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A quantitative trait locus genome scan for porcine muscle fiber traits reveals overdominance and epistasis¹

J. Estellé,*² F. Gil,† J. M. Vázquez,† R. Latorre,† G. Ramírez,† M. C. Barragán,‡
J. M. Folch,* J. L. Noguera,§ M. A. Toro,‡ and M. Pérez-Enciso*^{#2}

*Departament de Ciència Animal i dels Aliments, Facultat de Veterinària, Universitat Autònoma de Barcelona, 08193 Bellaterra, Spain; †Departamento de Anatomía Veterinaria, Universidad de Murcia, Campus de Espinardo, Apartado 4021, 30100 Murcia, Spain; ‡Departamento de Mejora Animal, INIA, 28040 Madrid, Spain; §Genética i Millora Animal, Centre IRTA-Lleida, 25198 Lleida, Spain; and #Institut Català de Recerca i Estudis Avançats, Lluís Companys 23, 08010 Barcelona, Spain

ABSTRACT: Muscle histochemical characteristics are decisive determinants of meat quality. The relative percentage and diameters of the different muscular fiber types influence crucial aspects of meat such as color, tenderness, and ultimate pH. Despite its relevance, however, the information on muscle fiber genetic architecture is scant, because histochemical muscle characterization is a laborious task. Here we report a complete QTL scan of muscle fiber traits in 160 animals from a F₂ cross between Iberian and Landrace pigs using 139 markers. We identified 20 genome regions distributed along 15 porcine chromosomes (SSC1, 2, 3, 4, 6, 7, 8,

9, 10, 11, 12, 13, 14, 15, and X) with direct and(or) epistatic effects. Epistasis was frequent and some interactions were highly significant. Chromosomes 10 and 11 seemed to behave as hubs; they harbored 2 individual QTL, but also 6 epistatic regions. Numerous individual QTL effects had cryptic alleles, with opposite effects to phenotypic pure breed differences. Many of the QTL identified here coincided with previous reports for these traits in the literature, and there was overlapping with potential candidate genes and previously reported meat quality QTL.

Key words: epistasis, muscle fiber, overdominance, pig, quantitative trait locus

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INTRODUCTION

Modern animal breeding has focused on increasing lean percentage in meat animals to provide an abundant source of protein for human nutrition. Although selection has succeeded in enhancing muscular growth (Weiler et al., 1995), a reduction in meat quality has occurred during the process. Muscle fibers are a major component of muscles and play a crucial role in the determination of lean content and meat quality. Pig skeletal muscle fibers have been routinely categorized into 3 major fiber types, designated I, IIA, and IIB,

using conventional histochemical reaction for myosin adenosine triphosphatase (**mATPase**) activity after acid pH preincubation (reviewed by Lefaucheur, 2001). Whereas type I are oxidative and IIA oxido-glycolytic, type IIB fibers can be either oxido-glycolytic (**IIBr**) or glycolytic (**IIBw**; Larzul et al., 1997). Each fiber type has different biochemical characteristics, and porcine muscle fiber type composition has been correlated with meat color, ultimate pH, and tenderness, thereby largely determining meat quality (Karlsson et al., 1999; Ryu and Kim, 2005; Ryu et al., 2008). It is documented that an increment of the type IIB muscular fibers has been produced during selection (Brocks et al., 1998).

Despite its relevance, however, the information on muscle fiber genetic architecture is limited because histochemical muscle characterization is a laborious task. Previous QTL scans on porcine muscle fiber characteristics detected significant effects on most porcine chromosomes (Malek et al., 2001; Nii et al., 2005; Wimmers et al., 2006). Herein we report a QTL scan in an Iberian by Landrace swine F₂ cross. We have previously shown that the Iberian and Landrace breeds have large phenotypic differences for a variety of traits including muscle

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²Corresponding authors: Jordi.Estelle@uab.es or Miguel.Perez@uab.es

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Table 1. Means and SD of the porcine muscle fiber traits analyzed in this study and comparisons with the pure breed phenotypes described by Serra et al. (1998)

Trait	Abbreviation	IBMAP F ₂ cross ¹			Iberian ²		Landrace ²	
		n	Mean	SD	Mean	SD	Mean	SD
Percentage of type I fibers	PER _I	160	12.2	3.9	12.1	0.7	9.1	0.5
Minimum diameter of type I fibers, μm	DIAM _I	156	46.1	5.7	44.4	1.3	40.8	1
Percentage of type IIA fibers	PER _{IIA}	160	9.2	3.4	4	0.6	4	0.5
Minimum diameter of type IIA fibers, μm	DIAM _{IIA}	156	43.8	7.1	43.3	1.2	41.2	0.9
Percentage of type IIB fibers (w+r) ³	—	—	—	—	83.9	0.9	86.9	0.7
Percentage of type IIB glycolytic fibers	PER _{IIBw}	160	72.8	5.8	—	—	—	—
Minimum diameter of type IIB fibers, μm	DIAM _{IIB}	156	57.8	6.3	48	1.2	41.2	0.9
Percentage of type IIB oxidative fibers	PER _{IIBr}	133	6.8	4.3	—	—	—	—

¹Generated by crossing Iberian and Landrace porcine breeds.

²Serra et al. (1998).

