Quantitative Trait Loci Variation for Growth and Obesity Between and Within Lines of Pigs (*Sus scrofa*)

Yoshitaka Nagamine,* Chris S. Haley,* Asheber Sewalem* and Peter M. Visscher†,[1]

**Division of Genetics and Biometry, Roslin Institute (Edinburgh), Roslin, Midlothian EH25 9PS, United Kingdom and †Institute of Cell, Animal and Population Biology, University of Edinburgh, Edinburgh EH9 3JT, United Kingdom*

Manuscript received December 13, 2002
Accepted for publication February 15, 2003

ABSTRACT

The hypothesis that quantitative trait loci (QTL) that explain variation between divergent populations also account for genetic variation within populations was tested using pig populations. Two regions of the porcine genome that had previously been reported to harbor QTL with allelic effects that differed between the modern pig and its wild-type ancestor and between the modern pig and a more distantly related population of Asian pigs were studied. QTL for growth and obesity traits were mapped using selectively genotyped half-sib families from five domesticated modern populations. Strong support was found for at least one QTL segregating in each population. For all five populations there was evidence of a segregating QTL affecting fatness in a region on chromosome 7. These findings confirm that QTL can be detected in highly selected commercial populations and are consistent with the hypothesis that the same chromosome locations that account for variation between populations also explain genetic variation within populations.

DESPITE the characterization of many genes and mutations for Mendelian disorders in humans and animals, relatively little is known about the nature and maintenance of genetic variation underlying quantitative traits and complex disease (*e.g.*, Mackay 2001; Wright and Hastie 2001; Barton and Keightley 2002). For example, we do not know the number of genes involved in quantitative genetic variation, the number and effects of alleles at these genes, or the gene action. To date, genes and causal variants have been detected for very few quantitative traits (*e.g.*, Grobet *et al.* 1998; Frary *et al.* 2000; Kim *et al.* 2000; Milan *et al.* 2000; Wilson *et al.* 2001), and the effects of the mutations in the majority of these examples are so large that the phenotypes segregate almost as Mendelian traits.

To understand and exploit the genetics of complex quantitative traits, experimental populations derived from two lines differing widely for traits of interest have been successfully used in model species (Belknap *et al.* 1993; Talbot *et al.* 1999), plants (Paterson *et al.* 1988), and livestock (Andersson *et al.* 1994) to detect quantitative trait loci (QTL). These studies have succeeded in mapping QTL for which alleles differ in frequency between the parental populations, for example, between commercial agricultural cultivars and wild-type populations (Paterson *et al.* 1988; Andersson *et al.* 1994). In addition to understanding the architecture of quantitative traits, crosses involving agricultural species are also motivated by the potential to exploit variation within elite populations; commercial plant and animal populations are usually not based upon the same crosses that are used in the QTL detection studies but the power of linkage studies in line crosses is generally greater than that of studies within populations. In commercial pig breeding populations, for example, elite populations comprise closed outbred populations that have been subjected to selection over a number of generations to improve their commercial performance, whereas wild boar (Andersson *et al.* 1994) and Chinese Meishan (Walling *et al.* 1998; De Koning *et al.* 1999; De Koning *et al.* 2000; Bidanel *et al.* 2001) populations have been employed in QTL studies. The implicit hypothesis in many QTL studies using divergent lines is that knowledge of between-population genetic variation can be extrapolated to genetic variation in other populations or species. Segregation at QTL in commercial populations can be utilized by breeders through gene- or marker-assisted selection programs (*e.g.*, Dekkers and Hospital 2002).

