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Genetic analyses and quantitative trait loci detection, using a partial genome scan, for intramuscular fatty acid composition in Scottish Blackface sheep[1]

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ABSTRACT: Genetic parameters for LM fatty acid composition were estimated in Scottish Blackface sheep, previously divergently selected for carcass lean content (LEAN and FAT lines). Furthermore, QTL were identified for the same fatty acids. Fatty acid phenotypic measurements were made on 350 male lambs, at approximately 8 mo of age, and 300 of these lambs were genotyped across candidate regions on chromosomes 1, 2, 3, 5, 14, 18, 20, and 21. Fatty acid composition measurements included in total 17 fatty acids of 3 categories: saturated, monounsaturated, and polyunsaturated. Total i.m. fat content was estimated as the sum of the fatty acids. The FAT line had a greater i.m. fat content and more oleic acid, but less linoleic acid (18:2 n-6) and docosapentaenoic acid (22:5 n-3) than did the LEAN line. Saturated fatty acids were moderately heritable, ranging from 0.19 to 0.29, and total SFA were highly heritable (0.90). Monounsaturated fatty acids were moderately to highly heritable, with *cis*-vaccenic acid (18:1 n-7) being the most heritable (0.67), and total MUFA were highly heritable (0.73). Polyunsaturated fatty acids were also moderately to highly heritable; arachidonic acid (20:4 n-6) and CLA were the most heritable, with values of 0.60 and 0.48, respectively. The total PUFA were moderately heritable (0.40). The QTL analyses were performed using regression interval mapping techniques. In total, 21 chromosome-wide QTL were detected in 6 out of 8 chromosomal regions. The chromosome-wide, significant QTL affected 3 SFA, 5 MUFA, and 13 PUFA. The most significant result was a QTL affecting linolenic acid (18:3 n-3) on chromosome 2. This QTL segregated in 2 of the 9 families and explained 37.6% of the phenotypic variance. Also, 10 significant QTL were identified on chromosome 21, where 8 out of 10 QTL were segregating in the same families and detected at the same position. The results of this study demonstrate that altering carcass fatness will simultaneously change i.m. fat content and oleic, linoleic, and docosapentaenoic acid content. The heritabilities of the fatty acids indicate opportunities for genetically altering most fatty acids. Moreover, this is the first report of detection of QTL directly affecting fatty acid composition in sheep.

Key words: fatty acid, genetic parameter, intramuscular fat, quantitative trait locus, sheep

INTRODUCTION

Sales of meat in many countries have remained static or fallen slightly in recent years. In the United Kingdom and other countries, red meat (beef and lamb) has been less popular than poultry (Wood et al., 1999). These changes have led to a reappraisal of factors influencing the appeal of meat to consumers, which together constitute quality. These include freedom from microbiological hazards, sensory appeal of meat and perceived healthiness (Wood et al., 1998). There is particular concern over the fat content of the human diet, with calls for fat intake to be reduced, as it impacts human cardiovascular diseases, obesity, and cancer (Simopoulos, 2001).

Sheep meat has been criticized because of high concentration of SFA, presumed to increase the risk of heart disease, and a low PUFA to SFA ratio (Enser et al., 1996). Recently, nutritionists have focused on the types of PUFA that lower blood cholesterol concentrations, and the balance in the diet between n-3 PUFA formed from linolenic acid (18:3) and n-6 PUFA formed from linoleic acid (18:2; Williams, 2000).

Fatty acid composition is influenced by both genetic and environmental factors. Genetic factors have not been widely investigated in sheep, and it is not known whether fatty composition can be genetically manipulated toward a more favorable profile. In this paper, we studied muscle fatty acid composition because i.m. fat cannot be easily removed and, thus, inevitably has an impact on human health.

The aims of this study were, first, to investigate the inheritance of fatty acid composition in sheep meat; second, to estimate genetic relationships between fatty acids and computer tomograph-assessed muscle density (a visual predictor of i.m. fatness); and third, to identify QTL for fatty acid composition, as a means to determine options for genetically improving the fatty acid profile of sheep meat.

MATERIALS AND METHODS

Animals

All experiments were undertaken in accordance with the UK Animals (Scientific Procedures) Act 1986, under project license PPL60/2639.

Blackface lambs born at Roslin Institute's Blythbank farm, Scotland, during the period 2000 to 2003, were used as the experimental resource. These lambs were from a flock that had been divergently selected for carcass lean content from 1988 to 1996, creating LEAN and FAT lines, after which the lines were maintained as closed populations with no further selection. A description of the selection procedures and initial responses to selection is given by Bishop (1993).

The flock consisted of 200 ewes, split approximately equally between the LEAN and FAT lines. A small proportion of reciprocal LEAN × FAT-line crosses were made at the 1999 matings, so that a cohort of F_1 lambs was born in April 2000, along with a majority of purebred LEAN- and FAT-line lambs. The male F_1 lambs were then backcrossed to the purebred LEAN- and FAT-line ewes to create a population of F_1 × LEAN and F_1 × FAT lambs from 2001 to 2003, for the purpose of QTL detection. This design created 9 half-sib families for QTL detection. On average, families contained 33 male offspring for measurement of fatty acids traits, as described below, with a range from 12 to 46.

Standard husbandry procedures were applied in this flock; all lambs were tagged at birth, with parentage, day of birth, gender, and mortalities recorded. Each year the lambs were kept in 2 groups (i.e., on 2 separate fields) for ease of management. Parentage information was maintained for all animals born after 1986, giving a total of 4,847 known animals in the flock pedigree. Male lambs were not castrated.

