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Mapping QTL for growth and muscling traits in three connected porcine F_2 crosses

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Abstract

QTL experiments in pigs are often analysed separately, although similar or same founder breeds are frequently used to establish the experimental design. The aim of the present study was to jointly analyse three porcine F_2-crosses for six growth and four muscling traits. The crosses were a Meishan × Pietrain cross, a Wild Boar × Pietrain cross, and a Wild Boar × Meishan cross. In some cases, same founder animals were used to establish the crosses. 966 F_2-individuals were genotyped for 242 genetic markers (mostly microsatellites) and phenotyped for birth weight, 21 and 35 day weight, slaughter weight, carcass length, food conversion ratio, ham meat weight, shoulder meat weight, loin and neck meat weight, and meat area. A multi-allele multi-QTL model was applied that estimated an additive QTL effect for each founder breed and parental origin (either paternally or maternally derived), and a dominant QTL effect for each cross. This model was previously introduced in plant breeding. Numerous QTL were mapped on the autosomes. Most QTL were localised on SSC1, 2, 3, 4, 6 and 8, and no QTL were on SSC9, 11, 13, 15, 17 and 18. The confidence intervals were short in many cases. QTL with an exceptionally high test statistic were found for carcass length on SSC1, 4, 7 and 17. The coefficient of variation was remarkably small for this trait, which suggests that carcass length is affected by only a few genes with large effects. Positional and functional candidates underlying promising QTL are suggested for further study.

Keywords: joint analysis, QTL, growth and muscling traits

Introduction

QTL mapping has received considerable attention in animal breeding over the last two decades. Experimental designs can be classified into two groups: those using existing family structure, e.g. half-sib families, or those based on experimental crosses. For mapping QTL on the pig genome, F_2-experimental crosses were often established from two founder breeds (Andersson *et al.* 1994, Rothschild *et al.* 2007). Although numerous F_2-designs with same founder breeds exist, they were usually analysed separately, probably because they were established by different research groups. However, it has frequently been shown that a combined analysis of QTL experiments boosts the statistical power substantially (Walling *et al.* 2000, Bennewitz *et al.* 2003). The three F_2-designs established by Geldermann *et al.* (2003) are especially well suited for a joint analysis, because not only same founder breeds, but also same founder animals were used to set up the designs.

Rückert & Bennewitz (2010) proposed a model adapted from plant breeding for analysis of connected F_2-experiments and showed the benefit of a joint analysis of these three designs. It was shown that the model not only increased the statistical power in a joint analysis, but also the confidence intervals of QTL positions were remarkably small given that only linkage information was used. This model was successfully applied to map QTL for metabolic and cytological fat traits by Rückert *et al.* (2012). Stratz *et al.* (2012) mapped QTL for meat quality traits considering main and pairwise epistatic effects. The aim of the present study was to map QTL for growth and muscling traits in the three F_2-designs from Geldermann *et al.* (2003) using the approach of Rückert & Bennewitz (2010).

Material and methods

The experimental design consisted of a Meishan (M) × Pietrain (P) F_2 cross (M × P), a European Wild Boar (W) × P F_2 cross (W × P), and a W × M F_2 cross. The number of individuals in each cross and generation can be found in Table 1. Some founder animals were the same in different crosses, e.g. the same W boar was used to generate the W × P and the W × M cross. A detailed description of the design can be found in Geldermann *et al.* (2003). The F_2-individuals were phenotyped for numerous traits. In this study, growth traits (birth weight, 21 day weight, 35 day weight, live weight at slaughter, food conversion ratio, and carcass length) and muscling traits (ham meat weight, shoulder meat weight, loin and neck meat weight and meat area between the 13 th/14 th rib in the *m. longissimus dorsi*) were analysed, see Table 2.

Table 1
Overview of the three crosses generated by mating Meishan (M) with Pietrain (P), Wild Boar (W) with P and W with M

Cross	M × P		W × P		W × M		Σ
Sex	♂	♀	♂	♀	♂	♀	
No. of founder animals	1	8	1	9	1	4	24
No. of animal in the F_1	3	19	2	26	2	21	73
No. of animal in the F_2	170	146	150	165	169	166	966

Table 2
Traits and the abbreviations used in this paper

Group	Trait	Abbr.	Symbols used in Figure 1
Growth	Birthweight	BW	▽
	21 day weight	W21	△
	35 day weight	W35	+
	Live weight at slaughter	SW	○
	Food conversion ratio	FCR	×
	Carcass length	CL	□
Muscling	Ham meat weight	HMW	◇
	Sholder meat weight	SMW	■
	Loin and neck meat weight	LNMW	●
	Meat area between 13th/14th rib in *m. longissimus dorsi*	MA	▲

Data recording took place under standardised conditions at one experimental farm. The means and standard deviations of the traits in the crosses are shown in Table 3. The data were pre-corrected for the effect of the litter, the sex and age at slaughter.

