



Genetic mapping of quantitative trait loci for milk production in sheep

R. G. Mateescu* and M. L. Thonney[†]

*Department of Animal Science, Oklahoma State University, Stillwater, OK 74078, USA. [†]Department of Animal Science, Cornell University, Ithaca, NY 14853, USA

Summary

A backcross pedigree using dairy East Friesian rams and non-dairy Dorset ewes was established specifically to map quantitative trait loci (QTL) affecting milk production in sheep. Ninety nine microsatellite markers of an initial set of 120 were successfully genotyped and informative on 188 animals of this backcross pedigree. Test-day milk records on individual ewes were used to estimate several milk yield related traits, including peak milk yield and cumulative milk yield to 50 (MY50), 100 (MY100) and 250 days (MY250). These traits, as well as estimated breeding value of backcross ewes extracted from the genetic evaluation file of the entire flock, were used in interval mapping. Ovine chromosomes 2, 12, 18, 20 and 24 were identified to harbour putative QTL for different measures of milk production. The QTL on *Ovis aries* chromosomes (OAR) 2 and 20 mapped to locations where similar trait QTL have already been mapped in other studies, whereas QTL on OAR 12, 18 and 24 were unique to our backcross pedigree and have not been reported previously. In addition, all identified QTL regions were syntenic with bovine chromosomal segments revealed to harbour QTL affecting milk production traits, providing supporting evidence for the QTL identified here.

Keywords milk production, quantitative trait loci, sheep.

Introduction

Consumers in the United States have shown an increased interest in sheep milk cheeses in recent years, meaning that sheep milk production is becoming an economically important trait. Imports of sheep milk cheeses have increased from 14.5 million kg in 1986 to 33.1 million kg in 2006 (FAO 2006). Of the 24 countries that report imports of sheep milk cheeses, the US accounts for just over one-half of the sheep milk cheese imported by all countries (FAO 2006). Domestic production of sheep milk and sheep milk products in the United States is very low. Neither the USDA nor state departments of agriculture collect production figures, but it has been estimated that there are 125–150 dairy sheep farmers in the United States producing approximately 4 million kg of sheep milk annually (David Thomas, personal communication). This amount of milk will produce 700 000–800 000 kg of cheese. Therefore,

almost 40 times as much sheep milk cheese is imported into the United States as is produced domestically, indicating tremendous opportunity for growth of the dairy sheep industry in the United States.

In contrast with many European and Mediterranean countries, which have a long-standing tradition in dairy sheep production and where the implementation of selection programmes have resulted in highly selected dairy breeds with high genetic potential for milk yields, most of the sheep breeds available to US producers have been selected for meat and wool, and there has been little selection for milk. Improvement of milk production through selection can be expected to be successful given the moderate heritability reported for this trait. Phenotypic selection is more difficult for milk yield than other traits, however, because of the repetitive nature of the phenotype (milk production over a 200- to 250-day lactation), which requires multiple measurements for an accurate description and also because the expression is limited to females only. Therefore, knowledge of the genes controlling this trait, or markers linked to these genes to be used in marker-assisted selection, should provide tools needed to implement effective (more accurate and faster) genetic improvement programmes for increased milk production in sheep.

Address for correspondence

R. G. Mateescu, Department of Animal Science, Oklahoma State University, 206D Animal Science, Stillwater, OK 74078, USA.
E-mail: raluca@okstate.edu

Accepted for publication 7 February 2010

To systematically map quantitative trait loci (QTL) contributing to milk production, we developed a backcross pedigree founded on phenotypically disparate breeds: East Friesian, a specialized dairy breed; and Dorset, a meat breed. The purpose of the project was to identify QTL for milk production in sheep, which should lead to a better understanding of the molecular mechanism of this complex trait and provide a basis for genetic improvement using marker-assisted selection.