Phenotypic Measurements

Phenotypic measurements of fatty acids were made on three hundred fifty 8-mo-old, male, grass-fed lambs, composed of 300 male lambs from the 9 backcross families, plus 25 LEAN- and 25 FAT-line male lambs born in 2000. Measurements were performed at the University of Bristol, on cohorts of 20 animals treated identically during their growth, transportation, and pre-slaughter periods.

Lipids were extracted from duplicate 10-g samples of LM, essentially as per Folch et al. (1957), separated into neutral and phospholipid, saponified and methylated, and individual fatty acids were separated by column chromatography and quantified as described by Demirel et al. (2004). Total fatty acids (as used in this study) was taken as the sum of all the phospholipid and neutral lipid fatty acids quantified. Total fatty acids included some unassigned fatty acids.

Fatty acid results are reported for major fatty acids and minor identifiable fatty acids relevant to the study. As a result of incomplete resolution, the *trans*-18:1 isomers are reported as a single value that does not include minor isomers (*trans*-13, *trans*-16-18:1) not resolved from *cis*-18:1n-9 and *cis*-18:1n-7. In addition to the minor crosscontamination of the latter 2 fatty acids, the fatty acid listed as *cis*-16:1 consists of n-9 and n-7 isomers. Fatty acid data are presented as weight of fatty acids, in milligrams, per 100 g of muscle tissue.

Additional phenotypic measurements of carcass composition and meat quality were also taken on this population of lambs (Karamichou et al., 2006a). In particular, computerized tomography (**CT**) assessments of carcass composition were obtained on these lambs at 5 mo of age, plus 350 females from the same families. From each scan image, the areas and image densities were obtained for the fat, muscle, and bone components of the carcass. Our previous study (Karamichou et al., 2006a) showed that muscle density was highly heritable and also was correlated with many meat quality traits influenced by i.m. fat content. Thus, we assessed phenotypic and genetic correlations of muscle density with fatty acids.

Genotyping

The DNA was extracted from blood samples for the 9 sires and their 300 progeny for a partial genome scan covering chromosomes 1, 2, 3, 5, 14, 18, 20, and 21. These 8 chromosomes were chosen because previous work had revealed QTL affecting meat and carcass traits on these chromosomes in sheep or on equivalent regions in other species (Nicoll et al., 1998; Walling et al., 1998a; Elo et al., 1999; Freking et al., 1999; Kmiec, 1999; Stone et al., 1999; Broad et al., 2000; Freking et al., 2002).

Informative marker panels were developed separately for each sire, containing an average of 16, 8, 10, 6, 7, 6, 7, and 4 informative microsatellite markers per sire on chromosomes 1, 2, 3, 5, 14, 18, 20, and 21, respectively. Initially, each sire was genotyped for all available microsatellite markers across each candidate region, and heterozygous markers were then selected

at approximately 10-cM intervals, wherever possible. All offspring were subsequently genotyped for selected markers that were heterozygous in their sire. In total, 139 markers were included in this study.

Data Analysis

All fatty acid measurement traits were right-skewed and were therefore log-transformed before further analysis. Restricted maximal likelihood methods were used to estimate variance components using an animal model, fitting the complete pedigree structure (4,847 animals), using the ASReml package (Gilmour et al., 2004). The fixed effects included in this analysis were year of birth (2000, 2001, 2002, and 2003), management group (1 or 2), litter size (1 = single or 2 = twins and triplets), and year × slaughter day (15 classes). Triplets comprised proportionately less than 0.02 of the data, and hence were combined with the twin lambs in the litter size classification. The only significant interaction was between year and group.

Heritability estimates were calculated for each log-transformed fatty acid, for total SFA (i.e., the sum of the saturated fatty acids), for total MUFA, and for total PUFA, using a bivariate analysis with CT-assessed muscle density. These analyses also yielded genetic and phenotypic correlations between each fatty acid measurement and muscle density.

Line Effects. To estimate genetic differences between the LEAN and FAT lines for each trait, using all of the data rather than just the 50 pure-line lambs, true line effects were estimated as the generalized least squares solutions to equations describing the genetic composition of each line or cross. Details of the methodology for predicting means and variances for line categories have been provided elsewhere (Karamichou et al., 2006a). Line effects were estimated using untransformed fatty acid data.

QTL Analysis

The QTL analysis was performed on the log-transformed data for each fatty acid, and for the 3 categories of total fatty acids (SFA, MUFA, and PUFA).

Map Construction. Linkage analysis was carried out with the CriMap program, option build (Green et al., 1990). Marker locations were in close agreement with previous studies (Maddox et al., 2001). In cases in which there was a disagreement with the published linkage map, the marker order was checked using the CriMap flips option. The marker order with the greatest likelihood was chosen to create a consensus linkage map that was used in subsequent QTL analyses.

QTL Detection. Marker information contents were obtained as in Knott et al. (1998). A regression method for QTL detection was applied according to Knott et al. (1996). The analysis used the multimarker approach for interval mapping in half-sib families. The method contained the following steps: for each offspring the

probability of inheriting a particular sire haplotype was calculated at 1-cM intervals conditional on the linkage phase of the sire and marker genotypes of the individual and its sire. For a given position, the conditional probabilities of the offspring provided independent variables on which the trait score can be regressed. Therefore, the regression model, in which fixed effects were simultaneously fitted, may be represented as

$$y_{ij} = a_i + b_{ik}p_{ijk} + e_{ij}, \qquad [1]$$

where y_{ij} denotes the trait score of the jth individual originating from sire i; a_i is the average effect for half-sib family i; b_{ik} is the effect of one of the paternal haplotypes at interval k within half-sib family i; p_{ijk} is the probability for individual j of inheriting the first paternal haplotype at interval k conditional on the marker genotypes; and e_{ij} is the residual effect for individual j. Fixed effects fitted in these analyses were those found to be significant, for each trait, by the variance analysis. To remove possible body size effects, fatty acids were also corrected for carcass weight at slaughter and the QTL reestimated.