All animals were genotyped for 242 genetic markers. These marker data were linked to the pedigree and a common genetic map was calculated and presented by Rückert & Bennewitz (2010). Because many markers were genotyped in two or three crosses this calculation was straightforward. QTL analysis was done using the multi-allele multi-QTL model of Rückert & Bennewitz (2010). The model assumes that two founder breeds *i* and *j* of an F_2 individual are divergent homozygous at a putative QTL. Under this assumption, for each F_2 individual and each chromosomal position (i.e. each cM) the following four genotype probabilities were estimated, $pr(Q_i^p Q_i^m)$, $pr(Q_j^p Q_i^m)$ $pr(Q_i^p Q_j^m)$ and $pr(Q_j^p Q_j^m)$, using a modified version of BigMap (Reinsch 1999).

Table 3
Number of observations (n), mean, standard deviation (SD), minimum (Min) and maximum (Max) of the phenotypic observations and coefficient of variation (CV)

Trait	Cross	n	Mean	SD	Min	Max	CV
BW	M×P	316	14.01	3.15	5.00	23.00	22.49
[kg*10]	W×P	315	14.06	2.99	5.00	26.00	21.30
	W×M	335	12.60	2.04	7.00	20.00	16.19
	Joint	966	13.54	2.84	5.00	26.00	20.97
W21	M×P	303	60.22	11.02	16.00	90.00	18.30
[kg*10]	W×P	315	45.49	12.01	14.00	81.00	26.40
	W×M	334	46.64	11.12	17.00	80.00	23.84
	Joint	952	50.58	13.16	14.00	90.00	26.02
W35	M×P	316	88.60	15.66	39.00	135.00	17.67
[kg*10]	W×P	315	68.67	16.29	28.00	116.00	23.72
	W×M	329	64.95	17.97	21.00	115.00	27.66
	Joint	960	73.96	19.63	21.00	135.00	26.55
SW	M×P	316	96.07	16.84	27.00	139.00	17.53
[kg]	W×P	314	72.37	14.62	28.00	108.00	20.20
	W×M	335	71.16	13.79	23.00	107.00	19.38
	Joint	965	79.71	18.94	23.00	139.00	23.76
CL	M×P	316	91.33	6.08	63.50	106.00	6.66
[cm]	W×P	315	79.89	5.19	62.50	94.00	6.50
	W×M	335	78.21	5.40	56.00	92.50	6.90
	Joint	966	83.05	8.05	56.00	106.00	9.69
FCR	M×P	316	3.88	0.88	2.60	11.46	22.59
[kg/kg]	W×P	315	3.42	0.50	2.54	8.83	14.66
	W×M	335	4.32	0.68	2.81	7.03	15.64
	Joint	966	3.88	0.79	2.54	11.46	20.38
HMW	M×P	316	7.09	1.26	2.00	11.20	17.78
[kg]	W×P	315	6.58	1.33	2.60	10.70	20.25
	W×M	335	4.44	0.76	1.55	6.35	17.08
	Joint	966	6.00	1.62	1.55	11.20	27.02
SMW	M×P	316	3.64	0.63	1.15	5.65	17.25
[kg]	W×P	315	3.27	0.67	1.30	5.35	20.51
	W×M	335	2.41	0.45	1.00	3.90	18.53
	Joint	966	3.09	0.78	1.00	5.65	25.34
LNMW	M×P	316	6.48	1.17	1.70	10.10	18.11
[kg]	W×P	315	5.55	1.26	1.95	10.05	22.65
	W×M	335	3.82	0.70	1.30	6.05	18.32
	Joint	966	5.25	1.54	1.30	10.10	29.28
MA	M×P	316	29.29	5.35	14.56	49.31	18.26
[cm*cm]	W×P	313	32.71	6.40	12.93	50.05	19.57
	W×M	335	19.42	3.13	7.73	31.81	16.13
	Joint	964	26.97	7.64	7.73	50.05	28.32

The upper subscripts denote the parental origin of the alleles (i.e. paternally (*p*) or maternally (*m*) derived) and the lower subscripts denote the breed origin of the alleles (i.e. breed *i* or *j*, with *i, j* being breed M, P, or W). These probabilities were used in a regression framework to estimate an additive QTL effect for each founder breed and each parental origin, i.e. $\hat{a}^p_M$, $\hat{a}^m_M$, $\hat{a}^p_P$, $\hat{a}^m_P$, $\hat{a}^p_W$, $\hat{a}^m_W$, where the lower subscript denotes the breed and the upper subscript denotes the parental origin. Additionally, a dominant QTL effect was estimated for each cross. The effect of the crosses was included and the residual variance was modelled to be heterogeneous across the crosses. The model was fitted for each cM on the autosomes. The test statistic was an F-test. The null hypothesis was that every estimate (i.e. each additive and dominant QTL effect estimated) at the position with the highest test statistic on a chromosome was equal to zero. The alternative hypothesis was that at least one effect was different from zero at this position. Correction for multiple testing on a chromosome was done using the quick method of Piepho (2001), accepting a 5 % error probability for significance. This somewhat loose threshold value was chosen because it was shown that many QTL with small effects segregate in these crosses (Bennewitz & Meuwissen 2010). At significant chromosomal positions it was tested if the additive and / or the imprinting and / or the dominant QTL effect were significant. These tests were conducted by building linear contrasts and resulted in the three error probabilities p_{add}, p_{dom}, and p_{imp} for additive, dominance and imprinting QTL, respectively. Additionally, the number of QTL alleles was determined based on their mendelian effects (i.e. ignoring parental origin of the alleles, $\hat{a}_P$, $\hat{a}_M$, $\hat{a}_W$). QTL confidence intervals were obtained by the one LOD drop method (Lynch & Walsh 1998). For this purpose, *F*-values were converted into LOD-scores. Multiple QTL were included as cofactors in the model using a forward selection approach. This increased statistical power and enabled the detection of multiple QTL on a chromosome. A more detailed description of this procedure can be found in Rückert & Bennewitz (2010).

