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Epistatic analysis of carcass characteristics in pigs reveals genomic interactions between quantitative trait loci attributable to additive and dominance genetic effects[1]

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ABSTRACT: The present study focused on the identification of epistatic QTL pairs for body composition traits (carcass cut, lean tissue, and fat tissue weights) measured at slaughter weight (140 kg of BW) in a 3-generation full-sib population developed by crossing Pietrain sires with a crossbred dam line. Depending on the trait, phenotypic observations were available for 306 to 315 F_2 animals. For the QTL analysis, 386 animals were genotyped for 88 molecular markers covering chromosomes SSC1, SSC2, SSC4, SSC6, SSC7, SSC8, SSC9, SSC10, SSC13, and SSC14. In total, 23 significant epistatic QTL pairs were identified, with the additive × additive genetic interaction being the most prevalent. Epistatic QTL were identified across all chromosomes except for SSC13, and epistatic QTL pairs accounted for between 5.8 and 10.2% of the phenotypic variance. Seven epistatic QTL pairs were between QTL that resided on the same chromosome, and 16 were between QTL that resided on different chromosomes. *Sus scrofa* chromosome 1, SSC2, SSC4, SSC6, SSC8, and SSC9 harbored the greatest number of epistatic QTL. The epistatic QTL pair with the greatest effect was for the entire loin weight between 2 locations on SSC7, explaining 10.2% of the phenotypic variance. Epistatic associations were identified between regions of the genome that contain the *IGF-2* or melanocortin-4 receptor genes, with QTL residing in other genomic locations. Quantitative trait loci in the region of the melanocortin-4 receptor gene and on SSC7 showed significant positive dominance effects for entire belly weight, which were offset by negative dominance × dominance interactions between these QTL. In contrast, the QTL in the region of the *IGF-2* gene showed significant negative dominance effects for entire ham weight, which were largely overcompensated for by positive additive × dominance genetic effects with a QTL on SSC9. The study shows that epistasis is of great importance for the genomic regulation of body composition in pigs and contributes substantially to the variation in complex traits.

Key words: carcass characteristic, epistasis, fatness, leanness, pig, quantitative trait locus

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INTRODUCTION

Numerous QTL have been reported for carcass characteristics in pigs (e.g., Geldermann et al., 2003; Karlskov-Mortensen et al., 2006; Liu et al., 2007). These studies have focused on identifying the individual QTL effects (additive, dominance, and imprinting), without considering interactions between loci (epistasis). When epistasis is ignored, some QTL may remain undetected, and the effects of the identified QTL can be severely biased (Carlborg, 2006). Furthermore, the inclusion of epistasis provides a better understanding of the genomic control of economically important traits.

Evidence exists for epistatic QTL in pigs for reproductive traits (Bidanel, 1993; Rodríguez et al., 2005; Noguera et al., 2006), coat color (Hirooka et al., 2002), meat quality (Ovilo et al., 2002; Szyda et al., 2006), and muscle fiber traits (Estellé et al., 2008). Studies in chickens have shown that epistasis is involved in the genomic regulation of growth traits (Carlborg et al., 2003, 2004). Moreover, studies in mice have identified

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epistatic QTL for growth and obesity (e.g., Brockmann et al., 2000; Yi et al., 2004a,b, 2006). Generally, these studies suggest that different networks of interactions are involved in the genomic regulation of different groups of traits.

Body composition of pigs may be controlled by a complex set of interactions; however, there is currently a lack of knowledge of epistatic QTL involved in the genomic regulation of the lean and fat tissue of pigs. This is most likely because of the computational demand associated with this type of analysis, rather than epistasis not being important for the genomic regulation of these traits.

In the present study, we investigated epistatic QTL pairs for several carcass cuts as well as lean and fat tissue traits in a commercial pig population, developed by crossing Pietrain sires with a crossbred dam line.

MATERIALS AND METHODS

All animal care and handling procedures in the federal testing station were reviewed and approved by the Landwirtschaftskammer Schleswig-Holstein, Rendsburg, Germany.

Design and Data

The QTL mapping experiment in this study was based on data from a resource family of a 3-generation full-sib design. The resource family was created by mating 7 Pietrain grandsires, which were unrelated, to 16 grandams of a crossbred dam line [Leicoma × (Landrace × Large White)]. The Pietrain sires were all heterozygous at the ryanodine receptor 1 (***RYR1***) locus. Eight boars and 40 sows of the F_1 generation were mated to produce 2 litters of the F_2 generation, comprising 315 pigs from 49 families. Animals of the F_2 generation were housed either individually or in groups of up to 15 pigs of mixed sex in straw-bedded pens. Individually housed pigs (48 gilts and 46 barrows) were fed manually, and feed consumption was recorded for these animals weekly. Group-housed animals (117 gilts and 104 barrows) were supplied food by an electronic feeding station (ACEMA 48, ACEMO, Pontivy, France), which recorded feed consumption at every visit. All animals were provided with 1 of 3 pelleted diets containing 13.8 MJ of ME/kg and 1.2% lysine, 13.8 MJ of ME/kg and 1.1% lysine, or 13.4 MJ of ME/kg and 1.0% lysine for BW ranges 30 to 60, 60 to 90, and 90 to 140 kg of BW, respectively. All animals were provided with ad libitum access to diets, which were formulated above requirements to reach maximal protein deposition. For a more detailed description of data, see Landgraf et al. (2006a,b) and Mohrmann et al. (2006a,b).

Carcass Composition

Phenotypic data on body composition were collected from pigs slaughtered in a commercial abattoir at 140 kg of BW. Measurements of valuable carcass cuts were obtained using an AutoFOM device (SFK Technology, Søborg, Denmark). This device uses an automatic ultrasound scanning technique to produce a 3-dimensional image of the carcass (Brondum et al., 1998). With the AutoFOM device, measurements were obtained for average fat thickness, belly weight, lean content, lean content of the belly, and weights of the entire and trimmed shoulder, loin, and ham without bones. Thereafter, the right carcass side of each pig was dissected into the primal carcass cuts neck, shoulder, loin, ham, and belly. Neck, shoulder, loin, and ham cuts were further dissected into lean and fat tissue. Moreover, weights of the jowl, thick rib, flank, front and hind hock, tail, and claw were recorded. From the cold left carcass side, further measurements were obtained, including carcass length, sidefat thickness; at the 13th/14th-rib interface, loin eye area, fat area, and thinnest fat measures were obtained; and fat content and area of the belly were obtained. Protein content of the loin and intramuscular fat content were measured in the musculus longissimus thoracis et lumborum using near-infrared reflectance spectroscopy. Additional information about the dissection of carcasses is presented in the study by Landgraf et al. (2006a). Table 1 outlines mean values and SD of traits analyzed in the present study.

Genotypic Data

From the F_0, F_1, and F_2 animals, blood samples of 9 mL were collected by puncture of the vena jugularis and their genomic DNA was extracted using the silica-gel method following Myakishev et al. (1995). Chromosomes SSC1, SSC2, SSC4, SSC6, SSC7, SSC8, SSC9, SSC10, SSC13, and SSC14 were chosen for genotyping because of their likely associations with carcass cuts as well as lean and fat tissue. All pigs were genotyped for 88 informative microsatellite markers, of which 10, 9, 9, 9, 10, 8, 9, 9, 8, and 7 genomic markers were located on SSC1, SSC2, SSC4, SSC6, SSC7, SSC8, SSC9, SSC10, SSC13, and SSC14, respectively. Based on the published USDA linkage map, markers and their distances were selected (http://www.marc.usda.gov; Rohrer et al., 1996). This linkage map provided all information relating to their position and alleles, as outlined in Table 2. The average distances between markers were 16.0, 16.5, 16.3, 20.6, 17.3 18.4, 17.3, 16.0, 18.0, and 17.4 cM and the largest gaps between markers were 27.7, 25.2, 26.5, 28.7, 26.2, 23.1, 21.7, 20.8, 24.0, and 23.6 cM on SSC1, SSC2, SSC4, SSC6, SSC7, SSC8, SSC9, SSC10, SSC13, and SSC14, respectively.