For each regression, an F-ratio of the full model including the inheritance probabilities vs. the same model without the inheritance probabilities was calculated across families. In a 1-QTL model, the location with the largest F-ratio was taken to be the best estimated position for a QTL for each trait.

Size of QTL Effects. For cases where QTL effects were significant, the within-sire substitution effects were obtained for each sire. The average substitution effect was calculated for those sires that showed significant evidence of a segregating QTL (i.e., for which the sire-specific t-statistic was nominally significant at $P < 0.05$).

For single-QTL analyses, the proportion of the phenotypic variance explained by the QTL ($\sigma^2_{QTL}/\sigma^2_P$) was calculated as $4 \times [(1 - \text{Mean Square}_{\text{full}})/\text{Mean Square}_{\text{reduced}}]$ (Knott et al., 1996), where σ^2_{QTL} is the additive variance at the QTL.

Significance Threshold. Chromosome-wide empirical threshold values of the test statistics from the regression analysis, at and $\alpha = 0.05$ chromosome level, were estimated with the permutation test procedure of Churchill and Doerge (1994). The thresholds varied between chromosomes depending on their length and the markers they contain.

Confidence Intervals. Bootstrap confidence intervals were estimated, as described by Visscher et al. (1996). Additionally, 95% support intervals for QTL location were obtained using the 1-LOD drop approximation (Lander and Botstein, 1989).

Two-QTL Model. Once a single QTL on a chromosome had been identified, the presence of a second QTL was investigated by performing a grid search at 1-cM intervals. The 2-QTL model was accepted if there was a significant improvement over the best possible 1-QTL model at $P < 0.05$ using a variance ratio (F) test with

Table 1. Line means (mg/100 g), line differences[1] (with SED), and trait phenotypic SD for LM fatty acids

Fatty acid	FAT Line	LEAN Line	Line difference (FAT − LEAN)[2]	SED	SD
Saturated					
Myristic acid–14:0	86.27	62.0	**24.3**	1.93	62.0
Palmitic acid–16:0	515.1	509	6.1	4.44	515.1
Stearic acid–18:0	405.4	389.1	**16.3**	2.20	405.4
Monounsaturated					
Palmitoleic acid–*cis* 16:1 (n-7, n-9)	54.78	55.92	−1.14	1.42	19.07
Oleic acid–*cis* 18:1 n-9	820.6	768.8	**51.8**	4.68	286
Cis-Vaccenic acid–*cis* 18:1 n-7	13.55	13.5	0.05	0.73	13.55
Vaccenic acid–*trans* 18:1 n-7	90.92	87.59	3.33	2.00	39.57
Gadoleic acid–20:1	1.726	1.806	−0.08	0.25	0.654
Polyunsaturated					
Linoleic acid–*cis* 18:2 n-6	92.07	86.98	**5.09**	0.22	22.8
Linolenic acid–*cis* 18:3 n-3	39.47	40	−0.53	0.68	12.6
Dihomo-γ-linolenic acid–20:3 n-6	3.894	3.518	0.376	0.27	0.76
Arachidonic acid–20:4 n-6	34.36	32.46	**1.90**	0.85	6.95
EPA (Eicosapentanoic acid)–20:5 n-3	29.93	28.14	1.79	1.11	6.69
Adrenic acid–22:4 n-6	1.138	1.007	0.131	0.19	0.33
DPA (Docosapentaenoic acid)–22:5 n-3	26.73	24.59	**2.14**	0.55	5.52
DHA (Docosahexaenoic acid)–22:6 n-3	9.328	9.242	0.086	0.41	2.78
Conjugated					
CLA–9-*cis*, 11-*trans* 18:2	32.89	36.67	**−3.78**	1.30	15.2
Total	2,258	2,150	**108**	7.80	795

[1]Line differences were estimated using the raw fatty acid data.
[2]Significant ($P < 0.05$) line differences are shown in bold.

2 df (for the additional additive effect and position estimated for the second QTL) as an approximate significance test.

RESULTS

Summary Statistics

Summary statistics and estimated line differences for the fatty acid content of LM are shown in Table 1. Concentrations of linoleic acid, arachidonic acid, and docosapentaenoic acid (**DPA**; 22:5 n-3) were lower in the LEAN line. The FAT line had a higher concentration of i.m. fat (total fatty acids) than the LEAN line. Significant trends were also seen for myristic and stearic acid, with the FAT line having higher concentration of saturated fatty acids than did the LEAN line. The FAT line also had a higher content of oleic acid than the LEAN line, whereas CLA was at a lower concentration in the FAT line.

Genetic Parameters

Heritability estimates for fatty acids are shown in Table 2. Almost all of the fatty acids were moderately heritable, with the exception of *cis*-vaccenic, vaccenic, CLA, and arachidonic acid, which were highly heritable. Traits describing combinations of fatty acids (i.e., total SFA, MUFA, and PUFA) were generally moderately to highly heritable.

Phenotypic and genetic correlations between average muscle density and fatty acids are also presented in Table 2. Phenotypic correlations were low, except for i.m. fat content, which was strongly negatively correlated with muscle density. Genetic correlations tended to be stronger than the phenotypic correlations. In particular, muscle density was strongly negatively genetically correlated with vaccenic acid, CLA, i.m. fat content, total MUFA, and total PUFA. Genetic correlations with the proportions of total fatty acids that were SFA, MUFA, and PUFA were −0.23, −0.54, and 0.39, respectively.