Results and discussion

The summary statistics in Table 1 reveal substantial variation for all traits within and across the three crosses. However, a low coefficient of variation was observed for CL. For the growth traits W21, W35 and CL, and SW the mean of the M×P cross is substantially higher than the mean of the other two crosses. For BW, HMW, and MA the W×M cross mean is substantially lower. This is in agreement with the history of the breeds. The Pietrain breed is a typical sire line used to generate crosses for slaughter pigs, and was selected for growth and meat quality during the last decades. The Meishan breed is known to be a fatty and fertile breed. Wild Boar is a small size breed. It was not subject to artificial selection and hence little or no selection pressure was on growth traits. The QTL results for growth traits and muscling traits are shown in Table 4 and 5, respectively. For many QTL with significant additive effects three Mendelian alleles could be observed. In this case, the order of effects was often, but not always, $\hat{a}_P > \hat{a}_M > \hat{a}_W$. If only two Mendelian alleles were observed, the order of effects was often $\hat{a}_P = \hat{a}_M > \hat{a}_W$, *or* $\hat{a}_P > \hat{a}_M = \hat{a}_W$. This was expected due to the selection history of the breeds mentioned above, but it also indicates genetic variation for these traits within the founder breeds.

Table 4
QTL results for growth traits

Trait	SSC	Pos	CI	F-value	P_{add}	P_{dom}	P_{imp}	Mode	Order of effects
BW	8	6	[0.0; 18.0] [SW905; SW933]	3.97	0.0005	0.0172	0.1980	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
W21	6	101	[96.4; 106.0] [RYR; SKI]	4.62	0.0017	0.0050	0.1273	(- -)	$\hat{a}_M>\hat{a}_P=\hat{a}_W$
	8	3	[0.0; 18.0] [SW905; SW933]	3.99	<0.0001	0.1194	0.6099	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	15	99	[71.9; 99.4] [SW2053; SW1983]	3.27	0.6207	0.0150	0.0030	(nc)	$\hat{a}_M=\hat{a}_P=\hat{a}_W$
	16	10	[0.0; 33.3] [S0111; SW419]	3.24	0.0327	0.0363	0.0139	(nc)	$\hat{a}_W>\hat{a}_M=\hat{a}_P$
W35	6	100	[96.4; 106.0] [RYR; SKI]	4.21	0.0014	0.0152	0.1513	(- -)	$\hat{a}_M>\hat{a}_P=\hat{a}_W$
	8	5	[0.0; 34.0] [SW905; SW933]	3.82	<0.0001	0.0393	0.8651	(- -)	$\hat{a}_P>\hat{a}_M=\hat{a}_W$
	12	1	[0.0; 10.8] [S0143; EAD]	3.22	0.7210	0.0748	0.0006	(mat)	$\hat{a}_M=\hat{a}_P=\hat{a}_W$
	12	75	[64.5; 99.3] [SW874; S0174]	3.45	0.2497	0.0577	0.0016	(nc)	$\hat{a}_M=\hat{a}_P>\hat{a}_W$
	14	132	[105.1; 151.3] [SW2488; SW2515]	2.60	0.0081	0.0544	0.9052	(- -)	$\hat{a}_P>\hat{a}_M=\hat{a}_W$
SW	1	90	[77.3; 104.1] [SW2130; IGFR]	7.99	<0.0001	0.9368	0.0118	(nc)	$\hat{a}_M=\hat{a}_P>\hat{a}_W$
	2	76	[70.6; 78.3] [MYOD1; INSR]	4.84	<0.0001	0.0095	0.3624	(- -)	$\hat{a}_M>\hat{a}_P>\hat{a}_W$
	3	59	[50.8; 74.0] [OIF; SW828]	3.18	0.0205	0.0038	0.6224	(- -)	$\hat{a}_M=\hat{a}_P>\hat{a}_W$
	4	71	[62.1; 75.3] [SW1073; S0073]	5.62	<0.0001	0.1687	0.4926	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	5	156	[110.0; 157.9] [IGF1; SW967]	3.76	0.6173	0.6432	<0.0001	(mat)	$\hat{a}_M=\hat{a}_P=\hat{a}_W$
	6	85	[73.7; 94.4] [FTO; ETH5001]	3.43	0.0036	0.0573	0.0700	(- -)	$\hat{a}_M=\hat{a}_P>\hat{a}_W$
	7	63	[0.0; 73.3] [S0025; CYPD]	3.56	<0.0001	0.2359	0.4437	(- -)	$\hat{a}_M>\hat{a}_P>\hat{a}_W$
	8	12	[0.0; 34.0] [SW905; SW933]	5.18	<0.0001	0.2696	0.0707	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
CL	1	110	[77.3; 119.2] [SW307; S0082]	3.73	0.0873	0.0248	0.0021	(mat)	$\hat{a}_M=\hat{a}_P>\hat{a}_W$
	1	161	[149.6; 178.5] [TGFBR1; SW705]	9.26	<0.0001	0.1989	0.2241	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	3	58	[35.9; 74.0] [S0206; SW828]	3.63	0.1496	0.0005	0.3775	(- -)	$\hat{a}_M=\hat{a}_P=\hat{a}_W$
	4	73	[62.1; 81.0] [SW1073; CASQ1]	9.45	<0.0001	0.0053	0.0424	(nc)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	7	73	[61.3; 75.2] [ID4_ECO; KE6]	15.32	<0.0001	0.1573	0.2116	(- -)	$\hat{a}_M=\hat{a}_P>\hat{a}_W$
	8	13	[0.0; 34.0] [SW905; SW933]	3.89	<0.0001	0.4477	0.2922	(- -)	$\hat{a}_M=\hat{a}_P>\hat{a}_W$
	10	65	[52.5; 74.1] [SW497; GAS1]	3.03	0.1906	0.1264	0.0083	(mat)	$\hat{a}_M=\hat{a}_P=\hat{a}_W$
FCR	1	105	[77.3; 119.2] [SW2130; S0082]	4.23	0.0856	0.0018	0.0105	(mat)	$\hat{a}_M>\hat{a}_P=\hat{a}_W$
	3	41	[11.6; 74.0] [SW72; SW828]	3.46	0.0021	0.0605	0.7272	(- -)	$\hat{a}_M>\hat{a}_P>\hat{a}_W$
	6	99	[80.0; 102.4]	3.25	0.0003	0.1463	0.9540	(- -)	$\hat{a}_M>\hat{a}_P=\hat{a}_W$

