.14 \pm 0.08^{b,d}$
Last rib back fat (cm)	3.19 ± 0.07^{c}	3.16 ± 0.06^{c}	2.99 ± 0.08^{d}
Lumbar back fat (cm)	3.60 ± 0.09	3.61 ± 0.07^{c}	3.41 ± 0.10^{d}
Tenth rib back fat (cm)	3.12 ± 0.09	3.17 ± 0.08^{a}	3.02 ± 0.10^{b}
16-day weight (kg)	4.64 ± 0.19^{e}	5.04 ± 0.17^{f}	5.31 ± 0.21^{f}
Average daily gain to weaning (kg)	$0.22 \pm 0.01^{c,e}$	0.24 ± 0.01^{d}	0.26 ± 0.01^{f}
ATP2B1	-	n = 157	n = 301
Carcass length (cm)	-	84.37 ± 0.22^{c}	83.82 ± 0.19^{d}
Tenth rib back fat (cm)	-	3.04 ± 0.08^{a}	3.16 ± 0.07^{b}
Marbling (1–5)	-	3.58 ± 0.08^{c}	3.76 ± 0.07^{d}
DUSP6	n = 132	n = 257	n = 103
Carcass weight (kg)	86.75 ± 0.24^{c}	87.25 ± 0.20^{d}	87.50 ± 0.28^{d}
Average back fat (cm)	3.11 ± 0.07^{e}	3.28 ± 0.06^{f}	3.38 ± 0.08^{f}
Last rib back fat (cm)	2.96 ± 0.07^{e}	3.16 ± 0.06^{f}	3.22 ± 0.08^{f}
Lumbar back fat (cm)	$3.39 \pm 0.08^{c,e}$	3.56 ± 0.07^{d}	3.66 ± 0.09^{f}
Tenth rib back fat (cm)	$2.96 \pm 0.08^{a,e}$	3.10 ± 0.07^{b}	$3.24 \pm 0.09^{a,f}$
16-day weight (kg)	5.22 ± 0.17^{c}	4.85 ± 0.16^{d}	4.93 ± 0.200
Average daily gain to weaning (kg)	0.25 ± 0.01^{c}	0.23 ± 0.01^{d}	0.24 ± 0.01

Significance levels for the differences between genotypic means: a, b, $p < 0.1$; c, d, $p < 0.05$; e, f, $p < 0.01$.

gene is deleted, that did not seem to be the case in this pig population since all animals analysed amplified the PCR fragment designed in the 5′UTR region. This was further confirmed by direct sequencing of this gene region in the BY founder animals. However, it is possible that other regions of the *CRADD* gene not analysed in this study may be absent in this or other pig populations. Animals carrying genotype 12 for both *PLXNC1* and *CRADD* were significantly associated with higher growth rates. In pig production, it is commonly assumed that selection for increased leanness and less backfat is associated with decreased meat quality. For the *PLXNC1* gene the best genotype for growth was related to poorer meat quality (lower pH and higher chew score). Since it was not possible to determine if the increased weight gain was due to an increase in lean growth rate it is unclear why these associations were detected, since an increase in body weight is not necessarily associated with decreased meat quality. However, for *CRADD* no significant associations with any of the meat quality traits analysed were detected. For this marker, the genotype associated with faster growth also displayed higher values for several fat traits (total lipid percentage, marbling and lumbar backfat). It is unclear why this was observed, but the low variability observed for these markers may have contributed for this situation, since in both cases only genotypes 11 and 12 were detected. It is not uncommon to observe low variability for markers analysed in QTL mapping populations because the amount of linkage disequilibrium is usually higher in these populations. It is also possible that some of the significant associations detected for CRADD could be due to random chance. The low variability registered for three of the genes mapped to SSC5, namely *PLXNC1*, *CRADD* and *ATP2B1*, for which only two (out of the possible three) genotypes were included in the association analyses performed was one limitation in this study. This may be a consequence of the allele frequency observed in the parental generation, in which the Berkshire boars were fixed for allele 1 (*PLXNC1*) or allele 2 (*ATP2B1*). The association of the *CRADD* polymorphism with fat traits in pigs is not surprising, given the role of the *CRADD* gene with adipocytes in the mouse, where overexpression of *CRADD* inhibits

Table 3 Least squares means and standard errors for the association analysis of *PLXNC1*, *ATP2B1* and *DUSP6* with meat quality phenotypes in an F2 Berkshire × Yorkshire pig population