Materials and methods

Animal pedigree

An experimental population of animals was created by crossing East Friesian rams from Old Chatham Sheepherding Company (OCSC), a sheep dairy farm near Albany, NY, with Dorset ewes from the Cornell Sheep Farm. The East Friesian dairy breed is known for high milk production, while the Cornell Dorset ewes are non-dairy sheep that have been selected for aseasuality and prolificacy. The two parental populations were appropriate for this project, with one line likely to carry predominantly favourable alleles and the other line likely to carry predominantly unfavourable alleles with respect to the milk production trait. The statis-

tical power of this pedigree to detect a QTL located in an interval flanked by two markers was assessed using the method developed by Hu & Xu (2008) based on the simple regression method. Based on this method, the current pedigree had a power of 52.2%, at significance level (α) of 0.05 and mapping density corresponding to 99 microsatellites, to detect an underlying QTL explaining 1% of the phenotypic variance for the milk production trait.

Four East Friesian rams and 37 Dorset ewes were used to generate 44 F₁ ewes, which were subsequently mated to 11 East Friesian rams to create 92 backcross ewes (Fig. 1). All sheep were housed, bred and fed under similar conditions at the OCSC.

Phenotypes

Ewes were milked twice daily and individual milk yields were recorded once monthly in the OCSC database for the entire lactation period. Lactation curves were fitted to each backcross and F₁ ewe by Wood's incomplete gamma function (1967):

$$y(t) = at^b e^{-ct},$$

where $y(t)$ is the average daily production at time t , a is an estimate of average milk yield, b is a measurement of the