Statistical Analysis

Because of the computational demand of a genomic scan for epistatic QTL, the analysis was performed in 2 stages following the procedure of Estellé et al. (2008). In the first stage, a 5-cM scan was carried out across all genomic positions. Individual additive and dominance

Table 1. Means and SD of carcass characteristics measured on pigs of the F_2 generation

Trait	Mean	SD	No. of records
AutoFOM[1] (AF) trait			
AF average fat thickness, mm	22.295	4.989	313
AF entire shoulder wt, kg	6.176	0.406	313
AF shoulder lean meat wt, kg	4.577	0.408	313
AF entire loin wt, kg	6.265	0.396	313
AF loin lean meat wt, kg	3.764	0.352	313
AF entire ham wt, kg	13.573	0.814	313
AF ham lean meat wt, kg	9.511	1.052	313
AF entire belly wt, kg	9.168	0.548	313
AF lean content, %	50.509	6.403	313
AF lean content of belly, %	43.741	7.891	313
Carcass characteristic—dissected carcass cuts			
Entire neck wt, kg	5.316	0.505	306
Neck wt without external fat, kg	4.160	0.430	306
External neck fat wt, kg	1.156	0.285	306
Entire shoulder wt, kg	8.452	0.564	307
Shoulder wt without external fat, kg	5.910	0.584	307
External shoulder fat wt, kg	1.403	0.261	307
Entire loin wt, kg	9.163	0.730	308
Loin wt without external fat, kg	6.650	0.624	308
External loin fat wt, kg	2.513	0.645	308
Entire ham wt, kg	16.908	0.997	310
Ham wt without external fat, kg	11.568	1.087	310
External ham fat wt, kg	2.566	0.493	310
Belly wt, kg	6.461	0.655	308
Jowl wt, kg	1.914	0.284	306
Thick rib, kg	1.441	0.217	307
Flank wt, kg	1.789	0.407	308
Front hock wt, kg	1.139	0.189	307
Hind hock wt, kg	1.430	0.141	310
Tail wt, kg	0.429	0.134	310
Hind claw, kg	0.914	0.122	310
Carcass characteristic—standard performance test			
Carcass length, cm	105.192	3.024	310
Sidefat thickness,[2] cm	3.847	0.866	315
Thinnest fat measure,[2] cm	1.725	0.552	314
Loin eye area M.l.t.l.,[2,3] cm^2	54.160	6.767	314
Fat area M.l.t.l.,[2,3] cm^2	24.514	5.884	314
Fat content of belly, %	53.508	8.272	306
Fat area of belly, cm^2	23.789	6.782	306
Intramuscular fat content, %	1.343	0.542	313
Protein content of loin, %	24.215	2.066	313

[1]AutoFOM device (SFK Technology, Søborg, Denmark).
[2]Collected at the 13th/14th-rib interface.
[3]Measured on musculus longissimus thoracis et lumborum.

effects were excluded from the first stage of analysis because of the substantial computing demand. As a result, all possible pairwise combinations between QTL at only 5-cM intervals were considered, to preselect potential candidate regions with epistatic effects with the model

$$y_i = sex_i + MHS_i + batch_i + \beta slwt_i + C_{aa}I_{aa} + C_{ad}I_{ad} + C_{da}I_{da} + C_{dd}I_{dd} + e_i, \quad [1]$$

where y_i is the ith individual phenotype. Fixed effects and covariates were fitted in the model, depending on their significance for the trait. For all traits, *sex*, *RYR1* genotype (*MHS*), and *batch* (1 to 9; animals beginning the performance test at the same time were grouped together as 1 batch) were included as fixed class variables in the model, and slaughter weight (*slwt*) was considered covariate β. The effect of housing system was tested in a preliminary analysis and found not to be significant for the analyzed traits, and was therefore not included in the model. I_{aa}, I_{ad}, I_{da}, and I_{dd} are the additive × additive ($\mathbf{A}\times\mathbf{A}$), additive × dominance ($\mathbf{A}\times\mathbf{D}$), dominance × additive ($\mathbf{D}\times\mathbf{A}$), and dominance × dominance ($\mathbf{D}\times\mathbf{D}$) epistatic effects, respectively; and e_i is the residual effect. These 4 epistatic effects were estimated, following the Cockerham decomposition (Cockerham, 1954), by regressing on a linear combination of the individual QTL origin probabilities:

Table 2. Markers used in the present QTL mapping project, their relative map position using the Meat Animal Research Center pig map, number of different alleles, polymorphic information content (PIC) in the F_2 generation, and heterozygosity in the F_1 generation (H)

Marker	SSC	Position, cM	H	No. of alleles	PIC
SW1514	1	0	0.79	8	0.75
SW1515	1	16.4	0.67	8	0.68
SW1332	1	29.2	0.63	4	0.37
SW1851	1	44.6	0.73	4	0.53
SW1430	1	58.5	0.81	6	0.76
SWR982	1	86.2	0.88	7	0.77
SW1311	1	100.8	0.58	6	0.62
SW1828	1	118.5	0.90	7	0.69
SW1301	1	140.5	0.83	5	0.67
SW2512	1	144	0.77	6	0.55
SWR2516	2	0	0.67	5	0.48
SW2623	2	9.8	0.68	5	0.63
SWR783	2	23.7	0.51	3	0.30
SW240	2	42	0.84	7	0.78
SW1026	2	60.6	0.47	6	0.55
SW1370	2	74.8	0.91	8	0.69
SWR2157	2	89.2	0.78	8	0.68
SWR345	2	114.4	0.87	8	0.75
S0036	2	132.1	0.85	7	0.80
SW2404	4	0	0.91	10	0.81
SW489	4	8	0.66	5	0.53
S0301	4	27.1	0.72	6	0.56
S0001	4	41.8	0.66	6	0.65
SW839	4	62.3	0.44	4	0.45
S0214	4	79.3	0.80	6	0.74
SW445	4	105.8	0.91	10	0.77
MP77	4	120	0.87	8	0.74
SW856	4	130.1	0.98	14	0.84
MP35	6	0	0.70	6	0.59
SW2406	6	21.4	0.74	8	0.61
SW1841	6	41.5	0.98	15	0.88
S0087	6	62.8	0.75	5	0.59
SW122	6	83.3	0.85	7	0.69
S0228	6	105.2	0.69	6	0.68
SW1881	6	121.1	0.96	8	0.76
SW322	6	149.8	0.79	8	0.72
SW2052	6	164.6	0.79	9	0.78
SW2564	7	0	0.69	5	0.49
SWR1343	7	12.2	0.83	4	0.53
SW2155	7	32.9	0.67	4	0.48
SW1369	7	48.2	0.77	8	0.68
SW1856	7	61.5	0.69	5	0.48
SWR2036	7	78.2	0.81	9	0.77
SW632	7	104.4	0.77	6	0.67
SWR773	7	117.3	0.56	3	0.46
SW2537	7	139.5	0.69	7	0.63
SW764	7	156	0.76	5	0.65
SW2410	8	−1.3	0.42	4	0.44
SW905	8	20.8	0.71	6	0.71
SWR1101	8	38.3	0.88	12	0.75
SW444	8	52.5	0.85	7	0.76
S0086	8	62.2	0.69	6	0.56
SW374	8	82.8	0.88	5	0.63
SW1551	8	105.9	0.75	6	0.66
S0178	8	127.7	0.54	7	0.68
SW983	9	4	0.81	6	0.61
SW21	9	15.1	0.65	5	0.50
SW911	9	36.8	0.75	7	0.68
SW2401	9	57.1	0.71	6	0.68
SW2571	9	73.3	0.46	6	0.61
S0019	9	86.4	0.75	6	0.62
SW2093	9	103.6	0.90	6	0.77