³Note that no distinction was made between IIBw and IIBr fibers in the Serra et al. (1998) report. w = nonoxidative; r = oxidative.

fiber characteristics; Iberian pigs showed more oxidative metabolism and greater proportion and diameter of type I fibers than Landrace; the opposite occurred with type IIB fibers (Serra et al., 1998).

MATERIALS AND METHODS

All procedures involving animal management were standard commercial protocols, as applied in the experimental farm of Nova Genética S.A. and under the supervision of IRTA authorities.

Animal Material and Traits Analyzed

Complete details of the Iberian by Landrace (**IBMAP**) cross are described in Varona et al. (2002). In brief, 3 Iberian boars were crossed with 31 Landrace sows producing 79 F₁ and 321 F₂ individuals. The histochemical analyses were performed as follows in a subset of 160 F₂ pigs, corresponding to 3 slaughter batches. There should be no bias because animals were randomly allocated to slaughter batch. Within 1 h after slaughter, a sample was taken from the longissimus lumborum muscle at the level of the last rib. Muscle samples were frozen in isopentane cooled with liquid nitrogen and stored at -65°C until further analysis. Transversal serial sections (10 μm thick) were cut in a cryostat (Leica CM 1850, Nussloch, Germany) at -20°C and stained for mATPase activity after acid preincubation at pH 4.3, 4.55, and 4.6, according to Latorre et al. (1993). Type I, IIA, and IIB fibers were identified by mATPase staining (Gil et al., 2001). Sections were also stained for activity of nicotinamide adenine dinucleotide tetrazolium reductase (**NADH-TR**), an enzyme frequently used as a marker for the oxidative capacity (Dubowitz and Brooke, 1973). In these sections, muscle fibers were classified into oxidative (**r**) and nonoxidative (**w**). Consequently, as described by Larzul et al. (1997), 4 types of muscle fibers were identified by combining mATPase and NADH-TR staining: types I, IIA, IIBr, and IIBw. Percentages (**PER**) of these muscle fiber types were

estimated from 4 corresponding fields (mATPase and NADH-TR) per section, each containing 200 to 300 muscle fibers. Additionally, mATPase-stained sections were used to estimate the smaller diameter (**DIAM**) (Dubowitz et al., 1985) of fiber types I, IIA, and IIB (IIBr + IIBw) by computer-assisted image analysis system (SigmaScan Pro 5.0, SPSS Inc., Chicago, IL). The means and standard deviations of the traits analyzed, together with the acronyms used, are shown in Table 1.

Linkage Maps

A total of 139 markers distributed along the porcine genome were genotyped. Sex-average linkage maps (supplementary Table S1; available online at <http://jas.fass.org/content/vol86/issue12>) were constructed with CRIMAP 2.4 software (Green et al., 1990). The map used here is slightly different from the one used previously by Varona et al. (2002), because some additional markers have been genotyped.

Statistical Analyses

Single QTL genome scans, 2 dimensional epistasis analyses, and estimates of heritability and genetic and environmental correlations were done with Qxpak 3.0 (Pérez-Enciso and Misztal, 2004). The single QTL scan was performed using the following model:

$$y_i = \text{sex}_i + \beta w_i + C_a a + C_d d + u_i + e_i, \quad [1]$$

where y_i is the i th individual phenotype; sex_i is the i th sex fixed effect; β is the covariate coefficient of carcass weight (w_i); C_a is the additive QTL coefficient (a) for that individual and position [i.e., the probability of the individual being homozygous for alleles of Iberian origin (**QQ**) minus the probability of being homozygous for alleles of Landrace origin (**qq**) at the position of interest], and C_d the dominance QTL coefficient (d) (i.e., the probability of being heterozygous for the Lan-

drace origin; Haley and Knott, 1992); u_i is the infinitesimal genetic effect, which is distributed as $N(\mathbf{0}, \mathbf{A}\sigma_u^2)$;

\mathbf{A} is the numerator relationship matrix; and e_i is the residual effect. Additional cofactors such as age or batch at slaughter were tested, but they were not retained in the final model due to lack of significance. The QTL scans were performed every centimorgan, and nominal P -values were obtained via maximum likelihood ratio tests by removing the QTL effect in [1]. The dominant effect d was deleted in [1] when not significant ($P < 0.05$). We have argued elsewhere (Mercadé et al., 2005) that a nominal P -value of 0.001 would correspond, roughly, to a 1% significance level in the IB-MAP cross. In this study, we considered QTL with nominal P -value ≤ 0.001 as significant and QTL with P -values ≤ 0.01 as suggestive.

Because of the high computational cost of a whole-genome epistatic QTL scan, epistasis analyses were performed using a 2-step approach. In the first step, we preselected potential candidate interacting regions carrying out a 5-cM step scan along the complete genome with the model:

$$y_i = \text{sex}_i + \beta w_i + C_{a \times a} I_{a \times a} + C_{a \times d} I_{a \times d} + C_{d \times a} I_{d \times a} + C_{d \times d} I_{d \times d} + u_i + e_i, \quad [2]$$

where $I_{a \times a}$, $I_{a \times d}$, $I_{d \times a}$, and $I_{d \times d}$ are the additive \times additive, additive \times dominance, dominance \times additive, and dominance \times dominance epistatic interaction effects, respectively. Following the Cockerham (1954) decomposition, the 4 epistatic components were estimated by regressing on a linear combination of the individual QTL origin probabilities (P_1 refers to QTL 1 and P_2 to QTL 2) as (Varona et al., 2002):

$$\begin{aligned} C_{a \times a} &= P_1(QQ)P_2(QQ) - P_1(QQ)P_2(qq) \\ &\quad - P_1(qq)P_2(QQ) + P_1(qq)P_2(qq), \\ C_{a \times d} &= P_1(QQ)P_2(Qq) - P_1(qq)P_2(Qq), \\ C_{d \times a} &= P_1(Qq)P_2(QQ) - P_1(Qq)P_2(qq), \text{ and} \\ C_{d \times d} &= P_1(Qq)P_2(Qq). \end{aligned}$$

