Detection of quantitative trait loci for growth and fatness in pigs.

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Detection of quantitative trait loci for growth- and fatness-related traits in a large-scale White Duroc × Erhualian intercross pig population

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Summary

Growth and fatness are economically important traits in pigs. In this study, a genome scan was performed to detect quantitative trait loci (QTL) for 14 growth and fatness traits related to body weight, backfat thickness and fat weight in a large-scale White Duroc × Erhualian F_2 intercross. A total of 76 genome-wide significant QTL were mapped to 16 chromosomes. The most significant QTL was found on pig chromosome (SSC) 7 for fatness with unexpectedly small confidence intervals of ~2 cM, providing an excellent starting point to identify causal variants. Common QTL for both fatness and growth traits were found on SSC4, 5, 7 and 8, and shared QTL for fat deposition were detected on SSC1, 2 and X. Time-series analysis of QTL for body weight at six growth stages revealed the continuously significant effects of the QTL on SSC4 at the fattening period and the temporal-specific expression of the QTL on SSC7 at the foetus and fattening stages. For fatness traits, Chinese Erhualian alleles were associated with increased fat deposition except that at the major QTL on SSC7. For growth traits, most of White Duroc alleles enhanced growth rates except for those at three significant QTL on SSC6, 7 and 9. The results confirmed many previously reported QTL and also detected novel QTL, revealing the complexity of the genetic basis of growth and fatness in pigs.

Keywords growth- and fatness-related traits, pig, quantitative trait loci.

Introduction

Growth and fatness traits, as typical complex and economically important traits, are of great interest and have been widely studied in pig genetics. Low growth rate and high fat deposition lead to poor feed efficiency and are not appreciated by producers. Dissection of the genetic architecture of growth and fatness in the pig not only benefits the pig industry but also provides implications for understanding human obesity, because pigs possess greater similarity with humans in nutritional and metabolic physiology compared with other model animals (Miller & Ullrey 1987).

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Many factors contribute to phenotypic variation in growth and fat deposition. Diet composition, age and gender have profound effects on fat deposition and growth rate. Other environmental factors, such as housing systems, lighting regimes and ambient temperature, influence individual maintenance requirements and consequently affect the fat content of livestock animals. Differences in growth and fat deposition among divergent pig breeds indicate the importance of genetic factors. In pigs, the heritability estimates of fatness and growth traits are approximately 0.45 and 0.25 respectively (Hetzer & Harvey 1967; Siers & Thomson 1972).

As the first step to identify the responsible gene(s) underlying growth and fatness, genome scans have been performed to detect quantitative trait loci (QTL) for growth- and fatness-related traits in pigs. The first one was conducted by Andersson *et al.* (1994) using a wild boar × Large White cross. Then, a series of experiments were performed to detect or confirm QTL affecting growth- and fatness-related traits using different or combined pig resource populations, repeatedly identifying major QTL on SSC1, 2, 4, 6, 7 and X

(Marklund *et al.* 1999; Walling *et al.* 2000; Bidanel *et al.* 2001; Quintanilla *et al.* 2002; Liu *et al.* 2007). The significant QTL on SSC2p has been shown to be caused by a single nucleotide substitution in intron 3 of the *IGF2* gene (Van Laere *et al.* 2003). More recently, the effects of several positional candidate genes corresponding to growth and fatness traits, such as *high mobility group AT-hook 1* (*HMGA1*, Kim *et al.* 2006), *leptin receptor* (*LEPR*, Ovilo *et al.* 2005; Munoz *et al.* 2009) and *melanocortin 4 receptor* (*MC4R*, Fan *et al.* 2009b), were investigated. However, a long road still remains to decipher the majority of genetic variants underlying growth and fat deposition in pigs.

Chinese Erhualian pigs are a subpopulation of the Taihu breed that shows divergent performance traits from western commercial breeds. It is characterized by high subcutaneous and intramuscular fat content, appreciated and priced meat quality, high prolificacy and slow growth rate (Zhang *et al.* 1986). The Duroc breed is widely used as a terminal sire line with an excellent growth rate and low carcass fat content. Previously, we have constructed a large-scale White Duroc × Erhualian intercross resource population (Guo *et al.* 2009) and recorded a set of diverse traits including growth and fatness traits. In this paper, we report QTL for growth and fatness traits using a genome scan in the population and show QTL effects on growth at different stages and fat deposition at different body sites.

