Joint analysis of two breed cross populations in pigs to improve detection and characterization of quantitative trait loci[1]

J.-J. Kim*[2], M. F. Rothschild*, J. Beever†, S. Rodriguez-Zas†, and J. C. M. Dekkers*[3]

*Department of Animal Science, Center for Integrated Animal Genomics, Iowa State University, Ames 50011; and †Department of Animal Science, University of Illinois, Champaign-Urbana 61801

ABSTRACT: The purpose of this study was to develop and implement least squares interval-mapping models for joint analysis of breed cross QTL mapping populations and to evaluate the effect of joint analysis on QTL detected for economic traits in data from two breed crosses in pigs. Data on 26 growth, carcass composition, and meat quality traits from F_2 crosses between commercially relevant pig breeds were used: a Berkshire × Yorkshire cross at Iowa State University (ISU) and a Berkshire × Duroc cross at the University of Illinois (UOI). All animals were genotyped for a total of 39 (ISU) and 32 (UOI) markers on chromosomes 2, 6, 13, and 18. Marker linkage maps derived from the individual and joint data were similar with regard to order and relative position, but some differences in absolute distances existed. Maps from the joint data were used in all analyses. The individual and joint data sets were analyzed using several least squares interval-mapping models: line-cross (LC) models with Mendelian and parent-of-origin effects; halfsib models (HS); and combined models (CB) that included LC and HS effects. Lack-of-fit tests between the models were used to characterize QTL for mode of expression and to identify segregation of QTL within parental breeds. A total of 26 (8), 47 (18), and 53 (16) QTL were detected at the 5% chromosome (genome)-wise level in the ISU, UOI, and joint data for the 26 analyzed traits. Of the 53 QTL detected in the joint data, only six were detected in both populations and for many, allele effects differed between the two crosses. Despite the lack of overlap between the two populations, joint analysis resulted in an increase in significance for many QTL, including detection of ten QTL that did not reach significance in either population. Confidence intervals for position also were smaller for several QTL. In contrast, 24 QTL, most of which were detected at chromosome-wise levels in the ISU or UOI population, were not detected in the joint data. Presence of paternally expressed QTL near the IGF2 region of SSC2 was confirmed, with major effects on backfat and loin muscle area, particularly in the UOI population, as well as one or more QTL for carcass composition in the distal arm of Chromosome 6. Results of this study suggest that joint analysis using a range of QTL models increases the power of QTL mapping and QTL characterization, which helps to identify genes for subsequent marker-assisted selection.

Key Words: Imprinting, Joint Analysis, Quantitative Trait Loci, Swine

 J. Anim. Sci. 2005. 83:1229–1240

Introduction

Over the past decades, several resource populations have been developed from breed crosses to detect chromosomal regions associated with traits of economic importance (i.e., QTL; Andersson, 2001). Although these studies have identified many QTL, their power and mapping resolution (precision of QTL location estimates) has been limited by size of the individual mapping populations. One approach to overcome the limited power of individual studies is to combine data from different populations. The feasibility and power of this approach was demonstrated by Walling et al. (2000) in a joint analysis of seven independent, divergent F_2 crosses between a Western commercial breed and either the Meishan or European Wild Boar to detect QTL for birth weight, backfat, and growth rate on chromosome 4. Whereas most QTL analyses of breed crosses, including the joint analysis by Walling et al. (2000), used the line cross model of Haley et al. (1994) to detect Mendelian QTL that differ in frequency between the parental breeds,

[1]This research was financially supported by National Pork Board, Iowa Pork Producers Association, Iowa Purebred Swine Council, Babcock Swine, Danbred USA, DEKALB Swine Breeders, Sygen International/PIC, Seghers Genetics USA, Shamrock Breeders, and USDA/CSREES IFAFS Grant No. 00-52100-9610.

[2]Present address: School of Biotechnology, Yeungnam University, Gyeongsan, Korea.

[3]Correspondence: 239 Kildee Hall (phone: 515-294-7509; fax: 515-294-9150; e-mail: jdekkers@iastate.edu).

Received November 21, 2004.

Accepted February 23, 2005.

several alternative models have now been developed and implemented to enhance detection and characterization of QTL in breed crosses, including imprinting models to detect parent-of-origin effects (de Koning et al., 2000; Thomsen et al., 2004), half-sib models (de Koning et al., 1999), and combined line-cross and half-sib models (Dekkers et al., 2003). Characterization of the detected QTL for their mode of expression and for their segregation within and between parental breeds provides valuable information for subsequent QTL analyses and marker-assisted selection. The purpose of this study was to further develop and implement these models for detection of QTL for growth, composition, and meat quality traits in a joint analysis of two independent QTL mapping populations created by crossing commercially relevant pig breeds.

Materials and Methods

Populations and Phenotypic and Molecular Data

Data from two F_2 QTL mapping resource populations of commercial pig breeds were used: 1) a Berkshire × Yorkshire population developed at Iowa State University (**ISU**); and 2) a Berkshire × Duroc population that was developed at the University of Illinois (**UOI**), Champaign-Urbana. The ISU population was created by crossing two purebred Berkshire sires and nine Yorkshire dams. Eight F_1 boars and 26 F_1 sows were used to produce 64 full-sib families, with a total of 510 F_2 progeny. The UOI mapping population was created from three Berkshire sires and 19 Duroc dams, from which seven F_1 boars and 56 F_1 sows were used to produce 88 full-sib families, with a total of 825 F_2 offspring. Details about raising and management of the two populations were given by Malek et al. (2001a) and Rodriguez-Zas et al. (2003).

Among the traits that were measured on these two populations, 26 traits that were common to both populations were included in a joint analysis. These included traits related to preweaning growth (birth weight, weaning weight [at d 16 and d 21 in the ISU and UOI populations], and ADG from birth to weaning), post-weaning growth (ADG from weaning to slaughter and live weight at slaughter), body composition (carcass weight, carcass length, loin muscle area, and backfat at the 10th, lumbar, and last rib, and average backfat), fat content (lipid % in the loin and marbling score), glycogen (glycogen content, lactate content, glycolytic potential), color (color score, 24-h Hunter reflectance in the loin), 24-h loin pH, sensory measures (juiciness and tenderness score), and other taste-related measures (firmness, percent cooking loss, average star probe force, and average drip loss). Further descriptions of the trait measures and descriptive statistics are provided in Malek et al. (2001a,b) and Rodriguez-Zas et al. (2003).

Fifty-nine genetic markers, mainly microsatellites, in four chromosomes (2, 6, 13, and 18) that were genotyped in one or both populations, were used to generate linkage maps and to perform QTL analyses. The number of markers for each chromosome (ISU, UOI) was 18 (13, 9), 19 (11, 10), 15 (9, 9), and 7 (6, 4), respectively (Figure 1). Numbers of markers that were common to both populations were limited because of differences in informativeness in the two populations, and were 4, 2, 3, and 3 for chromosomes 2, 6, 13, and 18. Linkage maps based on the ISU, UOI, and joint data were constructed using Crimap Version 2.4 (Green et al., 1994) by using the flips and all options to get the best order. To perform QTL analyses, linkage maps generated from the joint data were used.

QTL Analysis Models

Phenotypes were standardized by dividing by population specific residual SD before QTL analysis. Residual SD were obtained after adjustment for fixed effects (except F_1 sire) that were specified by Malek et al. (2000a,b) for the ISU data and by Rodriguez-Zas et al. (2003) for the UOI data.