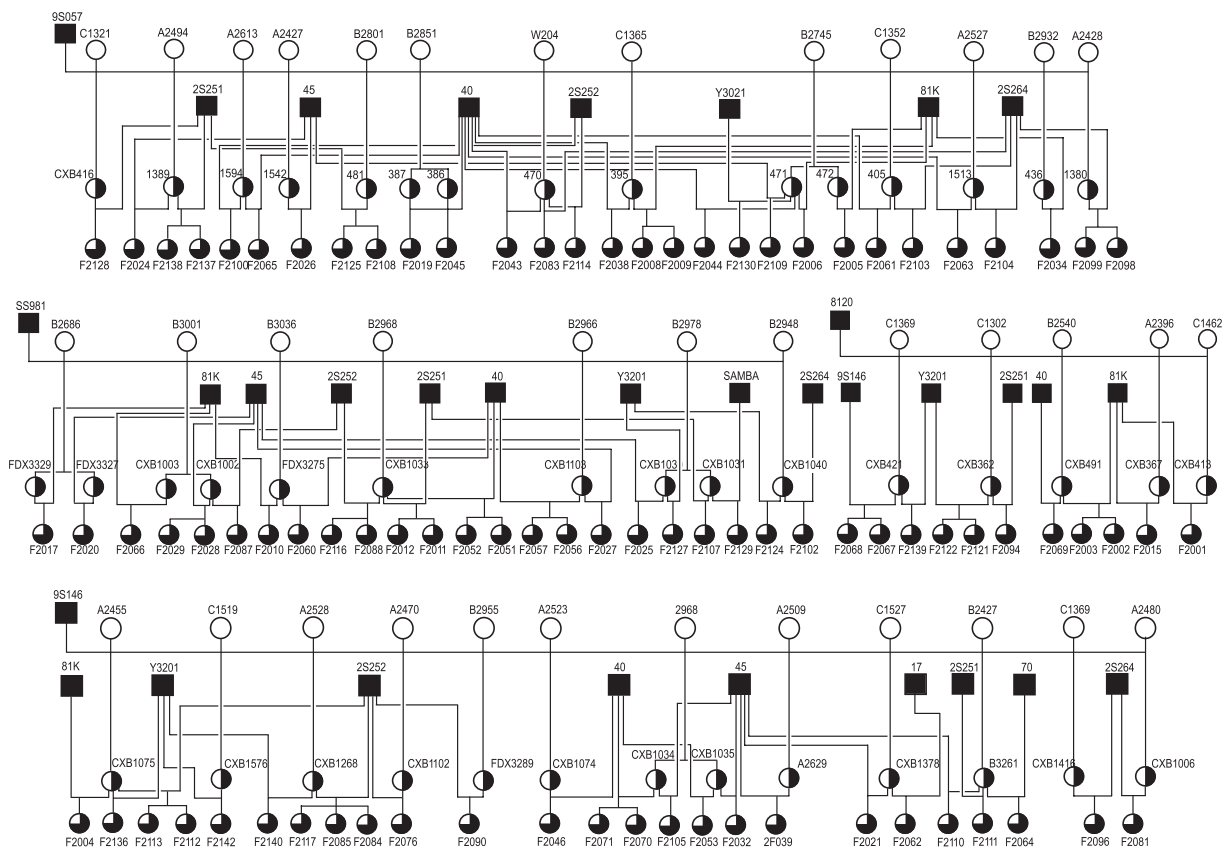


Figure 1 Diagram of the backcross pedigree used to identify QTL associated with milk production, founded on dairy East Friesian rams and Dorset ewes. Open and filled portions of each symbol represent the respective proportion of Dorset and East Friesian alleles possessed by each individual.

rate of milk yield increase until the peak, and c is a measurement of the rate of decreasing milk yield after the peak. Peak milk yield (PMY) and cumulative milk yield to 50 (MY50), 100 (MY100) and 250 days (MY250) were estimated from the first lactation curves for individual backcross ewes and were analysed in the QTL mapping analysis. In addition, average lactation curves were estimated for all backcross and F₁ ewes grouped by lactation (1, 2 and >2).

For the last 10 years, OCSC has implemented a within-flock selection programme to increase milk production. A genetic evaluation to support the breeding programme is performed twice every year to estimate the breeding value of all animals. The routine genetic evaluation is performed using a test-day animal model (Stanton *et al.* 1992; Carvalheira *et al.* 1998) and includes monthly test-day production collected from the ewes in the flock from 1 January 1997 to the day of evaluation. The (co)variance components and genetic parameters for test-day records are estimated using an autoregressive test-day model and a genetic evaluation for ewes and rams in the flock is performed using an animal model and BLUP methodology. The following model is used to describe the data:

$$Y_{ijklmnpq} = YM_j + DIM_j(L_k) + A_m + LTE_n + STE_p + E_{ijklmnpq},$$

where Y is the test-day observation, YM is the fixed effect of year-month, $DIM(L)$ is the fixed effect of the number of days in milk nested within the lactation, A is the random effect of the animal, LTE is the random long-term environmental effects that account for the autocorrelations generated by the ewe across lactations, STE includes the random short-term environmental effects that account for the autocorrelations caused by the ewe within each lactation, and E is the random residual effect that is assumed to have a normal distribution. The estimated variance components are used as inputs for the second stage of the analysis in which the breeding values (EBV) and accuracies of EBVs are estimated for all animals in the data set.

For this study, we had access to the July 2007 genetic evaluation that was performed using milk production and pedigree information available from January 1997 through the end of July 2007. The pedigree file consisted of 365 rams and 3219 ewes that included 41 F₁ and 92 backcrosses used for QTL mapping, for a total of 3584 animals.

Genotyping and linkage maps

Using the latest sheep linkage map available (version 4.7), 120 microsatellite markers were identified to provide uniform coverage of the genome and to maximize the polymorphic information content (PIC). These markers were distributed in 26 autosomes at an average marker interval of 29 cM. Genotyping of all 188 animals on the backcross pedigree (37 Dorset and 15 East Friesian founders, 44 F₁

ewes and 92 backcrosses to East Friesian) was performed at GeneSeek Inc.