QTL Results

A total of 21 QTL, significant at chromosome-wide level, were detected in 6 out of 8 chromosomal regions, for 14 out of 17 fatty acids, and for every category of fatty acid. All families produced evidence for significant QTL in 1 or more regions. A summary of the chromosome-wide significant QTL, along with the proportions of variance attributable to the QTL and the confidence intervals for QTL location are presented in Table 3. The profile for the QTL affecting linolenic acid is shown in Figure 1. Results for fatty acids corrected for live weight were essentially identical to those for uncorrected fatty acids. Additionally, the 2-QTL analyses never gave a significantly better fit than the single QTL analyses; hence, all results presented in Table 3 are from the single QTL analyses.

Table 2. Bivariate heritabilities (h^2) for LM fatty acids, and phenotypic and genetic correlations of LM fatty acids with CT-assessed muscle density[1]

Fatty acid	h^2 (s.e.)	Phenotypic correlation (SE)	Genetic correlation (SE)
Saturated			
Myristic acid–14:0	0.19 (0.14)	0.01 (0.06)	−0.09 (0.15)
Palmitic acid–16:0	0.29 (0.17)	−0.07 (0.07)	−0.30 (0.10)
Stearic acid–18:0	0.24 (0.15)	−0.01 (0.06)	−0.10 (0.16)
Monounsaturated			
Palmitoleic acid–*cis* 16:1 (n-7, n-9)	0.31 (0.18)	0.02 (0.07)	−0.17 (0.15)
Oleic acid–*cis* 18:1 n-9	0.27 (0.17)	−0.02 (0.07)	−0.30 (0.15)
Cis-Vaccenic acid–*cis* 18:1 n-7	0.67 (0.16)	−0.35 (0.06)	−0.47 (0.14)
Vaccenic acid–*trans* 18:1 n-7	0.49 (0.17)	−0.11 (0.07)	−0.50 (0.18)
Gadoleic acid–20:1	0.30 (0.17)	0.01 (0.07)	−0.24 (0.15)
Polyunsaturated			
Linoleic acid–*cis* 18:2 n-6	0.10 (0.09)	−0.19 (0.06)	−0.45 (0.14)
Linolenic acid–*cis* 18:3 n-3	0.30 (0.02)	0.01 (0.07)	−0.24 (0.15)
Dihomo-γ-linolenic acid–20:3 n-6	0.12 (0.10)	−0.05 (0.06)	−0.22 (0.13)
Arachidonic acid–20:4 n-6	0.60 (0.17)	0.08 (0.07)	0.28 (0.18)
EPA (Eicosapentanoic acid)–20:5 n-3	0.21 (0.13)	0.01 (0.06)	−0.35 (0.16)
Adrenic acid–22:4 n-6	0.22 (0.13)	−0.09 (0.06)	0.12 (0.15)
DPA (Docosapentaenoic acid)–22:5 n-3	0.13 (0.12)	0.12 (0.06)	0.12 (0.12)
DHA (Docosahexaenoic acid)–22:6 n-3	0.16 (0.10)	−0.14 (0.06)	−0.47 (0.15)
Conjugated			
CLA–9-*cis*, 11-*trans* 18:2	0.48 (0.16)	−0.15 (0.06)	−0.60 (0.17)
Total fatty acid	0.32 (0.09)	−0.57 (0.04)	−0.67 (0.14)
SFA	0.90 (0.16)	−0.30 (0.06)	−0.45 (0.14)
MUFA	0.73 (0.18)	−0.35 (0.06)	−0.60 (0.13)
PUFA	0.40 (0.16)	−0.26 (0.06)	−0.56 (0.17)

[1]Heritabilities, and phenotypic and genetic correlations were estimated using transformed fatty acid data.

The QTL tended to be observed for individual fatty acids, rather than totals. In fact, the only QTL for combinations of fatty acids was for PUFA on chromosome 1. Bootstrapped confidence intervals were very large, typically covering the whole chromosome; however, it is known that this technique produces conservative intervals around areas of higher marker density (Walling et al., 1998b; 2002) and typically produces intervals covering the whole chromosome. The 1-LOD drop 95% support intervals (results not shown) were much smaller, typically 37 cM on average, ranging from 5 to 84 cM.

The most remarkable results were on chromosome 21 where 10 significant QTL were identified. Five of these were at position 58 cM, and a further 3 at position 57 cM. Moreover, apart from arachidonic acid, these QTL all segregated in the same families (S3 and S7). However, these individual fatty acids were not necessarily strongly correlated with each other. Residual correlations between the individual fatty acids were calculated as an approximation of phenotypic correlations. The correlations were seldom strong, ranging from 0.03 to 0.50.

DISCUSSION

This study has produced novel information on the genetic control of fatty acid composition in sheep. The heritabilities indicate opportunities for genetically altering fatty acid composition, and the genetic correlations with muscle density suggest a means of genetic selection using in vivo measurements. Additionally, the study was successful in identifying 21 QTL for a range of fatty acids. The QTL tended to be for the individual fatty acids rather than for trait combinations, and QTL were found for each category of fatty acid (i.e., SFA, MUFA, and PUFA).

