Detection of Quantitative Trait Loci for Meat Quality and Carcass Composition Traits in Blackface Sheep

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Abstract. Quantitative trait loci (QTL) were identified for traits related to carcass and meat quality in Scottish Blackface sheep. The population studied comprised a double backcross between lines of sheep previously divergently selected for carcass lean content (LEAN and FAT lines), comprising nine half-sib families. Carcass composition (600 lambs) was assessed non-destructively using computerised tomography (CT) scanning and comprehensive meat quality measurements (initial and final pH of meat, flavour, colour and carcass weight) were taken on 300 male lambs. Lambs and their sires were genotyped across candidate regions on chromosomes 1, 2, 3, 5, 14, 18, 20 and 21. QTL analyses were performed using regression interval mapping techniques. In total, eight genome-wise significant and 12 chromosome-wise and suggestive QTL were detected in seven out of eight chromosomal regions. The genome-wise significant QTL (chromosomes 1, 2, 3 and 5) affected flavour, meat colour, muscle density, bone density and live weight-related traits. The most significant QTL affected meat flavour and was segregating in several families on chromosome 1. This study provides information on new QTL affecting meat quality and carcass composition traits in sheep. Verification of these results is now required in independent sheep populations.

Introduction

Selection objectives in sheep breeding are changing as the nature of the pressures upon the sheep industry change. Sheep breeders particularly need to address product quality traits, as these will determine consumer acceptance of lamb, thus the long-term market prospects.

Critical traits determining product quality are carcass composition and meat quality. A number of selection experiments have documented rapid changes in composition that are possible by selecting on live animal estimates of carcass weight. New measurement technologies, such as computerised tomography (CT), offer the potential for more accurate measurement of carcass traits in the live animal and consequently improved genetic gains. On the other hand, meat quality traits pose particular problems for improvement, as measurement is generally restricted to the slaughtered animal. Therefore, for meat quality quantitative trait loci (QTL) will be particularly important.

The development of genetic markers and their application to farm animals has progressed rapidly, opening new prospects for identifying chromosomal regions defining QTL. There is less activity in QTL identification in sheep populations compared to other livestock species, and surprisingly few QTL have been published for traits of direct relevance to meat production, apart from studies of individual major genes such as the callipyge locus (Freking *et al.,* 2002). This suggests there may be QTL effects for meat traits still to be found in sheep.

The aim of this study is to identify QTL for carcass composition and meat quality traits. This will provide a basis for targeting genomic regions to verify QTL in independent sheep populations.

Material and Methods

Animals

The population studied comprised lambs derived from LEAN (**L**) and FAT (**F**) lines of Blackface sheep, previously divergently selected for predicted carcass composition (Bishop, 1993). A double backcross design created 9 half-sib families for QTL detection, ranging from 23 to 141 individuals per family. Phenotypic measurements taken on cross-sectional scans at the ischium (ISC), the 5th lumbar vertebrae (LV5) and the 8th thoracic vertebrae (TV8) were obtained by computerised tomography (CT) on 600 5-month old lambs, from these 9 families. From each scan image the areas and image densities were obtained for the fat, muscle and bone components of the carcass. Additionally, meat quality measurements were made on 300 8-month old male lambs that had previously been CT scanned. Traits including initial and final pH of the meat, colour, flavour and carcass weight traits.

Genotyping and Map Construction

Eight chromosomes (1, 2, 3, 5, 14, 18, 20 and 21) were selected for further analyses, based on current knowledge of QTL for meat and carcass traits, containing an average of 9 to 34 informative microsatellite markers each. All sires were genotyped for markers across all candidate chromosomal regions outlined above. All lambs were subsequently genotyped for the markers that were heterozygous in their sire. For each chromosome a linkage map was then constructed using Cri-Map (Green *et al.,* 1990).

QTL Analysis

Preparation of Phenotypic Data: QTL analyses were performed for all meat quality traits, but a rationalised set of traits was chosen for the CT measures (only areas and densities of the three sites). Genetic correlations were calculated between all equivalent CT measures taken at different sites. When the correlation between measures was greater than 0.8, the measures were averaged (after scaling by their standard deviations), otherwise they were treated as separate traits.