CI: confidence interval, P_{add}: error probability for additive effects, P_{dom}: error probability for dominant effects, P_{imp}: error probability for imprinting effects, Mode: mode of imprinting; (--) imprinting not significant, (mat) maternal imprinting, (pat) paternal imprinting, (nc) not consistent), $\hat{a}_P$: estimated effect of Pietrain breed, $\hat{a}_M$: estimated effect of Meishan breed, $\hat{a}_W$: estimated effect of Wild Boar breed

Table 5
QTL results for muscling traits

Trait	SSC	Pos	CI	F-value	P_{add}	P_{dom}	P_{imp}	Mode	Order of effects
HMW	1	66	[43.5; 77.3] [SWR2300; SW2130	5.81	<0.0001	0.9619	0.0899	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	1	119	[110.3; 126.3] [SW307; SW780	3.36	0.0004	0.1097	0.2797	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	2	34	[14.9; 68.0] [SW2623; MLP	4.23	0.0080	0.7878	0.0006	(mat)	$\hat{a}_M=\hat{a}_P>\hat{a}_W$
	3	0	[0.0; 11.6] [SERPINE1; SW72	3.94	<0.0001	0.6002	0.3853	(- -)	$\hat{a}_M=\hat{a}_P>\hat{a}_W$
	4	71	[62.1; 75.3] [SW1073; S0073	6.95	<0.0001	0.2454	0.2363	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	5	120	[110.0; 150.4] [IGF1; MYF5	5.18	0.0002	0.9961	<0.0001	(mat)	$\hat{a}_M=\hat{a}_P>\hat{a}_W$
	6	98	[80.0; 106.0] [S0087; SKI	5.76	<0.0001	0.3880	0.2407	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	7	73	[61.3; 86.5] [ID4_ECO; S0102	4.06	<0.0001	0.5281	0.4518	(- -)	$\hat{a}_M>\hat{a}_P>\hat{a}_W$
	8	15	[0.0; 34.0] [SW905; SW933	5.49	<0.0001	0.4905	0.3259	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	10	63	[52.5; 74.1] [SW497; GAS1	5.03	0.0723	0.0052	0.0003	(mat)	$\hat{a}_P>\hat{a}_M=\hat{a}_W$
	12	95	[51.0; 109.8] [S0083; S0106	2.85	0.0037	0.3635	0.0770	(- -)	$\hat{a}_P>\hat{a}_M=\hat{a}_W$
	14	91	[78.0; 105.1] [ACTA1; SW2488	6.12	0.0001	0.5692	0.6072	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
SMW	1	119	[110.3; 126.3] [SW307; SW780	5.39	<0.0001	0.1457	0.0350	(pat)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	2	48	[0.0; 77.8] [SW2443; UBL5	4.44	0.0001	0.5542	0.0107	(nc)	$\hat{a}_M=\hat{a}_P>\hat{a}_W$
	3	0	[0.0; 11.6] [SERPINE1; SW72	4.73	<0.0001	0.1081	0.6617	(- -)	$\hat{a}_M=\hat{a}_P>\hat{a}_W$
	3	56	[35.9; 74.0] [S0206; SW828	3.40	0.0993	0.0007	0.5296	(- -)	$\hat{a}_P>\hat{a}_M=\hat{a}_W$
	4	68	[62.1; 75.3] [SW1073; S0073	8.98	<0.0001	0.4658	0.2340	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	5	120	[77.3; 150.4] [S0005; MYF5	3.69	0.0043	0.9294	0.0011	(mat)	$\hat{a}_P>\hat{a}_M=\hat{a}_W$