Continued

Table 2 (Continued). Markers used in the present QTL mapping project, their relative map position using the Meat Animal Research Center pig map, number of different alleles, polymorphic information content (PIC) in the F_2 generation, and heterozygosity in the F_1 generation (H)

Marker	SSC	Position, cM	H	No. of alleles	PIC
SW174	9	122.9	0.81	3	0.51
SW1349	9	142.5	0.81	7	0.75
SW830	10	0	0.67	7	0.64
SWR136	10	7.6	0.77	6	0.72
SW1894	10	23.2	0.65	4	0.50
SW2195	10	44	0.48	3	0.42
SW173	10	56.1	0.35	4	0.39
SW1041	10	67.5	0.46	3	0.41
SW2043	10	87.7	0.56	5	0.72
SW1626	10	108	0.79	11	0.68
SW2067	10	128	0.81	7	0.69
S0282	13	0	0.90	8	0.77
SWR1941	13	14.1	0.87	7	0.71
SW1407	13	27.2	0.88	11	0.83
SW864	13	43.1	0.63	5	0.64
S0068	13	62.2	0.78	9	0.72
SW398	13	79.3	0.69	6	0.66
SW2440	13	102.2	0.96	6	0.79
S0291	13	126.2	0.83	8	0.79
SW857	14	7.4	0.87	9	0.74
S0089	14	14	0.67	7	0.71
SW245	14	32	0.77	7	0.71
SW342	14	53.2	0.79	7	0.71
SW1081	14	72.1	0.87	6	0.65
SW1557	14	87.9	0.64	4	0.49
SWC27	14	111.5	0.45	8	0.41

$$C_{aa} = P_1(QQ)P_2(QQ) - P_1(QQ)P_2(qq) - P_1(qq)P_2(QQ) + P_1(qq)P_2(qq),$$

$$C_{ad} = P_1(QQ)P_2(Qq) - P_1(qq)P_2(Qq),$$

$$C_{da} = P_1(Qq)P_2(QQ) - P_1(Qq)P_2(qq), \text{ and}$$

$$C_{dd} = P_1(Qq)P_2(Qq),$$

where P_1 and P_2 refer to the probability of QTL at locations 1 and 2, respectively, and $P(QQ)$ is the probability of the grandpaternal sire line (Pietrain) being homozygous, $P(qq)$ is the probability of the grandmaternal dam line being homozygous, and $P(Qq)$ is the probability of being heterozygous (Varona et al., 2002). Model [1] was tested against a null model in which no epistatic effects were estimated; that is,

$$y_i = sex_i + MHS_i + batch_i + \beta slwt_i + e_i.$$

Interacting QTL pairs with P-values <0.001 were selected for further analyses.

In the second stage, a complete epistatic model including the individual QTL effects was applied using a 1-cM scan around the preselected positions obtained in the first stage. This model included, besides all environmental effects, the individual additive and dominance genetic effects as well as epistatic genetic effects:

$$y_i = sex_i + MHS_i + batch_i + \beta slwt_i + C_{a1}a_1 + C_{a2}a_2 + C_{d1}d_1 + C_{d2}d_2 + C_{aa}I_{aa} + C_{ad}I_{ad} + C_{da}I_{da} + C_{dd}I_{dd} + e_i, \quad [2]$$

where a denotes the individual additive genetic effect and C_a represents the difference in probabilities of being homozygous for alleles of the grandpaternal sire line (QQ) and being homozygous for alleles of the grandmaternal dam line (qq). A positive additive genetic value indicates that the allele originating from the grandpaternal sire line (Pietrain) showed a greater effect than the allele from the grandmaternal dam line, and vice versa. The effect d represents the individual dominance genetic effects and C_d gives the probability of being heterozygous. The dominance effect is defined as the deviation of heterozygous animals from the mean of both types of homozygous animals. A positive dominance value indicates an increase in the trait of interest resulting from a heterozygous genotype, and vice versa. Model [2] was tested against a null model that contained only the individual QTL effects; that is,

$$y_i = sex_i + MHS_i + batch_i + \beta slwt_i + C_{a1}a_1 + C_{a2}a_2 + C_{d1}d_1 + C_{d2}d_2 + e_i. \quad [3]$$

Epistatic interactions were reported as significant if they had a nominal P-value of <0.001. All analyses

Table 3. Evidence of epistatic interactions for carcass characteristics measured after dissection and by the AutoFOM device[1] (AF)