Estimation of QTL Position: The genotype pedigree contained nine half-sib families with 600 or 300 progeny, depending upon the trait. These were analysed with a regression-based interval mapping method, developed from the method of Knott *et al.* (1996), using QTL Express (Seaton *et al.,* 2002). Briefly, the probability of inheriting a particular sire haplotype at a particular position was calculated for each offspring at 1 centiMorgans (cM) intervals along each chromosome:

$$y_{ij} = m_i + b_{ik} p_{ijk} + e_{ij}$$

where y_{ij} denotes the phenotype of the j^{th} individual (adjusted for fixed effects) originating from sire i; m_i is the average effect for half-sib family i; b_{ik} is the effect of one of the paternal haplotypes for marker k within half-sib family i; p_{ijk} is the probability for individual j of inheriting the first paternal haplotype of marker k conditional on the marker genotypes; and e_{ij} is the residual effect for individual j. To test for the presence of a QTL, test statistics similar to an F-ratio were calculated for every position on all chromosomes. This test statistic is the ratio of the difference in residual sums of squares under the null hypothesis (no QTL) and residual sums of squares under the QTL model. In a one-QTL model, the location with the largest F-ratio was taken to be the best estimated position for a QTL for each trait. In addition, an alternative approximate log-likelihood ratio test statistic was provided, for each regression, by:

$$n \log_e \left(\frac{\text{residual sum of squares reduced model}}{\text{residual sum of squares full model}} \right)$$

where n is the number of observations (Haley *et al.*, 1994). This test statistic is distributed approximately as a chi-square with degrees of freedom equal to the number of parameters included in the full model (i.e., estimating the QTL effects) but omitted from the reduced model (i.e., omitting QTL) (Aitken *et al.*, 1989). The LOD score was calculated by dividing this test statistic by ($2\log_e 10$).

Estimation of QTL effects: Estimates for the substitution effects (α) were calculated for each sire at the position with the highest F-ratio, and results were averaged across families in which there was significant evidence of a segregating QTL. Results were expressed in residual standard deviation units (RSD). For single-QTL analyses, the variance explained by the QTL under the regression approach obtained by considering the difference in residual MS between a model fitting the QTL and one in which it is omitted. This difference is equal to $\sigma^2_{QTL}/4$ (Knott *et al.*, 1996), where σ^2_{QTL} is the additive variance at the QTL. Using phenotypic and genetic variances (σ_p^2 and σ_g^2) obtained from the variance component analyses (Karamichou *et al.*, 2005 submitted), the heritability of the QTL was estimated by $h^2_{QTL} = \sigma^2_{QTL}/\sigma_p^2$ and the proportion of genetic variance attributable to the QTL was estimated as $\sigma^2_{QTL}/\sigma_g^2$.

Significance Thresholds: Three significance thresholds were applied. The **first** level was the chromosome wise threshold, which takes account of multiple tests on a specific chromosome but does not correct for testing on the entire genome. Although calculated as an F-ratio, the distribution of the test statistic under the H_0 of no QTL is unknown for half-sib analyses (de Koning *et al.,* 2001). Therefore, chromosome-wise significance thresholds were determined empirically by permutation for individual chromosome (Churchill and Doerge, 1994). One thousand permutations were studied for each trait and the relevant fixed effects and covariates were fitted. The **second** level was a suggestive linkage, where one false positive is expected in a genome scan (Kruglyak and Lander, 1995). The suggestive level (where, by chance, we expect to

obtain one significant result per genome analysis) was obtained by considering that we were analysing 27 (independent) chromosomes, each with probability P of having a significant result. Assuming the number of significant chromosomes to follow a binomial distribution, we set the required threshold, P, such that the expected number of significant chromosomes, 27P, is equal to one. Therefore, the suggestive significance level for a specific chromosome would be P ~ 0.037. **Third**, the genome-wise significance levels (where, by chance, we expect 0.05 significant results per genome analysis) was obtained using the Bonferroni correction: $p_{genome\text{-}wise} = 1 - (1-p_{chromosome\text{-}wise})^{n}$ (Knott *et al.,* 1998). For example, assuming 27 chromosomes are being analysed (i.e. there are 27 independent tests), the chromosomal test significance level would be 0.001898 to give the genome-wise 0.05 level ($(1-0.001898)^{27}=1-0.05$). None of these significance levels take the testing of multiple traits in the present and future studies into account. For the genome-wise threshold levels, little variation was found in equivalent significance thresholds across different traits and across different chromosomes. Therefore a rounded value for 5% genome-wise significance of 3.0 was used.