Selection for meat and fat production in pigs has taken place for centuries, but intense selection using modern statistical methods has been practiced for only the past ~50 years (Clutter and Brascamp 1998). Stock used in present-day breeding programs consists of pure closed lines, which are selected for clearly defined breeding objectives, for example, lean tissue growth rate, decreased fatness, and increased litter size. The nature and maintenance of quantitative genetic variation in elite populations and their wild-type ancestors is not well understood, but the application of simple

[1]*Corresponding author:* University of Edinburgh Institute of Cell, Animal and Population Biology, W. Mains Rd., Edinburgh EH9 3JT, United Kingdom. E-mail: peter.visscher@ed.ac.uk

TABLE 1

Summary of populations and traits

Company	Population type	Minimum no. of yr closed	N_e[a]	Traits	Selection of progeny for genotyping
A	Large White	15	200	Growth rate pretest (g/day) Growth rate on test (g/day) Fat-P_1, fat-P_3, fat-loin, fat-shoulder (all in mm)	BLUP index of all six traits
B	Duroc-Large White synthetic	10	85	Growth rate pretest (g/day) Growth rate on test (g/day) Growth rate birth to end of test (g/day) Back fat (mm)	EBV[b] for growth rate birth to end of test[c]
C	Yorkshire/Large White	10	60	Growth rate pretest (g/day) Growth rate on test (g/day) Growth rate birth to end of test (g/day) Back fat P_1 (mm) Back fat P_2 (mm) Muscle depth (mm)	EBV for growth rate birth to end of test
D	Large White	16	300	EBV for growth rate (g/day) Fat-P_1, fat-P_3 (mm) Loin area (mm^2) Growth rate pretest (g/day) Growth rate on test (g/day)	EBV for growth rate
E	Landrace	20	190	EBV for growth rate (g/day) Back fat (mm) Lean % Growth rate on test (g/day) Growth rate birth to end of test (g/day)	EBV for growth rate[d]

[a] N_e estimated by individual companies.
[b] EBV, estimated breeding value, the best linear unbiased prediction (BLUP) of an individual's breeding value. EBVs were adjusted for the average EBV of the parents, to give an estimate of the within-family Mendelian sampling term.
[c] Selection was in two stages. First, 10 half-sib families were selected with the largest within-family variance, and second, within each selected half-sib family the extreme progeny from both tails were selected.
[d] Tail selection was practiced for 8 half-sib families. For the remaining 4 half-sib families, full-sib families were selected on the basis of within-full-sib family variance.

quantitative biometrical "black-box" methods pioneered by Galton, Fisher, and Wright have been highly efficient in changing livestock appearance and performance (*e.g.*, in Hill *et al.* 2000, pp. 1–38).

We have previously shown that QTL in a particular region can be identified in quite distinct experimental crosses as well as in replicated studies of the same experimental cross (Walling *et al.* 1998). The aim of this study was to test the hypothesis that the same QTL that account for variation between divergent populations also account for genetic variation within populations, using modern pig populations. To our knowledge, this study and that of Evans *et al.* (2003, this issue) are the first to specifically test this hypothesis.

MATERIALS AND METHODS

Two chromosome regions on porcine chromosomes 4 and 7 that were shown previously to harbor QTL for growth and obesity traits in Meishan × Large White (Rohrer and Keele 1998; Walling *et al.* 1998; De Koning *et al.* 1999; Andersson 2001; Bidanel *et al.* 2001) and wild boar × Large White (Andersson *et al.* 1994; Knott *et al.* 1998) crosses were investigated. From each of five commercial pig genetics companies, blood (or other tissue) from ~10 males from an elite breeding population was supplied. Males were selected on the basis of having at least 100 progeny with phenotypic records and were therefore extensively used as sires in these populations. A summary of the types of populations used is given in Table 1. Animals were performance tested to measure their individual growth rates over the weight range of ~30–100 kg. At the end of the test fat depth at various points on the back was recorded using an ultrasonic scanner. None of the populations had a recent history of intercrossing with either Meishan or wild boar genotypes.

A set of 30 microsatellite genetic markers from the two regions was supplied to a commercial laboratory, to determine heterozygosity for each male and to test the repeatability and reliability of genotyping. A subset of 19 were selected as technically tractable and heterozygous in one or more sires and finally15 markers (8 on chromosome 4 and 7 on chromosome 7) were used for subsequent genotyping of females and progeny (Table 2).