Trait	LR[2]	*P*-value	Q0 chr[3] (pos[4])	Q1 chr (pos)	% var[5]	Q0_a ± SE[6]	Q0_d ± SE[6]	Q1_a ± SE[6]	Q1_d ± SE[6]	Q01_aa ± SE[7]	Q01_ad ± SE[7]	Q01_da ± SE[7]	Q01_dd ± SE[7]
Entire carcass characteristic (lean + fat)													
AF entire belly wt, kg	21.68	2.3E-04	1 (88)	7 (148)	6.7	−0.086 ± 0.075	0.309 ± 0.118[a]	0.033 ± 0.070	0.663 ± 0.130[a]	0.061 ± 0.069	−0.122 ± 0.130	−0.021 ± 0.108	−1.040 ± 0.212[a]
Hind hock wt, kg	22.52	1.6E-04	1 (35)	8 (107)	6.5	−0.035 ± 0.028	0.126 ± 0.053	0.036 ± 0.028	0.066 ± 0.052	0.120 ± 0.025[a]	0.049 ± 0.050	−0.038 ± 0.048	−0.190 ± 0.091[a]
Hind claw, kg	22.33	1.7E-04	1 (63)	9 (23)	7.1	0.031 ± 0.023	0.073 ± 0.038	0.010 ± 0.021	0.072 ± 0.042	−0.074 ± 0.021[a]	−0.061 ± 0.040	−0.055 ± 0.035	−0.196 ± 0.068[a]
Entire ham wt, kg	23.51	1.0E-04	2 (10)	9 (66)	7.3	−0.213 ± 0.124	−0.408 ± 0.194[a]	−0.177 ± 0.119	−0.369 ± 0.231	−0.242 ± 0.118[a]	0.881 ± 0.225[a]	0.436 ± 0.187[a]	0.529 ± 0.345
Belly wt, kg	27.93	1.3E-05	4 (130.1)	4 (31)	8.7	0.043 ± 0.085	−0.282 ± 0.127[a]	−0.140 ± 0.084	−0.187 ± 0.143	−0.410 ± 0.083[a]	−0.170 ± 0.142	0.170 ± 0.123	0.433 ± 0.209[a]
Entire neck wt, kg	21.50	2.5E-04	6 (71)	6 (86)	6.8	−0.876 ± 0.380[a]	0.015 ± 0.457	0.844 ± 0.389[a]	−0.191 ± 0.441	−0.450 ± 0.328	1.067 ± 0.473[a]	−1.145 ± 0.503[a]	−0.322 ± 0.565
Entire loin wt, kg	33.11	1.1E-06	7 (77)	7 (86)	10.2	1.227 ± 1.537	2.197 ± 1.142	−1.451 ± 1.509	2.571 ± 1.353	2.954 ± 0.953[a]	−0.524 ± 1.990	1.282 ± 1.779	−1.764 ± 1.467
Flank wt, kg	19.90	5.2E-04	7 (88)	10 (23)	6.2	0.056 ± 0.067	0.086 ± 0.124	0.037 ± 0.069	0.121 ± 0.113	0.249 ± 0.066[a]	−0.167 ± 0.106	−0.227 ± 0.118	−0.308 ± 0.197
AF entire shoulder wt, kg	24.97	5.1E-05	8 (21)	8 (37)	7.7	0.849 ± 0.273[a]	−0.491 ± 0.340	−0.729 ± 0.254[a]	−0.699 ± 0.397	−0.684 ± 0.225[a]	−0.991 ± 0.415[a]	0.665 ± 0.343	0.484 ± 0.504
Lean tissue characteristic													
Protein content of loin, %	21.64	2.4E-04	2 (93)	2 (117)	6.7	1.160 ± 0.323[a]	1.208 ± 0.405[a]	−1.225 ± 0.323[a]	1.204 ± 0.402[a]	1.378 ± 0.317[a]	−1.142 ± 0.406[a]	1.162 ± 0.408[a]	−1.049 ± 0.504[a]
AF lean content of belly, %	21.87	2.1E-04	2 (9)	8 (55)	6.7	1.973 ± 1.168	5.305 ± 1.773	0.130 ± 1.057	4.762 ± 2.012[a]	−3.022 ± 1.058[a]	−1.582 ± 1.990	−3.089 ± 1.631	−10.239 ± 2.954[a]
Loin eye area M.l.t.l.,[8,9] cm^2	27.71	1.4E-05	2 (22)	9 (136)	8.4	−2.565 ± 1.318	−4.516 ± 2.300	−1.856 ± 1.255	−3.497 ± 2.459	4.275 ± 1.170[a]	6.658 ± 2.314[a]	5.782 ± 2.110[a]	11.189 ± 4.045[a]
Protein content of loin, %	19.69	5.7E-04	4 (121)	7 (1)	6.1	−0.149 ± 0.089	0.067 ± 0.128	0.142 ± 0.090	0.127 ± 0.127	−0.140 ± 0.089	0.522 ± 0.127[a]	−0.145 ± 0.128	−0.036 ± 0.186
Loin wt without external fat, kg	22.05	2.0E-04	4 (89)	14 (66)	6.9	0.088 ± 0.113	−0.358 ± 0.196	−0.226 ± 0.105[a]	−0.022 ± 0.202	0.328 ± 0.102[a]	0.034 ± 0.196	0.505 ± 0.178[a]	0.508 ± 0.334
Loin wt without external fat, kg	18.71	9.0E-04	6 (28)	8 (60)	5.9	0.094 ± 0.116	0.061 ± 0.213	−0.086 ± 0.108	0.335 ± 0.223	0.409 ± 0.101[a]	−0.188 ± 0.207	0.271 ± 0.190	−0.468 ± 0.379
Neck wt without external fat, kg	19.64	5.9E-04	6 (145)	9 (58)	6.3	−0.099 ± 0.070	0.323 ± 0.131[a]	0.130 ± 0.071	0.431 ± 0.121[a]	0.158 ± 0.065[a]	0.249 ± 0.112[a]	−0.047 ± 0.124	−0.776 ± 0.225[a]
Fat tissue characteristic													
External ham fat wt, kg	21.79	2.2E-04	1 (48)	1 (118)	6.8	−0.080 ± 0.071	0.168 ± 0.108	0.107 ± 0.072	−0.073 ± 0.101	−0.131 ± 0.072	−0.092 ± 0.100	−0.367 ± 0.106[a]	−0.185 ± 0.150
Intramuscular fat content, %	20.82	3.4E-04	1 (126)	4 (94)	6.4	0.257 ± 0.090[a]	0.087 ± 0.151	0.102 ± 0.088	0.246 ± 0.154	−0.036 ± 0.085	−0.721 ± 0.150[a]	−0.171 ± 0.142	−0.288 ± 0.258
AF average fat thickness, mm	19.56	6.1E-04	1 (142)	6 (119)	6.1	−1.656 ± 0.672[a]	−0.419 ± 0.988	0.217 ± 0.652	1.858 ± 1.159	2.293 ± 0.651[a]	4.014 ± 1.153[a]	−1.053 ± 0.956	0.248 ± 1.700
External neck fat wt, kg	19.61	6.0E-04	4 (1)	4 (120)	6.1	0.015 ± 0.033	−0.075 ± 0.048	−0.050 ± 0.033	−0.056 ± 0.049	−0.139 ± 0.033[a]	−0.031 ± 0.048	0.005 ± 0.048	0.130 ± 0.070
Fat content of belly, %	19.54	6.2E-04	4 (106)	6 (12)	6.2	1.027 ± 1.069	0.734 ± 1.572	−0.478 ± 1.007	−0.788 ± 1.858	−4.737 ± 1.020[a]	−2.345 ± 1.885	−0.796 ± 1.478	−0.003 ± 2.669

Continued

Table 3 (Continued). Evidence of epistatic interactions for carcass characteristics measured after dissection and by the AutoFOM device[1] (AF)

Trait	LR[2]	*P*-value	Q0 chr[3] (pos[4])	Q1 chr (pos)	% var[5]	Q0_a ± SE[6]	Q0_d ± SE[6]	Q1_a ± SE[6]	Q1_d ± SE[6]	Q01_aa ± SE[7]	Q01_ad ± SE[7]	Q01_da ± SE[7]	Q01_dd ± SE[7]
Thinnest fat measure,[8] cm	18.70	9.0E-04	6 (42)	8 (56)	5.8	−0.131 ± 0.088	−0.462 ± 0.145[a]	−0.121 ± 0.079	−0.369 ± 0.155[a]	−0.234 ± 0.078[a]	0.112 ± 0.153	0.166 ± 0.134	0.789 ± 0.248[a]
External loin fat wt, kg	18.90	8.2E-04	6 (150)	9 (57)	6.0	0.130 ± 0.099	−0.115 ± 0.174	−0.078 ± 0.097	−0.336 ± 0.165[a]	−0.235 ± 0.093[a]	−0.325 ± 0.159[a]	−0.023 ± 0.165	0.901 ± 0.299[a]

[a]Values represent significant additive, dominance, or epistatic effects ($P < 0.001$).
[1]AutoFOM device (SFK Technology, Søborg, Denmark).
[2]LR = likelihood ratio.
[3]chr = chromosome.
[4]Positions of the QTL in cM.
[5]Percentages of F_2 variance explained by the QTL calculated as the proportion of residual variances attributable to the QTL effect on the residual variances excluding the QTL effect.
[6]Estimated additive (a) and dominance (d) effects and their SE of the individual QTL.
[7]Estimated additive × additive (aa), additive × dominance (ad), dominance × additive (da), and dominance × dominance (dd) effects and their SE.
[8]Collected at the 13th/14th-rib interface.
[9]Measured on musculus longissimus thoracis et lumborum.

were performed with QxPak software (Pérez-Enciso and Misztal, 2004).

RESULTS AND DISCUSSION

In total, 23 significant epistatic QTL pairs were identified. Of these, 9 epistatic QTL pairs were identified for entire carcass characteristics, 7 were identified for lean tissue characteristics, and 7 were identified for fat tissue characteristics (Table 3). Epistatic interactions were identified between QTL on SSC1, SSC2, SSC4, SSC6, SSC7, SSC8, SSC9, SSC10, and SSC14. No epistatic QTL were identified on or with SSC13. Epistatic QTL pairs explained between 6.2 and 10.2% of the phenotypic variance for entire carcass characteristics (lean + fat), between 5.9 and 9.5% for lean tissue characteristics, and between 5.8 and 6.8% for fat tissue characteristics. Seven of the significant epistatic QTL pairs were between QTL that resided on the same chromosome, on SSC1, SSC2, SSC4, SSC6, SSC7, and SSC8. All types of epistatic effects were identified (A×A, A×D, D×A, and D×D) in this study, with the A×A interaction being the most prevalent. The epistatic QTL pair with the greatest effect was for entire loin weight between 2 locations on SSC7. This QTL explained a large proportion of the phenotypic variance, at 10.2%. However, the locations are close together; therefore, this interaction has to be interpreted with care. Interactions between QTL that lie in close proximity have been reported for 3 additional traits (Table 3). Future fine mapping analyses are necessary to confirm these interactions.