QTL analysis

A QTL interval-mapping analysis was performed using the web-accessible program `GRIDQTL` (<https://gridqt1.cap.ed.ac.uk/gridsphere>) (Seaton *et al.* 2006) and was based on a least-squares method (Haley *et al.* 1994). This method assumes that alleles at the QTL are fixed in the original lines, therefore the East Friesian and the Dorset founders were assumed to be homozygous for the alternate allele at the QTL locus controlling the milk production phenotype. The software allows for the analysis of data from different mating schemes including the backcross design employed for our crossbreed pedigree. The general linear model for all traits included the genetic background (two founder groups, F₁'s and backcross groups) as fixed effect.

An F -ratio of the variance explained by the QTL (after fitting all fixed effects in the model) to the residual MS was used to test for the significance of the QTL effects. The location giving the highest F -ratio statistic was considered to be the best estimate for the position of the QTL. Estimates were obtained for the additive effect of the putative QTL at that location in the backcross population. Additive QTL effects (a) correspond to genotype values of $+a$ and $-a$ for individuals having inherited two East Friesian alleles and individuals with two Dorset alleles respectively. Positive additive effects indicate that East Friesian alleles increase the milk production while negative additive effects indicate that East Friesian alleles have a negative effect on milk production. When the plot of the F -value against the chromosomal location suggested the presence of two QTL, the analysis was repeated with a test for two vs. one QTL. Chromosome- and experiment-wide significance thresholds for each trait were determined (Churchill & Doerge 1994); the threshold at $P < 0.05$ and $P < 0.01$ was obtained from a 10 000 permutation test implemented through the `GRIDQTL` software. Bootstrap analysis was carried out to determine 95% confidence intervals for each detected QTL (Visscher *et al.* 1996).

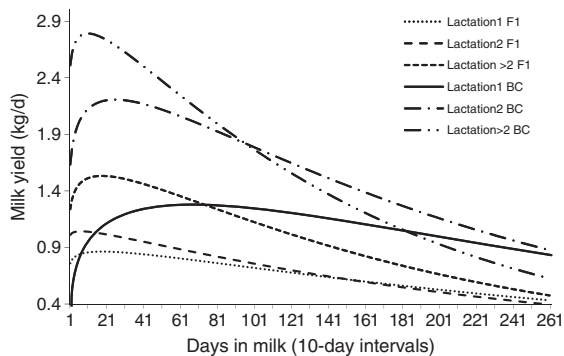
Results and discussion

Milk production phenotypes

Summary statistics for M50, M100, M250 (kg), day of peak milk yield, and PMY (kg) from first lactation for all 92 backcross ewes are presented in Table 1. Average lactation curves for backcross and F₁ ewes, shown in Fig. 2, were of the expected shape, with lower total yield and flatter curve for first lactation and higher total yield, higher peak yield and lower persistency for subsequent lactations. The lactation peak occurred between 20 and 60 days in milk. These results are in agreement with those for other dairy breeds

Table 1 Summary statistics for cumulative milk yield (kg) to 50, 100, 250 days, peak DIM (day), peak milk yield (kg) and EBV(g/day) for 92 backcross ewes.

	Milk 50 days	Milk 100 days	Milk 250 days	Peak DIM	Peak yield	EBV
Minimum	26.34	50.57	66.47	4.69	0.68	-371.08
Maximum	154.28	280.69	549.29	79.07	3.36	631.88
Mean	70.73	143.01	265.46	38.88	1.66	79.69
SD	26.08	47.42	91.58	18.21	0.55	191.58

**Figure 2** Lactation curves for milk yield (kg/day) of F_1 and backcross (BC) ewes for first, second and greater than second parity groups.

(Carta *et al.* 1995; Cappio-Borlino *et al.* 1997) as well as dairy cows (Stanton *et al.* 1992). Milk production for backcross ewes was higher in all lactations (1st, 2nd and >2nd) than for F_1 ewes, suggesting that the two parental populations are genetically different for milk yield (which is one of the assumptions for using the least-squares methods for QTL mapping) and that the backcross design should have been successful in generating an informative pedigree.