In each of five collaborating pig genetics companies, phenotypic performance data were collected from half-sib progeny of each selected male. Traits recorded depended upon the prevailing practice within each company and are detailed in Table 1. Where possible, selective genotyping was practiced by identifying the 20% best and 20% worst animals with respect to growth rate within each sire family. Collection of phenotypic records and identification of extreme performing animals were carried out by the collaborating companies. Genetic marker genotypes were determined on males, their mates, and the extreme progeny, using family-specific informative

TABLE 2

Genetic markers used in the study

Chromosome 4			Chromosome 7		
	Relative position (cM)			Relative position (cM)	
Marker	This study	USDA map[a]	Marker	This study	USDA map[a]
S0001	0	0	SW1354	0	0
SW45	12	14	S0064	6	8
SW35	12	14	SWR1078	9	11
SW839	16	20	SW1344	17	26
S0107	17	24	TNF-β	28	33
S0217	20	28	SW2019	30	29
SW841	24	29	S0102	39	38
S0073	29	32			

See http://www.ri.bbsrc.ac.uk/cgi-bin/mapviewer for marker details.
[a] See http://www.genome.iastate.edu/maps/marcmap.html for map details.

markers. In total, nearly 3000 animals were genotyped, and ~28,000 individual marker genotypes were determined by a commercial laboratory. A summary of the data is given in Table 3.

Marker information was used to detect genotype inconsistencies between relatives. Progeny with multiple marker genotypes that were inconsistent with Mendelian inheritance were excluded. In total, this resulted in the exclusion of 110 progeny (<5%). Sporadic marker genotypes that were inconsistent with Mendelian inheritance were set to unknown. Subsequently, for each company a linkage marker map was estimated using CRI-MAP (Green *et al.* 1990) and the order of the markers was compared to the published consensus maps (http://www.thearkdb.org/). Finally, a joint linkage analysis of all marker data across all five populations was performed to create a consensus linkage map that was used in subsequent QTL analyses.

For each of the five populations, data were analyzed by a half-sib regression-based method (Knott *et al.* 1996), as implemented in our web-based software package QTL Express (Seaton *et al.* 2002). From these analyses, the mean square due to the putative QTL, the residual mean square, and the within-sire substitution effects were obtained. To compare these results with those reported from line crosses, the proportion of within-sire variance explained by the QTL was calculated (Knott *et al.* 1996). In addition, the average substitution effect was calculated for those sires that showed the strongest evidence of being heterozygous, *i.e.*, for which the absolute value of the sire-specific *t*-statistic was >2.0. Results were expressed in phenotypic standard deviations, adjusting the results for selective genotyping a fraction (20%) of each tail (Darvasi and Soller 1992) and adjusting the results for the proportional reduction in phenotypic variance within sire families of $\frac{1}{4}h^2$. For all traits, a heritability of 0.4 was assumed, which is consistent with published estimates of genetic parameters of these traits in commercial populations (see Clutter and Brascamp 1998 for a literature review). The adjustment for selective genotyping was performed for the growth rate traits (on which selection was based) but not for back fat, which is phenotypically only moderately correlated with growth rate. *P* values calculated from test statistics are nominal, because we specifically set out to test the hypothesis that a particular small region of the genome harbored QTL. The samples will not be used for further genome analyses, so that whole chromosome-wise or genome-wise significance levels are inappropriate for our study.

TABLE 3

Summary of family structure and marker genotypes

Company	No. males	No. mates	No. progeny	No. genotypes
A	10	156	431	5,640
B	10	179	393	5,516
C	10	102	395	5,166
D	11	141	429	5,412
E	12	135	461	5,910
Total	53	713	2,109	27,644