Confidence Intervals: If the largest *F*-ratio indicated a QTL at the genome wise level, one and two LOD support intervals were produced by taking the region of the chromosome encompassed when reducing the largest *F*-ratio by the equivalent of a LOD score of either 1.0 or 2.0, to get 95% and 99% confidence intervals (Lander and Botstein, 1989). This calculation was preferred to the bootstrap method (Visscher *et al.,* 1996), which produces conservative intervals, sometimes covering the whole chromosome, as expected from previous results (Walling *et al.,* 2002). However, for comparison bootstrap confidence intervals were also calculated.

Results

This study was successful in detecting QTL at both the genome-wise and chromosome-wise level for traits of relevance to carcass and meat quality, in seven out of eight chromosomal regions. A summary of significant QTL is presented, in decreasing order of significance, in Table 1. Highly significant QTL have been observed for a range of traits, particularly flavour, muscle densities, live weight-related traits, and colour traits. The most significant result in the analyses was evidence for a QTL affecting flavour on chromosome 1 (Figure 1). A highly significant QTL affecting muscle density (LV5-TV8) was identified on chromosome 2, and a QTL affecting bone density (ISC) was located on chromosome 1 close to the transferrin gene. A further 12 QTL achieved significance at the 5% chromosome-wise level. These were for slaughter live weight (chromosome 2), hot carcass weight (chromosome 1), lightness (colour L*) (chromosome 20), bone area (TV8) (chromosome 20), lightness (chromosome 18), hot carcass weight (chromosome 21), yellowness (colour b*) (chromosome 1), bone density (ISC) (chromosome 20), bone area (LV5) (chromosome 20), muscle area (chromosome 5), live weight at CT scanning (chromosome 21) and bone area (LV5) (chromosome 18). Of particular interest are the QTL for muscle density, as this measure is related to intramuscular fat content. Surprisingly, of these QTL, four are located in the major histocompatibility complex (MHC) region on chromosome 20.

Table 1 *Summary of significant QTL from across families analyses (suggestive or stronger linkage), presented in order of decreasing significance for CT traits and meat quality traits*

Trait	Chromosome	Position, (cM)	Marker Region	*F*-statistic	5% Chr-Wise Threshold	1% Chr-Wise Threshold
Flavour (units)	1	119	MAF64	4.80	3.15	3.91
Muscle density LV5-TV8	2	28	CSSM47-FCB226	3.45	3.45	3.95
Redness (a*) (units)	3	113	KD0103-BL4	3.31	2.68	3.26
Slaughter live weight (kg)	1	229	LCV105-BMS1789	3.23	2.98	3.66
Cold carcass weight (kg)	5	0	TGLA176	3.23	2.56	3.25
Muscle density ISC	3	172	BM6433-BMS772	3.16	2.60	3.15
Bone density ISC	1	261	BM3205-OarHH36	3.15	2.70	3.26
Hot carcass weight (kg)	5	0	TGLA176	3.07	2.72	3.27
Slaughter live weight (kg)	2	262	BM6444-BMS356	3.02	2.88	3.49
Hot carcass weight (kg)	1	227	LCV105-BMS1789	2.97	2.86	3.44
Lightness (L*) (units)	20	42	BM1815-DRB1	2.94	2.43	2.94
Bone area TV8 (mm^2)	20	55	OMHC1	2.90	2.50	3.08