Estimated breeding values for milk production

The genetic merit was estimated relative to the average production in the entire population, which for July 2007 was 1171 g of milk per day. The ratio of genetic variance relative to phenotypic variance provided estimates of heritability for each lactation, ranging from 0.32 to 0.39. From the OCSC genetic evaluation file, we extracted the EBVs for the 92 genotyped backcross individuals. Summary statistics for EBVs for this group of individuals are presented in Table 1. The accuracy of the EBVs varied from 0.52 to 0.90 with a mean of 0.77.

Marker informativeness

Among 120 microsatellite markers genotyped, 18 amplified poorly during genotyping and were removed from the analysis. This left chromosome 23 with no microsatellite markers, while chromosomes 10 and 11 had only one microsatellite marker left, both of which were subsequently

removed from the dataset. One other microsatellite marker was removed from the analysis because it was fixed for a single allele. The final dataset used in the QTL analysis therefore included 99 informative microsatellite marker loci on 23 of 26 ovine autosomes.

The average number of alleles for the 99 microsatellite marker loci in the entire population was 7.03 (range 2–21). The observed heterozygosity ranged from 0.07 to 0.97 with a mean of 0.65 and the PIC ranged from 0.06 to 0.89 with a mean of 0.63. The average information content was 0.41 with the lowest value on *Ovis aries* chromosomes (OAR) 5 (0.06) and the highest value on OAR 22 (0.83).

QTL analysis

Five chromosomes were identified to harbour putative QTL for different milk production-related traits at the 5% and 1% chromosome-wise significance level. The QTL locations giving the highest test statistic and the parameter estimates obtained at each location for chromosomes with a significant QTL are shown in Table 2. No QTL reached the experiment-wide significance threshold. The least squares method used for QTL analysis assumed that the founder breeds were fixed for alternate alleles at a QTL and, based on very different selection strategies, the two parental populations used to develop this pedigree were likely to be fixed for different alleles at many QTL with respect to milk production. However, it is expected that many QTL were still segregating in the two parental lines, which allowed detection only of those QTL which differ in allele frequency between the two parental populations. This could have reduced the power of QTL detection of this experiment and might explain the limited number of QTL identified as well as the fact that no QTL reached the experiment-wide significance threshold. Other factors limiting the ability to detect QTL in this experiment included a limited number of backcross individuals and the sparse marker coverage on some chromosomes for optimum coarse screening. Therefore, it is very likely that the QTL identified represent some of the major loci contributing to milk production.

QTL for several traits (on chromosomes 2, 20 and 24) had East Friesian alleles with a positive effect (increased milk production), while the estimated additive effect for QTL identified on chromosomes 12 and 18 indicated lower milk production of individuals inheriting East Friesian alleles.

Table 2 Parameter estimates for QTL with *F*-tests significant at $P < 0.05$ (chromosome-wide) for milk yield estimated breeding value (EBV), cumulative milk yield at 50 days (MY50) and 100 days (MY100) and peak milk yield (PMY) following a genome-wide screen for QTL. Chromosomal (OAR), position and the 95% confidence interval of this position (CI), *F*-statistic, log of the odds (LOD) ratio score and the additive (*a*) effect and SE are shown.

Trait	OAR	Position ¹	Flanking markers	CI (cM)	<i>F</i>	LOD	<i>a</i>
MY50 (kg)	2	251.4	BMS1126–BMS2626	220–282	7.78*	1.61	26.98 (9.67)
EBV (g/day)	12	59.4	BM4025–CSSM3	37–82	5.12*	1.11	–172.87 (75.39)
MY100 (kg)	18	56.1	BM3413–UWCA4	43–69	5.02*	1.07	–33.83 (15.10)
PMY (kg)	18	56.1	BM3413–UWCA4	44–69	6.95*	1.44	–0.46 (0.17)
EBV (g/day)	20	64.1	INRA064–BM1818	52–77	5.56*	1.14	266.97 (113.20)
EBV (g/day)	24	0	BMS514–BM4005	0–25	11.73**	2.37	223.94 (65.39)

OAR, *Ovis aries* chromosome.