Various QTL models that have been developed using the least squares regression framework for analysis of data from an F_2 cross between two outbred breeds were applied, following Dekkers et al. (2003) and Thomsen et al. (2004). All models were based on a one QTL single-trait model and fitted at each 1 cM position to data from each population separately and to the joint data. The most parsimonious Mendelian model fitted to the joint data combined QTL effects fitted in line-cross and half-sib models, following Dekkers et al. (2003), and allowed for interactions of QTL effects with population:

$$\text{Model } \mathbf{CB\text{-}i}\text{: } y_{ijk} = \mathbf{X}_{ijk}\mathbf{b}_{ijk} + s_{ik} + a_k P_{(a)ijk} + d_k P_{(d)ijk} + \alpha_{ik} P_{(\alpha)ijk} + e_{ijk};$$

where y_{ijk} is the standardized phenotype for F_2 progeny j of F_1 sire i in population k (ISU or UOI), $\mathbf{X}_{ijk}$ and $\mathbf{b}_{ijk}$ are the design matrix and solution vector for fixed effects and covariates (same effects as fitted by Malek et al. [2000a,b] and Rodriguez et al. [2003], in addition to the effect of population), s_{ik} is the fixed effect of the ith F_1 sire in population k, and e_{ijk} is a residual. Following the line-cross model of Haley et al. (1994), coefficients a_k and d_k are the additive and dominance effects of breed-origin alleles of a putative QTL at the fitted position for population k, and coefficients $P_{(a)ijk}$ and $P_{(d)ijk}$ are the corresponding breed-origin coefficients. Following the half-sib model of Knott et al. (1996), α_{ik} represents the substitution effect for the two putative QTL alleles carried by the F_1 sire ik and $P_{(\alpha)ijk}$ the probability that the F_2 offspring inherited the one vs. the other QTL allele from its F_1 sire. Reduced Mendelian models were derived from Model CB-i by including only the line-cross components a_k and d_k (Model **LC-i**), only the half-sib components α_{ik} (Model **HS-i**), and by dropping population interaction effects (Models **CB**, **LC**, and **HS**).

To identify parent-of-origin effects, models described by De Koning et al. (2001a) and Thomsen et al. (2004)

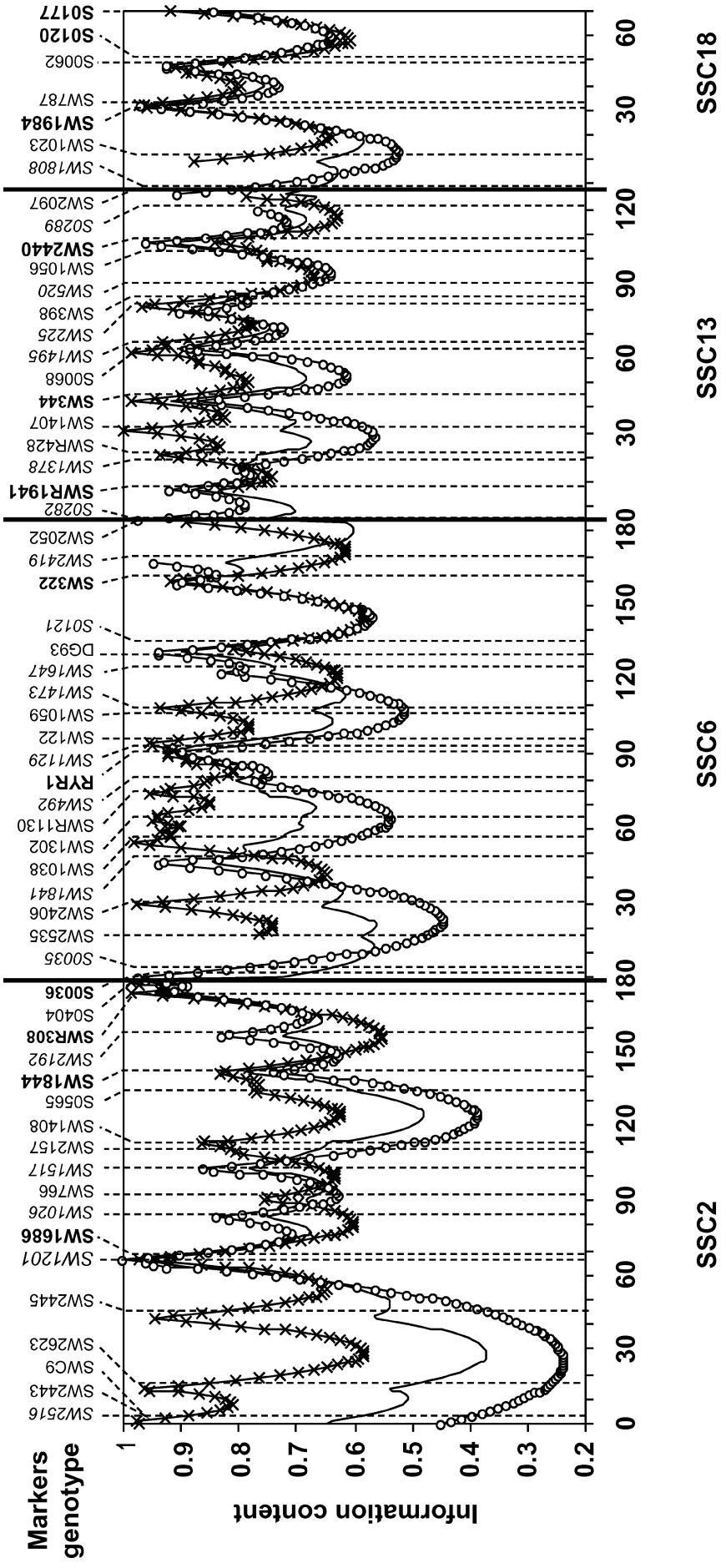

Figure 1. Markers genotyped in only the Iowa State University (ISU) Berkshire × Yorkshire cross (regular font), the University of Illinois (UOI) Berkshire × Duroc cross (italic font), and in both populations (bold font) on SSC 2, 6, 13, and 18, their map distance based on the joint data, and information content for detection of Mendelian QTL under the line-cross model using marker data from the ISU (—o—), UOI (—×—), and joint data (——).

were fitted to the data from each population and the joint data. The most parsimonious imprinting model fitted to the joint data was:

$$\text{Model } \mathbf{FULL\text{-}i}\text{: } y_{ijk} = \mathbf{X}_{ijk}\mathbf{b}_{ijk} + s_{ik} + a_{(pat)k}P_{(pat)ijk} + a_{(mat)k}P_{(mat)ijk} + d_kP_{(d)ijk} + e_{ijk};$$

where $a_{(pat)k}$ and $a_{(mat)k}$ are paternally and maternally inherited effects for population k, and coefficients $P_{(pat)ijk}$ and $P_{(mat)ijk}$ are as defined by De Koning et al. (2001a). Reduced imprinting models were derived from Model FULL-i by including only paternal effects $a_{(pat)k}$ (Model **PAT-i**), only maternal effects $a_{(mat)k}$ (Model **MAT-i**), and by dropping the population interaction effects (Models **FULL**, **PAT**, and **MAT**). All models, except PAT(-i) and MAT(-i) were used to detect QTL in the joint and individual data sets, based on tests against the no QTL model at a 5% chromosome-wise (**ChW**) level.