RESULTS

Heterozygosity was calculated per boar across 19 markers (a subset of the original 30 markers) and ranged from 0.5 to 0.6, with a standard deviation of 0.10–0.15. Fifteen markers were typed across sufficient animals (>300 informative meioses per population) to build linkage maps for further analyses. All marker linkage maps were consistent with the published linkage maps for chromosomes 4 and 7 (see Table 2 for marker order and relative positions). The best order of the markers in the linkage groups was not significantly better (LOD < 2) than the order of the published maps, and, given this order, there was little evidence of heterogeneity of map length. For the chromosome 4 region, the map lengths varied from 22 to 36 cM between populations, whereas for the chromosome 7 region the range was (only) 37–42 cM. Overall results by chromosome, company, and trait are shown in Table 4. Significant QTL effects were detected in two of five populations for chromosome 4 and in all populations for chromosome 7. Overall, 16 out of 50 trait-by-company-by-chromosome tests were significant at the 5% level, substantially more than might be expected due to chance. For

TABLE 4

Evidence for QTL by chromosome and company (*P* values)

Company	Trait	Chromosome 4	Chromosome 7
A	Growth rate pretest	NS[a]	NS
	Growth rate on test	NS	0.01
	Fat-C	NS	0.03
	Fat-K	NS	NS
	Fat-L	NS	NS
	Fat-S	NS	NS
B	Growth rate pretest	NS	NS
	Growth rate on test	0.04	NS
	Growth rate (all)[b]	0.009	NS
	Back fat	0.04	0.05
C	Growth rate pretest	NS	NS
	Growth rate on test	NS	NS
	Growth rate (all)[b]	NS	NS
	Back fat P_1	NS	0.002
	Back fat P_2	NS	0.006
	Muscle depth	NS	0.03
D	EBV growth rate	NS	0.009
	Back fat P_1	NS	($P = 0.063$)
	Back fat P_3	NS	NS
	Loin area	NS	0.012
	Growth rate pretest	NS	0.049
	Growth rate on test	NS	0.042
E	EBV growth rate	0.035	NS
	Back fat	NS	0.021
	Lean %	NS	0.012

[a] NS, nonsignificant, $P > 0.05$.
[b] Growth rate from birth until the end of test.

the on-test growth rate traits, 4 out of 10 statistical tests were significant at the 5% level, 2 on chromosome 4 and 2 on chromosome 7. When selecting a single representative back fat measurement per population (P_1 fat measurement or one nearest to its physical location), 5 out of 10 tests were significant at the 5% level, 1 on chromosome 4 and 4 on chromosome 7. The *P* value for the P_1 fat measurement in company D was 0.063, so the data are consistent with a QTL for back fat segregating on chromosome 7 for all companies. The results for the back fat traits for chromosome 7 are shown in Figure 1, for each of the five populations. This figure demonstrates that, as expected, where a putative QTL is identified, only a proportion of the sires appear significant for that QTL (as judged by a *t*-statistic >2).

The standardized estimated effects of segregating sires and the proportion of variance explained by the QTL are shown in Table 5. The effects are in the range of 0.5–0.6 phenotypic standard deviations for growth rate and 0.8–1.3 for back fat. The proportion of phenotypic variance explained by the QTL varied from 7 to 18%. If the heritability of the traits is 0.4, then these results imply that one-quarter to one-half of additive genetic variance is explained by the reported QTL.

DISCUSSION

We have tested the hypothesis that QTL that explain between-line genetic variation also explain variation within commercial lines and presented evidence that is consistent with this hypothesis.

There are a number of different explanations of the observations: (i) false-positive results, (ii) locus heterogeneity, (iii) segregation of ancestral QTL alleles, and (iv) allelic heterogeneity at previously published QTL. The first explanation is highly unlikely, because our study was based upon targeted genome regions, rather than upon a genome scan, and for these regions 16 out of 50 tests (32%) were significant at the 5% level (Table 4). Furthermore, a number of these traits are phenotypically highly correlated, for example, the four fat measurements from company A. If we restrict ourselves to the commonly measured traits growth rate and back fat, then 9 of the 20 tests are significant at the 5% level (Table 4). At a more stringent significance level of 0.0125, accounting for two regions and two independent traits tested, 7/50 tests are significant for all traits and 4/20 for growth rate and back fat, respectively, when we would expect none to be significant by chance under the null hypothesis. We cannot rule out explanation ii, *i.e.*, that polymorphisms at different loci in the same region contribute to genetic variation in different populations. To our knowledge, there is no evidence, either for or against, of clustering of different QTL in the same linkage groups. However, the resolution of linkage mapping studies is not large enough to exclude the existence of multiple linked QTL affecting the same trait in the same genome region (Keightley and Knott 1999; Mackay 2001). A joint analysis of all populations was performed for standardized back fat traits on chromosome 7, and the resulting *F* value was 1.62 for 52 and 1922 d.f., which is highly significant ($P < 0.004$). However, the resolution of the QTL position was not improved (results not shown). A two-QTL model on the combined data set did not explain a significantly larger proportion of the variance ($P > 0.10$). Precise estimates of QTL locations on the two chromosomes vary between published studies. However, published joint estimates in large data sets put a QTL affecting growth rate on chromosome 4 at around the S0217–SW841 interval (Walling *et al.* 1998) and put a fatness QTL on chromosome 7 close to TNF-β (S. MacGregor and C. S. Haley, unpublished observation).