*Chromosome-wise 5% significance; **chromosome-wise 1% significance.

¹Position (cM) on the chromosome where the maximum *F*-statistic value was obtained.

There was a putative QTL for MY50 at the distal end of OAR 2, with an estimated additive QTL effect (East Friesian homozygotes deviated from the mean of homozygotes for the alternative QTL allele) indicating a mean superiority of the East Friesian QTL allele of 26.98 kg of milk to 50 days of lactation. This QTL was accompanied by a parallel behaviour of the statistical profile for EBV, PMY, MY100 and MY250, but these effects did not reach the significance threshold. Although no QTL for milk yield has been reported on OAR2, QTL for other milk-related traits have been identified on this chromosome. Gutierrez-Gil *et al.* (2009) reported a QTL for fat percentage approximately 25 cM proximal from this location in a commercial population of Spanish Churra sheep, while Barillet *et al.* (2005) identified the same chromosomal region to have a significant effect on protein percentage in a granddaughter design study in French dairy sheep. Considering the high genetic correlation among the milk yield traits analysed in the present study and among fat and protein percentage traits from other studies, the QTL identified by several studies suggest that this region of OAR2 is very likely to contain one or more QTL influencing milk production traits. This is further supported by the report of a QTL for milk yield in Finnish Ayrshire dairy cattle (Viitala *et al.* 2003) in the corresponding orthologous bovine region on *Bos taurus* chromosome (BTA) 2.

A QTL for EBV was identified in the middle of OAR 12 with an estimated additive effect of –172.87 g of milk per day (deviation from the average milk production in the OCSC population), suggesting lower genetic merit for milk production for homozygotes inheriting East Friesian alleles. Although a shadow effect was observed for the other milk-related traits used in this study in the same region of OAR 12, no milk production QTL have been reported previously on this ovine chromosome. However, the QTL identified on OAR 12 was located approximately 30 and 10 cM proximal to the homologous cattle BTA 17 region, which contains a QTL for milk yield (Zhang *et al.* 1998) and a QTL for fat yield respectively (Casas *et al.* 2003). A similar situation

was encountered for the QTL identified in the first third of OAR 18 and at the proximal end of OAR 24, where no previous QTL have been mapped in sheep, but the orthologous bovine regions on BTA 21 and BTA25 contain QTL for MY (Viitala *et al.* 2003) and protein yield (Ashwell *et al.* 1998) respectively. The coincidence with milk production QTL mapped in dairy cattle provides support for our results and suggests similar genetic mechanisms underlying these traits in the two species.

The QTL mapped in the last third of OAR 20 for EBV had an estimated additive effect, suggesting homozygotes for the East Friesian allele at this position have the genetic ability to produce 266.97 g more milk per day in comparison with the mean of homozygote animals for East Friesian and Dorset alleles. The same region of OAR 20 showed significant effects on fat percentage (Gutierrez-Gil *et al.* 2009) as well as MY, fat yield and protein yield (Barillet *et al.* 2005), providing supporting evidence for the importance of this chromosomal region for several milk-related traits. This QTL is of particular importance because the chromosomal region harbouring this QTL is in immediate proximity to the *prolactin* gene (*PRL*), which was shown to be associated with milk production traits in both sheep and cattle (Brym *et al.* 2005; Alipanah *et al.* 2007; Staiger *et al.* 2009). While *PRL* has been shown to be a likely positional candidate gene, until fine-mapping of this region is performed we cannot rule out the possibility of more than one QTL in this region.