	6	72	[58.1; 80.0] [SW1057; S0087	3.90	0.0024	0.1828	0.0106	(mat)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	7	70	[61.3; 86.5] [ID4_ECO; S0102	6.98	<0.0001	0.5094	0.1476	(- -)	$\hat{a}_M>\hat{a}_P>\hat{a}_W$
	8	12	[0.0; 34.0] [SW905; SW933	5.67	<0.0001	0.3958	0.6961	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	10	65	[30.6; 74.1] [SW443; GAS1	3.75	0.2838	0.1446	0.0004	(mat)	$\hat{a}_M=\hat{a}_P>\hat{a}_W$
LNMW	1	66	[43.5; 77.3] [SWR2300; SW2130	7.10	<0.0001	0.9358	0.1127	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	1	119	[110.3; 126.3] [SW307; SW780	1.93	0.0336	0.1941	0.5139	(- -)	$\hat{a}_P>\hat{a}_M=\hat{a}_W$
	1	162	[149.6; 178.5] [TGFBR1; SW705	3.28	0.0121	0.0133	0.1105	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	2	25	[5.2; 52.9] [SWC9; SW240	3.36	0.0033	0.1639	0.1554	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	3	55	[35.9; 74.0] [S0206; SW828	4.65	0.0003	0.0006	0.9149	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	4	71	[50.9; 75.3] [SW2128; S0073	7.33	<0.0001	0.2312	0.2368	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$

Table 5 continued
QTL results for muscling traits

Trait	SSC	Pos	CI		F-value	P_{add}	P_{dom}	P_{imp}	Mode	Order of effects
	5	118	[92.3; [SW152;	150.4] MYF5	3.69	0.0046	0.8156	0.0011	(nc)	$\hat{a}_W>\hat{a}_M=\hat{a}_P$
	6	88	[80.0; [S0087;	99.5] TGFB1	4.91	<0.0001	0.0385	0.2132	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	8	13	[0.0; [SW905;	34.0] SW933	4.89	<0.0001	0.2773	0.1846	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	10	61	[30.6; [SW443;	74.1] GAS1	3.97	0.6031	0.0090	0.0006	(nc)	$\hat{a}_M=\hat{a}_P=\hat{a}_W$
	14	65	[43.8; [SW2038;	105.1] SW2515	3.70	0.0070	0.0031	0.2850	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
MA	1	160	[144.7; [TPM2;	178.5] SW705	5.74	<0.0001	0.4987	0.0042	(pat)	$\hat{a}_P>\hat{a}_W>\hat{a}_M$
	2	4	[0.0; [SW2443;	14.9] SW2623	4.72	0.0049	0.0019	0.0053	(mat)	$\hat{a}_M=\hat{a}_P>\hat{a}_W$
	4	71	[62.1; [SW1073;	75.3] S0073	4.27	<0.0001	0.9746	0.6095	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	6	94	[80.0; [S0087;	99.5] TGFB1	4.65	<0.0001	0.0444	0.2910	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$
	8	23	[0.0; [SW905;	49.4] SW1070	4.31	<0.0001	0.2301	0.1895	(- -)	$\hat{a}_P>\hat{a}_M=\hat{a}_W$
	8	96	[49.4; [SW1070;	110.1] SW16	3.04	0.0164	0.0095	0.6006	(- -)	$\hat{a}_P>\hat{a}_M=\hat{a}_W$
	14	77	[60.7; [SW540;	105.1] SW2488	5.69	<0.0001	0.5742	0.5435	(- -)	$\hat{a}_P>\hat{a}_M>\hat{a}_W$