Tests to Determine the Nature of Detected QTL

A series of tests of alternate models was applied to characterize the QTL detected. In a first set of tests, QTL with parent-of-origin expression were differentiated from Mendelian QTL by testing the LC, FULL, PAT, and MAT models against each other, following the decision tree described in Thomsen et al. (2004). Then, for QTL regions detected using the LC, HS, or CB models and for which no imprinting was detected, a series of tests between the LC, HS, and CB models was applied, following Dekkers et al. (2003), to determine whether the F_0 parents of the two parental breeds that contributed to the cross were fixed for alternate QTL alleles, which will be referred to as LC QTL, or whether the two parental breeds were segregating for the QTL at similar (HS QTL) or different frequencies (CB QTL). These tests are described in further detail below. In all cases, final estimates of QTL effects and QTL position were derived using the inferred mode of expression.

For the joint analyses, breed origin alleles were assumed to be unique *a priori*; thus, the population interaction models were used for QTL detection and for tests for parent-of-origin effects. Significance of population-specific QTL effects were then tested for the inferred mode of expression based on a lack of fit test between the interaction and single effect models. These tests were conducted at the 5% comparison-wise level at the best position for the inferred population-interaction model.

Significance Tests

Empirical significance thresholds against the null model at the 5 and 1% ChW level were derived for each QTL model based on 10,000 permutations for each trait and each data set. Threshold values at the 5 and 1% genome-wise (GW) level were then obtained based on size of the chromosome relative to the whole genome, following de Koning et al. (2001a). These thresholds were used to detect QTL as described above. Tests of alternate models for parent-of-origin expression were conducted at the 5% ChW level, following Thomsen et al. (2004). But, to decrease computing, tests were not conducted at every position in the QTL region, as in Thomsen et al. (2004), but at the best position of the full model in tests of the FULL against the LC model, and at the best position of the PAT or MAT models in tests against the FULL model. In addition, ChW thresholds for these tests were set equal to thresholds obtained for *F*-test statistics against the null hypothesis of no QTL with equivalent numerator degrees of freedom, as suggested by Thomsen et al. (2004). Thus, thresholds for tests of the PAT against the null model were used for tests of the FULL against the LC model because both have 1 df.

For QTL that were not determined to be imprinted based on tests described above, the following tests were conducted to identify segregation of QTL within the parental breeds and to declare a QTL to be a LC, HS, or CB QTL:

LC QTL = the QTL was detected under the LC model, but an *F*-test of the CB over the LC model at the most likely position under the LC model was not significant at the 5% comparison-wise level.

HS QTL = the QTL was detected under the HS model, not significant under the LC model, and an *F*-test of the CB over the HS model at the most likely position under the HS model was not significant at the 5% comparison-wise level:

CB QTL = the QTL was detected with the CB model but could not be defined as a LC or HS QTL based on the previous tests.

Confidence Interval for QTL Position

Confidence intervals (**CI**) for position of QTL were obtained by applying an empirical non-parametric bootstrap method (Visscher et al., 1996) to phenotypes that were pre-adjusted for fixed effects and covariates. For chromosome-trait combinations with significant QTL, 300 bootstrap samples were generated using the inferred QTL model. To decrease the effect of other QTL on the chromosome and of bias of estimates toward marker positions, the distribution of bootstrap estimates was evaluated for clear discontinuities along the chromosome and only estimates that fell within a continuous cluster of estimates around the QTL were used to determine the confidence interval for the QTL. Although this could lead to an underestimate of the confidence interval, this was preferred to having substantial overestimates because of presence of multiple QTL on the chromosome.

Results

Phenotypes

Comparing descriptive statistics presented in Malek et al. (2001a,b) and Rodriguez-Zas et al. (2003), traits

Table 1. Number of QTL detected at various significance levels in the breed cross data from Iowa State University (ISU), the University of Illinois (UOI), and in the joint data (JOINT) on SCC 2, 6, 13, and 18, and the number of QTL detected at various significance levels in the joint data that also were detected in the ISU or UOI data at the 5% chromosome-wise level or better

	QTL detected in			JOINT QTL also detected in:			
Significance level	ISU data	UOI data	JOINT data	ISU + UOI	ISU only	UOI only	Neither data
5% chromosome-wise	13	20	25	1	5	11	8
1% chromosome-wise	5	9	12	0	3	7	2
5% genome-wise	1	5	4	0	1	3	0
1% genome-wise	7	13	12	5	1	6	0
Total	26	47	53	6	10	27	10
QTL not significant in JOINT				0	10	14	—

generally had similar means, ranges, and standard deviations in the two populations. Berkshire-Yorkshire progeny had slightly thicker backfat and a smaller loin muscle than Berkshire-Duroc progeny. Measures related to glycolytic potential had higher means and some extreme phenotypes in the UOI progeny. Tenderness and other taste-related measures were not much different between the two populations, but the Berkshire-Yorkshire progeny had greater drip loss in the fresh product and smaller cooking loss.

Marker Linkage Maps

Marker orders and relative locations obtained from each data set were in good agreement with the USDA-MARC swine genome map (http://www.marc.usda.gov/genome/genome.html). Marker orders were the same for all maps, except for some tightly linked markers (Supplemental Figure, available online). For most chromosomes, map lengths based on the joint and UOI data were larger than distances between corresponding external markers in the USDA and ISU maps.

Information contents across the four chromosomes to detect Mendelian QTL, computed following Knott et al. (1998), are in Figure 1. Average information content was greatest for the ISU data, least for the UOI data, and intermediate for the joint data. Information contents for paternal and maternal expression models (not shown) were slightly higher but had similar patterns as in Figure 1. No region on the four chromosomes showed segregation distortion for additive, dominance, or parent-of-origin effects.

QTL Results

Chromosome-wise significance thresholds for tests against the null model were similar across models, traits, and chromosomes when expressed in terms of the corresponding comparison-wise *P*-value for the *F*-statistic (results not shown). Thus, to allow comparison between models, the $-\log_{10}$ of the comparison-wise *P*-value was used to present the level of significance of QTL results and was 2.2 ± 0.1 for 5% ChW thresholds and 3.5 ± 0.1 for 5% GW thresholds across models, traits, and chromosomes. Thresholds for SSC18 were slightly lower because of its smaller size.

Table 1 summarizes the number of QTL-trait combinations that were significant at the 5% ChW level in analyses of the individual and joint data. The total number of QTL detected was slightly greater for the joint (53) than for the UOI analyses (47), but the number significant at the 5% GW level or better was slightly lower for the joint analyses (16 vs. 18 QTL). The ISU analyses resulted in substantially fewer QTL detected (26 total and eight at the GW level), consistent with its smaller population size.

Only six QTL were significant in all three data sets (joint, ISU, and UOI) and five of these were located in the IGF2 region on SSC2 (see later), which were all significant at the 1% GW level (Table 1). Of the other QTL that were significant in the joint data, 27 were significant in the UOI population but not in the ISU data, 10 were significant in the ISU population but not in the UOI data, and 10 were not detected in either population. The latter represent newly detected QTL through joint analysis and included eight QTL that were significant at the 5% ChW level (for color score at 159 cM on SSC2, reflectance at 151 cM on SSC2, firmness at 75 cM on SSC2, birth weight at 112 cM on SSC6, lipid % at 39 cM on SSC6, live weight at 25 cM on SSC13, growth on test at 25 cM on SSC13, and loin muscle area at 67 cM on SSC18) and two QTL significant at the 1% ChW level (drip loss at 154 cM on SSC2 and average backfat at 183 on SSC6). For most of these QTL there was a peak that approached significance in the individual analyses, but joint analysis allowed the suggestive evidence in each population to reach significance (results not shown). A total of 24 QTL were significant in one individual population (10 for ISU and 14 for UOI) but did not reach significance in the joint analysis.