Note that these equations imply unlinked interacting loci (Kao and Zeng, 2002). Model [2] was tested against the null model $y_i = \text{sex}_i + \beta w_i + u_i + e_i$. Interacting QTL pairs with P -value < 0.001 were selected for further analyses. In a second step, a complete epistatic model, including the individual QTL effects, was applied every centimorgan on the 20-cM region around the preselected positions:

$$y_i = \text{sex}_i + \beta w_i + C_{a1} a_1 + C_{d1} d_1 + C_{a2} a_2 + C_{d2} d_2 + C_{a \times a} I_{a \times a} + C_{a \times d} I_{a \times d} + C_{d \times a} I_{d \times a} + C_{d \times d} I_{d \times d} + u_i + e_i. \quad [3]$$

Model [3] was tested against a null model that contained only the individual QTL effects; that is:

$$y_i = \text{sex}_i + \beta w_i + C_{a1} a_1 + C_{d1} d_1 + C_{a2} a_2 + C_{d2} d_2 + u_i + e_i.$$

We reported epistatic interactions with nominal P -values around 10^{-4} or lower. Epistatic models were not applied to SSCX.

RESULTS

Heritabilities and Correlations

The means and standard deviations of the different traits are in Table 1. Percentages and diameters of different fiber types showed medium to high heritabilities (Table 2). Diameters showed much greater heritabilities than percentages: 0.70 vs. 0.35 on average. Correlations between percentages were negative, although moderate, which was as expected because percentages sum to 1. In contrast, diameters of the different fiber types were positively correlated, whereas correlations between percentages and diameters were negligible. Larzul et al. (1997) also reported that, although correlations between fiber type cross-sectional areas were all positive and highly significant, correlations between fiber percentages and areas were low: fiber type relative areas were much more related to fiber percentages than to cross-sectional areas.

Single QTL Genome Scan

A summary of the single QTL analyses performed with model [1] is presented in Table 3; QTL profiles are shown in Figure 1. There are several remarkable observations. The first is that the magnitude of heritability is no indication of QTL architecture. We did not find any QTL for DIAM_{IIB} and only one for DIAM_{I} , 2 traits with $h^2 = 0.80$ (Table 2). On average, we identified 2 QTL for the rest of traits, for which heritabilities were much lower. Although the interpretation of heritability in F_2 crosses is not standard, these observations suggest that DIAM_{IIB} and DIAM_{I} might be affected by a greater number of loci, each of smaller effect, than the rest of traits. The second result is that the 2 most significant QTL were located in the same region of chromosome X (the pseudoautosomal region) and affected DIAM_{I} and DIAM_{IIA} . The rest of the effects were distributed across 9 autosomes; overdominance was detected in 7 of the 11 QTL on autosomes. Several QTL regions coincided on SSC11 (PER_{IIBw} and PER_{IIBr}), SSC14 (DIAM_{IIA} and PER_{IIBr}), and, as mentioned, SSCX. We did not specifically test the hypothesis of pleiotropy vs. linkage, because the QTL fell within the same marker intervals and results would not be conclusive. Finally, it is also remarkable that some QTL effects for the same trait were of opposite effect (i.e., there was evidence of cryptic alleles or alleles whose effects were opposite to the phenotypic differences between Iberian and Landrace breeds; Serra et al., 1998). We found such evidence for PER_{IIA} (SSC1 vs. SSC2), DIAM_{IIA} (SSC9 vs. SSC14

Table 2. Heritabilities (diagonal, boldface), genetic (below diagonal), and environmental (above diagonal) correlations between the porcine muscle fiber traits analyzed in this study

Trait ¹	PER _I	DIAM _I	PER _{IIA}	DIAM _{IIA}	PER _{IIBw}	DIAM _{IIB}	PER _{IIBr}
PER _I	0.35	0.05	-0.19	0.17	-0.33	0.18	-0.16
DIAM _I	0.10	0.81	-0.08	0.61	-0.07	0.57	0.03
PER _{IIA}	-0.17	-0.13	0.34	0.03	-0.41	-0.02	-0.09
DIAM _{IIA}	0.38	0.69	0.02	0.48	-0.53	0.46	0.20
PER _{IIBw}	-0.39	-0.03	-0.40	-0.06	0.36	-0.15	-0.62
DIAM _{IIB}	0.23	0.65	-0.08	0.65	-0.13	0.80	0.07
PER _{IIBr}	-0.13	0.02	-0.15	0.22	-0.56	0.03	0.35

¹PER = percentage of fibers; DIAM = minimum diameter of fibers; subscripts I, IIA, IIBw, and IIBr indicate each fiber type. w = nonoxidative; r = oxidative.

and SSCX), PER_{IIBw} (SSC11 vs. SSC12), and PER_{IIBr} (SSC4 and SSC11 vs. SSC14).