Line Differences

Selection for increased leanness changed some aspects of fatty acid composition; the FAT line had a significantly higher i.m. fat content (total fatty acids), and a higher content of stearic (18:0), oleic (18:1 n-9), linoleic (18:2 n-6), and DPA (22:5 n-3) fatty acids than the LEAN line. Stearic acid accounts for 18% of the total fatty acid in lamb meat (Rhee, 1992; Enser et al., 1996). Several studies have shown that stearic acid is essentially neutral in its effects on serum total cholesterol, similar to oleic acid (Bonanome and Grundy, 1988; Zock and Katan, 1992; Kris-Etherton et al., 1993; Grundy, 1994; Judd et al., 2002). It is not clear why dietary stearic acid does not raise human serum cholesterol level as do other SFA. Oleic acid is the primary MUFA in lamb meat and accounts for about 32% of the total fatty acids (Rhee, 1992; Enser et al., 1996). Available

Table 3. Most likely locations and effects of QTL detected for LM fatty acids

Fatty acid	Chromosome	Location (cM)[1]	F-ratio 5% threshold[2]	F-ratio 1 vs. 0 QTL	Estimated effect[3] Additive (SE)	Families significant	% of phenotypic variance[4]
Saturated							
Myristic acid–14:0	21	57 (6, 100)	3.02	3.14	3.03 (1.03)	S3, S7	26.1
Palmitic acid–16:0	21	57 (0, 100)	2.94	3.17	3.03 (1.03)	S3, S7	29.0
Stearic acid–18:0	21	58 (0, 85)	3.13	3.25	2.81 (1.00)	S3, S7	30.1
Monounsaturated							
Palmitoleic acid–cis 16:1 (n-7, n-9)	5	12 (0, 139)	2.63	2.77	1.07 (0.24)	S1, S5, S7	27.5
Oleic acid–cis 18:1 n-9	21	58 (0, 90)	2.98	3.23	2.80 (1.00)	S3, S7	27.2
Cis-Vaccenic acid–cis 18:1 n-7	21	58 (0, 85)	2.99	3.26	2.81 (1.00)	S3, S7	30.2
Gadoleic acid–20:1	21	21 (0, 106)	3.03	3.49	2.39 (1.31)	S3, S7	33.1
	18	97 (23, 105)	2.01	2.38	0.82 (0.23)	S2, S3, S9	18.4
Polyunsaturated							
Linoleic acid–cis 18:2 n-6	21	58 (0, 85)	3.14	3.22	2.80 (1.00)	S3, S7	29.7
Linolenic acid–cis 18:3 n-3	2	269 (6, 294)	2.89	3.97	1.66 (0.31)	S1, S8	37.6
	21	57 (0, 88)	3.08	3.17	3.03 (1.04)	S3, S7	29.1
Arachidonic acid–20:4 n-6	21	58 (0, 72)	2.41	3.84	3.61 (0.32)	S5	20.3
	2	21 (0, 250)	2.73	2.75	1.62 (0.37)	S1, S3, S4	36.1
EPA (Eicosapentanoic acid)–20:5 n-3	2	229 (6, 294)	2.70	3.05	1.34 (0.16)	S5, S8, S9	28.1
	1	79 (50, 280)	3.00	3.02	2.09 (0.45)	S1, S8	26.6
DPA (Docosapentaenoic acid)–22:5 n-3	1	168 (50, 286)	3.19	3.52	1.63 (0.35)	S2, S6	32.7
	2	87 (6, 290)	3.32	3.49	1.60 (0.32)	S2, S3, S6	32.2
	21	0 (0, 107)	2.66	3.07	2.71 (0.65)	S6, S7	27.9
DHA (Docosahexaenoic acid)–22:6 n-3	18	105 (25, 107)	2.31	2.32	0.94 (0.25)	S4, S8	24.2
CLA	3	159 (83, 205)	2.51	3.22	1.50 (0.40)	S2	28.6
PUFA	1	85 (56, 286)	2.59	2.84	1.87 (0.41)	S1, S8	23.9

[1]The 95% confidence intervals by bootstrap analysis are given in parentheses. The QTL were classified as significant at the 5% chromosome-wide level.

[2]The chromosome-specific 5% F-value thresholds estimated via permutation analyses.

[3]The additive effects are given as the average effects within significant families.

[4]The proportion of phenotypic variance explained by the QTL is given as $\sigma^2_{QTL}/\sigma^2 p$.

evidence indicates that, whereas the shorter chain saturated fatty acids raise human serum cholesterol concentrations, the monounsaturated oleic acid does not (Denke, 1994). The fatty acid composition of muscle influences important components of meat quality, such as meat flavor, flavor liking, and overall acceptability. In the study of Cameron et al. (2000), where the effects of genotype, diet, and their interaction on fatty acid composition of i.m. fat in pigs were examined, it was found that linoleic acid was positively correlated with pork flavor (0.33), taste panel-assessed flavor liking (0.23), and overall acceptability (0.23), whereas DPA was negatively correlated with pork flavor (–0.30), flavor liking (–0.33) and overall acceptability (–0.30). In particular, linoleic acid (18:2 n-6), which is low in ruminant tissues (Wood et al., 1999; about 3.5% of total fatty acids), is a plant fatty acid that can be transformed to conjugate linolenic acid by bacteria in the rumen (Kepler et al., 1966). This low level of linoleic acid causes the polyunsaturated:saturated fatty acid ratio (an important nutritional index) to be below the recommended dietary value, which is 0.45 (Department of Health, 1994).

The LEAN line had more CLA than the FAT line, in agreement with the results of Wachira et al. (2002) in a comparison between (lean) Soay and (relatively fat) Suffolk breeds. Interest in CLA research has increased in the past few years as a result of reports of CLA consumption providing several health benefits (Kramer et al., 1998). Because plants do not synthesize CLA, ruminant fats in meat are the primary dietary source of CLA for humans (Herbein et al., 2000). It has been found that CLA has positive effects of reducing cardiovascular risk, protecting against atherosclerosis, is anticarcinogenic, reduces intake, reduces body content of adipose tissue and lipid, and enhances the immune system (Cook et al., 1993; Ip et al., 1994; Lee et al., 1994; Nicolosi et al., 1997; West et al., 1998). In summary, these results show that, as the lamb becomes leaner, the PUFA of muscle increase and, in particular, quantities of the beneficial CLA increase.