Entire Carcass Characteristics

Weights of important carcass cuts are economically important for the market value of the carcass. In the present study, we identified 10 epistatic interactions for entire carcass cuts. A D×D interaction was identified between QTL on SSC1 and SSC7 for entire belly weight measured by the AutoFom device. The QTL on SSC1 was previously identified in individual QTL mapping analyses by Mohrmann et al. (2006a), and in both studies, this QTL showed a significant dominance effect. Around this location of SSC1, numerous QTL have been reported for lean tissue and fat tissue (Nezer et al., 2002; Beeckmann et al., 2003b; Karlskov-Mortensen et al., 2006). No individual QTL were identified in previous analyses of the data on SSC7, which was surprising because there is strong evidence for QTL on SSC7 in the literature (e.g., Milan et al., 2002; Nezer et al., 2002; Yue et al., 2003a; Kim et al., 2005; Sanchez et al., 2006; Table 4). Therefore, the QTL identified on SSC7 has only expressed its effects through D×D interactions with SSC1.

A QTL on SSC1 showed an interaction with a QTL on SSC8 for hind hock weight. Neither of these QTL were identified in previous analyses of the present data, which may be expected because the negative interaction effect is almost as large as the sum of the indi-

Table 4. Reports of QTL in the literature around similar locations as the QTL identified in the present study

Trait	SSC (position[1])	Marker interval	Other studies confirming the QTL[2]
Entire carcass characteristic (lean + fat)			
Hind hock wt, kg	1 (35)	*SW1332–SW1851*	de Koning et al. (2001)
Hind claw, kg	1 (63)	*SW1430–SWR982*	Beeckmann et al. (2003b)
AF[3] entire belly wt, kg	1 (88)	*SWR982–SW1311*	Nezer et al. (2002); Beeckmann et al. (2003b); Karlskov-Mortensen et al. (2006)
Entire ham wt, kg	2 (10)	*SW2623–SWR783*	de Koning et al. (2001); Milan et al. (2002); Geldermann et al. (2003); Lee et al. (2003)
Belly wt, kg	4 (31)	*S0301–S0001*	Cepica et al. (2003b); Geldermann et al. (2003); Kim et al. (2006)
Belly wt, kg	4 (130.1)	*SW856*	Knott et al. (2002)
Entire neck wt, kg	6 (71)	*S0087–SW122*	Yue et al. (2003b)
Entire neck wt, kg	6 (86)	*SW122–S0228*	Rohrer (2000); Grindflek et al. (2001); Varona et al. (2002); Yue et al. (2003b); Edwards et al. (2008b)
Entire loin wt, kg	7 (77)	*SW1856–SWR2036*	Malek et al. (2001b); Milan et al. (2002); Geldermann et al. (2003); Yue et al. (2003a)
Entire loin wt, kg	7 (86)	*SWR2036–SW632*	Nezer et al. (2002); Kim et al. (2005); Ponsuksili et al. (2005); Edwards et al. (2008a)
Flank wt, kg	7 (88)	*SWR2036–SW632*	Nezer et al. (2002); Kim et al. (2005); Ponsuksili et al. (2005); Edwards et al. (2008a)
AF entire belly wt, kg	7 (148)	*SW2537–SW764*	—
AF entire shoulder wt, kg	8 (21)	*SW905–SWR1101*	Quintanilla et al. (2002); Sato et al. (2003)
AF entire shoulder wt, kg	8 (37)	*SW905–SWR1101*	Beeckmann et al. (2003a)
Hind hock wt, kg	8 (107)	*SW1551–S0178*	—
Hind claw, kg	9 (23)	*SW21–SW911*	—
Entire ham wt, kg	9 (66)	*SW2401–SW2571*	Cepica et al. (2003a)
Flank wt, kg	10 (23)	*SWR136–SW1894*	Quintanilla et al. (2002)
Lean tissue characteristic			
AF lean content of belly, %	2 (9)	*SWR2516–SW2623*	de Koning et al. (2001); Milan et al. (2002); Geldermann et al. (2003); Lee et al. (2003)
Loin eye area M.l.t.l.,[4,5] cm^2	2 (22)	*SW2623–SWR783*	Lee et al. (2003)
Protein content of loin, %	2 (93)	*SWR2157–SWR345*	Malek et al. (2001b); Lee et al. (2003)
Protein content of loin, %	2 (117)	*SWR345–S0036*	—
Loin wt without external fat, kg	4 (89)	*S0214–SW445*	Pérez-Enciso et al. (2000); Varona et al. (2002); Cepica et al. (2003b); Geldermann et al. (2003)
Protein content of loin, %	4 (121)	*MP77–SW856*	Malek et al. (2001b); Cepica et al. (2003b)
Loin wt without external fat, kg	6 (28)	*SW2406–SW1841*	de Koning et al. (2000); Milan et al. (2002)
Neck wt without external fat, kg	6 (145)	*SW1881–SW322*	Malek et al. (2001b); Edwards et al. (2008a)
Protein content of loin, %	7 (1)	*SW2564–SWR1343*	—
AF lean content of belly, %	8 (55)	*SW444–S0086*	—
Loin wt without external fat, kg	8 (60)	*SW444–S0086*	Casas-Carrillo et al. (1997); Milan et al. (2002); Kim et al. (2005)
Neck wt without external fat, kg	9 (58)	*SW2401–SW2571*	Rohrer et al. (2005)
Loin eye area M.l.t.l.,[4,5] cm^2	9 (136)	*SW174–SW1349*	Cepica et al. (2003a); Kim et al. (2006)
Loin wt without external fat, kg	14 (66)	*SW342–SW1081*	Dragos-Wendrich et al. (2003); Geldermann et al. (2003); van Wijk et al. (2006)
Fat tissue characteristic			
External ham fat wt, kg	1 (48)	*SW1851–SW1430*	Malek et al. (2001b); Beeckmann et al. (2003b); Geldermann et al. (2003)
External ham fat wt, kg	1 (118)	*SW1311–SW1828*	Beeckmann et al. (2003b); Geldermann et al. (2003); Kim et al. (2006)
Intramuscular fat content, %	1 (126)	*SW1828–SW1301*	Rohrer and Keele (1998a,b); Rohrer (2000); Beeckmann et al. (2003b); Edwards et al. (2008a)
AF average fat thickness, mm	1 (142)	*SW1301–SW2512*	Rohrer and Keele (1998a); Bidanel et al. (2001); Quintanilla et al. (2002); Beeckmann et al. (2003b); Sanchez et al. (2006)
External neck fat wt, kg	4 (1)	*SW2404–SW489*	Marklund et al. (1999); Milan et al. (2002)
Intramuscular fat content, %	4 (94)	*S0214–SW445*	Pérez-Enciso et al. (2000); Varona et al. (2002); Cepica et al. (2003b); Geldermann et al. (2003)
Fat content of belly, %	4 (106)	*SW445–MP77*	Cepica et al. (2003b); Geldermann et al. (2003)
External neck fat wt, kg	4 (120)	*MP77*	Malek et al. (2001b); Cepica et al. (2003b)
Fat content of belly, %	6 (12)	*MP35–SW2406*	van Wijk et al. (2006)
Thinnest fat measure,[4] cm	6 (42)	*SW1841–S0087*	—
AF average fat thickness, mm	6 (119)	*S0228–SW1881*	Varona et al. (2002); Sato et al. (2003); Kim et al. (2006); Edwards et al. (2008a)
External loin fat wt, kg	6 (150)	*SW322–SW2052*	Kim et al. (2005)
Thinnest fat measure,[4] cm	8 (56)	*SW444–S0086*	—
External loin fat wt, kg	9 (57)	*SW911–SW2401*	Rohrer et al. (2005)

[1]Positions of the QTL in cM.
[2]References of other studies reporting QTL for similar traits in similar regions of the genome.
[3]AF = AutoFOM device (SFK Technology, Søborg, Denmark).
[4]Collected at the 13th/14th-rib interface.
[5]Measured on musculus longissimus thoracis et lumborum.

vidual QTL effects. Around the same location of SSC1, a QTL has been reported for growth rate (de Koning et al., 2001). However, there are no reports in the literature confirming the QTL on SSC8.