Epistatic QTL Analyses

A total of 40 candidate interacting pairs were preselected with model [2], and 10 epistatic pairs were finally deemed as significant after analysis with the complete model [3]. They were located on chromosomes 2, 3, 4, 6, 7, 8, 10, 11, 12, 13, and 14 (Table 4; Figures 1 and 2). All epistatic interactions except one were found for percentages rather than diameters. There was no clear preeminence of any of the epistatic components, a×a, a×d, or d×d; using the rule of thumb of the effect being at least twice the SD, 2 or more components were significant in all cases. Often, but not always, the marker interval of the individual QTL and the epistatic interaction coincided (scheme in Figure 2). Overall, PER_{IIBr} was the trait for which we identified the most significant effects: 3 QTL (SSC4, 11, and 14) and 3 interacting pairs, one of which was between SSC4 and SSC11, and the other between SSC11 and SSC14. These 3 epistatic pairs were the most significant ones. An epistatic

pair appeared for DIAM_{IIB}, although no direct effect was found in single QTL analyses (Table 3).

DISCUSSION

We have reported a detailed QTL scan for traits of high potential economic and technological interest; that is, the histochemical composition of porcine muscle. Numerous putative QTL regions were identified. Because the number of phenotyped individuals is limited, the identification of only those QTL with large effects may be expected. In agreement with previous genome scans (Malek et al., 2001; Nii et al., 2005; Wimmers et al., 2006), we found QTL on most porcine chromosomes for these traits. In addition, we detected the presence of cryptic alleles in numerous single QTL effects reported. Our results also suggest a complex genetic architecture that includes overdominance, epistatic interactions, and, probably, pleiotropy. Although epistasis can be important in the determination of the genetic architecture of complex traits (Carlborg and Haley, 2004), full-genome QTL scans accounting for epistasis are not yet widespread.

Table 3. Results of the single QTL analyses for the porcine muscle fiber traits analyzed in this study

Trait ¹	Chromosome	Position, cM	Marker interval	QTL effects (SD) ²			
				a	d	LR ³	P-value
PER _I	SSC10	25	<i>S0038-S0070</i>	-1.77 (0.64)	—	7.42	0.0064
	SSC15	10	<i>SW919-SW1111</i>	-0.53 (0.47)	2.28 (0.79)	9.61	0.0082
DIAM _I	SSCX	20	<i>SW949-SW2126</i>	0.38 (1.39)	6.98 (1.70)	16.82	2.2 × 10 ⁻⁴
PER _{IIA}	SSC1	1	<i>SW1515-CGA</i>	-0.70 (0.40)	-1.61 (0.54)	10.59	0.0050
	SSC2	71	<i>SW395-S0226</i>	0.28 (0.46)	2.68 (0.81)	16.11	3.2 × 10 ⁻⁴
DIAM _{IIA}	SSC9	152	<i>SW2093-SW1349</i>	2.44 (0.94)	5.97 (1.98)	13.75	0.001
	SSC14	25	<i>SW1125-SW210</i>	-2.22 (0.78)	—	7.63	0.0057
	SSCX	11	<i>SW949-SW2126</i>	-2.64 (1.55)	7.67 (2.29)	18.40	1.0 × 10 ⁻⁴
PER _{IIBw}	SSC11	22	<i>S0385-S0071</i>	-2.11 (0.88)	3.89 (1.80)	10.34	0.0057
	SSC12	102	<i>S0106-SWR1021</i>	2.22 (0.76)	-3.11 (1.25)	12.99	0.0015
PER _{IIBr}	SSC4	128	<i>SW445-SW58</i>	1.48 (0.54)	—	7.21	0.0072
	SSC11	24	<i>S0385-S0071</i>	1.72 (0.74)	-3.01 (1.56)	9.83	0.0073
	SSC14	19	<i>SW1125-SW210</i>	-1.34 (0.50)	—	6.93	0.0085

¹PER = percentage of fibers; DIAM = minimum diameter of fibers; subscripts I, IIA, IIBw, and IIBr indicate each fiber type. w = nonoxidative; r = oxidative.

²QTL effects: Iberian – Landrace allele effects, a positive additive effect indicates that Iberian alleles increase the trait. a = additive QTL effect; d = dominant QTL effect.

³LR = likelihood ratio values.

A Network of QTL

Figures 1 and 2 aim to show the complexity encountered. The individual QTL scans in the margins are superimposed on the epistatic interactions in the square. In the square, each circle represents 2 putative interacting QTL, with the size of the circle representing the approximate strength of epistasis. Figure 2 is a network interpretation: lines connecting the chromosomes

indicate epistatic interactions and vertical lines within chromosomes represent individual effects. Most epistatic interactions were complex and involved more than one type of epistasis. Moreover, these epistatic interactions often form a network of connected epistatic pairs. Recently, a similar epistatic network has also been reported in chicken (Carlborg et al., 2006). It is possible then that such epistatic networks are a common phenomenon. Chromosomes 10 and 11 seem to behave as