Inheritance of Fatty Acids

The heritability estimates for most of the fatty acids measured in this study indicate that there is substantial genetic variation in these traits, such that fatty acid composition can potentially be improved, probably through indirect selection. In particular, SFA were moderately heritable. The additive genetic coefficient
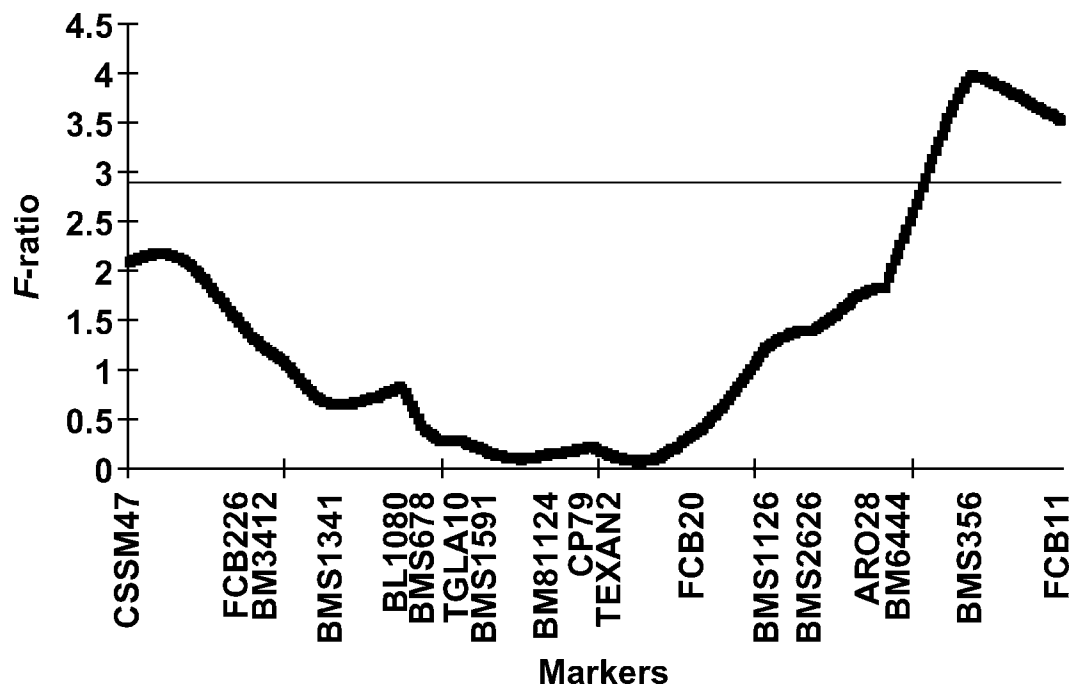
Figure 1. *F*-ratio profile for across-family QTL on sheep chromosome 2, affecting linolenic acid (18:3 n-3) in LM. Marker positions are indicated on the lower X-axis. The thin horizontal line indicates the 5% chromosome-wide significance threshold.

of variation for these traits was 0.45 for myristic and 0.09 for palmitic and stearic acids (results not shown), indicating that genetic alteration of these fatty acids is feasible. Due to lack of information on heritabilities of fatty acids in sheep, we will compare our results to published studies in other species. In pigs, heritability estimates for the content of palmitic and stearic fatty acids, obtained by Fernandez et al. (2003) for Iberian pigs, were 0.31 for palmitic and 0.41 for stearic acid. The estimate for palmitic acid is similar to the one obtained in the current study. The review by Sellier (1998) of 3 previous studies indicated that stearic acid had a higher heritability (0.51) than found in the current study.

The heritability estimates for monounsaturated fatty acids were high for *cis*-vaccenic (18:1 n-7), and vaccenic (*trans* 18:1 n-7) acid, and moderate for palmitoleic (16:1), gadoleic (20:1), and oleic (18:1 n-9) acid. In the study of Fernandez et al. (2003), the heritability of oleic acid was almost the same (0.30) as in our study.

The heritability of polyunsaturated fatty acids was variable with an average of 0.23. In pigs, Fernandez et al. (2003) and Sellier (1998) presented heritabilities for linoleic acid of 0.29 and 0.58, respectively. Linoleic acid appears to be more heritable in pigs than in sheep, although it should be noted that linoleic acid is much lower in ruminant tissues than in pigs and in all species is obtained from the diet rather than being synthesized in the animal. The rumen biohydrogenates a high proportion of linoleic and linolenic acid, reducing concentrations in body tissues (Wood et al., 1994; 1999). Significant heritabilities for fatty acids not synthesized by

the animal may be a result of different rates of fatty acid catabolism between animals.

Intramuscular fat (total fatty acids) was moderately heritable, although the value reported here is slightly lower than results from studies done in pigs. Malmfors and Nilsson (1979) obtained heritability estimates of 0.58 and 0.68 for Swedish Landrace and Large White pigs, respectively. Scheper (1979) reported a heritability estimate of 0.35 for German Landrace pigs, and a heritability of 0.55 was reported for Landrace pigs in Denmark (Just et al., 1986) and in Switzerland (Schworer et al., 1987). The average heritability weighted by number of sires for i.m. fat content from previous reports is 0.53 (Sellier, 1998).

The heritabilities of trait combinations were surprisingly high in our data set. One possible reason for this result is that, by combining correlated traits, the random measurement error or imprecision associated with individual fatty acids is reduced.