Lightness (L*) (units)	18	80	ILSTS54-MCMA26	2.74	2.24	2.75
Hot carcass weight (kg)	21	88	HH22-BMC1948	2.72	2.48	3.14
Yellowness (b*) (units)	1	165	INRA11-BMS527	2.55	2.55	2.95
Bone density ISC	20	52	OLARDB-OMHC1	2.46	2.47	3.00
Bone area LV5 (mm^2)	20	21	MCMA36-CP73	2.45	2.46	3.24
Average muscle area (mm^2)	5	116	MCM527-CSRD2134	2.44	2.88	3.27
CT live weight (kg)	21	11	BMC2228-BMC1206	2.41	2.08	2.76
Bone area LV5 (mm^2)	18	83	OB2-CSSM018	2.26	2.21	2.6

The size of effects and the proportions of variance attributable to the QTL significant at the genome level are presented in Table 2. The QTL effect for flavour was on average 1.89 residual standard deviation (RSD) in families S1, S3, S4 and S6. The proportion of the genetic variance due to QTL for flavour was 41.0%. The QTL affecting muscle density (LV5-TV8) had an effect of 1.51 RSD. Also, the significance of that QTL is reflected by the 39.5% of the genetic variance that the QTL explains. Additionally, the QTL for redness of meat had a size effect of almost 2 RSD and the genetic variance due to the QTL was 20.1%. On chromosome 5, the QTL for both cold and hot carcass weight explained, approximately, the 49% of the genetic variance, with an effect of 1.22 kg and 1.20 kg, respectively. A QTL affecting bone density (ISC) was located on chromosome 1 close to the transferrin gene, with size effect of 1.14 RSD. The QTL explained 13.8% of the genetic variance. The traits slaughter live weight and muscle density (ISC) produced evidence for a QTL at the 5% genome-wise level, on chromosomes 1 and 3 respectively, however the genetic variance due to QTL was only 7.4% and 12.5% respectively.

Table 2 *Summary of phenotypic and genetic variance explained by the genome level significant QTL for CT traits and meat quality traits*

Trait	Chromosome	Families significant	Effect ±SE	%Phenotypic Variance due to QTL	%Genetic Variance due to QTL
Flavour (units)	1	S1, S3, S4, S6	1.89±0.65	10.3	41.0
Muscle density LV5-TV8	2	S3, S4	1.51±0.28	14.4	39.5
Redness (a*) (units)	3	S1	1.91±0.58	14.8	20.1
Slaughter live weight (kg)	1	S3, S4, S8	1.29±0.28	35.4	7.40
Cold carcass weight (kg)	5	S3, S4, S5	1.22±0.27	23.2	49.3
Muscle density ISC	3	S1, S6	1.51±0.41	4.10	12.5
Bone density ISC	1	S2, S3, S5	1.14±0.26	5.40	13.8
Hot carcass weight (kg)	5	S3, S4, S5	1.20±0.27	23.2	49.2

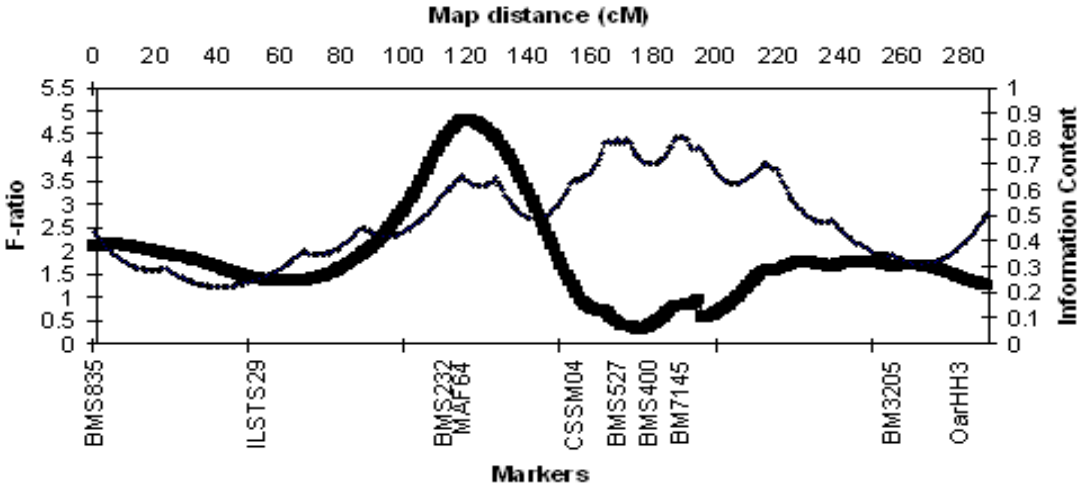

Figure 1: F-ratio profile for across-family QTL on sheep chromosome 1, affecting flavour (thick line), and information content (thin line). Marker positions are indicated on the lower X-axis and map distances in cM are shown on the upper X-axis.