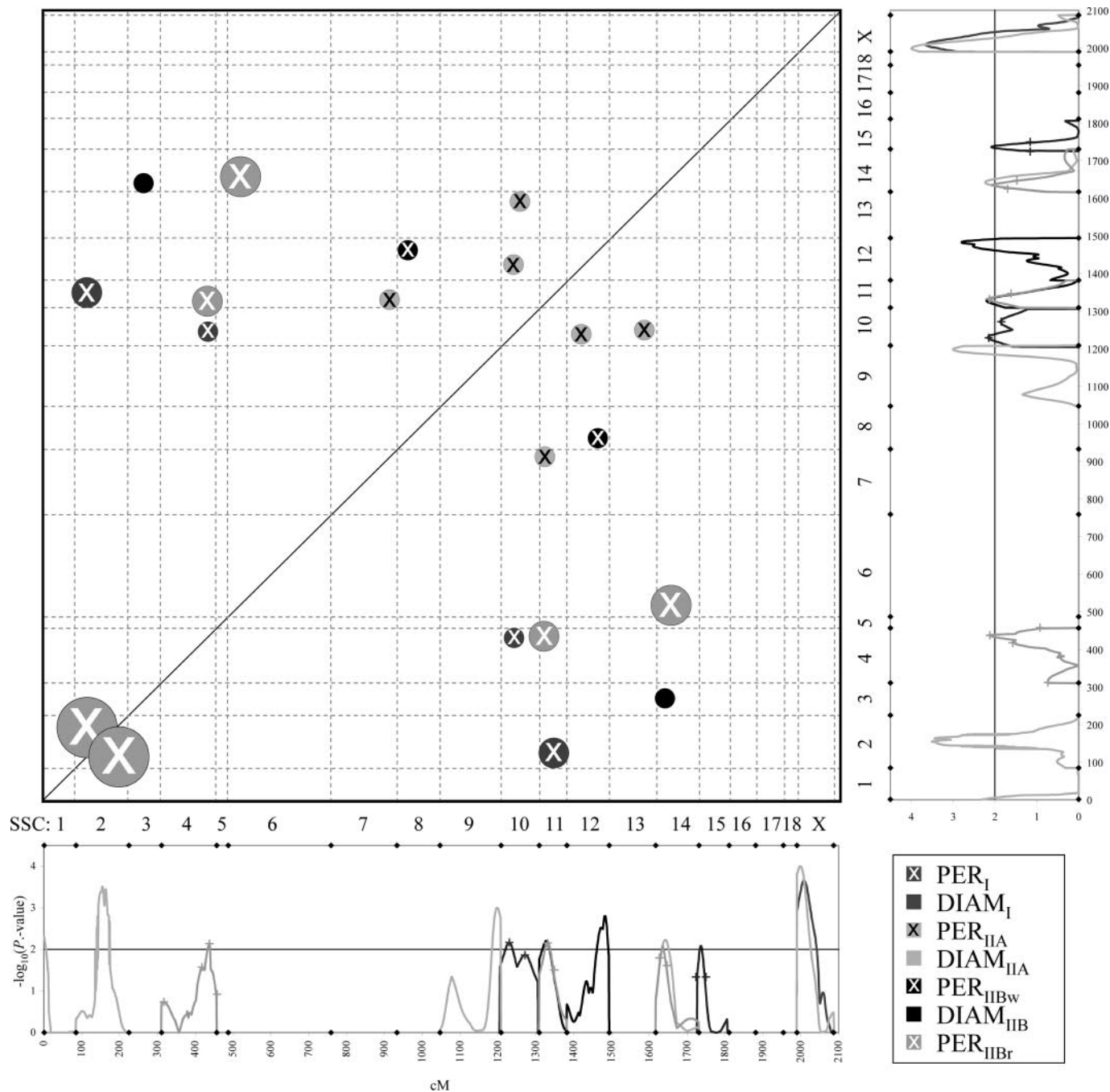


Figure 1. Graphical scheme of the single QTL and the epistatic QTL interactions. Profiles $[-\log_{10}(P\text{-values})]$ of the single QTL analyses (Table 3) are on the margins, numbers refer to SSC number; and the horizontal line is the 0.01 significance level. The QTL epistatic interactions are represented as circles in the square, with the circle size proportional to the significance (Table 4). PER = percentage of fibers; DIAM = minimum diameter of fibers; subscripts I, IIA, IIB, IIBw, and IIBr indicate each fiber type. w = nonoxidative; r = oxidative. Color figure available online at <http://jas.fass.org/content/vol86/issue12/>.

hubs for this network; they harbor 2 individual QTL, but, more importantly, 6 epistatic regions, 4 of them also mapping the individual loci. The power to detect epistatic interactions varies with the size of the analyzed populations; small populations allow detection of only highly significant effects (Carlborg and Haley, 2004). Thus, given the moderate number of phenotypes here, additional epistatic interaction must have remained uncovered. In addition to low power, an additional matter of concern is false-positive results. For that reason, it is necessary to find the biological cause for the statistical results reported here (Carlborg and Haley, 2004). As a first step, we provide a reconstruction of genetic networks with the identified effects, which have been proposed as a method to increase the confidence in the identified QTL interacting effects (Carlborg and Haley, 2004).