Tables 2, 3, and 4 present detailed results of QTL that were detected at the 5% GW level in the joint or individual analyses. In these tables, which will be described further by chromosome in the following, results

Table 2. Quantitative trait loci detected on SSC2 at the 5% genome-wise level in the joint or individual population analyses

Trait	Analysis	Position, cM		Significance (logP^c)	QTL type[d]	Estimates of QTL effects	
		Estimate[a]	CI[b]			Additive[e]	Dominance
Last rib backfat	Joint	2	1 to 8	18.8****	Pat-i	0.177 ± 0.045	
						0.446 ± 0.053	
	ISU	1	0 to 5	6.4****	CB	0.140 ± 0.088	–0.044 ± 0.088
	UOI	5	0 to 13	17.1****	Pat	0.483 ± 0.055	
Lumbar backfat	Joint	9	5 to 24	22.7****	Pat-i	0.197 ± 0.046	
						0.545 ± 0.057	
	ISU	1	0 to 10	10.6****	CB	0.185 ± 0.086	–0.087 ± 0.086
	UOI	16	8 to 23	20.5****	Pat	0.585 ± 0.059	
Tenth-rib backfat	Joint	9	3 to 22	24.8****	Pat-i	0.208 ± 0.046	
						0.570 ± 0.057	
	ISU	1	0 to 6	10.1****	CB	0.092 ± 0.086	–0.049 ± 0.086
	UOI	16	7 to 23	22.5****	Pat	0.613 ± 0.059	
Average backfat	Joint	6	2 to 21	28.9****	Pat-i	0.228 ± 0.045	
						0.537 ± 0.056	
	ISU	1	0 to 5	13.2****	CB	0.161 ± 0.085	–0.071 ± 0.085
	UOI	12	3 to 20	21.7****	Pat	0.583 ± 0.059	
Loin muscle area	Joint	24	18 to 29	29.1****	Pat-i	–0.263 ± 0.052	
						–0.674 ± 0.063	
	ISU	5	1 to 8	6.5****	Pat	–0.235 ± 0.045	
	UOI	24	17 to 32	24.4****	Pat	–0.651 ± 0.061	
Lipid %	Joint	108	92 to 116	5.4****	LC-i	0.031 ± 0.071	–0.286 ± 0.102
						0.268 ± 0.060	–0.189 ± 0.096
	ISU	*109*		*1.6^{NS}*	*LC*	—	—
	UOI	97	92 to 121	5.6****	LC	0.264 ± 0.058	–0.225 ± 0.092
Marbling score	Joint	52	44 to 63	3.7***	LC-i	–0.038 ± 0.073	–0.307 ± 0.121
						0.216 ± 0.063	–0.232 ± 0.119
	ISU	*51*		*1.3^{NS}*	LC	—	—
	UOI	63	52 to 103	3.3**	LC	0.166 ± 0.050	–0.165 ± 0.076
Juiciness score	Joint	90	75 to 98	6.1****	LC	0.240 ± 0.047	–0.096 ± 0.071
	ISU	*87*		*2.2^{NS}*	LC	—	—
	UOI	88	69 to 97	4.6****	LC	0.235 ± 0.060	–0.217 ± 0.096
Tenderness score	Joint	42	NA[f]	6.8****	CB-i	–0.060 ± 0.113	–0.094 ± 0.114
						0.480 ± 0.114	0.067 ± 0.169
	ISU			*<1*	CB	—	—
	UOI	40	NA	8.9****	CB	0.475 ± 0.116	0.066 ± 0.178
Tenderness score	Joint	100	91 to 113	9.6****	LC-i	0.069 ± 0.078	0.001 ± 0.119
						0.388 ± 0.056	0.134 ± 0.085
	ISU	*90*		*<1*	LC	—	—
	UOI	104	92 to 118	10.7****	LC	0.365 ± 0.054	0.168 ± 0.080
Star probe force	Joint	100	91 to 109	13.0****	CB-i	–0.034 ± 0.105	0.011 ± 0.121
						–0.523 ± 0.081	–0.166 ± 0.085
	ISU	*92*		*1.2^{NS}*	CB	—	—
	UOI	102	92 to 109	14.4****	CB	–0.500 ± 0.077	–0.154 ± 0.077
Drip loss	Joint	48	32 to 66	3.8**	CB	–0.055 ± 0.073	0.024 ± 0.087
	ISU	50	32 to 66	4.5***	CB	0.097 ± 0.110	0.062 ± 0.120
	UOI	*30*		*1.1^{NS}*	CB	—	—

[a]Position at which the test-statistic value was maximized for the inferred QTL model.
[b]95% confidence interval for location estimates for the inferred mode of expression.
[c]Negative logarithm of the comparison-wise *P*-value of the test-statistic against the null hypothesis of no QTL at the most likely position for the inferred QTL model.
[d]Declared QTL type: LC = line-cross QTL; HS = half-sib QTL; CB = combined type QTL; Pat = QTL with paternal expression; Mat = QTL with maternal expression; Partial = parent-of-origin QTL with expression of both parental alleles. For the joint analyses, -i indicates significance of the population interaction term with the assumption of different effects for the two maternal breed alleles (or populations).
[e]Estimates of additive effects for LC or CB QTL and of paternal and maternal effects for parent-of-origin QTL. Estimates in first and second lines for type -i QTL in the joint analyses represent estimates for the Iowa State University and University of Illinois populations. All estimates are expressed in residual phenotype standard deviations.
[f]Confidence interval could not be derived because of multiple QTL detected on the chromosome.
*Significant at the 5% chromosome-wise level.
**Significant at the 1% chromosome-wise level.
***Significant at the 5% genome-wise level.
****Significant at the 1% genome-wise level.
NS = QTL not significant but included for completeness, with position estimate denoted in italic font.