Materials and methods

Experimental animals and phenotype measurements

A three-generation F_2 population was established by crossing Chinese Erhualian and White Duroc pigs as described previously (Guo *et al.* 2009). Briefly, two White Duroc boars were mated to 17 Erhualian sows. Nine F_1 boars and 59 F_1 sows were then mated to produce a total of 1912 F_2 animals in six batches. All piglets were weaned at 46 days of age, and the males were castrated at 90 days of age (d). The fattening pigs were then housed at a consistent indoor condition at the experimental farm of Jiangxi Agricultural University or the testing station of Jiangxi Province. After the fattening period, a total of 1037 F_2 animals at 240 ± 3 d were slaughtered in a commercial slaughter facility following Chinese industry standards. From this intercross population, a total of six growth- and eight fatness-related traits were recorded, including body weight at birth (BW0) and at days 21 (BW21), 46 (BW46), 120 (BW120), 210 (BW210), 240 (BW240); average backfat thickness (ABFT) and backfat thickness at four different sites including at the shoulder (SBFT), the first rib (FRBFT), the last rib (LRBFT) and the hip (HBFT); and weight of leaf fat (LFW), veil fat (VFW) and abdominal fat (AFW).

Genotyping and map construction

Genomic DNA was extracted from pig tail or spleen tissues. A set of 194 informative microsatellite markers covering the pig genome were genotyped across the entire White Duroc × Erhualian resource population as described previously (Guo *et al.* 2009). A comprehensive linkage map was constructed with CRIMAP version 2.4 as described in Guo *et al.* (2009). The number of markers on each chromosome ranged from five on SSC 16 to 24 on SSC13 with a total length of 2344.9 cM and an average interval of 13.40 cM. The information content of each marker was >0.5.

Statistical analyses

Descriptive statistics of growth- and fatness-related traits in the F_2 population were analysed by SAS version 9.0 (SAS Institute Inc.). Phenotypic values were tested for approximate Gaussian distribution. The PROC GLM procedure of SAS version 9.0 was used to determine the fixed effects and covariates in the following QTL model. Biologically correlated traits that showed significant effects on a given trait were treated as covariates in the QTL model for the trait. In this study, sex and batch were considered the fixed effects with covariates of carcass weight for fatness traits and birth weight for body weight at different growth stages. A QTL interval mapping analysis was performed with QTL EXPRESS (accessible at http://www.gridqtl.org.uk/) based on a least-squares method. This analysis assumed that the founder breeds were fixed for alternative alleles at a QTL, and two alleles at a putative QTL at a given location were denoted by Q and q. Probabilities of QTL genotypes, denoted by Prob(QQ), Prob(Qq), Prob(qQ) and Prob(qq), were computed from the observed genotypes of markers linked to the QTL. The QTL analysis was fitted at 1-cM intervals along each chromosome, and the *F* value for the QTL effect was calculated at each point. A genome scan was performed in a forward and backward selection interval mapping manner as described in Guo *et al.* (2008). Briefly, after the first-round scan, the most significant QTL was considered to be the first QTL and was included in the model as a genetic background effect for the second-round scan. The first and second QTL were then used as genetic background effects to search the third QTL. Sequentially, all detected QTL were included in the model for the next-round search until 5% chromosome-wide significant QTL was not detected any more. The position of each detected QTL was then re-estimated using the remaining QTL as genetic background. If the position of one QTL changed, the new parameters of this QTL were used as a genetic background effect to re-estimate the positions of the remaining QTL. This iteration was continued until the positions of all QTL remained unchanged. After that,

the effects of all QTL were finally determined. Genome-wide significance thresholds were empirically calculated with 1000 repetitions of the permutation test (Doerge & Churchill 1996). Suggestive QTL are defined as the 5% chromosome-wide significant QTL, and the threshold was determined in the permutation test, as described by de Koning *et al.* (2001), as: $P_{\text{Genome–wide}} = 1 - (1 - P_{\text{Chromosome–wide}})^{1/r}$, where r is the proportion of total genome length attributed to the chromosome. The 95% confidence intervals for the location of the QTL were obtained by a bootstrap method with 2000 iterations (Visscher *et al.* 1996). Percentage of variance explained by each QTL was calculated using the following formula:

$$\text{Var}\% = (\text{MS}_{\text{reduce1}} - \text{MS}_{\text{full}})/\text{MS}_{\text{reduce}} \times 100$$

where MS_{full}, $\text{MS}_{\text{reduce1}}$ and $\text{MS}_{\text{reduce}}$ were the mean squares of the models with all the detected QTL, with all the detected QTL except for the current focused one and without all of the detected QTL respectively.