It should also be mentioned that although all traits analyzed here are related to muscle fiber characteristics, each has a different genetic architecture. For instance, a single epistatic pair was found for $DIAM_{IIB}$, but several individual loci and interacting pairs were found for PER_{IIBr} . Overdominance appeared to predominantly affect fiber diameters, whereas epistasis was more common for fiber percentages. Thus, different numbers of genes with disparate effects should be expected for each trait.

Relation with Other Reported QTL and Hypothetical Positional Candidate Genes

We did a literature search to gain some insight into potential pleiotropic QTL effects and to identify hypothetical positional candidate genes for future studies. Although some contradictory results have been reported, it is generally accepted that relative proportions and diameters of porcine muscle fiber types are correlated with meat color, pH, and tenderness (Klont et al., 1998; Karlsson et al., 1999) and it has been proposed that selection for decreased IIBw fibers may improve meat quality by reducing the postmortem pH decline (Larzul et al., 1997). Thus, we paid attention to colocalization of fiber trait QTL with those affecting meat quality traits, as a single genetic causal factor may have pleiotropic effects on both sets of phenotypes.

Table 5 shows the published QTL that approximately coincided with the regions detected here. Among the meat quality traits, the most related seem to be color traits, in both IIBMAP and the other experiments. In addition, other QTL studies for muscle fibers agree in many regions, in particular with Wimmers et al. (2006). Those authors described a QTL for fiber diameter and proportion of giant fibers close to the QTL for PER_{IIA} on SSC1. This position coincides with the *ESR1* gene, whose protein product is present in muscular tissue and is more expressed in slow oxidative muscles than in fast glycolytic muscles (Lemoine et al., 2002). We reported 3 main QTL regions on SSC2. A highly significant epistatic QTL pair on its 2 telomeres for PER_{IIBr} colocal-

Table 4. Results of the QTL epistatic analyses for the porcine muscle fiber traits analyzed in this study

Trait ¹	QTL positions (chromosome: cM)		LR ²	P-value	Epistatic QTL effects (SD) ³			
	QTL1 (marker interval)	QTL2 (marker interval)			I _{a×a}	I _{a×d}	I _{d×a}	I _{d×d}
PER _I	SSC4: 128 (SW445-SW58)	SSC10: 34 (S0038-S0070)	20.80	3.4 × 10 ⁻⁴	-2.82 (0.79)	-3.34 (1.86)	-3.49 (1.31)	2.81 (2.86)
	SSC11: 51 (S0071-SW703)	SSC2: 14 (JGF2QTN-S0141)	26.02	3.1 × 10 ⁻⁵	4.34 (1.01)	4.40 (1.83)	-2.82 (1.67)	0.22 (3.20)
PER _{IIA}	SSC7: 151 (S0101-SW764)	SSC11: 1 (S0385-S0071)	19.89	5.2 × 10 ⁻⁴	-1.26 (0.56)	2.63 (0.84)	-0.93 (0.95)	-3.03 (1.38)
	SSC10: 85 (S0070-SW1026)	SSC13: 102 (SW1056-SW769)	22.67	1.5 × 10 ⁻⁴	4.31 (0.97)	-0.46 (1.75)	-4.14 (2.07)	-4.28 (3.86)
PER _{IIBw}	SSC12: 49 (SW1307-SW874)	SSC10: 11 (S0038-S0070)	22.20	1.8 × 10 ⁻⁴	1.29 (0.76)	-1.03 (1.39)	3.40 (1.15)	7.93 (2.07)
	SSC8: 2 (SW2410-SW905)	SSC12: 100 (S0106-SWR1021)	21.49	2.5 × 10 ⁻⁴	-3.22 (0.99)	1.52 (1.63)	0.51 (1.47)	-7.80 (2.36)
DIAM _{IIB}	SSC3: 53 (S0206-S0216)	SSC14: 26 (SW1125-SW210)	21.67	2.3 × 10 ⁻⁴	4.20 (1.03)	5.64 (1.82)	-0.25 (1.50)	0.17 (2.66)
	SSC2: 25 (JGF2QTN-S0141)	SSC2: 135 (S0378-SWR308)	36.74	3.3 × 10 ⁻⁷	0.57 (1.16)	5.14 (1.98)	-5.11 (2.12)	-20.40 (3.54)
PER _{IIBr}	SSC4: 121 (SW524-SW445)	SSC11: 11 (S0385-S0071)	24.28	7.0 × 10 ⁻⁵	-0.88 (0.91)	4.52 (1.61)	1.26 (1.44)	-8.56 (2.65)
	SSC6: 11 (MC1R-S0035)	SSC14: 80 (S0007-SW1557)	31.99	1.9 × 10 ⁻⁶	4.40 (1.07)	1.39 (1.81)	0.09 (1.78)	11.58 (3.09)

¹PER = percentage of fibers; DIAM = minimum diameter of fibers; subscripts I, IIA, IIB, IIBw, and IIBr indicate each fiber type. w = nonoxidative; r = oxidative.

²LR = likelihood ratio values.

³Estimates of each of the epistatic interactions between the QTL pairs; I_{a×a}, I_{a×d}, I_{d×a}, and I_{d×d} are the additive × additive, additive × dominance, dominance × additive, and dominance × dominance epistatic interaction effects, respectively.