Table 3. Quantitative trait loci detected on SSC6 at the 5% genome-wise level in the joint or individual population analyses

Trait	Analysis	Position, cM		Significance (logP^c)	QTL type[d]	Estimates of QTL effects	
		Estimate[a]	CI[b]			Additive[e]	Dominance
Carcass length	Joint	135	115 to 143	4.4***	LC	0.193 ± 0.044	–0.068 ± 0.070
	ISU	*135*		*<1^{NS}*	LC	—	—
	UOI	131	107 to 142	4.3***	LC	0.225 ± 0.051	–0.067 ± 0.074
Last rib backfat	Joint	168	142 to 183	3.3**	Pat-i	0.067 ± 0.053	
						–0.137 ± 0.037	
	ISU	*168*		*<1^{NS}*		—	—
	UOI	167	140 to 183	3.7***	Pat	–0.137 ± 0.037	
Tenth-rib backfat	Joint	122	NA[f]	4.6****	CB	0.078 ± 0.064	0.172 ± 0.068
	ISU	108	NA	2.3*	HS	—	—
	UOI	*122*		*<1^{NS}*		—	—
Tenth-rib backfat	Joint	167	NA	4.4***	CB-i	–0.340 ± 0.110	0.240 ± 0.121
						0.063 ± 0.078	0.055 ± 0.075
	ISU	165	NA	3.4**	CB	–0.333 ± 0.106	0.220 ± 0.115
	UOI	*167*		*1.1^{NS}*	CB	—	—
Average backfat	UOI	86	70 to 100	3.5***	Mat	0.146 ± 0.039	
Loin muscle	Joint	100	87 to 122	5.2****	LC	–0.228 ± 0.047	–0.056 ± 0.076
	ISU	*89*		*2.2^{NS}*	LC	—	—
	UOI	107	59 to 125	4.8****	LC	–0.306 ± 0.065	–0.067 ± 0.115
Lipid %	ISU	167	158 to 173	4.1****	Partial	0.101 ± 0.051[g]	0.347 ± 0.051
						–0.168 ± 0.051	

[a,b,c,d,e,f]See Table 2 for a description of column headings.
[g]Estimate of the paternal effect in the first line and of the maternal effect in the second line.
*Significant at the 5% chromosome-wise level.
**Significant at the 1% chromosome-wise level.
***Significant at the 5% genome-wise level.
****Significant at the 1% genome-wise level.
NS = QTL not significant but included for completeness, with position estimate denoted in italic font.

of the individual population analyses were included for all QTL that were significant in the joint analyses for comparison purposes.

QTL on SSC2. Several QTL for backfat measures, muscle, fat, and tenderness traits were detected on SSC2 with high statistical evidence, in particular in the UOI data (Table 2, Figure 2). A strong QTL (significant at the 1% GW level) was detected for each backfat trait and in each data set in the proximal region of the chromosome (0 to 16 cM). This is near IGF2, which is located around 1 cM on the joint map, near SWC9 (Nezer et al., 2003). These QTL were declared to be paternally expressed following the decision tree of Thomsen et al. (2004) based on the UOI and the joint data, but as CB QTL in the ISU data. Parent-of-origin effects were, however, close to significant in the ISU data and the paternal expression model itself was significant at the 5% GW level (Figure 2). Point estimates for the backfat QTL were at the beginning of the chromosome for the ISU data, but at positions further down the chromosome for the UOI and joint data. Confidence intervals for the UOI and joint data did not always include the IGF2 location. In both populations, the Berkshire allele resulted in greater backfat (Table 2), but this effect was much stronger in the UOI data (> 0.5 SD or 0.22 cm).

The same proximal region of SSC2 also contained a strong (1% GW level) QTL for loin muscle area (Table 2; Figure 2) with a paternal expression mode in all data sets. Similar to backfat, effects of this QTL on loin muscle area were substantially greater for the UOI (0.65 SD or 3 cm^2) than the ISU data (0.24 SD), but the Berkshire allele resulted in lower loin muscle area in both populations. In the near proximal region (52 cM), a strong QTL was detected in the joint analysis for marbling (Table 2; Figure 3). This so-called 5% GW LC-i QTL was declared to be a LC QTL, had a significant population interaction effect (–i), and was significant at a 5% GW level for its declared mode of expression (i.e., the LC-i model). This QTL was not significant in the ISU but suggestive in the UOI data. For both populations, heterozygous individuals had the lowest degree of marbling for the QTL at 52 cM (–0.31 and –0.23 SD for ISU and UOI; see Table 2).

In the same region as the marbling QTL (at 42 cM), a QTL for tenderness was detected in the UOI and joint data (1% GW CB-i QTL). In contrast to the marbling QTL, which was declared to be a LC QTL, evidence of segregation was detected at this QTL (CB QTL), but on average, the Berkshire allele resulted in greater tenderness, consistent with the greater marbling score. There was no evidence for dominance at the tenderness QTL; however, in contrast to the marbling QTL. Also in this same region (at 48 cM), but now in the ISU data, a QTL for drip loss was detected (Table 2).

Around 100 cM on the joint map, close to the second QTL for marbling in the UOI data, strong QTL were detected for lipid % (1% GW LC-i at 108 cM), juiciness (1% GW LC at 90 cM), tenderness (1% GW LC-i at 100

Table 4. Quantitative trait loci detected on SSC13 and SSC18 at the 5% genome-wise level in the joint or individual population analyses

Trait	Analysis	Position, cM		Significance	QTL	Estimates of QTL effects	
		Estimate[a]	CI[b]	(log*P*[c])	type[d]	Additive[e]	Dominance
				Chromosome 13			
Loin muscle area	Joint	77	66 to 98	3.4***	HS	—	—
	ISU	*77*		*<1*	HS	—	—
	UOI	74	66 to 100	4.3****	CB	0.206 ± 0.080	0.061 ± 0.087
Cooking loss	UOI	86	75 to 106	3.6***	Mat	0.137 ± 0.038	
				Chromosome 18			
Lipid %	Joint	70	62 to 72	3.5**	LC-i	–0.096 ± 0.071	0.098 ± 0.100
						0.222 ± 0.056	0.135 ± 0.086
	ISU	*66*		*<1*		—	—
	UOI	72	62 to 73	3.9***	LC	0.220 ± 0.055	0.112 ± 0.082
Glycogen content	Joint	40	36 to 52	3.2**	Pat-i	–0.186 ± 0.050	
						0.040 ± 0.041	
	ISU	38	36 to 48	3.8****	Pat	–0.181 ± 0.048	
	UOI	*51*		*1.1*^{NS}	Pat	—	
24-h loin pH	Joint	10	0 to 18	2.6*	Mat-i	0.000 ± 0.050	
						–0.177 ± 0.051	
	ISU	*10*		*<1*	Mat	—	
	UOI	10	0 to 18	3.2****	Mat	–0.177 ± 0.051	

[a,b,c,d,e]See Table 2 for a description of column headings.
*Significant at the 5% chromosome-wise level.
**Significant at the 1% chromosome-wise level.
***Significant at the 5% genome-wise level.
****Significant at the 1% genome-wise level.
NS = QTL not significant but included for completeness, with position estimate denoted in italic font.

cM), and Star probe force (1% GW CB-i at 100 cM; Table 2). All these QTL were detected at 1% GW level in the UOI data but not significant in the ISU data. For the QTL in this region, the Berkshire allele in the UOI population had greater lipid %, marbling, juiciness, and tenderness, and lower force required to puncture the meat compared with the Duroc allele (Table 2).

QTL on SSC6. Toward the end of chromosome 6 (at 167 cM), QTL associated with backfat at the last and 10th rib were detected in the joint analysis (Table 3), but with evidence for the last rib QTL coming from the UOI data and for the 10th rib QTL from the ISU data. For both QTL, the Berkshire allele resulted in less backfat but with evidence of paternal-only expression for the last-rib QTL in the UOI population, and with segregation and increased backfat for the heterozygote for the tenth-rib QTL in the ISU population. These could represent the same QTL but with their expression being dependent on developmental stage and population background. The same region also showed QTL significant at the 5% ChW level for lumbar and average backfat in the same region in the joint analyses (data not shown). The ISU data also showed a QTL for lipid % in the same region, with evidence for partial imprinting, with greater lipid % for the heterozygote and lower lipid % for the Berkshire allele when inherited through the maternal side (Table 3). The ISU data also showed evidence for HS QTL for 10th-rib backfat (at 108 cM), whereas the UOI data showed evidence of a QTL for loin muscle area at 107 cM. Both these QTL also were significant in the joint analyses at the GW level but with segregating vs. fixed breed alleles, respectively (Table 3).