A further location of SSC1 showed an interaction with SSC9 for weight of the hind claw. These QTL were not identified in previous analyses. These QTL showed no significant additive or dominance effects and expressed their effects only through novel interactions between additive as well as dominance effects. The QTL on SSC1 for the hind claw was close to *SW1430*. Many QTL for carcass traits have been identified around this location (Beeckmann et al., 2003b).

Several epistatic effects were identified between the telomeric end of the p-arm of SSC2 and 66 cM of SSC9 for entire ham weight. In the present study, the QTL on SSC2 and SSC9 showed substantial interactions between additive and dominance effects, which more than offset the negative effects associated with dominance and A×A genetic effects. From previous analysis of these data, numerous QTL were identified around this location of SSC2, where Pietrain alleles were associated with increased lean tissue and reduced fatness (Duthie et al., 2008). Whereas the QTL on SSC2 was affected by individual dominance effects, the QTL on SSC9 showed no significant ($P > 0.001$) individual QTL effects in the present study. However, in previous analyses, QTL were identified in this genomic location for entire shoulder weight and shoulder weight without external fat (Duthie et al., 2008). There are reports of QTL around this location of SSC2 for carcass traits, lean tissue, and fat tissue and around the region of SSC9 for BW (de Koning et al., 2001; Milan et al., 2002; Geldermann et al., 2003; Lee et al., 2003). In the region of the QTL on SSC2, a paternally expressed QTL that affects growth and fat deposition has been mapped to the *IGF-2* locus (Jeon et al., 1999; Nezer et al., 1999). In the present analysis, imprinting effects have not been included in the model because of the substantial increase in complexity of the epistatic QTL analysis. This exclusion may reduce the power of detecting epistatic effects between QTL expressing imprinting at one or more loci. Therefore, including the *IGF-2* genotypes and considering their imprinting in an epistatic QTL analysis would be of interest for identifying *IGF-2* genomic interactions in further analyses.

Interactions between additive or dominance effects were identified between 2 locations of SSC4, on the p-arm (31 cM) and the telomeric end of the q-arm (130.1 cM), for belly weight. The QTL on the p-arm was not identified in previous individual QTL analyses of the data, whereas a QTL was identified for lean content at 33 cM, for which Pietrain alleles were associated with decreased lean tissue (Duthie et al., 2008). Quantitative trait loci have been reported around 31 cM for numerous carcass traits as well as lean and fat tissue; however, only a single QTL has been reported at the telomeric end of the q-arm for daily BW gain (Knott et al., 2002).

For entire neck weight, A×D and D×A interactions were identified between 2 close genomic locations of SSC6 (71 and 86 cM). There are numerous reports in the literature for QTL associated with carcass traits, lean tissue, and fat tissue in these locations (Rohrer et al., 2000; Grindflek et al., 2001; Varona et al., 2002; Yue et al., 2003b; Edwards et al., 2008b). No QTL were detected near 71 cM from previous individual QTL analyses of these data, but Mohrmann et al. (2006a) reported a large number of QTL around the QTL at 86 cM for several carcass cuts (lean + fat), fat tissue, lean tissue characteristics, and chemical body composition, at which Pietrain alleles were associated with decreased fat tissue and increased lean tissue. The significant additive effect identified at the QTL (86 cM) in the present study indicated that Pietrain alleles were associated with increased neck weight. This QTL is in the same genomic location as the *RYR1* locus (Rohrer et al., 1996); however, it is independent from the *RYR1* locus because its effect has been adjusted for as a fixed effect in the model.

A novel epistatic A×A QTL pair was identified on 2 locations of SSC7 for entire loin weight. No individual QTL effects were identified at either of these QTL, outlining why they were not identified from previous individual QTL analyses. There are reports of QTL around these locations for numerous carcass characteristics (Malek et al., 2001; Milan et al., 2002; Nezer et al., 2002; Geldermann et al., 2003; Yue et al., 2003a; Kim et al., 2005; Ponsuksili et al., 2005; Edwards et al., 2008a).

An A×A interaction was identified between SSC7 and SSC10 for flank weight. Again, at these QTL no individual QTL effects were identified. The QTL on SSC7 was located around the same region as for entire loin weight in the present study. Around this location of SSC7, there are reports of QTL for leanness, fatness, and growth (Nezer et al., 2002; Kim et al., 2005; Ponsuksili et al., 2005; Edwards et al., 2008a), whereas around this location of SSC10, a QTL has been reported for backfat (Quintanilla et al., 2002).

For entire shoulder weight, A×A and A×D interactions were identified between 2 close genomic locations of SSC8 (21 and 37 cM). Duthie et al. (2008) identified QTL at 37 cM for protein content of the loin, at which Pietrain alleles were associated with less protein content. In this study, Pietrain alleles were associated with less shoulder weight at this QTL. The QTL at 21 cM was not identified previously; therefore, it exhibits effects only through the interactions. Quantitative trait loci have been reported around these locations for numerous carcass traits, daily BW gain, and lean tissue (Quintanilla et al., 2002; Beeckmann et al., 2003a; Sato et al., 2003).

Lean Tissue Characteristics

One of the main goals of commercial pig production has been to increase lean tissue. A large number of stud-

ies have investigated QTL for lean tissue (e.g., Rohrer and Keele, 1998b; Malek et al., 2001a; Geldermann et al., 2003) from individual QTL analyses. In the present study, we identified 7 epistatic QTL pairs for lean tissue characteristics.

For protein content of the loin tissue, all fitted interactions and all individual QTL effects were significant between 2 genomic locations on SSC2 (93 and 117 cM). A QTL was previously identified at 92 cM for shoulder weight without external fat (Duthie et al., 2008). Around this location (93 cM), QTL have been reported for daily BW gain and backfat (Malek et al., 2001b; Lee et al., 2003).

At the telomeric end of the p-arm of SSC2, additive as well as dominance interactions were detected with SSC8 for lean content of the belly. Numerous QTL were previously identified for lean and fat tissue QTL around this location of SSC2 (Duthie et al., 2008). The dominance effects of the QTL on SSC8, however, were not detected in previous individual QTL mapping analyses of the data.

A slightly different location of SSC2 (22 cM) showed further interactions of all fitted combinations with SSC9 for loin eye area. No individual QTL effects were identified at these QTL; however, QTL were reported in this resource family for lean tissue at the same location on SSC2 (Duthie et al., 2008). Interestingly, all interactions were positive, and may thus be an explanation for heterosis of these crosses in lean content. Around this location of SSC2, QTL have been reported for lean tissue as well as backfat (Lee et al., 2003), and on SSC9, QTL have been reported for fatness, daily BW gain, and BW (Cepica et al., 2003a; Kim et al., 2006).

In previous individual QTL mapping of the present resource family, no QTL were identified on SSC7 and only a few QTL were identified on SSC4. In the present study, we identified A×D interactions between these chromosomes for protein content of the loin. Quantitative trait loci have been reported around this location of SSC4 for carcass weight, BW, and liver weight (Malek et al., 2001b; Cepica et al., 2003b).

Moreover, SSC4 showed positive interaction effects with SSC14 for loin weight without external fat. These positive interaction effects were almost 4 times as large as the negative additive genetic effects of the QTL on SSC14. These negative additive genetic effects at the QTL on SSC14 indicated that Pietrain alleles were associated with less lean meat of the loin. The QTL on SSC14 was at the same genomic location of SSC14 as the reported QTL for ham lean meat weight (Duthie et al., 2008), where Pietrain alleles were also associated with decreased lean tissue weight, interpreted as a cryptic allele. Around both of these QTL, there are reports in the literature for QTL associated with numerous carcass characteristics, including lean and fat tissue (Perez-Enciso et al., 2000; Varona et al., 2002; Cepica et al., 2003b; Dragos-Wendrich et al., 2003; Geldermann et al., 2003; van Wijk et al., 2006).