When analysing the sex chromosome, we calculated QTL genotype probabilities using QXPAK 5 (Pérez-Enciso & Misztal 2004). The pseudoautosomal region is assumed to be flanked by markers *SW949* and *SW980* (~25 cM). The QTL genotype probabilities in this region were calculated in the same way as those on the autosomes. We denoted the QTL genotypes in the sex-specific region of White Duroc sires and Erhualian dams as QY and qq respectively, where Y indicates chromosome Y. The possible QTL genotypes were QY and qY for F_2 males and QQ and Qq for F_2 females. Thus, effects corresponding to the difference between the two possible genotypes of QTL (male, QY-qY; female, QQ-Qq), instead of additive and dominance effects, were used for the analyses of the sex-specific region on the sex chromosome. The genome-wide threshold of the X chromosome was determined in the same way as the autosomal chromosome scans.

Results and discussion

Descriptive statistics of phenotypic data

The descriptive statistics of growth- and fatness-related traits are summarized in Table 1. Phenotypic correlation coefficients among the tested traits are presented in Table S1. Backfat thickness at different measured sites showed a high correlation with a range of 0.75–0.95 ($P < 0.0001$), and the correlation coefficients among abdominal, veil and LFW varied from 0.67 to 0.77 ($P < 0.0001$). Between backfat thickness and fat weight, the correlation coefficients ranged from 0.60 to 0.83 ($P < 0.0001$). Among body weight at six different growth stages, the correlation coefficient between BW0 and BW240 was lowest ($r = 0.24$), while that between BW210 and BW240 was up to 0.92.

General description of the detected QTL

In total, 76 genome-wide significant QTL were mapped to 16 chromosomes for the tested growth- and fatness-related traits, including 63 at the 1% genome-wide significance level and 13 at the 5% genome-wide significance level. Details of the genome-wide significant QTL for growth and fatness are presented in Table 2, and suggestive QTL are given in Table S2. The *F*-statistic curves indicating significant and multifaceted-effect QTL on SSC1, 2, 4, 5, 7, 8 and X are depicted in Fig. S1.

For fatness-related traits, all Chinese Erhualian alleles were associated with increased fat weight or backfat thickness except for that at the prominent QTL on SSC7. The largest effects were observed around 57 cM on SSC7, accounting for 7.49–38.01% of the phenotypic variance in fat deposition, followed by the significant QTL on SSC4 explaining 1.55–9.00% of phenotypic variance. A majority

Table 1 Descriptive statistics of growth- and fatness-related traits in the White Duroc × Erhualian intercross.

Trait	Symbol	No.	Mean	SD	Min.	Max.
Growth						
Birth weight, kg	BW0	1894	1.18	0.26	0.35	2.05
Body weight at 21 day, kg	BW21	1757	5.23	1.28	1.25	9.40
Body weight at 46 day, kg	BW46	1713	11.22	2.70	2.70	20.10
Body weight at 120 day, kg	BW120	611	30.71	6.90	8.50	53.50
Body weight at 210 day, kg	BW210	1174	78.39	16.75	33.50	132.00
Body weight at 240 day, kg	BW240	1319	94.91	17.88	26.60	146.20
Fatness						
Backfat thickness at the shoulder, cm	SBFT	1037	3.93	0.95	1.34	7.30
Backfat thickness at the first rib, cm	FRBFT	1037	3.13	0.96	0.14	6.85
Backfat thickness at the last rib, cm	LRBFT	1037	2.34	0.86	0.21	6.93
Backfat thickness at the hip, cm	HBFT	1037	2.55	1.02	0.24	7.01
Average backfat thickness, cm	ABFT	1037	2.99	0.88	0.48	6.51
Leaf fat weight, kg	LFW	1033	2.08	1.10	0.70	6.06
Veil fat weight, kg	VFW	1035	1.30	0.44	0.22	3.35
Abdominal fat weight, kg	AFW	1035	1.23	0.43	0.11	2.74

Table 2 Details of genome-wide significant quantitative trait loci (QTL) for growth- and fatness-related traits in the White Duroc × Erhualian intercross.