QTL on SSC13. One QTL affecting loin muscle area was detected in the interstitial region of SSC13 at the 5% GW level in the joint and UOI data (Table 4). This QTL had significant evidence of segregation in the parental breeds. In the same region, QTL for lipid %, 10th-rib and average backfat, and carcass weight and length were detected at the 5% ChW level in the joint and UOI data (data not shown). One maternally expressed QTL for cooking loss was detected at the 5% GW level in the UOI data, but this QTL was not significant in the joint data.

QTL on SSC18. Three QTL were detected at the 5% GW level in SSC18 (Table 4); a LC QTL for lipid % at 72 cM in the UOI data; a paternally expressed QTL for glycogen content at 38 cM in the ISU data; and a maternally expressed QTL for 24-h loin pH at 10 cM in the UOI data. None of these QTL was significant in the other population and, as a result, they were detected with a lower level of statistical evidence (at the 1 and 5% ChW level) in the joint data, and had different allele effects in the two populations.

Discussion

QTL Detection Using Joint Data

This study reports on the use of a comprehensive set of models for joint QTL analysis of two F_2 pig populations

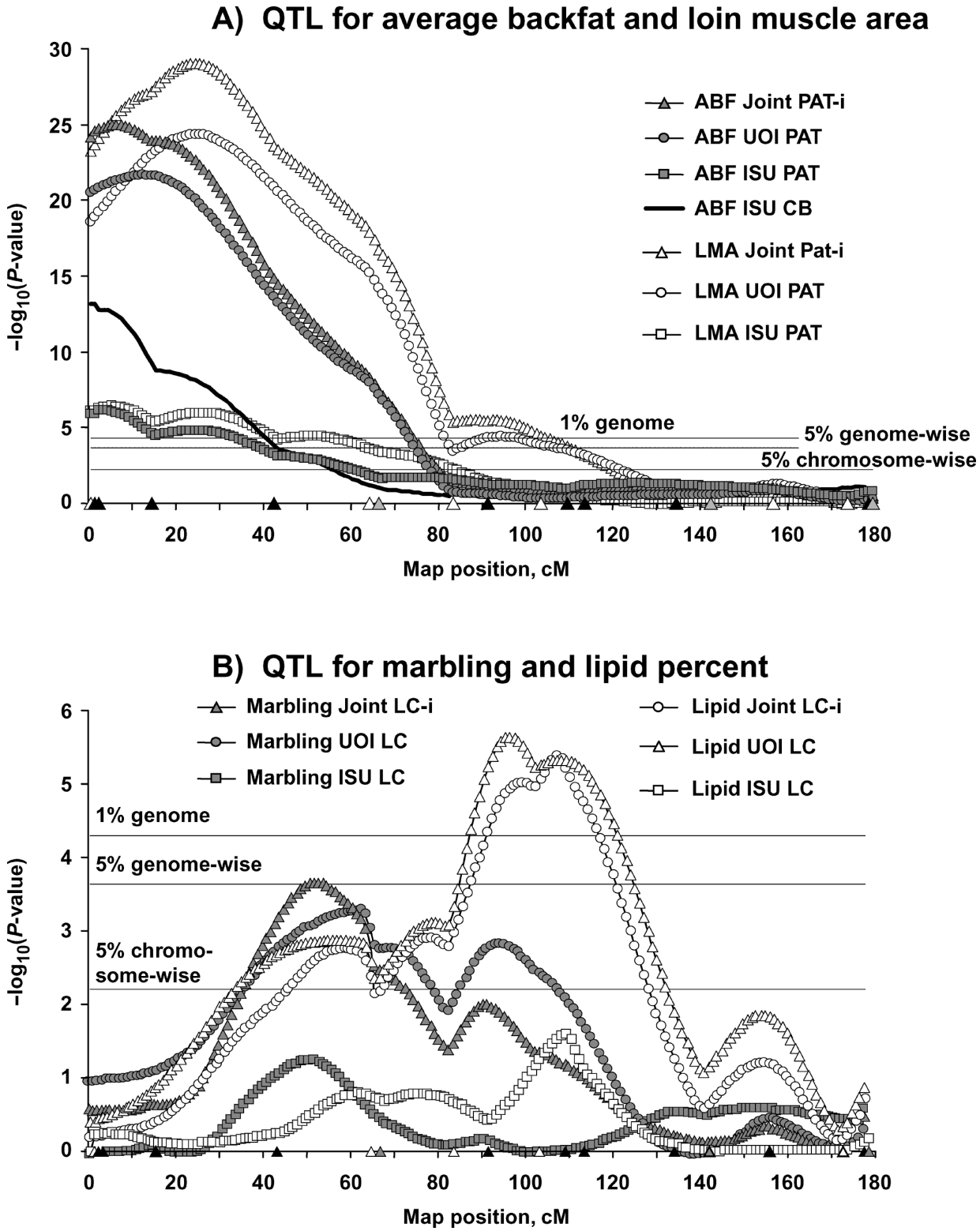

Figure 2. Profiles for QTL on SSC 2 using data from the Iowa State University (ISU) Berkshire × Yorkshire cross, the University of Illinois (UOI) Berkshire × Duroc cross, and the joint data. Shown is the negative of the logarithm of the comparison-wise significance value for the inferred QTL models against position on the joint linkage map. Markers genotyped in the ISU and UOI population are indicated by open and closed triangles on the x-axis, with shaded triangles indicating markers genotyped in both populations. Shown are (A) profiles for the inferred models for average backfat (ABF) and loin muscle area (LMA), which was the paternal (PAT) expression model for all cases, except for the combined (CB) model for average backfat in the ISU data, and (B) profiles for the inferred models for marbling and lipid %, which was the line-cross model for all cases. For all four traits, QTL effects were significantly different ($P < 0.05$) between the two populations.

generated from commercial breeds. All models were based on the least squares framework, which facilitates implementation. Advantages of combined analysis of QTL data to improve power for QTL detection and mapping precision have been suggested (Allison and Heo, 1998) but only a limited number of studies have reported on results from such analyses (Walling et al., 2000), despite a large number of reports on individual populations (Bidanel and Rothschild, 2002).

Separate analyses of the ISU and UOI populations resulted in substantial numbers of QTL detected, but there was generally limited overlap between QTL detected in the two populations (Table 1). This lack of overlap may be due to the difference in the F_0 parents that were used to create these two populations (i.e., Yorkshire vs. Duroc as the maternal breed). Although the Berkshire breed was common to both populations, only two Berkshire sires contributed to the ISU population and a different set of three sires to the UOI population. Thus, QTL alleles present in the F_0 parents could have differed substantially between the two populations. The difference in the genetic basis of these two populations was further substantiated by the fact that of the 16 QTL that were significant at the GW level in the joint analysis, 12 had significant evidence of a QTL by population interaction (Tables 2, 3, 4). Presence of a population interaction can be caused by different effects of the QTL in the two populations, but it is more likely caused by different QTL frequencies in the F_0 parents between the two populations or that the QTL is segregating in the one population but not in the other.