A further interaction between additive genetic effects was identified between QTL on SSC6 and SSC8 for loin weight without external fat. No individual QTL effects were identified at these QTL, and these were not identified in previous analyses. Around the location of the QTL on SSC6, QTL have been identified for loin and ham percentage in the carcass and intramuscular fat content (de Koning et al., 2000; Milan et al., 2002), and in the region of SSC8, QTL have been reported for several weights of carcass cuts and daily BW gain (Casas-Carrillo et al., 1997; Milan et al., 2002; Kim et al., 2005).

The SSC6 showed further epistatic effects with SSC9 for neck weight without external fat. At both individual QTL, heterozygote animals were associated with increased lean weight. Mohrmann et al. (2006a) reported, for the same resource family, QTL around this location of SSC6 for lean and fat tissue showing dominance effects, whereas the QTL on SSC9 was not identified previously. The negative D×D effects may be the reason for not detecting the QTL on SSC9 in an individual QTL mapping approach. Quantitative trait loci have been reported around this location of SSC6 for carcass length and loin eye area (Malek et al., 2001b; Edwards et al., 2008a), and have been reported on SSC9 for lean weight and loin eye area (Rohrer et al., 2005).

Fat Tissue Characteristics

Selection for reduced fatness has been an important goal within pig breeding over the last 50 yr. Fat tissue has negative associations with consumer acceptability and the economic value of the carcass, and it has waste and environmental impacts. In the present study, we identified epistatic interactions for 7 traits associated with fatness.

Epistatic D×A genetic effects were identified in 2 genomic locations of SSC1 for external ham fat weight (48 and 118 cM). This QTL for external ham fat weight at 48 cM was identified close to *SW185* on SSC1. In a previous individual QTL analysis of the data, Mohrmann et al. (2006a) reported QTL at 119 cM of SSC1 for the entire loin weight and the external loin fat weight, attributed to dominance effects. The QTL on SSC1 for external ham fat weight at 118 cM is close to *SW1828*. At both of these QTL, a large number of QTL have been reported for carcass traits, lean tissue, fat tissue, and daily BW gain (Malek et al., 2001b; Beeckmann et al., 2003b; Geldermann et al., 2003; Kim et al., 2006).

Sus scrofa chromosome 1 also showed an A×D interaction with SSC4 for intramuscular fat content. Significant additive effects at the QTL on SSC1 indicated that the alleles from the Pietrain breed were associated with greater intramuscular fat content. However, this positive additive genetic effect was offset by an almost 3 times greater negative interaction effect with SSC4. The QTL on SSC1 and SSC4 were not identified in previous individual QTL mapping of the data.

Table 5. Potential candidate genes in locations of the epistatic QTL of the present study

QTL (SSC, position)	Trait	Candidate gene	Role of candidate gene
Entire carcass characteristic			
SSC1, 88 cM	Entire belly wt	Melanocortin-4 receptor	• Important for controlling energy balance and BW; hence, is a candidate gene for traits associated with feed intake and energy homeostasis-related traits (Meidtner et al., 2006). • Reports of an association with growth and fatness (Kim et al., 2000; Park et al., 2002; Houston et al., 2004; Meidtner et al., 2006). • Could be a useful marker to increase growth of the slow-growing Pietrain breed by increasing feed intake (Meidtner et al., 2006).
SSC1, 63 cM	Weight of hind claw	*IGF-1* receptor	• Role in regeneration, metabolism, and proliferation in a variety of cell types (Schweiger et al., 2005).
SSC1, 59 cM	Carcass length		• Regulates growth and differentiation of a variety of cells and controls BW (Kopečný et al., 2002).
SSC2, 10 cM	Entire ham wt	*IGF-2*	• Paternally expressed (Jeon et al., 1999; Nezer et al., 1999). • Caused by a nucleotide substitution in intron 3 (Van Laere et al., 2003).
SSC4, 31 cM	Belly wt	*F-BOX* protein 32	• Expression increased in myotubules during muscle atrophy, whereas mice deficient in this gene were resistant to atrophy (Bodine et al., 2001, Yu et al., 2005). • Could be an important gene for muscle mass development (Glass, 2003).
		Exostosis (multiple) 1	• Candidate gene for growth-related traits (Cepica et al., 2002).
SSC6, 86 cM	Entire neck wt	Ryanodine receptor 1	• A mutation at this locus is associated with malignant hyperthermia syndrome (Fujii et al., 1991). • Significantly associated with production traits in pigs (Kadarmideen, 2008).
SSC7, 86 cM	Entire loin wt	Proteasome (prosome, macropain) activator subunit 1 (*PA28α*) and proteasome (prosome, macropain) activator subunit 2 (*PA28β*)	• Encodes proteasome activators PA28α and β subunits, 2 subunits of PA28, which is an activator of the proteosome and plays an important role in antigen presentation mediated by the major histocompatibility complex class I (Dubiel et al., 1992). • Evidence that a polymorphism in this gene is associated with weaning weight (Wang et al., 2004).
Lean tissue characteristic			
SSC2, 9 cM	Lean content of belly	*IGF-2*	•Role outlined above.
SSC4, 121 cM	Protein content of loin	Transforming growth factor, β receptor III	• Mediates the diverse effects of transforming growth factor-*β*, which is involved in tissue development and repair processes (Johnson et al., 1995).
SSC4, 89 cM	Loin wt without external fat	Myocyte enhancer factor 2D	• Member of the myocyte enhancer binding factor 2 gene family (Wagenknecht et al., 2003). • Thought to be involved in myogenesis (Breitbart et al., 1993).
		Myelin protein zero	• Identified in the same location as QTL for carcass traits (lean and fat mass; Cepica et al., 2003b, Wagenknecht et al., 2005).
		Lamin A/C	• Encodes lamins A and C (Wagenknecht et al., 2006). • Mice lacking lamin A have severely retarded postnatal growth and premature death, and developed cardiac and skeletal myopathy (Sullivan et al., 1999). • QTL for carcass traits identified around this region (Cepica et al., 2003b); therefore, is a candidate gene for muscle development and growth.
		Thioredoxin-interacting protein	• Role in cell proliferation and growth (Yu et al., 2007). • Significant effects on several important growth traits, including carcass weight as well as daily BW gain in pigs (Yu et al., 2007).
SSC9, 58 cM	Neck wt without external fat	Succinate dehydrogenase complex, subunit D	• One of the subunits of the succinate dehydrogenase complex. • Candidate for production traits because of its role in this complex in the process of aerobic respiration. Expression of this gene was associated with growth and meat quality traits in pigs (Guimaraes et al., 2007). • Associated with loin muscle area (Zhu et al., 2005).

However, numerous QTL have been identified around both of these QTL for carcass characteristics, lean and fat tissue, and BW (Rohrer and Keele, 1998a,b; Perez-Enciso et al., 2000; Rohrer, 2000; Varona et al., 2002; Beeckmann et al., 2003b; Cepica et al., 2003b; Geldermann et al., 2003; Edwards et al., 2008a).

Furthermore, SSC1 showed interactions with SSC6 for average fat thickness measured by the AutoFom device. The QTL on SSC6 was previously reported by Mohrmann et al. (2006a). However, they estimated a significant individual dominance effect, whereas the present study showed that it is more likely due to an interaction between additive and dominance effects. Around this location of SSC1, there are a large number of reports for fat tissue, along with lean tissue and growth (Rohrer and Keele, 1998a; Bidanel et al., 2001; Quintanilla et al., 2002; Beeckmann et al., 2003b; Sanchez et al., 2006), and around the location of SSC6, there are reports for fatness, leanness, and growth (Varona et al., 2002; Sato et al., 2003; Kim et al., 2006; Edwards et al., 2008a).

An A×A genetic interaction was identified between the 2 telomeric ends of SSC4 for external neck fat weight. No individual QTL effects were identified at these QTL, and they were not identified in previous analyses of the data. At the telomeric end of the p-arm, there are reports of QTL for fat tissue, as well as BW and belly weight (Marklund et al., 1999; Milan et al., 2002). At the telomeric end of the q-arm, there are no reports of QTL for fatness; however, there are reports for carcass weight, BW, and liver weight (Malek et al., 2001b; Cepica et al., 2003b).