Chr	Position (cM)	Trait	*F*-value[1]	Origin[2]	ADD ± SE[3]	Dom ± SE[4]	CI_{95} (cM)[5]	Var.[6]
1	146	ABFT	19.26**	ER	−0.14 ± 0.02	−0.02 ± 0.04	133.5–153.5	1.56
	150	FRBFT	16.46**	ER	−0.15 ± 0.03	−0.07 ± 0.04	139.0–157.0	1.44
	135	HBFT	11.04**	ER	−0.14 ± 0.03	0.03 ± 0.05	53.0–151.0	1.00
	146	LFW	10.62**	ER	−0.13 ± 0.03	−0.01 ± 0.04	53.5–153.5	1.06
	146	LRBFT	11.86**	ER	−0.13 ± 0.03	0.02 ± 0.04	9.5–157.0	1.32
	147	SBFT	9.46*	ER	−0.12 ± 0.03	−0.03 ± 0.05	4.5–159.0	1.21
	145	VFW	13.43**	ER	−0.07 ± 0.01	0.02 ± 0.02	135.5–156.0	1.92
2	85	ABFT	11.55**	ER	−0.08 ± 0.02	0.13 ± 0.04	72.0–93.0	0.94
	20	ABFT	10.43*	ER	−0.10 ± 0.02	0.05 ± 0.04	0.0–98.5	0.85
	88	AFW	12.66**	ER	−0.05 ± 0.01	0.02 ± 0.02	2.0–93.0	1.48
	19	AFW	11.66**	ER	−0.05 ± 0.01	0.02 ± 0.02	0.0–103.0	1.68
	82	FRBFT	16.71**	ER	−0.14 ± 0.03	0.13 ± 0.04	66.0–88.0	1.46
	24	FRBFT	11.85**	ER	−0.13 ± 0.03	0.01 ± 0.04	0.0–59.0	1.03
	16	HBFT	13.64**	ER	−0.15 ± 0.03	0.08 ± 0.05	0.0–27.0	1.23
	88	LFW	14.06**	ER	−0.14 ± 0.03	0.08 ± 0.04	70.0–124.0	1.40
	79	SBFT	21.42**	ER	−0.17 ± 0.03	0.08 ± 0.04	32.0–84.0	2.75
3	79	BW240	23.25**	D	4.46 ± 0.70	2.40 ± 1.09	43.0–86.0	3.56
	119	VFW	16.8**	ER	−0.08 ± 0.01	0.01 ± 0.02	90.0–129.0	2.40
4	74	ABFT	76.78**	ER	−0.28 ± 0.02	−0.02 ± 0.04	71.0–77.0	6.23
	71	AFW	56.25**	ER	−0.10 ± 0.01	−0.02 ± 0.01	64.0–75.0	7.05
	60	BW120	10.98**	D	1.71 ± 0.37	−0.46 ± 0.58	53.0–105.0	3.41
	65	BW210	22.5**	D	4.02 ± 0.60	−0.43 ± 0.89	56.0–72.0	3.12
	65	BW240	38.82**	D	5.39 ± 0.67	−1.32 ± 0.91	59.0–75.0	5.94
	52	BW46	9.96*	D	0.32 ± 0.09	0.30 ± 0.13	39.0–130.0	1.11
	75	FRBFT	64.26**	ER	−0.31 ± 0.03	0.04 ± 0.01	72.0–78.0	5.60
	73	HBFT	75.03**	ER	−0.38 ± 0.03	0.01 ± 0.05	70.0–76.0	6.79
	74	LFW	90.23**	ER	−0.36 ± 0.03	−0.12 ± 0.04	71.0–77.0	9.00
	72	LRBFT	46.93**	ER	−0.25 ± 0.03	−0.07 ± 0.04	67.0–77.0	5.22
	74	SBFT	27.61**	ER	−0.22 ± 0.03	−0.02 ± 0.04	60.0–79.0	3.54
	63	VFW	10.86**	ER	−0.05 ± 0.01	−0.05 ± 0.02	13.0–84.5	1.55
5	59	ABFT	25.11**	ER	−0.15 ± 0.02	−0.04 ± 0.04	53.0–73.0	2.04
	105	BW240	17.88**	D	3.45 ± 0.60	1.43 ± 0.88	78.0–109.0	2.74
	58	FRBFT	13.13**	ER	−0.12 ± 0.03	−0.08 ± 0.04	26.0–110.5	1.15
	54	HBFT	17.49**	ER	−0.18 ± 0.03	−0.07 ± 0.05	36.0–110.0	1.58
	60	LRBFT	35.98**	ER	−0.21 ± 0.03	−0.08 ± 0.04	55.0–71.0	4.00
	56	SBFT	10.92**	ER	−0.13 ± 0.03	−0.04 ± 0.05	35.0–114.0	1.40
6	84	BW46	10.28*	ER	−0.29 ± 0.08	0.33 ± 0.12	21.0–127.0	1.15
7	58	ABFT	442.58**	D	0.65 ± 0.02	−0.23 ± 0.03	57.0–59.0	35.92
	57	AFW	151.97**	D	0.16 ± 0.01	−0.04 ± 0.01	55.0–58.0	19.05
	57	BW0	14.2**	ER	−0.04 ± 0.01	0.03 ± 0.01	53.0–94.0	1.59
	52	BW210	29.52**	ER	−3.89 ± 0.61	3.40 ± 0.86	50.0–59.0	4.10
	58	BW240	28.25**	ER	−4.49 ± 0.75	4.30 ± 0.92	51.0–59.0	4.32
	58	FRBFT	435.78**	D	0.76 ± 0.03	−0.26 ± 0.04	57.0–59.0	38.01
	57	HBFT	386.58**	D	0.79 ± 0.03	−0.29 ± 0.04	57.0–58.0	34.96
	58	LFW	317.93**	D	0.62 ± 0.03	−0.21 ± 0.04	58.0–60.0	31.72
	58	LRBFT	262.58**	D	0.54 ± 0.03	−0.21 ± 0.04	57.0–59.0	29.19
	59	SBFT	168.66**	D	0.47 ± 0.03	−0.13 ± 0.04	56.0–60.0	21.62
	58	VFW	52.44**	D	0.13 ± 0.01	−0.03 ± 0.02	54.0–60.0	7.49
8	93	AFW	9.27*	ER	−0.04 ± 0.01	−0.00 ± 0.01	28.5–125.5	1.16
	53	BW210	8.91*	D	2.54 ± 0.61	0.30 ± 0.87	5.0–90.0	1.24
	42	BW240	11.51**	D	3.03 ± 0.63	−0.13 ± 0.94	12.0–86.0	1.76
	51	HBFT	11.26**	ER	−0.13 ± 0.03	−0.05 ± 0.04	16.0–94.5	1.02
	54	LFW	35.56**	ER	−0.21 ± 0.03	−0.07 ± 0.04	36.5–75.5	3.55
	40	VFW	22.7**	ER	−0.09 ± 0.01	−0.01 ± 0.02	23.0–81.0	3.24