Relationships between Fatty Acids and Muscle Density

The results of our previous study (Karamichou et al., 2006a), where we estimated genetic parameters for carcass composition, assessed in the live animal, and meat quality traits in these same sheep, demonstrated that altering carcass fatness will simultaneously change muscle density and aspects of i.m. fat content. Hence, muscle density was chosen as the trait to be used for estimating phenotypic and genetic correlations
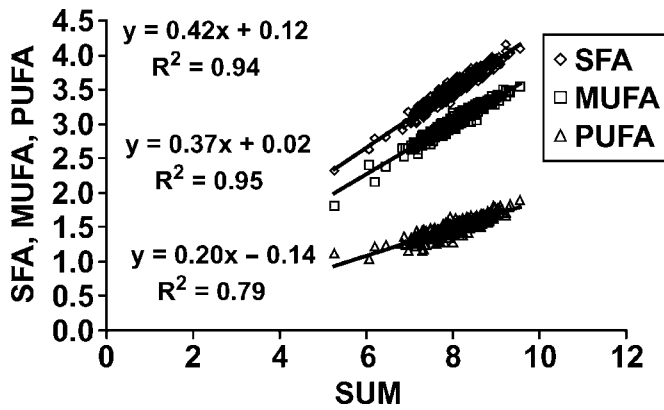
Figure 2. Relationships between total SFA, MUFA, and PUFA contents and their sum (mg per 100 g of muscle) in LM fat content.

with fatty acids, and we observed that muscle density was indeed strongly correlated with i.m. fat content.

There is no published information on genetic relationships between muscle density, assessed by CT, and fatty acids in any species. Genetic correlations of SFA and MUFA with muscle density were negative, with correlations involving vaccenic and *cis*-vaccenic acids being the strongest. Genetic correlations of polyunsaturated fatty acids with muscle density were mostly negative, except for arachidonic, adrenic, and DPA fatty acids. The CLA, docosahexaenoic acid, and linoleic fatty acids were strongly negatively correlated with muscle density. This result indicates that selection for decreased muscle density increases the concentration of CLA, docosahexaenoic acid, and linoleic fatty acids in lambs. In summary, selection to decrease muscle density, and hence increase i.m. fat, is expected to result in lamb meat with more total fatty acids, but proportionately increased MUFA and decreased PUFA. This is in accordance with the review of meat fatty acid composition by De Smet et al. (2004), where they reported that variation in fat content has an effect on fatty acid composition, independent of species or breed and dietary factors. Hence, the content of total SFA and total MUFA increases more rapidly with increasing fatness than does the content of total PUFA, leading to a decrease in the relative proportion of PUFA. This is shown at the phenotypic level in Figure 2.

Identified QTL

Chromosome 1 was chosen for study because of the presence of the transferrin gene, which has been shown to be associated with growth effects (Kmiec, 1999), at 272 cM. Significant QTL on this chromosome affected 2 individual long-chain fatty acids, the EPA (20:5 n-3) and DPA (22:5 n-3) acids, and the total PUFA. The QTL for DPA is at the same relative position as the meat color trait yellowness (b*), which was reported in an earlier publication on the same Blackface population

(Karamichou et al., 2006b). Regarding QTL for fatty acids in sheep populations, there in no comparable published information, although there have been some studies in pigs. The importance of the long-chain n-3 PUFA is that they are not incorporated into triacylglycerols to any important extent in ruminants, as they are in pigs (Wood et al., 1999). They are restricted to phospholipids (mainly in membranes) and, therefore, are found in muscle but not fat tissue, except at very low levels in the total lipid (Enser et al., 1996). This fact has important implications for PUFA supply in the diet of individuals consuming muscle and fat in the usual portions. Pig meat contributes about 80% of the total PUFA provided by pork, lamb, and beef, and about 60% of the n-3 PUFA, 50% coming from pig fat (Enser et al., 1996).

Chromosome 2 showed significant QTL for linolenic acid (18:3 n-3), DPA (22:5 n-3), EPA (20:5 n-3), and arachidonic acid (20:4 n-6). The QTL for linolenic acid mapped to the same position as slaughter live weight in these sheep (Karamichou et al., 2006b), and it was located 23 cM distal to the myostatin locus, which is responsible for the double muscling phenotype in cattle. Chromosome 2 was chosen for the mounting evidence of 1 or several QTL for carcass composition segregating around the myostatin locus (Broad et al., 2000; Walling et al., 2001; Johnson et al., 2005a,b; Clop et al., 2006). In the study of Clop et al. (2003), a significant QTL for linolenic fatty acid was identified on pig chromosome 12 (conservation of synteny with sheep chromosome 11). In the current study, the QTL on chromosome 2 affecting arachidonic fatty acid mapped to the same position as a QTL for muscle density in Blackface sheep (Karamichou et al., 2006b).

One QTL for CLA was found on chromosome 3, at 159 cM, excluding the candidate locus this chromosome was chosen for, IGF-I at 227 cM. The QTL for muscle density was also significant and mapped to a position (172 cM) close to the CLA fatty acid content QTL. The concentration of CLA in lamb muscle is important in human nutrition because it has been linked to a multitude of metabolic effects, including inhibition of carcinogenesis, reduced fat deposition, altered immune response, and reduced serum lipids (Mulvihill, 2001).