Confidence intervals for the most significant QTL at the genome-wise level are explored in Table 3. The one- and two-LOD support intervals were on average 17 and 41 cM long, respectively. The QTL for flavour, muscle density, bone density, redness and slaughter live weight all show reasonably tight confidence intervals as assessed by the LOD-drop method. As expected, the bootstrap confidence intervals are wider, often covering the majority of the chromosome.

Table 3 *Confidence intervals for QTL significant at the 5% genome-wise level*

Trait	LOD Score	1 LOD CI (95% CI)	2 LOD CI (99% CI)	Bootstrap C.I.	Position, (cM)	Chromosome
Flavour (units)	8.79	111-131	106-136	5-269	119	1
Muscle density LV5-TV8	6.60	17-40	7-49	6-227	28	2
Redness (a*) (units)	6.20	106-117	93-125	63-205	113	3
Cold carcass weight (kg)	6.06	0-15	0-21	0-133	0	5
Muscle density ISC	6.05	158-195	149-205	83-197	172	3
Bone density ISC	6.03	246-279	234-287	0-287	261	1
Hot carcass weight (kg)	5.78	0-15	0-21	0-139	0	5
Slaughter live weight (kg)	5.31	218-239	209-287	117-287	229	1

Discussion

This study has successfully identified 20 significant QTL for a range of meat quality and carcass traits. Of these, eight were genome-wise significant and 12 chromosome-wise significant (Table 1). Thus, even with highly stringent significance thresholds, convincing QTL have been found for various definitions of carcass and live weight, for flavour, meat colour, muscle density, muscle area, bone area and bone density. The last trait, bone density, possibly has a lesser relevance to meat production but it may be of particular importance as an animal model for osteoporosis. The eight discrete traits that are significant at the genome-wise level (Table 3) all have tight confidence intervals.

Chromosome 1. Chromosome 1 was chosen because of the presence of the transferrin gene at 272cM, which has been shown to be associated with growth effects (Kmiec, 1999). Five QTL were found to be segregating on chromosome 1 in this Blackface sheep population. The half-sib analysis found genome-wise significant QTL for flavour, slaughter live weight, bone density (ISC) and hot carcass weight and yellowness of meat were significant at the chromosome-wise level. Regarding the QTL for the most significant trait, flavour, there is no published information available on meat flavour in sheep or other species except for studies being done in pigs for 'boar taint' traits (androstenone, indole and skatole). The first study by Quintanilla *et al.* (2003), who recorded laboratory measurements of androstenone in the fat at several ages, but not included sensory panel evaluations, showed evidence for QTL for fat androstenone level on pigs' chromosomes 4 and 7. A second study by Lee *et al.* (2004) identified QTL for boar flavour traits, as detected by sensory panel evaluations, in the same or adjacent marker intervals as the QTL for the laboratory estimate of androstenone on pigs' chromosome 6. The QTL affecting slaughter live weight on chromosome 1 corresponds to QTL for live weight previously detected in Charollais sheep by (McRae *et al.,* 2005). The QTL for bone density was detected at 261cM near the transferrin region. Also, analyses of the phenotypes showed that the FAT line had significantly denser bone than the LEAN line (Karamichou *et al.,* 2005 submitted). This result was in agreement with the study by Campbell *et al.* (2003), for detecting the QTL for bone mineral density (BMD) in Coopworth sheep, who showed that bone density across lines was correlated with the amount of fat (subcutaneous, intramuscular, internal and total) ($p<0.01$), the amount of muscle ($p<0.01$) and the body weight ($p<0.01$). Body weight and fat and muscle components are also correlated with bone density in humans. Low BMD has been shown to be an important factor in osteoporotic fracture risk in humans (Cummings *et al.,* 1990). A number of QTL contributing to genetic variation in BMD were identified in that study. These results along with the present study indicate that bone density is a subject of importance for body composition studies in sheep.