Table 2 Continued.

Chr	Position (cM)	Trait	*F*-value[1]	Origin[2]	ADD ± SE[3]	Dom ± SE[4]	CI_{95} (cM)[5]	Var.[6]
9	111	ABFT	9.88*	ER	−0.10 ± 0.02	−0.02 ± 0.04	52.0–135.0	0.80
	92	AFW	10.75**	ER	−0.04 ± 0.01	0.00 ± 0.01	70.4–126.5	1.35
	75	BW21	8.83*	ER	−0.12 ± 0.04	−0.17 ± 0.06	68.0–128.0	1.01
	110	FRBFT	14.26**	ER	−0.15 ± 0.03	−0.01 ± 0.05	51.5–133.0	1.24
	93	LFW	8.58*	ER	−0.11 ± 0.03	0.01 ± 0.04	16.0–114.5	0.86
10	93	BW46	11.17**	D	0.34 ± 0.08	0.31 ± 0.13	73.0–103.0	1.25
12	82	LFW	9.68*	ER	−0.12 ± 0.03	0.01 ± 0.05	18.0–86.0	0.97
13	62	VFW	18.09**	ER	−0.08 ± 0.01	0.01 ± 0.02	35.5–86.0	2.58
14	5	AFW	10.32**	ER	−0.04 ± 0.01	−0.04 ± 0.02	0.0–54.5	1.29
	10	LFW	12.2**	ER	−0.11 ± 0.03	−0.15 ± 0.05	0.0–44.5	1.22
	29	VFW	10.91**	ER	−0.06 ± 0.01	−0.05 ± 0.02	6.0–66.0	1.56
15	87	AFW	8.8*	ER	−0.04 ± 0.01	−0.03 ± 0.02	67.0–111.0	1.10
	73	SBFT	24.22**	ER	−0.20 ± 0.03	−0.08 ± 0.05	57.0–80.5	3.10
	80	VFW	9.45*	ER	−0.05 ± 0.01	−0.04 ± 0.02	21.0–92.0	1.35
18	17	AFW	14.94**	ER	−0.06 ± 0.01	0.03 ± 0.02	2.0–43.0	1.87
	18	BW0	9.71*	D	0.04 ± 0.01	0.04 ± 0.02	9.0–45.0	1.09
X	56	ABFT	62.09**	ER	−0.43 ± 0.04	−0.18 ± 0.04	57.0–58.0	5.71
	56	FRBFT	34.39**	ER	−0.38 ± 0.05	−0.13 ± 0.05	56.0–61.0	3.14
	56	HBFT	78.23**	ER	−0.66 ± 0.05	−0.31 ± 0.06	57.0–58.0	8.23
	57	LRBFT	33.23**	ER	−0.36 ± 0.05	−0.17 ± 0.05	57.0–61.0	3.78
	56	SBFT	22.78**	ER	−0.33 ± 0.05	−0.08 ± 0.05	53.0–59.0	2.91
	56	VFW	31.27**	ER	−0.17 ± 0.02	−0.09 ± 0.02	52.0–58.0	4.63