A different location of SSC4 showed A×A genetic interactions with SSC6 for fat content of the belly. At these QTL, no individual QTL effects were identified and they were not identified in previous analyses. Around this location of SSC4, no QTL have been reported for fat tissue, but there are reports of QTL for lean tissue (Cepica et al., 2003b; Geldermann et al., 2003). In the region of the QTL on SSC6, there is only 1 report of QTL for ham weight (van Wijk et al., 2006).

For the thinnest fat measure, additive and dominance interactions were identified between SSC6 and SSC8. In addition, significant dominance effects were identified at both QTL, indicating that heterozygous animals were associated with thinner fat at both QTL. An interaction was described previously in this study for loin weight without external fat between SSC6 and SSC8. The QTL on SSC8 were both identified between *SW444* and *S0086*. The QTL on SSC6 were not identified in the same marker bracket. At the location of the QTL on SSC6, Mohrmann et al. (2006a) found significant dominance effects influencing chemical body composition (protein and lipid content) measured at 30 kg of BW. At these QTL, heterozygous animals were associated with less lipid and protein content of the empty body and less protein content of the fat-free substance. There are no reports in the literature of QTL for similar traits around either QTL.

For external loin fat weight, interactions were identified between genomic locations of SSC6 and SSC9 similar to that of neck weight without external fat. At the QTL on SSC9, heterozygous animals are associated with less fat weight of this carcass cut and increased lean. The QTL on SSC6 has been reported previously by Mohrmann et al. (2006a) for this resource family for many fat tissue characteristics. Furthermore, there are reports in the literature for fatness QTL around both QTL (Kim et al., 2005; Rohrer et al., 2005).

There are numerous reports of QTL in the literature for carcass characteristics and lean tissue and fat tissue characteristics in pigs in many genomic locations throughout the genome (e.g., Rohrer and Keele, 1998a,b; Bidanel et al., 2001; Milan et al., 2002; Geldermann et al., 2003; Sanchez et al., 2006; Liu et al., 2007). There are many potential candidate genes that can be found in locations similar to some of the QTL identified in the present study. These are outlined in Table 5. Previous analyses of the phenotypic data from the commercial population (Pietrain sires × crossbred dam line) of the present study identified numerous QTL for entire carcass characteristics, as well as lean and fat tissue characteristics (Mohrmann et al., 2006a; Duthie et al., 2008). However, in these studies the role of epistasis in the genomic regulation of body composition has not been considered. To date, there is limited evidence for epistatic QTL across all species of livestock. This is most likely because tools and methodologies have not been available for this type of research and because of the computational demand associated with the analysis.

In pigs, epistatic QTL have been reported so far for reproductive traits (Bidanel, 1993; Rodríguez et al., 2005; Noguera et al., 2006), coat color (Hirooka et al., 2002), meat quality traits (meat color and intramuscular fat content; Ovilo et al., 2002; Szyda et al., 2006), and muscle fiber traits (Estellé et al., 2008). No epistatic QTL have been reported for body composition, such as entire carcass cuts or lean tissue and fat tissue characteristics. The present study is, to our knowledge, the first report to estimate epistatic interactions for carcass characteristics measured at slaughter weight in the pig.

Carlborg and Haley (2004) outlined the importance of a relatively large data set for the analysis of epistatic QTL. Small data sets will detect only epistatic QTL pairs with large effects. In the present study, we identified a large number of epistatic QTL pairs; this study is only the first step in understanding the contribution of epistasis to the genetic control of body composition in pigs. We have not covered the whole genome; therefore, many more epistatic interactions are probably involved in the genomic regulation of body composition.

Estellé et al. (2008) identified numerous significant epistatic QTL pairs for muscle fiber traits in a pig popu-

lation of Iberian × Landrace F_2 cross, using a methodology similar to that in the present study. They identified all 2-locus epistatic effects (A×A, A×D, D×A, D×D) but did not find that any particular epistatic effect was prevalent in their study. The interactions identified in the present study were at different genomic locations than those of Estellé et al. (2008). This may be because muscle fiber traits are under different genomic control or because of breed differences, because the study by Estellé et al. (2008) was based on an experimental cross between Iberian and Landrace pigs. They found that the epistatic interactions formed a network of connected pairs of epistatic QTL. They also indicated that this may be a common phenomenon because Carlborg et al. (2006) reported similar networks. Estellé et al. (2008) found that SSC10 and SSC11 behaved as hubs for this network. There is no clear evidence of this type of network in our study. However, SSC1, SSC2, SSC4, SSC6, SSC8, and SSC9 seemed particularly active with respect to epistasis. *Sus scrofa* chromosome 10 did not seem as important in our study, with only 1 interaction being identified on SSC10; SSC11 was not genotyped in the present study.

Information about the involvement of epistatic QTL in the genomic regulation of body composition is limited in livestock. There is, however, some evidence of the involvement of epistasis in the genomic regulation of growth in chickens, particularly early growth (Carlborg et al., 2003, 2004). Furthermore, there is considerable evidence indicating an important role for epistatic interactions in the genomic control of growth and obesity in mice. Routman and Cheverud (1997) reported epistatic QTL for adult BW. Brockmann et al. (2000) reported epistatic effects for serum concentrations of leptin, insulin, and IGF-1 and for BW, abdominal fat weight, and muscle weight. They reported co-coordinated regulation of BW and muscle weight by the interaction of 2 pairs of loci, 1 of which also influenced serum concentrations of lipid. They indicated that these interactions may contribute to the strong genetic correlation between BW and muscle weight. Yi et al. (2004b) also found that epistasis played an important role controlling obesity in mice. They reported that different groups of traits were influenced by different interactions, such that a different genetic architecture was identified for obesity traits and total cholesterol. They also found that the total phenotypic variance explained by epistatic interactions was greater than those explained by main effects. The epistatic QTL pairs identified in the present study also contributed to greater proportions of the phenotypic variance than QTL identified from individual QTL analysis. In a further study of mice, Yi et al. (2004a) reported an epistatic effect between mouse chromosomes 7 and 3 for hepatic lipase activity. The QTL on chromosome 7 was detected in a nonepistatic analysis in the same location. The QTL on chromosome 3 had a weak main effect on hepatic lipase activity and was not detected in the nonepistatic analysis; however, chromosome 3 was found to interact strongly with chromosome 7. Further studies in mice reported epistatic QTL pairs for abdominal fat percentage, abdominal fat weight, BW, kidney weight, spleen weight (Carlborg et al., 2005), organ weights, and limb length traits (Wolf et al., 2006). Yi et al. (2006) found that epistasis was more important for BW in mice at older ages than at younger ages, in contradiction to the report of Ishikawa et al. (2005), who found that epistasis was more important for early growth than late stages of growth in mice. Yi et al. (2006) also found that epistasis influenced fatness and organ weights.

A concern in epistatic QTL analysis is multiple testing and the risk of false-positive results, based on the large number of tests that are carried out. Therefore, to minimize the risk of false-positive results, in the present study a more stringent threshold was applied to the epistatic analysis compared with the individual QTL analysis of previous work based on these data (Mohrmann et al., 2006a; Duthie et al., 2008).

In the present study, we have identified a large number of epistatic QTL pairs involved in the regulation of many carcass traits, including lean and fat tissue weights in pigs. It is obvious from this study and from studies of poultry and mice that epistasis is important for the genomic regulation of growth and body composition. Information about epistatic interactions can add to our understanding of the genomic networks that form the fundamental basis of biological systems. In addition to knowledge about the individual QTL or genes that influence a biological system, information about the effect of interactions between genes will build on the understanding of the genomic networks that influence variation in biological systems (Carlborg and Haley, 2004). Future QTL analyses should therefore focus their attention on uncovering the role of epistasis in the genomic regulation of economically important traits.

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