It would be surprising if ancestral wild-type QTL alleles that increase fatness and/or reduce growth are still segregating in the elite lines, because pigs are under intense selection pressure for reduced obesity and increased lean tissue growth rate (Clutter and Brascamp 1998; Andersson 2001). However, segregation

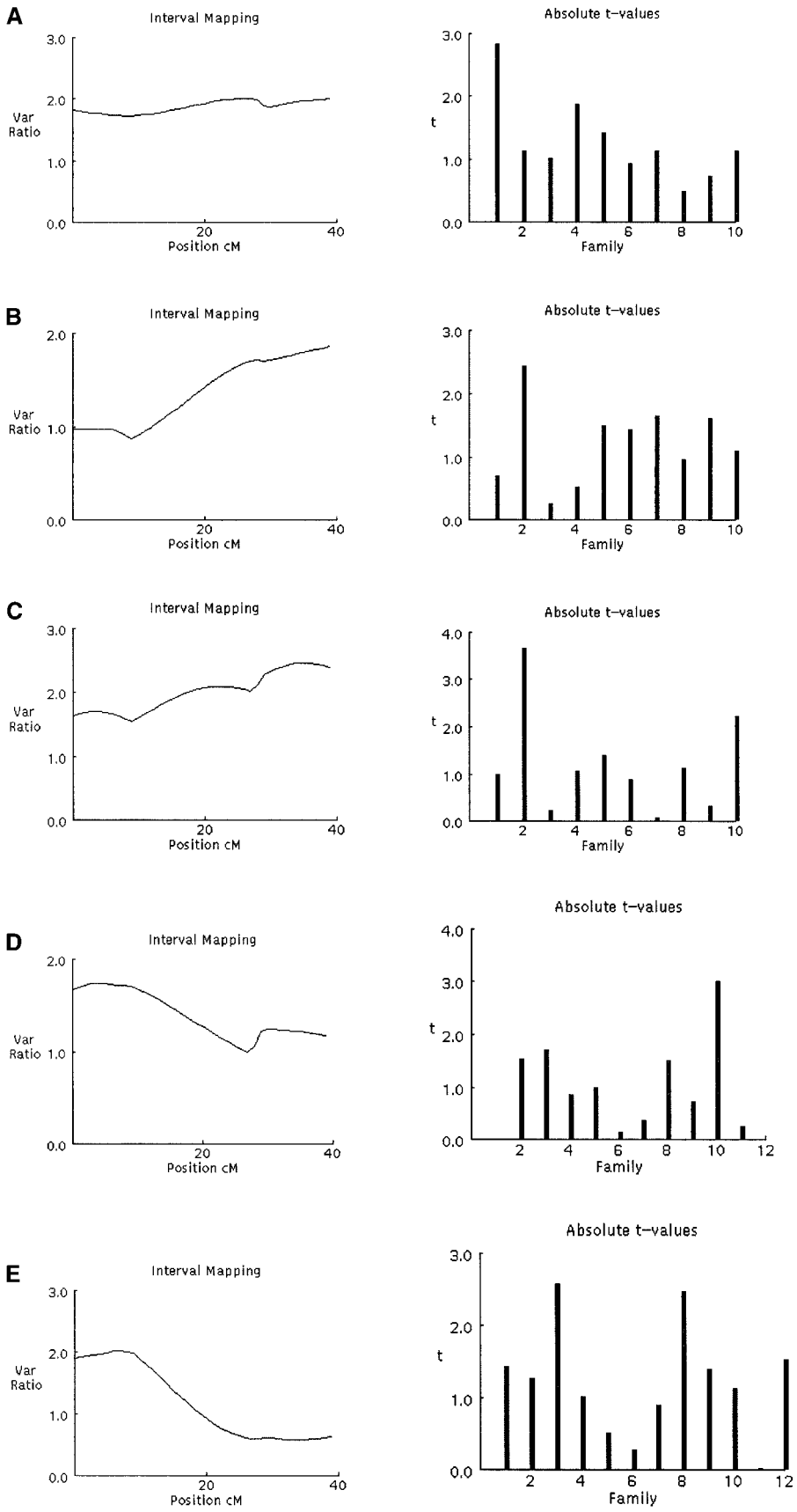

FIGURE 1.—Analysis of fatness traits on chromosome 7 for populations A–E. QTL plot across targeted region (left) and significance of gamete contrasts for each of the sires at the location with the highest test statistic (right) are shown. Fatness traits (see also Table 4) were fat-C (population A), back fat (B), back fat P_1 (C), back fat P_1 (D), and back fat (E). The approximate *F*-value thresholds for a type-I error of 0.05 and 0.01 are 1.8 and 2.3, respectively.

TABLE 5

Standardized effects for significant QTL on growth rate and back fat

		Chromosome 4		Chromosome 7	
Company	Trait	q^2 [a]	$\|a\|$ [b]	q^2	$\|a\|$
A	Growth rate on test	NS[c]	NS	0.12	0.60
	Back fat	NS	NS	0.09	1.04
B	Growth rate on test	0.14	0.60	NS	NS
	Back fat	0.09	0.83	0.08	0.95
C	Back fat	NS	NS	0.18	1.25
D	Growth rate	NS	NS	0.12	0.58
	Back fat	NS	NS	0.07[d]	1.04[d]
E	Growth rate	0.08	0.50	NS	NS
	Back fat	NS	NS	0.09	0.94

[a] q^2, proportion of phenotypic variance explained by QTL.
[b] $|a|$, average allelic substitution effect for sires with $|t\text{-statistic}| > 2.0$, in phenotypic standard deviations.
[c] NS, not significant, $P > 0.05$.
[d] $P < 0.063$.

of causal polymorphisms at candidate genes affecting growth rate and back fat has been demonstrated (*e.g.*, Kim *et al.* 2000). The maintenance of such alleles at intermediate frequencies would indicate strong pleiotropic effects, presumably on fitness traits such as survival and fertility. Our study was not designed to obtain unbiased estimates of QTL effects, but the within-sire allelic substitution effects presented here are of the same order of magnitude as the substitution effects estimated from the line cross populations, in the range of 0.4–0.8 phenotypic standard deviations (Hayes and Goddard 2001). The