[1]Significant level: *, 5% genome-wide significant; **, 1% genome-wide significant.
[2]Origin of allele increasing phenotypic values with respect to the founder breeds.
[3]Additive effects of QTL and their standard error. For chromosome X, values indicate additive effects of QTL and their standard error in males.
[4]Dominant effects of QTL and their standard error. For chromosome X, values indicate additive effects of QTL and their standard error in females.
[5]95% confidence interval.
[6]Percentage of the phenotypic variance explained by the QTL.

of White Duroc alleles were favourable for faster growth except for those at the QTL on SSC6, 7 and 9. Like the QTL for fatness, the effect of QTL on SSC4 and 7 was much stronger on growth than that at the other QTL. The proportions of phenotypic variance explained by the QTL on SSC7 were from 1.59% (BW0) to 4.32% (BW240), and the QTL on SSC4 explained 1.11% (BW46) to 5.94% (BW240) of phenotypic variance in growth traits.

Several significant QTL, including those on SSC4, 5, 7 and 8, showed pleiotropic effects on both growth traits and fat deposition, indicating the existence of common variants for these traits in these regions. However, we could not exclude the possibility that closely linked but distinct variants cause the QTL effect. We also observed common QTL for all fatness traits, such as the significant QTL on SSCX, and QTL specifically affecting one fatness trait, such as the 1% genome-wide significant QTL for VFW on SSC13. These results revealed the complexity of the genetic basis of growth and fatness traits.

QTL for growth-related traits

To date, 593 QTL for growth traits have been deposited in the pigQTL database (http://www.genome.iastate.edu/cgi-bin/QTLdb/SS/index), including 39 QTL for body weight at birth. In this study, one 1% genome-wide significant QTL for BW0 was mapped to SSC7, and a 5% genome-wide significant QTL was mapped to SSC18. Erhualian alleles were associated with increased body weight on SSC7 and decreased body weight on SSC18. For BW21, a 5% genome-wide significant QTL and a suggestive QTL were detected on SSC9 and 8 respectively. Erhualian alleles were associated with faster growth rates than were White Duroc alleles in both regions. The QTL on SSC9 is different from the previously reported suggestive QTL for weaned body weight and average daily gain from birth to weaning day (Malek *et al.* 2001; Liu *et al.* 2007). A 1% genome-wide significant and two 5% genome-wide significant QTL for BW46 were identified on SSC10, 4 and 6 respectively, and four suggestive QTL for this trait were observed on SSC3, 7, 8 and 13. For BW120, one 1% genome-wide significant QTL and two suggestive QTL were mapped to SSC4, 3 and 16 respectively. Bidanel *et al.* (2001) and Quintanilla *et al.* (2002) detected QTL for body weight at 17 weeks on SSC3 and 4, and Edwards *et al.* (2008) reported a suggestive QTL for body weight at 19 weeks on SSC16. These QTL overlapped with the corresponding QTL in this study. Three significant QTL for BW210 were detected on SSC4, 7 and 8 respectively. It should be mentioned that, in the

present genome scan, QTL for body weight at day 240 were reported for the first time. Five 1% genome-wide significant QTL for BW240 were detected on SSC3, 4, 5, 7 and 8, and those on SSC4, 7 and 8 overlapped with QTL for BW210. Compared with the 38 QTL for body weight at slaughter (~110 kg) in the pig QTL database (http://www.genome.iastate.edu/cgi-bin/QTLdb/SS/index), the major QTL on SSC4 and 7 were consistently evidenced, and the QTL for BW240 on SSC3 and 8 overlapped with those reported by Rohrer *et al.* (2006) and Beeckmann *et al.* (2003a).