Despite the lack of overlap between results from the two separate population analyses, joint analysis in general resulted in greater significance of QTL and greater mapping precision (i.e., smaller CI for QTL position). For example, joint analysis resulted in detection of nine QTL (at the 5% ChW level) that did not reach significance in either population (Table 1) and in greater levels of significance for many QTL for which only one of the populations was significant (Tables 2, 3, 4). Both these cases support increasing evidence of QTL from joint analysis. However, for six QTL, joint analysis resulted in lower significance of the detected QTL compared with the individual population analyses (Tables 2, 3, 4), and 24 QTL were not detected in the joint data (Table 1). These tended to be QTL for which one of the populations provided no indication of presence of a QTL. Some QTL had substantially different position estimates in the two populations and resulted in longer confidence intervals for the joint than for the individual analyses. Examples are the backfat and loin muscle area QTL on SSC2, for which position estimates were at the IGF2 gene for the ISU data, but 5 to 15 cM distal from IGF2 for the UOI data (Table 2). It is possible that two QTL were segregating in the UOI population, one at IGF2 and one further into the chromosome, but this could not be confirmed by a two-QTL analysis (data not shown). In addition, it must be noted that, although the first marker was at IGF2 (position 0), the second marker that was genotyped in the UOI population was at 60 cM (Figure 1). This large distance between markers and low information content in the region, may cause biased position estimates and CI, so position estimates from the UOI and joint data must be interpreted with care.

Data from the two populations were standardized by their respective residual SD before analysis to ensure homogeneous residual variance in the joint analyses. Residual SD can differ between populations because of differences in scale or accuracy of measurement or population differences in genetic or environmental variances. This adjustment assumes that differences in QTL effects between populations are multiplicative, which could introduce interactions between QTL and population if QTL effects are the same in both populations on the original scale. This could be tested by comparing population-specific QTL effect estimates after back-transformation to the original scale.

QTL Characterization

The QTL type declarations in the individual population analyses generally supported the QTL type designation in the joint analysis but with some exceptions. For example, the QTL for backfat and loin muscle area in the IGF2 region on SSC2 were detected as CB QTL in the ISU population but as paternally expressed QTL in the UOI and joint analyses. A previous analysis of the ISU data by Thomsen et al. (2004) declared the backfat QTL in this region to be paternally expressed, but this was with a model that did not include F_1 sire. In both their and the present analyses of the ISU data, the Mendelian (LC) model was significant in this region for all backfat traits, but in the present analysis, the subsequent test for presence of imprinting (i.e., the test of the FULL against the Mendelian model) only approached 5% ChW significance, implying no parent-of-origin effects. When characterizing these QTL further, all backfat QTL in this region were declared as CB QTL for the ISU data. It should be noted that this declaration may in fact be consistent with presence of paternal expression because the HS component in the CB model allows for differential allele effects, depending on parental origin, by fitting additional effects for one of the parental origin alleles. The CB model can, therefore, model parent-of-origin effects (paternal-only as well as maternal-only expression) and is confounded with the parent-specific expression models. Thus, although not significant, the present ISU results do not exclude paternal-only expression of these QTL. Indeed, paternal-only expression was confirmed in the joint analysis, but with different effects in the two populations (Table 2). Thus, QTL type declarations must be interpreted with care because of the confounding between some models.

The small number of QTL with evidence of segregation within the parental breeds (HS or CB QTL) does not imply that most QTL will be fixed in alternate breeds. In a simulation study, Kim and Dekkers (2004) demonstrated the greater power of F_2 designs to detect LC QTL

and the limited ability to determine that detected QTL that are declared to be HS or CB QTL are indeed segregating within the parental breeds. Nevertheless, the use of the CB and HS models aids in detecting more QTL than using the LC model alone (Dekkers et al., 2003).

Six additional QTL with parent-of-origin effects were detected at the GW level in individual populations, but for all these, no QTL was detected in the other population and the joint analysis reached significance at the 5 or 1% ChW level for only three of these QTL (Tables 2, 3, and 4). Parent-of-origin effects in these regions must be confirmed in other studies.

Comparison of QTL Results with Previous Studies

Previous results have extensively reported on QTL detected in the ISU population, including using linecross (Malek et al., 2000a,b), parent-of-origin (Thomsen et al., 2004), and QTL segregation models (Dekkers et al., 2003). Further discussion will, therefore, focus primarily on QTL detected at the GW level in the joint and UOI analyses.

Our results for paternally expressed QTL in the proximal region of SSC2 (Table 3; Figure 2) confirm previous evidence of similar results in several populations (Jeon et al., 1999; Nezer et al., 1999; de Koning et al., 2001b) and the recent identification of a causative SNP in the IGF2 gene (Nezer et al., 2003; van Laere et al., 2003). Bidanel et al. (2001) detected a Mendelian QTL for backfat thickness in this region in a Meishan and Large White cross but did not test for imprinting. Milan et al. (2002) detected QTL for backfat weight and loin weight in the same population and region but did not find evidence of parent-of-origin effects.

The QTL identified on SSC6 partially confirm results from other populations. De Koning et al. (1999) also found a QTL for backfat thickness in the distal region of the chromosome in a Meishan and Dutch White cross, where our study found conflicting parent-of-origin effects. However, further analyses by De Koning et al. (2001b) did not identify parent-of-origin effects. De Koning et al. (2001b) did detect a maternally expressed QTL for backfat in a similar region where the maternally expressed UOI QTL for average backfat resided (86 cM). Ovilo et al. (2000) detected a Mendelian QTL for loin muscle area and backfat in an Iberian and Landrace cross between our two QTL regions for 10th rib backfat. Rohrer (2000) and Bidanel et al. (2001) also detected a Mendelian backfat QTL in Meishan and Large White crosses, whose locations were close to the average back QTL and the 10th rib QTL region in SSC6, respectively, in our study. Combined, these studies clearly demonstrate the presence of one or more QTL for carcass composition on the distal arm of SSC6, although the mode of expression of these QTL remains unclear.

Our finding of a QTL for 24-h loin pH on SSC18 confirms a suggestive QTL for ham muscle pH at 24 h by De Koning et al. (2001a) in a Meishan and Dutch commercial pig cross. De Koning et al. (2001a) found no evidence of parent-of-origin effect for that QTL, in contrast to the evidence for maternal-only expression that was found here.

Implications

This study demonstrates the feasibility and usefulness of joint analysis of quantitative trait loci mapping experiments in terms of greater power to detect quantitative trait loci and greater quantitative trait loci mapping precision, even when breeds involved in the alternate crosses are quite different. Implementation of various Mendelian and parent-of-origin quantitative trait loci models allowed better quantitative trait loci detection and characterization, by utilizing the appropriate model according to the nature of quantitative trait loci. This enables proper definition of quantitative trait loci in terms of mode of gene action and of segregation of alleles within the parental breeds, which provides valuable information for subsequent quantitative trait loci analyses and marker-assisted breeding schemes. Many quantitative trait loci were not detected in both populations or had different effects or frequencies in the two populations, suggesting that quantitative trait loci must be validated in commercial populations before application. The quantitative trait loci identified and confirmed in this study have important economic effects for pork production.

Literature Cited

Allison, D. B., and M. Heo. 1998. Meta-analysis of linkage data under worst-case conditions: A demonstration using the Human OB region. Genetics 148:859–865.

Andersson, L. 2001. Genetic dissection of phenotypic diversity in farm animals. Nat. Rev. Genet. 2:130–138.