effect of the QTL for back fat on chromosome 7 appears to be larger than other effects in this study. Although our study used a targeted approach instead of a genome scan, we cannot rule out the possibility that the estimates obtained are biased upward. The presented data are consistent with the hypothesis that the same QTL alleles are segregating in all commercial populations. However, the sample size was such that only allelic substitution effects of more than half a phenotypic standard deviation could be detected, so we should be very cautious in drawing inference about allelic homogeneity within and between populations. The chromosome 7 QTL that was mapped from the Meishan and modern pig cross is unusual, in that the obesity decreasing allele originates from the (obese) Meishan genotype (Walling *et al.* 1998; De Koning *et al.* 1999; Bidanel *et al.* 2001). Breeders may have selected against this allele in the past when obesity was a desired trait and for this allele more recently when leanness was desired. However, given the apparent large allelic effects, it is surprising that the populations are still segregating at this QTL. Pleiotropy of the chromosome 7 QTL on fatness and growth was investigated by estimating a correlation between the within-sire allelic substitution effects for the two traits for each population and for all populations combined. None of these correlations were significantly different from zero ($P > 0.10$). Although the resolution of our study is not sufficient to fine map the QTL or to investigate positional candidate genes, it is interesting to note that the QTL for fatness on chromosome 7 maps close to the MHC region. Many genes in this region could be plausibly associated with either disease or growth and fatness. Thus it is possible that the favorable lean allele has an unfavorable pleiotropic effect on disease resistance or is in strong disequilibrium with an allele at another locus in the region that has an unfavorable effect on disease resistance; hence variation is maintained by the balancing effects of selection for leanness and disease resistance.