Time-series analysis of QTL for body weight from day 0 to 240 revealed that significant QTL on SSC4 and 7 were consistently detected at multiple stages. The locus on SSC4 showed increasing effects on body weight at 46, 120, 210 and 240 days, indicating that the major QTL influenced body weight during the fattening period. The significant QTL on SSC7 showed discontinuous effects on body weight at different stages. Strong association of the locus with body weight at days 0, 210 and 240 was observed. Nevertheless, no QTL was detected for body weight at day 21, and only a suggestive QTL was evidenced for body weight at day 46. The results indicated the temporal-specific expression of the QTL on SSC7 on the individual development at the foetus and fattening stages but not at the suckling period.

QTL for fat deposition

Common QTL on SSC1, 2, 4, 5, 7, 8 and X were found for backfat thickness at all measured sites; these QTL were also shared for abdominal, veil and/or LFW. Additional significant QTL for one or more fatness-related traits were evidenced on SSC3, 9, 12, 13, 15 and 18. Of the QTL for fatness traits, the effect of QTL on SSC7 was strongest with unexpectedly small confidence intervals of ~2 cM, providing an excellent starting point to identify causal variants underlying the major QTL. This chromosomal region has been consistently characterized as QTL for fat deposition and growth in different crosses between Chinese Meishan and commercial breeds (Rohrer & Keele 1998; de Koning *et al.* 1999; Wada *et al.* 2000; Walling *et al.* 2000; Bidanel *et al.* 2001). Interestingly, both Chinese Meishan and Erhualian alleles are associated with decreased fat deposition and enhanced growth rate, in contrast to their breed characteristics. The reasons for this discrepancy could be that the allele for leanness is of Chinese origin and remains segregated in Chinese pigs that have not undergone strong selection. Alternatively, the allele has strong pleiotropic effects, presumably on fitness traits, and thus has been favourably selected in Chinese pigs. Within the QTL region, *HMGA1* and *peroxisome proliferator-activated receptor-δ* (*PPARD*) are two interesting positional candidate genes. Kim *et al.* (2006) reported that *HMGA1* was significantly associated with fat deposition and growth traits. *PPARD* is involved in regulating fatty acid oxidation and utilization and serves as a potential target in the treatment of obesity and its associated disorders (Wang *et al.* 2003).

A 1% genome-wide significant QTL for all fatness traits and growth was detected at 71 cM on SSC4. This region has been known as FAT1 and, in the first genome scan for pig QTL (Andersson *et al.* 1994; Marklund *et al.* 1999), initially showed evidence for fat deposition and growth. The FAT1 region has been confirmed in different pig resource populations (Knott *et al.* 1998; Pérez-Enciso *et al.* 2000; Bidanel *et al.* 2001; Mercade *et al.* 2005; Liu *et al.* 2007). The region has been refined to a region of 3.3 cM that harbours about 20 genes including a cluster of *FABP* genes (Berg *et al.* 2006). However, the causative gene(s) and mutations underlying *FAT1* remain unknown. One of the reasons could be that at least two distinct QTL segregate in the *FAT1* region, complicating the search for causal mutations (Mercade *et al.* 2005; Berg *et al.* 2006).

On the distal tip of the p arm of SSC2 is a well-characterized imprinting QTL for muscle growth and fatness traits (de Koning *et al.* 1999), and a regulatory mutation in the *IGF2* gene has been explicitly identified as the causative mutation explaining the imprinting QTL (Van Laere *et al.* 2003). In this study, a prominent QTL for fat deposition was evidenced at 19 cM on SSC2 without significant effects on growth traits. The different location and fat-specific effect of the QTL indicate that *IGF2* might not be the candidate of the QTL. On this chromosome, we detected another significant QTL at the different position of 88 cM. Similarly, Jungerius *et al.* (2004) reported a minor QTL for growth and fatness traits around 40 cM on this chromosome.