Another significant region was detected on chromosome 21. Remarkably, 8 significant QTL (Figure 3) for arachidonic (20:4 n-6), *cis*-vaccenic (18:1 n-7), stearic (18:0), oleic (18:1 n-9), linoleic (18:2 n-6), palmitic (16:1), linolenic (18:3 n-3), and myristic (14:0) fatty acids were mapped to the same position (57–58 cM), and gadoleic (20:1) acid and DPA (22:5 n-3) were mapped to 21 and 0 cM, respectively. Additionally, the families segregating for 8 out of 10 QTL identified, at the genome level, were the same. Hence, these effects likely correspond to a single QTL. Results from other studies in Iberian × Landrace pigs have identified QTL affecting linoleic fatty acid on pig chromosome 4 (Perez-Enciso et al., 2000; Clop et al., 2003; conservation of synteny with sheep chromosome 25). Also, Perez-Enciso et al. (2000)
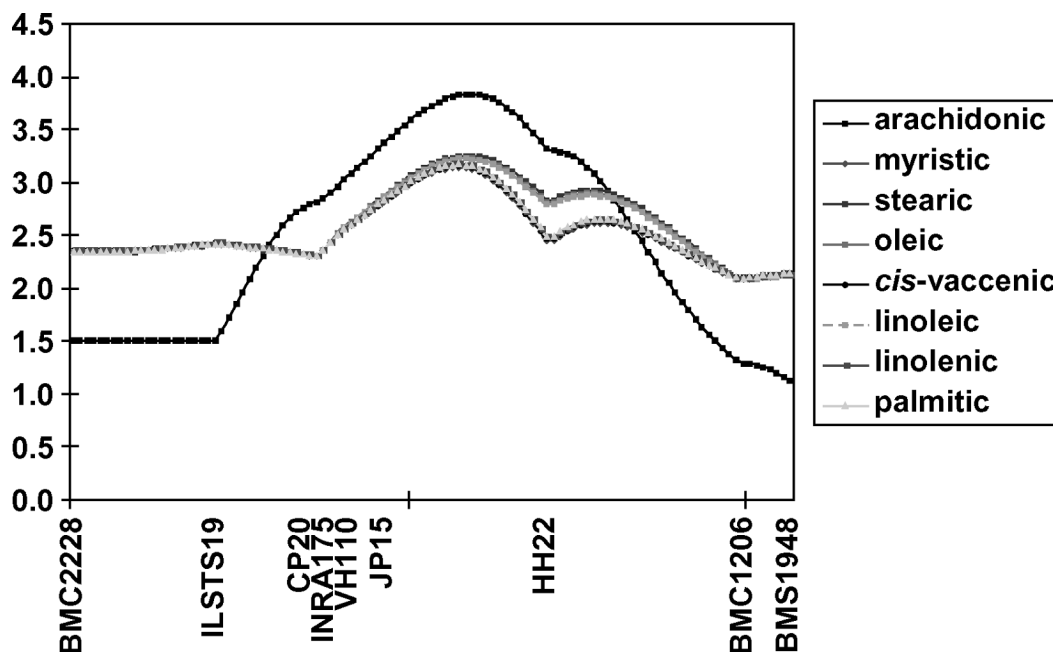
Figure 3. *F*-ratio profile for across-family QTL on sheep chromosome 21, affecting myristic acid (14:0), palmitic acid (16:0), stearic acid (18:0), oleic acid (*cis* 18:1 n-9), *cis*-vaccenic acid (*cis* 18:1 n-7), linoleic acid (*cis* 18:2 n-6), linolenic acid (*cis* 18:3 n-3), and arachidonic acid (20:4 n-6) in LM. Marker positions are indicated on the lower X-axis. The 5% chromosome-wide significance thresholds for each fatty acid are shown in Table 3.

have found that effects on backfat thickness, backfat weight, and LM area in pigs were also significant and mapped to the same position as the linoleic acid content QTL. Linoleic acid is an essential fatty acid for mammals because they lack desaturase capacity beyond the ninth carbon atom (Vance and Vance, 1996). It is a key component of cellular membranes and a precursor of prostaglandins and thromboxanes. It is also stored in adipose tissue or β-oxidized for energy production. In fact, it is highly digestible and preferentially deposited compared with other fatty acids (Lawrence and Fowler, 1997). High linoleic acid content is also associated with toughness and low consumer acceptability in pig meat (Whittington et al., 1986; Cameron and Enser, 1991; Lawrence and Fowler, 1997).

In summary, this study has shown that altering carcass fatness has simultaneously changed oleic acid (18:1 n-9), linoleic acid (18:2 n-6), DPA (22:5 n-3), CLA, and i.m. fatness (total fatty acids). Heritabilities for most of the fatty acids were moderate to high, suggesting that composition of lamb meat can be changed genetically. Also, selection to alter muscle density and i.m. fat content would also alter both the total quantities and proportions of SFA and MUFA in lamb meat. Hence, the opportunity exists to use muscle density as a tool to breed pasture-finished lambs that have the potential to compete as a health-promoting food with other health-oriented products on the market.

This study was also successful in detecting significant QTL related to fatty acid composition on sheep chromosomes 1, 2, 3, 5, 14, 18, and 21, and the same QTL were detected irrespective of whether the data were corrected

for live weight or not. These QTL are clearly of potential importance to the sheep industry; however, they first need to be confirmed in independent populations, and more precise genetic markers would be required. Several genes might be selected as functional candidate genes to explain the QTL found in this study, as fatty acid metabolism can be influenced by a large number of genes involved in complex metabolic routes (Clop et al., 2003). Association analyses between allelic variants of these genes and fatty acid content would need to be performed to find the necessary genetic markers.

IMPLICATIONS

This study has identified new information on the genetic basis of intramuscular fatty acid composition in sheep meat. We have demonstrated that quantities of different fatty acids are moderately to highly heritable; we have shown genetic correlations between live animal measurements and fatty acid composition; and we have found several quantitative trait loci for fatty acid composition. These include 8 quantitative trait loci in one location on chromosome 21 with large effects on myristic, palmitic, stearic, oleic, *cis*-vaccenic, arachidonic, linoleic, and linolenic acid content of intramuscular fat. Thus, we have demonstrated that it is possible, in principle, to breed for altered fatty acid composition, and we have gone a long way toward providing the tools for achieving this. The next step may involve finer mapping of the quantitative trait loci detected, and analysis of these quantitative trait loci in commercial populations.

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