CI: confidence interval, P_{add}: error probability for additive effects, P_{dom}: error probability for dominant effects, P_{imp}: error probability for imprinting effects, Mode: mode of imprinting; (--) imprinting not significant, (mat) maternal imprinting, (pat) paternal imprinting, (nc) not consistent), $\hat{a}_P$: estimated effect of Pietrain breed, $\hat{a}_M$: estimated effect of Meishan breed, $\hat{a}_W$: estimated effect of Wild Boar breed

Most of the QTL were found on SSC1, 2, 3, 4, 6 and 8, and no QTL were on SSC9, 11, 13, 15, 17 and 18 (Figure 1). For the six growth traits, a total of 28 QTL were found, 12 with a significant dominant QTL effect and 10 with a significant imprinting QTL effect. For the four muscling traits, 40 QTL were found, with 10 and 12 significant dominant and imprinting effects, respectively. Most QTL were significant due to their additive effects. Some QTL, however, showed only a significant dominant and/or a significant imprinting effect, but no significant additive effects. Consequently, no different Mendelian alleles could be observed for these QTL, and $\hat{a}_P=\hat{a}_M=\hat{a}_W$. For example, see QTL on SSC3 for CL and SMW, SSC5 for SW, SSC10 for HMW and SMW and SSC12 for W35. Many QTL showed similar position estimates and overlapping confidence intervals. The QTL with significant imprinting effects were mainly located on chromosomes 1, 2, 5 and 10. The mode of imprinting (paternal or maternal) was not always consistent across the three crosses. This can be interpreted as evidence against real imprinting effects, because it is not likely that an imprinted gene has a different mode in different crosses. As discussed in detail by Rückert & Bennewitz (2010), the test for imprinting as conducted in this study might also reveal significance due to within founder breed segregation rather than due to real imprinting.

Due to the high number of mapped QTL not all of them will be discussed. A comparison of the results and other literature results can be done using the pig QTL data base (Hu *et al.* 2005). In the following, some interesting chromosomal regions will be considered and putative candidate genes underlying the QTL will be discussed.

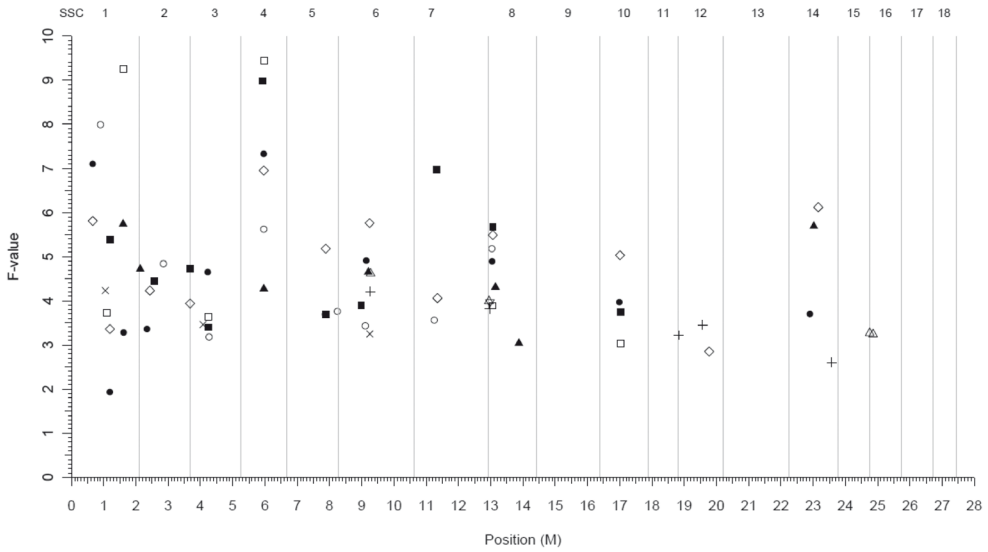

Figure 1
Overview of the QTL distribution of the porcine genome. Note that the test statistic of the QTL for CL on SSC7 was F>15 (not shown in the figure). The definition of the symbols is given in Table 2.

For all traits except BW, W21, and W35 one or two QTL were found on SSC1. These QTL were distributed over five confidence intervals (see also the plots of the test statistics in Figure 2). QTL affecting growth and muscling on this chromosome have previously been mentioned in other F_2 cross-studies (Bidanel *et al.* 2001, Milan *et al.* 2002), although the QTL were not always located at the same region as in this study.

QTL were found for all muscling traits on SSC2. This is in agreement with Varona *et al.* (2002). A maternal imprinting effect was found for HMW and MA. The confidence intervals of these two QTL contain the *IGF2* locus (co-localised with the microsatellite SWC9) which affects muscling and fattening traits and is known to be imprinted (Nezer *et al.* 1999). However, due to the large confidence intervals it might be that these imprinted QTL are caused by other imprinted genes, e.g. *INS2* (Jeon *et al.* 1999). For SW a QTL was mapped in the interval between *MYOD1* and *InsR*. Varona *et al.* (2002) also found significant QTL in this chromosomal region. *MYOD1* is known to be involved in muscle differentiation and is mentioned as a candidate gene for growth (Fan *et al.* 2011).