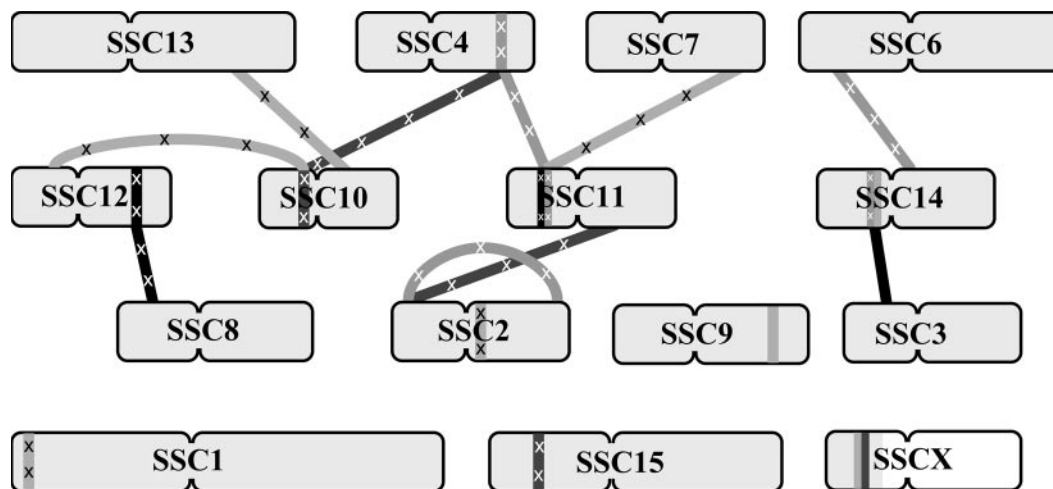


Figure 2. Network representation of the single QTL and the epistatic QTL interactions. Vertical lines in a chromosome represent individual QTL, and lines connecting chromosomes represent epistatic interactions. Chromosome lengths are approximately proportional to their size in the porcine cytogenetic map. The non-pseudoautosomal region in SSCX is white; the pseudoautosomal region and the autosomes are gray. Each shade corresponds to a different trait. Color figure available online at <http://jas.fass.org/content/vol86/issue12/>.

ized with meat quality QTL (Lee et al., 2003 and Malek et al., 2001, respectively). The growth factor gene *IGF2* is within the confidence interval of one of the epistatic regions, but the *IGF2* causal mutation (Van Laere et al., 2003) would not be involved in the QTL because it is segregating at a very low frequency in the IBMAP cross (Estellé et al., 2005). Fiber (Nii et al., 2005; Wimmers et al., 2006) and meat quality (Estellé et al., 2005) QTL were also found in the center of the chromosome at similar positions to the single QTL effect on PER_{IIA} . Calpastatin (*CAST*) is a major candidate gene within this central region, as it has been associated with porcine meat quality traits (Ciobanu et al., 2004; Meyers et al., 2007) as well as with muscle fiber characteristics (Wu et al., 2007).

The fiber QTL found here on SSC4 does not overlap with the *FAT1* locus (Andersson et al., 1994). Rather, it is close to a telomeric region that harbors a pH and color QTL found in IBMAP (Mercadé et al., 2005). Again, a significant association was reported in this region by Wimmers et al. (2006), who proposed *MEF2D* as a candidate gene. This gene is involved in the formation of slow oxidative fibers (Potthoff et al., 2007). *Sus scrofa* chromosome 7 is another chromosome where important effects have been found, often in the neighborhood of the swine leucocyte antigen (**SLA**) complex (Demars et al., 2006). The QTL found here (marker interval *S0101-SW764*) is distant from the SLA, but it overlaps with a suggestive QTL for the diameter of red fibers and proportion of white fibers (Wimmers et al., 2006) and a QTL for meat color in the IBMAP cross (Óviló et al., 2002). The porcine *FOS* proto-oncogene, which has been associated with relative percentages and diameters of porcine white fibers (Reiner et al., 2002), maps to this region.

We argued above that chromosomes 10 and 11 might play an important role as hubs for muscle fiber archi-

ture. A role was also supported by results of Wimmers et al. (2006). Although we did not find any other relevant meat quality QTL in the IBMAP cross, the literature suggests the presence of loci influencing color and biochemical properties such as drip loss or glycogen potential (Malek et al., 2001; Dragos-Wendrich et al., 2003a; van Wijk et al., 2006). Potential candidate genes include *TPM2*, *SGCG*, and *MTMR6*. Mutations in *TPM2* have been involved in human nemaline myopathy, a disease often characterized by fiber type disproportion and predominance of type I fibers (Donner et al., 2002). The main QTL region on SSC12 coincides again with previous fiber (Wimmers et al., 2006) and color (Malek et al., 2001) QTL and contains the fast skeletal myosin heavy chain gene cluster (Davoli et al., 1998), which represent, in consequence, major candidates.

Previous fiber muscle studies (Nii et al., 2005; Wimmers et al., 2006) also reported QTL on SSC14 and SSC15 for both size and percentage of fibers. These positions overlap with color and related biochemical muscle traits as in the case of SSC10 and SSC11. Nii et al. (2005) suggested *PPP3CC*, *PPP3CB*, and *NFAM1* genes as candidates in the SSC14 region. Finally, on SSC15, it is remarkable that the QTL confidence intervals probably include the porcine *PRKAG3* gene (Milan et al., 2000; Ciobanu et al., 2001) and the myostatin gene, which play an important role in muscle development and with major effect mutations discovered in cattle (reviewed by Bellingue et al., 2005) and in sheep (Clop et al., 2006).