Chromosome 2. A QTL on chromosome 2 for muscle density (LV5-TV8) was detected near the CSSM47 marker. Muscle density is related to intramuscular fat and the phenotype analysis of the FAT and LEAN lines, revealed that the FAT line had a lower muscle density than the LEAN line and this suggest more intramuscular fat, as fat is less dense tissue than muscle (results not shown) (Karamichou *et al.,* 2005 submitted). The evidence for a QTL on chromosome 2 affecting slaughter live weight was only significant

at chromosome-wise level, but it was located 23cM distal to the myostatin locus, responsible for the double muscling phenotype in cattle. Chromosome 2 was chosen for the mounting evidence of one or several QTL for carcass composition segregating around the myostatin locus (Broad *et al.,* 2000 and Walling *et al.,* 2001). However, the region covered by the one LOD support interval for muscle density is approximately 200cM proximal from the region around myostatin in which growth effects have been observed.

Chromosome 3. Two QTL were found on chromosome 3, one for each of muscle density (ISC) and redness of meat. The QTL affecting muscle trait and redness were located 55cM and 114cM, respectively, proximal to the *insulin-like growth factor I gene (IGF1)*, again excluding the candidate locus this chromosome was chosen for, IGF1 at 227cM. Other studies have identified QTL for carcass traits in homologous regions of chromosome 5 in cattle. The detected QTL for redness of meat was unique for sheep population as, so far, there are no studies available that concern meat quality traits in sheep. However, there some studies being done in pigs. De Koning *et al.* (2001) have found a suggestive QTL for redness in meat on chromosome 13 in pigs. Again in the phenotype study of that trait, the results showed that as lamb fatness increased the colour of meat became lighter (results not shown) (Karamichou *et al.,* 2005 submitted). Thus, there is evidence to support the existence of a QTL for growth and carcass traits on that chromosome, while further studies will be needed to ascertain whether the same gene or genes is/are responsible for the expression of the traits in different species.

Chromosome 5. The presence of three QTL, for cold and hot carcass weight and muscle areas, were observed on chromosome 5. The QTL for hot and cold carcass was located at 0cM, i.e. at the beginning of the mapped region of the chromosome, while the QTL for muscle areas was located at 116cM, near to the calpastatin region (139cM). It has been reported by Shackelford *et al.* (1994) that the decreased tenderness of meat seems to be highly related to increased calpastatin activity.

Chromosome 18. Another significant region detected in the half-sib analyses was on chromosome 18. Chromosome 18 contains the Callipyge gene (Cockett *et al.,* 1994), the rib-eye muscling locus (Nicholl *et al.,* 1998) and the Texel muscling QTL (Walling *et al.,* 2004). Two QTL were detected in that chromosome, one for lightness of meat and one for bone area (LV5). Both these QTL were located very close to the callipyge region, but biological inferences are difficult to draw for this result.

Chromosome 20. Four QTL for lightness of meat, bone areas (TV8 and LV5) and bone density, were identified on chromosome 20. The major histocompatibility complex (MHC) is located on sheep chromosome 20, and contains genes coding for antigen presentation, i.e. it is critical to the acquired immune response. Studies in cattle (Elo *et al.,* 1999) and pigs (Walling *et al.,* 1998) have found effects for growth and fatness in homologous regions of their genomes. Biological links between acquired immunity and bone and meat attributes are currently not obvious to us.

In summary, this study has been successful in detecting QTL, that meet highly stringent significance thresholds, for a range of meat quality and carcass traits, including carcass and live weight, flavour, meat colour, muscle density, muscle area, bone area and bone density. Bone density, may have a lesser relevance to meat production but it may be of particular importance as an animal model for osteoporosis. These QTL offer several possibilities to breed sheep for altered or improved meat quality. However, verification of these results in independent populations is required first. Furthermore, the QTL study will be extended to a wider range of meat quality traits, including chemical carcass composition, fatty acid profiles and taste panel assessments. Future work aims to evaluate and refine possible alternative breeding goals and selection strategies for meat quality traits.

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