An alternative explanation of the results is allelic heterogeneity, *i.e.*, the segregation of different QTL alleles in different populations. This is consistent with the reporting of multiple mutations in the myostatin gene giving rise to the same double muscling phenotype (Grobet *et al.* 1998) and the numerous examples of many mutations in the same gene affecting Mendelian disorders in human populations (Wright and Hastie 2001). In this case the segregation observed in commercial populations may not represent segregation of ancestral alleles but rather of more recent mutations. Our study was not designed to fine map the QTL on chromosomes 4 and 7 or to specifically test that the same QTL alleles that vary between wide crosses are segregating within lines. Using a denser marker map, an association [linkage disequilibrium (LD)] study should establish whether ancestral QTL alleles are still segregating in the commercial lines or if the observed QTL variation is due to allelic heterogeneity at major trait loci.

Our results show strong evidence of genes segregating in highly selected outbred populations and offer the opportunities to map QTL by linkage or LD within a population. In addition, breeders can utilize the detected QTL in their own populations using marker-assisted-selection breeding schemes.

We thank the commercial partners, Cotswold, JSR Healthbred, PIC International, Rattlerow Ltd., and Newsham Ltd., for their generous support in supplying blood or tissue samples and phenotypic information. We thank Mike Goddard, Sara Knott, Bill Hill, Rick Maizels, Graham Plastow, and D. J. de Koning for helpful discussions and comments. Both referees are thanked for their comments and suggestions. This project was funded by the Biotechnology and Biological Sciences Research Council under the Sustainable Livestock Production LINK program.

LITERATURE CITED

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

Andersson, L., C. S. Haley, H. Ellegren, S. A. Knott, M. Johansson *et al.*, 1994 Genetic mapping of quantitative trait loci for growth and fatness in pigs. Science **263:** 1771–1774.

Barton, N. H., and P. D. Keightley, 2002 Understanding quantitative genetics variation. Nat. Rev. Genet **3:** 11–21.

Belknap, J. K., P. Metten, M. L. Helms, L. A. O'Toole, S. Angeli-Gade *et al.*, 1993 Quantitative trait loci applications to substances of abuse physical dependence studies with nitrous oxide and ethanol in bxd mice. Behav. Genet. **23:** 213–222.

Bidanel, J. P., D. Milan, N. Iannuccelli, Y. Amigues, M. Y. Boscher *et al.*, 2001 Detection of quantitative trait loci for growth and fatness in pigs. Genet. Sel. Evol. **33:** 289–309.

Clutter, A. C., and E. W. Brascamp, 1998 Genetics of performance traits, pp. 427–462 in *The Genetics of the Pig*, edited by M. F. Rothschild and A. Ruvinsky. CAB International, Wallingford, UK.

Darvasi, A., and M. Soller, 1992 Selective genotyping for determination of linkage between a marker locus and quantitative trait loci. Theor. Appl. Genet. **85:** 353–359.

Dekkers, J. C. M., and F. Hospital, 2002 The use of molecular genetics in the improvement of agricultural populations. Nat. Rev. Genet. **3:** 22–32.

De Koning, D. J., L. L. Janss, A. P. Rattink, P. A. Van Oers, B. J. De Vries *et al.*, 1999 Detection of quantitative trait loci for backfat thickness and intramuscular fat content in pigs. Genetics **152:** 1679–1690.