The presented results suggest that muscle fiber traits are governed by many loci scattered throughout the genome. In addition, a complex genetic architecture characterized by overdominance and epistasis has been uncovered. Both overdominance and epistasis have been proposed as genetic causes of hybrid vigor or heterosis,

Table 5. Relation between QTL regions found and the previous meat quality QTL in the Iberian × Landrace (IBMAP) cross and the literature

SSC	Marker interval	Other muscle fiber QTL ¹	IBMAP QTL	Other meat quality QTL	Potential candidate genes ²
SSC1	<i>SW1515-CGA</i>	Percentages, diameters [1]	—	pH [2]	<i>ESR1</i>
SSC2	<i>IGF2QTN-S0141</i> <i>SW395-S0226</i> <i>S0378-SWR308</i>	— Percentages [1], diameters [4]	— Carcass weight, LM area, pH [5]	Conductivity, dressing [3] Shear force, tenderness [6] Color, water-holding capacity, drip loss, tenderness [7]	<i>IGF2</i> <i>MYOD1</i> , <i>CAST</i>
SSC3	<i>S0378-S0216</i>	Fiber number [1,8]	—	Dressing loss [9], pH [9,10], color [11]	—
SSC4	<i>SW445-SW58</i>	Diameters, fiber number [1]	Color, hematin, pH [12]	Dressing loss [13], color [7]	<i>MEF2D</i> , <i>PPOX</i>
SSC6	<i>MC1R-S0035</i>	Diameters [4]	—	Color [10]	—
SSC7	<i>S0101-SW764</i>	Percentages, diameters [1]	Color, hematin [14]	Sarcomere length [15]	<i>FOS</i>
SSC8	<i>SW2410-SW905</i>	—	—	Color [15], pH [16]	—
SSC9	<i>SW2093-SW1349</i>	Diameters [1]	—	Color [10], pH, and shear force [11]	<i>MYOG</i>
SSC10	<i>S0038-S0071</i> <i>S0071-SW703</i>	Percentages [1] —	— —	Color [16], tenderness [10] Dressing loss [17]	<i>TPM2</i>
SSC11	<i>S0385-S0071</i>	Percentages, diameters [1]	—	Drip loss, glycogen potential [7]	<i>SGCG</i> , <i>MTMR6</i>
SSC12	<i>S0071-SW703</i> <i>SW1307-SW874</i>	Percentages [1] —	— —	Color, drip loss [18], pH [11] —	— <i>MYH1</i> to 4, <i>MYH8</i> , <i>MYH13</i>
SSC13	<i>S0106-SWR1021</i>	Diameters, fiber number [1]	—	Color [7]	—
SSC14	<i>SW1056-SW769</i>	—	—	Color, pH [19]	—
SSC15	<i>SW1125-SW210</i>	Percentages, diameters [1,4]	—	Color [10], dressing loss [20]	<i>PPP3CC</i> , <i>PPP3CB</i> , <i>NEFAM1</i>
SSCX	<i>SW919-SW1111</i> <i>SW949-SW2126</i>	Percentages, diameters [1] —	— —	Color [4], pH, glycogen potential [7] pH, cooling loss [21]	<i>PRKAG3</i> , <i>MSTN</i> —

¹References: [1] Wimmers et al. (2006); [2] Su et al. (2004); [3] Lee et al. (2003); [4] Nii et al. (2005); [5] Estellé et al. (2005); [6] Meyers et al. (2007); [7] Malek et al. (2001); [8] Milan et al. (1998); [9] Beeckmann et al. (2003); [10] Edwards et al. (2008); [11] de Koning et al. (2001); [12] Mercadé et al. (2005); [13] Cepica et al. (2003b); [14] Ovilo et al. (2002); [15] Rohrer et al. (2006); [16] van Wijk et al. (2006); [17] Dragos-Wendrich et al. (2003a); [18] Kim et al. (2005); [19] Ponsuksili et al. (2005); [20] Dragos-Wendrich et al. (2003b); [21] Cepica et al. (2003a).

²Potential candidate genes are proposed for some of the QTL regions.

a phenomenon widely used in agronomy as a breeding strategy to increase product yield (Lippman and Zamir, 2007). In this sense, it will also be important to study the contribution of epistasis and overdominance to the heterosis commonly found in porcine commercial crossbreeding. Interestingly, our results largely agree with previous muscle fiber QTL scans, particularly that of Wimmers et al. (2006). A literature search showed that color QTL and, to a lesser extent, drip loss QTL often colocalized with the QTL regions detected in this study.

Identification of the causal genetic factors of these QTL would be of great utility to the pork industry. Table 5 lists some of the numerous positional and functional candidate genes that are of interest. Given that Duroc, a widely used breed known for its high meat quality, may have some Iberian origin (Porter, 1993; Jones, 1998), it would be of special interest to determine if some of the epistatic QTL found in the IBCMAP cross can be confirmed in this genetic background (i.e., the Duroc \times Pietrain experiment of Wimmers et al., 2006). Finally, the genetic causes of variation in muscle fiber characteristics are of major interest not only for the meat industry: the relative proportions of the different types of muscular fibers have also been related to a great variety of muscular and metabolic pathologies in humans (Clarke and North, 2003).

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