QTL for some growth and muscling traits were found at the distal part of SSC3, with the *SERPINE1* gene at the start of the confidence intervals. It codes for a protein called Serpine1, which is a molecule located in the extracellular space and is known to influence obesity and diabetes in humans (Kaur *et al.* 2010). *SERPINE1* may be seen as possible candidate gene for growth. Additional QTL with a highly significant dominance effect were found for SW, CL, FCR, and LNMW.

The SSC4 is known as the chromosome with the highest density of QTL in pigs (Rothschild *et al.* 2007). In our study QTL were found for every trait, with a remarkably consistent chromosomal position estimated in the centromeric region (see also Figure 2). In this interval two markers located in the gene coding regions of *VATP* (coding for the vacuolar ATPase

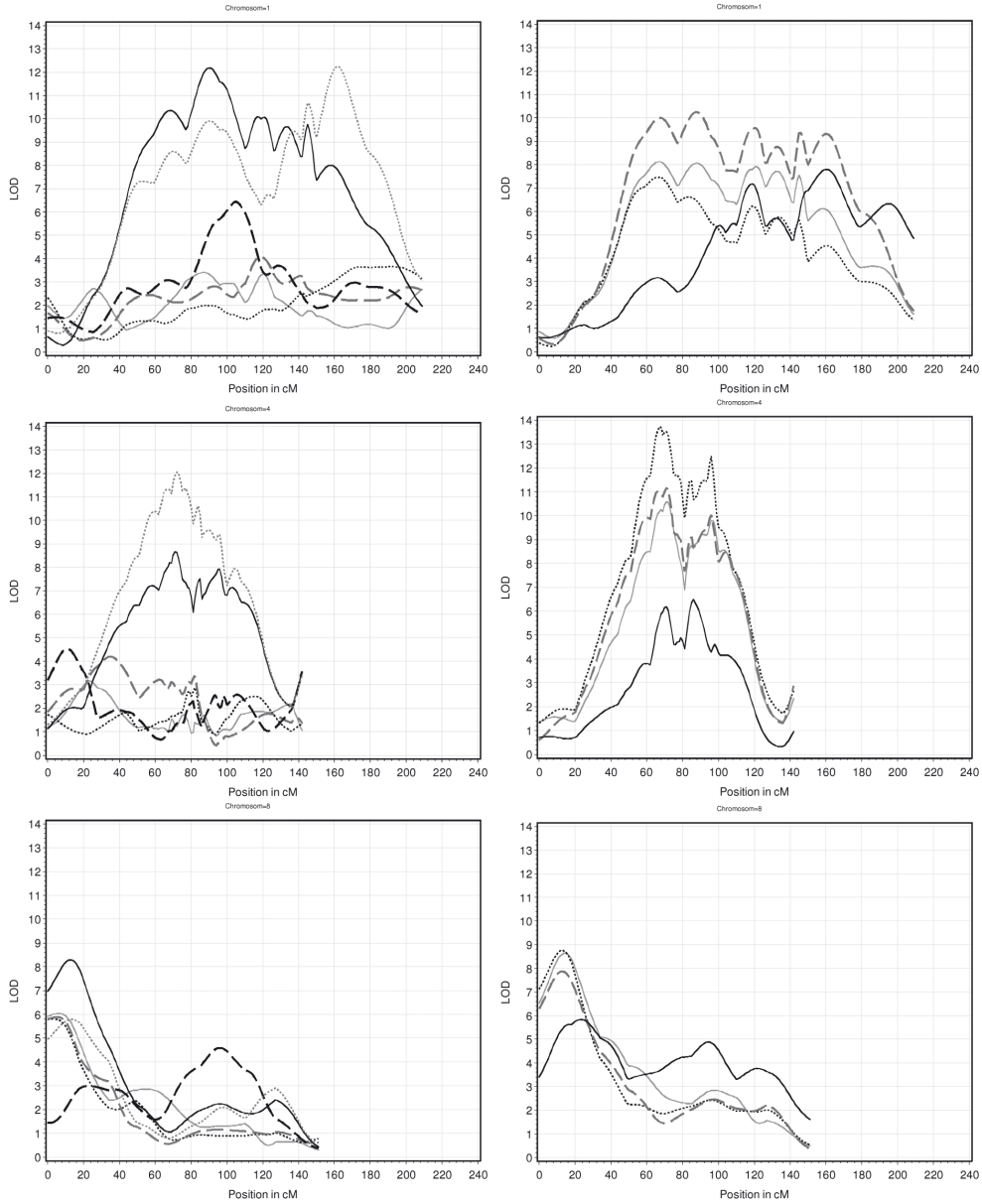

Figure 2
Plot of the test statistics for Chromosome 1 (top), 4 (middle) and 8 (bottom). Plots on the left show growth traits (BW: gray solid, W21: black dotted, W35: gray dashed, SW: black solid, CL: black dashed, FCR: gray dotted) and those on the right show muscling traits (HMW: gray solid, SMW: black dotted, LNMW: gray dashed, MA: black solid).

proton pump) and *ATP1B1* (coding for the sodium/potassium-dependent ATPase beta-1 subunit) are of interest. Both gene products are involved in the ATP-dependent pathway including protein synthesis.