	Genotypic least squares means		
Gene/trait	11	12	22
PLXNC1	n = 398	n = 95	
Chewiness score (1–10)	2.40 ± 0.09^{a}	2.66 ± 0.13^{b}	
24-h ham pH	5.92 ± 0.02^{c}	5.83 ± 0.03^{d}	
ATP2B1	-	n = 157	n = 301
Average glycogen (μmol/g)	-	9.44 ± 0.33^{c}	8.50 ± 0.29^{d}
Tenderness (1–10)	-	7.62 ± 0.13^{a}	7.86 ± 0.11^{b}
Cooking loss (%)	-	19.48 ± 0.44^{a}	18.61 ± 0.37^{b}
24-h loin pH	-	5.78 ± 0.01^{a}	5.75 ± 0.01^{b}
24-h loin Hunter *L*-value	-	43.86 ± 0.69^{c}	45.03 ± 0.60^{d}
DUSP6	n = 132	n = 257	n = 103
Average glycolytic potential (μmol/g)	103.90 ± 1.84^{c}	106.52 ± 1.53	109.08 ± 2.17^{d}
Average lactate (μmol/g)	$86.10 \pm 1.44^{a,c}$	88.57 ± 1.20^{b}	90.91 ± 1.70^{d}
24-h loin Hunter *L*-value	44.75 ± 0.70	44.83 ± 0.65^{a}	43.78 ± 0.80^{b}
24-h loin Minolta *L*-value	$21.16 \pm 0.55^{a,c}$	21.29 ± 0.50^{b}	22.30 ± 0.64^{d}

Significance levels for the differences between genotypic means: a, b, $p < 0.1$; c, d, $p < 0.05$; e, f, $p < 0.01$.

the differentiation of mouse preadipocytes (Felmer *et al.* 2003). These fat traits are very important for the pig producer, especially back fat thickness and also marbling scores, which correspond to intramuscular lipid content. Higher lipid content is generally considered more desirable because it adds to flavour and cooking properties.

The *SOCS2* gene was also significantly associated with growth and fat traits in the pig. However, unlike *PLXNC1* and *CRADD*, this gene was only associated with early growth. In fact, individuals with *SOCS2* genotype 22 were associated with higher weaning weight and faster growth from birth to weaning. This gene is an essential down regulator of growth and its absence leads to the high growth phenotype in mouse, due to significant increases in bone and body lengths, thickening of the skin due to collagen deposition, and increases in internal organ size (Metcalf *et al.* 2000; Horvat & Medrano 2001). *SOCS2* specifically interacts with IGF-1, GH and prolactin receptors (Wong *et al.* 2002) suggesting how it possibly plays a role in increasing carcass weight in swine.

The *ATP2B1* gene was also associated with meat quality traits and growth in this study. The animals with 22 genotype had decreased level of average glycogen, carcass length and percent cooking loss and increased marbling, tenth rib backfat and tenderness score. The *SOCS2* and *ATP2B1* polymorphisms were associated with the glycogen index. During the first 6–24 h postmortem, glycogen reserves in the muscle are reduced, lactic acid builds up, and muscle metabolism stops. Greater amounts of glycogen in the tissue at harvest provide the potential for sustained glycolysis in the muscle after slaughter, which could result in lower ultimate pH and negative meat quality traits. *DUSP6* was related with all backfat traits, and also with growth, since animals carrying genotype 11 for this marker grew faster and had less back fat. This gene has been associated with cellular proliferation and differentiation (Toyota *et al.* 2000). It is possible that it also plays a role in the regulation of pig growth and fat deposition, but further studies would be required to better define the role played by *DUSP6* in the regulation of these traits.

Conclusions

This study confirmed similar associations played by the genes involved in the mouse high growth mutation in the regulation of growth and body composition traits since all genes displayed significant associations with several porcine growth and carcass traits. However, the mechanism seems to be different in the pig since no animals with the *CRADD* gene deletion were detected in the pig population analysed. However, we can not rule out that other mechanisms may exist in other pig populations or breeds. Future studies should focus on the detection of additional mutations in these genes since it is possible that other mutations may exist.

Several interesting associations were detected for traits of economic importance for the pig industry. It is possible that selection for increased growth and leanness may have been acting upon these genes. However, these results were obtained in a mapping population, with significant linkage disequilibrium.

Hence, additional studies conducted with different swine breeds and polymorphisms are necessary in order to better define the nature of the influence of these genes on pig production traits.

Acknowledgements

Financial support for Antonio Marcos Ramos was provided by FCT Fellowship BD/6877/2001. The authors thank CAPES/Brazilian Ministry of Education, for their sponsorship of R.H. Pita during her stay at Iowa State University. This work was supported in part by funding from Sygen International, PIC USA and the Iowa Agriculture and Home Economics Experiment Station, Ames, Iowa and by Hatch Act and State of Iowa funds, Project 3600.

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