Bidanel, J. P., and M. Rothschild. 2002. Current status of quantitative trait locus mapping in pigs. Pig News Inf. 23 (2):39N–53N.

Bidanel, J., D. Milan, N. Iannuccelli, Y. Amigues, M. Boscher, F. Bourgeois, J. Caritez, J. Gruand, P. Le Roy, H. Lagant, R. Quintanilla, C. Renard, J. Gellin, L. Ollivier, and C. Chevalet. 2001. Detection of quantitative trait loci for growth and fatness in pigs. Genet. Sel. Evol. 33:289–309.

Dekkers, J., J.-J. Kim, M. Malek, H. Thomsen, H. Lee, H.-H. Zhao, and M. Rothschild. 2003. A genome scan to detect QTL affecting growth, composition, and meat quality trait in a Berkshire × Yorkshire cross. Pages 1–21 in Proc. 28th National Swine Improvement Federation, Des Moines, IA.

De Koning, D. J., L. L. G. Janss, A. P. Rattink, P. A. M. van Oers, B. J. de Vries, M. A. M. Groenen, J. J. van der Poel, P. N. de Groot, E. W. Brascamp, and J. A. M. van Arendonk. 1999. Detection of quantitative trait loci for backfat thickness and intramuscular fat content in pigs (*Sus scrofa*). Genetics 152:1679–1690.

De Koning, D. J., A. P. Rattink, B. Harlizius, J. A. M. van Arendonk, E. W. Brascamp, and M. A. M. Groenen. 2000. Genome-wide scan for body composition in pigs reveals important role of imprinting. Proc. Natl. Acad. Sci. USA 97:7947–7950.

De Koning, D. J., B. Harlizius, A. P. Rattink, M. A. M. Groenen, E. W. Brascamp, and J. A. M. van Arendonk. 2001a. Detection and characterization of quantitative trait loci for meat quality traits in pigs. J. Anim. Sci. 79:2812–2819.

De Koning, D. J., A. P. Rattink, B. Harlizius, M. A. M. Groenen, E. W. Brascamp, and J. A. M. van Arendonk. 2001b. Detection and characterization of quantitative trait loci for growth and reproduction traits in pigs. Livest. Prod. Sci. 72:185–198.

Green, P., K. Fallis, and S. Crooks. 1994. Documentation for CRIMAP version 2.4, Washington Univ. School of Med., St. Louis, MO.

Haley, C. S., S. A. Knott, and J.-M. Elsen. 1994. Mapping quantitative trait loci in crosses between outbred lines using least squares. Genetics 136:1195–1207.

Jeon, J. T., O. Carlborg, A. Toernsten, E. Giuffra, V. Amarger, P. Chardon, L. Andersen-Eklund, K. Andersson, I. Hansson, K. Lundstroem, and L. Andersson. 1999. A paternally expressed QTL affecting skeletal and cardiac muscle mass in pig maps to the IGF2 locus. Nat. Genet. 21:157–158.

Kim, J.-J., and J. C. M. Dekkers. 2004. A combined line-cross and halfsib model to detect and characterize QTL in an F_2 outbred cross population. J. Anim. Sci. 82(Suppl. 1):415. (Abstr.)

Knott, S. A., J. M. Elson, and C. S. Haley. 1996. Methods for multimarker mapping of quantitative trait loci in half-sib populations. Theor. Appl. Genet. 93:71–80.

Knott, S. A., L. Marklund, C. S. Haley, K. Andersson, W. Davis, H. Ellegren, M. Fredholm, I. Hansson, B. Hoyheim, K. Lundstrom, M. Moller, and L. Andersson. 1998. Multiple marker mapping of quantitative trait loci in a cross between outbred wild boar and Large White pigs. Genetics 149:1069–1080.

Malek, M., J. C. M. Dekkers, H. K. Lee, T. J. Baas, K. Prusa, E. Huff-Lonergan, and M. F. Rothschild. 2001a. A molecular genome scan analysis to identify chromosomal regions influencing economic traits in the pig. II. Meat and muscle composition. Mamm. Genome 12:637–645.

Malek, M., J. C. M. Dekkers, H. K. Lee, T. J. Baas, and M. F. Rothschild. 2001b. A molecular genome scan analysis to identify chromosomal regions influencing economic traits in the pig. I. Growth and body composition. Mamm. Genome 12:630–636.

Milan, D., J-P. Bidanel, N. Iannuccelli, J. Riquet, Y. Amigues, J. Gruand, P. Le Roy, C. Renard, and C. Chevalet. 2002. Detection of quantitative trait loci for carcass composition traits in pigs. Genet. Sel. Evol. 34:705–728.

Nezer, C., C. Collette, L. Moreau, B. Brouwers, J. J. Kim, E. Giuffra, N. Buys, L. Andersson, and M. Georges. 2003. Haplotype sharing refines the location of an imprinted quantitative trait locus with major effect on muscle mass to a 250-kb chromosome segment containing the porcine IGF2 gene. Genetics 165:277–285.

Nezer, C., L. Moreau, B. Brouwers, W. Coppieters, J. Detillieux, R. Hanset, L. Karim, A. Kvasz, P. LeRoy, and M. Georges. 1999. An imprinted QTL with major effect on muscle mass and fat deposition maps to the IGF2 locus in pigs. Nat. Genet. 21:155–156.

Ovilo, C., M. Perez-Enciso, C. Barragan, A. Clop, C. Rodrigues, M. A. Oliver, M. A. Toro, and J. L. Noguera. 2000. A QTL for intramuscular fat and backfat thickness is located on porcine chromosome 6. Mamm. Genome 11:344–346.

Rodriguez-Zas, S., T. Stearns, J. Beever, J. Hartschuh, M. Ellis, and F. McKeith. 2003. Mapping of quantitative trait loci for weight, carcass and meat quality traits on pig chromosomes six and thirteen. Pages 59–70 in Proc. 28th National Swine Improvement Federation, Des Moines, IA.

Rohrer, G. A. 2000. Identification of quantitative trait loci affecting birth characters and accumulation of backfat and weight in a Meishan-White composite resource population. J. Anim. Sci. 78:2547–2553.

Thomsen, H., H. K. Lee, M. F. Rothschild, M. Malek, and J. C. M. Dekkers. 2004. Characterization of quantitative trait loci for growth and meat quality in a cross between commercial breeds of swine. J. Anim. Sci. 82:2213–2228.

Van Laere, A. S., M. Nguyen, M. Braunschweig, C. Nezer, C. Collette, L. Moreau, A. L. Archibald, C. S. Haley, N. Buys, M. Tally, G. Andersson, M. Georges, and L. Andersson. 2003. A regulatory mutation in IGF2 causes a major QTL effect on muscle growth in the pig. Nature 425:832–836.

Visscher, P. M., R. Thompson, and C. S. Haley. 1996. Confidence intervals in QTL mapping by bootstrapping. Genetics 143:1013–1020.

Walling, G. A., P. M. Visscher, L. Andersson, M. F. Rothschild, L. Wang, G. Moser, M. A. M. Groenen, J.-P. Bidanel, S. Cepica, A. L. Archibald, H. Geldermann, D. J. de Koning, D. Milan, and C. S. Haley. 2000. Combined analyses of data from quantitative trait loci mapping studies: Chromosome 4 effects on porcine growth and fatness. Genetics 155:1369–1378.