Several QTL were found on SSC5 with highly significant imprinting effects and a consistent mode of imprinting, i.e. maternally imprinted. The confidence intervals included *IGF1*, which is known to be involved in a wide variety of growth responses (Fan *et al.* 2011) and has been suggested as a candidate gene (Roehe *et al.* 2003).

Porcine chromosome 6 is frequently mentioned in QTL studies, because several genes, such as the *RYR1* (frequency of 0.492 and 0.513 in W×P and M×P in that study) associated with pale, soft and exudative meat and *TGF-β-1*, which controls cell growth, cell performance and cell differentiation, are located there. These two markers are within the overlapping QTL confidence intervals for six traits in our study. Additionally, Fan *et al.* (2009) detected a polymorphism within the fat mass and obesity associated protein gene (*FTO*), which is associated with growth and fatness traits. This gene is located at the bound of the QTL confidence intervals for SW and SMW in our study.

Many QTL have been detected in the same region of SSC7. Demars *et al.* (2007) searched for body composition traits on SSC7. In this study the same traits as in our study (slaughter weight, carcass length, ham and sholder weight) showed significant QTL in very similar regions of porcine chromosome 7. A QTL for carcass length on SSC7 was found by Sanchez *et al.* (2006). An exceptionally high test statistic (F-value ~15) was found for a QTL for CL on SSC7 in this study. For this trait two other highly significant QTL (F-value >9) were also found. These high test statistic values were not observed for other traits. It seems that the low variation observed for CL is due to only a few genes with large effects. One possibly explanation might be that the genes affect the number of ribs. Therefore, candidate genes involved in determination of rib number were investigated. Two interesting candidate genes which are located close to the CL QTL on SSC7 were suggested. The first candidate gene is called *PPARD*, which is involved in cartilage development as well as in fat metabolism. Ren *et al.* (2011) described a missense mutation which is associated with ear size in Chinese pigs. The second one is the *Bmp5* gene located at the short ear locus, which was investigated by Kingsley *et al.* (1992). Among others, Kingsley *et al.* (1992) demonstrated that null mutations at the *Bmp5* locus reduce the number of ribs along the vertebral column. In further studies it should be investigated if the QTN in *PPARD* affects only the ear size or even CL (pleiotropy) or if the *PPARD* mutation is in LD with a mutation in the gene *Bmp5*. Therefore both candidate genes should be considered to unravel this exceptional QTL result.

Nine QTL were found on SSC8 (see Figure 2). In most cases the QTL were located in the distal region around the peroxisome proliferative activated receptor gamma coactivator 1 (*PGCMUT* or *PPARGC1*). *PPARGC1* is a candidate gene that regulates the determination of myofibre types and has an important influence on myofibre growth (Jiang *et al.* 2011). In the study of Jiang *et al.* (2011), strong differences in gene expression between Landrace pigs and Chinese Meishans were reported. The detected QTL on SSC10 were all located in one region near the growth arrest-specific protein 1 marker (*GAS1*). *GAS1* is an integral membrane protein and plays an important role in growth suppression in humans and mice (Del Sal *et al.* 1994).

The three QTL for muscling identified on SSC14 are located in the region around the marker actinin alpha 2 (*ACTN2*) and actin alpha 1 (*ACTA1*). Davoli *et al.* (2003) searched for polymorphisms in the myopalladine (*MYOP*) gene and placed the porcine *MYOP* gene, which is closely linked to *ACTA1*, on the genetic map of SSC14. Myopalladin (*MYOP* or *FLJ14437*) is

a 145-kDa sarcomeric protein, which binds α-actinin with nebulin in skeletal muscle and functions in the organisation and assembly of the Z-line (Bang *et al.* 2001). Due to its role as a skeletal muscle gene especially coding for a sarcomeric protein, *MYOP* may play a key role in muscle mass accretion. Wimmers *et al.* (2007) searched for associations between functional candidate genes derived from gene-expression profiles of prenatal porcine muscle tissue and meat quality and muscle deposition. For *MYOP* the authors were able to show association with ham weight and lean content.

In conclusion, in this study the three connected F_2-designs of Geldermann *et al.* (2003) were analysed jointly for muscling and growth traits using a multi-allele multi-QTL model. A large number of QTL was found compared to the separate analysis of crosses (see Geldermann *et al.* 2003). This underlines the high statistical power resulting from analysing the data jointly using an appropriate model. Based on small and overlapping confidence intervals, positional and functional candidate genes were suggested for most interesting QTL regions. In particular, the exceptional QTL for carcass length should be further investigated.

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