On SSC1, two major QTL affecting fatness traits have been previously detected. One was located at ~79 cM flanked by markers *S0313* and *SW745* (Malek *et al.* 2001; Beeckmann *et al.* 2003b; Hernández-Sánchez *et al.* 2003; Grapes & Rothschild 2006; Liu *et al.* 2007); the other was detected on the distal tip of the q arm of this chromosome proximal to marker *SW1301* (Rohrer & Keele 1998; Rohrer 2000; Bidanel *et al.* 2001; Geldermann *et al.* 2003). The QTL at ~79 cM harbours the *MC4R* gene that has a well-established role in fatness and obesity in humans (Loos *et al.* 2008) and has significant association with fat deposition traits in western commercial pig breeds (Kim *et al.* 2000, 2006; Houston *et al.* 2004; Bruun *et al.* 2006; Fan *et al.* 2009b). However, studies on a Large White × Wild Boar cross did not reveal any significant effects of *MC4R* variants on fat deposition (Park *et al.* 2002), and Stachowiak *et al.* (2006) doubted effects of the *MC4R* variants in Polish Landrace and Large White breeds. In the present study, we detected the significant QTL for all fatness-related traits peaking at ~146 cM rather than 79 cM, which are consistent with the QTL for shoulder external fat weight in a Meishan × Pietrain family and a wild boar × Meishan family studied by Geldermann *et al.* (2003). This excluded the *MC4R* gene as a candidate for the QTL.

In this study, a major QTL affecting fatness deposition was found on the X chromosome flanked by markers *SW2456* and *SW1943* and has been detected in the same region using several Meishan × Western breed pedigrees

(Rohrer 2000; Bidanel *et al.* 2001; Milan *et al.* 2002; Sato *et al.* 2003). However, the QTL region between *SW2456* and *SW1943* contained a large recombination coldspot of ~31 Mb (Ma *et al.* 2010). Low recombination rates might cause multiple independent genetic factors contributing to a trait to resemble a single QTL of large effect. Meanwhile, lack of recombination in such a large region makes it impossible to narrow the QTL interval using traditional fine-mapping approaches.

In humans, common variants for body mass index and obesity, such as the *fat mass- and obesity-associated* (*FTO*) gene variants, have been recently identified by genome-wide association analysis (Frayling *et al.* 2007) and confirmed by a battery of genetic and functional assays (Church *et al.* 2010). Recent studies showed that the *FTO* gene was associated with fat deposition in Italian Duroc pigs (Fontanesi *et al.* 2009, 2010) and intramuscular fat content and growth rate in a Berkshire × Yorkshire pig resource population (Fan *et al.* 2009a). The genomic location of the *FTO* gene is close to *S0067* at 83.9 cM on SSC6, which was evidenced as a significant QTL for BW46. However, no significant effect was found on fatness traits in the QTL region. Previously, a significant QTL for fatness and meat quality was detected in the *S0228–SW1881* interval on SSC6 in several mapping populations (Ovilo *et al.* 2005; Edwards *et al.* 2008), and the *LEPR* gene has been proposed as a candidate for the QTL (Ovilo *et al.* 2005; Munoz *et al.* 2009). However, *LEPR* is located in a region (~140 cM) that does not contain any significant QTL for fatness, indicating that *LEPR* variants did not contribute to phenotypic variance in fatness traits measured in the current resource population.

In conclusion, we detected a total of 76 significant QTL for growth and fatness traits in the White Duroc × Erhualian intercross. The results confirmed many previously reported QTL for growth and fat deposition and revealed several novel regions significantly associated with growth and fatness traits in the pig genome. The results shed new light on the genetic basis of growth and fatness traits in the pig. Future work will be directed toward fine mapping of the major QTL, such as those on SSC4 and 7, and ultimately identification of causal genes.

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Supporting information

Additional supporting information may be found in the online version of this article.

Figure S1 *F*-ration curves of the QTL on pig chromosomes 1, 2, 4, 7, 8 and X showing multiple associations with growth- and (or) fatness-related traits in the White Duroc × Erhualian.

Table S1 Phenotypic correlation coefficients among growth- and fatness-related traits in the White Duroc × Erhualian intercross[a].

Table S2 Details of suggestive QTL for growth- and fatness-related traits in the White Duroc × Erhualian intercross.

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