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

Evans, G. J., E. Giuffra, A. Sanchez, S. Kerje, G. Davalos *et al.*, 2003 Identification of quantitative trait loci for production traits in commercial pig populations. Genetics **164:** 621–627.

Frary, A., T. C. Nesbitt, S. Grandillo, E. Knaap, B. Cong *et al.*, 2000 A quantitative trait locus key to the evolution of tomato fruit size. Science **289:** 85–88.

Green, P., K. Falls and S. Crooks, 1990 *Documentation for CRI-MAP*, Version 2.4. Washington University School of Medicine, St. Louis.

Grobet, L., D. Poncelet, L. J. Royo, B. Brouwers, D. Pirottin *et al.*, 1998 Molecular definition of an allelic series of mutation disrupting the myostatin function and causing double muscling in cattle. Mamm. Genome **9:** 210–213.

Hayes, B., and M. E. Goddard, 2001 The distribution of the effects of genes affecting quantitative traits in livestock. Genet. Sel. Evol. **33:** 209–229.

Hill, W. G., S. C. Bishop, B. McQuirk, J. C. Mackay, G. Simm *et al.*, 2000 The challenge of genetic change in animal production. Occasional Publications of the British Society of Animal Science, Edinburgh, No. 27.

Keightley, P. D., and S. A. Knott, 1999 Testing the correspondence between map positions of quantitative trait loci. Genet. Res. **74:** 323–328.

Kim, K. S., N. Larsen, T. Short, G. Plastow and M. F. Rothschild, 2000 A missense variant of the porcine melanocortin-4 receptor (MC4R) gene is associated with fatness, growth, and feed intake traits. Mamm. Genome **11:** 131–135.

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

Knott, S. A., L. Marklund, C. S. Haley, K. Andersson, W. Davies *et al.*, 1998 Multiple marker mapping of quantitative trait loci in a cross between outbred wild boar and large white pigs. Genetics **149:** 1069–1080.

Mackay, T. F. C., 2001 Quantitative trait loci in *Drosophila*. Nat. Rev. Genet. **2:** 11–20.

Milan, D., J. T. Jeon, C. Looft, V. Amarger, A. Robic *et al.*, 2000 A mutation in PRKAG3 associated with excess glycogen content in pig skeletal muscle. Science **288:** 1248–1251.

Paterson, A. H., E. S. Lander, J. D. Hewitt, S. Peterson, S. E. Lincoln *et al.*, 1988 Resolution of quantitative traits into Mendelian factors by using a complete linkage map of restriction fragment length polymorphisms. Nature **335:** 721–726.

Rohrer, G. A., and J. W. Keele, 1998 Identification of quantitative trait loci affecting carcass composition in swine. J. Anim. Sci. **76:** 2247–2254.

Seaton, G., S. A. Knott, M. J. Kearsey, C. S. Haley and P. M. Visscher, 2002 QTL express: mapping quantitative trait loci in simple and complex pedigrees. Bioinformatics **18:** 339–340.

Talbot, C. J., A. Nicod, S. S. Cherny, D. W. Fulker, A. C. Collins *et al.*, 1999 High-resolution mapping of quantitative trait loci in outbred mice. Nat. Genet. **21:** 305–308.

Walling, G. A., A. L. Archibald, J. A. Cattermole, A. C. Downing, H. A. Finlayson *et al.*, 1998 Mapping of quantitative trait loci on porcine chromosome 4. Anim. Genet. **29:** 415–424.

Wilson, T., X. Y. Wu, J. L. Juengel, I. K. Ross, J. M. Lumsden *et al.*, 2001 Highly prolific Booroola sheep have a mutation in the intracellular kinase domain of bone morphogenetic protein IB receptor (ALK-6) that is expressed in both oocytes and granulosa cells. Biol. Reprod. **64:** 1225–1235.

Wright, A. F., and N. D. Hastie, 2001 Complex genetic diseases: controversy over the Croesus code. Genome Biol. **2:** 2007.1–2007.8.

Communicating editor: G. Churchill