Examination of chromosomes harbouring putative QTL revealed that on most of these chromosomes, many of the other traits analysed indicated the likely presence of an underlying QTL in the same position, even though QTL for those traits did not reach statistical significance. On OAR 24, for example, one QTL that contributed to EBV was identified at 0 cM with an estimated additive effect of 223.94 g milk per day. A high *F*-statistic at the same position was obtained for the MY50 without reaching the significance threshold (Fig. 3). The only chromosome where a significant QTL for more than one trait was identified was OAR 18, where a QTL for MY50 and PMY were mapped

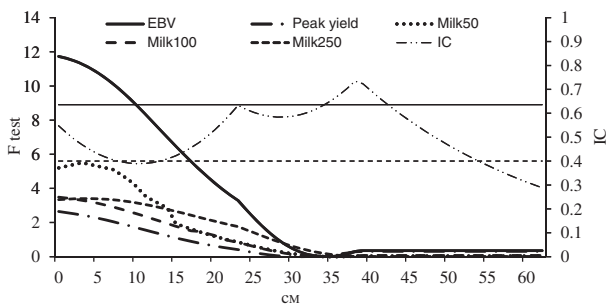


Figure 3 Statistical profile for chromosome 24 for estimated breeding value for milk yield (EBV), peak milk yield (Peak Yield) and cumulative milk yield at 50, 100 and 250 days (Milk50, Milk100 and Milk250). The x-axis indicates the relative position on the linkage map (cM Haldane). The y-axis represents the F -test statistic. The solid and dashed horizontal lines indicate the 1% and 5% chromosome-wide significance thresholds respectively. Information content (IC) obtained along the linkage groups is represented on the secondary y -axis.

around 56.1 cM. The exact same location of this QTL, the similar direction of the additive effect, and the high correlation (0.98) between these two traits suggest a pleiotropic QTL, but the possibility of two linked QTL cannot be excluded until fine-mapping of this region is performed. This pattern, where many traits suggest the presence of a QTL but only one or two traits reached significance thresholds, applied to most of the chromosomes where putative QTL were identified, providing some assurance of the significance of the mapped QTL.

To our knowledge, this is the only sheep milk yield QTL study that has used a cross between the East Friesian and Dorset breeds. It is therefore of great interest to know how these results compare with QTL identified in other studies. Gutierrez-Gil *et al.* (2009) identified one genome-wide significant QTL for milk protein percentage on OAR 3 and associations with several milk production traits on five other chromosomal regions of OAR 1, 2, 20, 23 and 25. The only association with milk yield, which is the phenotype used in our study, was identified on OAR 23. Our study provides supporting evidence for QTL on OAR 2 and 20, but no evidence of a QTL was detected on OAR 23. However, this is not surprising for a number of reasons, including the use of a crossbred pedigree between East Friesian and Dorset vs. pure breed Chura sheep, differences in marker coverage of the genome and in the power of the two pedigrees to detect QTL, and the use of slightly different phenotypes in the two QTL mapping studies. While not surprising, these differences highlight the importance of QTL discovery using the breed(s) which will be the subject of marker-assisted selection, as research findings from studies in other breeds may not be relevant to the target population.

Several candidate genes have been investigated for their potential association with milk production traits in both cattle and sheep, and an association between genetic variants of α_{s1} -casein, β -lactoglobulin (Pietrola *et al.* 2000;

Ramos *et al.* 2002; Dario *et al.* 2008) and PRL (Ramos *et al.* 2009; Staiger *et al.* 2009) have been previously reported in different populations. Because of marker genotyping failures, no markers were available in the present study for QTL analysis on OAR 11, where the β -lactoglobulin gene is located. Ovine chromosome 6, which contains the cluster of casein genes and was identified to harbour a putative QTL for protein percentage (Diez-Tascon *et al.* 2001), showed no evidence of a putative QTL in our study or the study of Gutierrez-Gil *et al.* (2009). This could be explained by the use in this study of only milk yield related traits and/or a reduced power of our study to detect QTL with small effects or multiple linked QTL with opposite effects on the trait.

The results presented here are a first step in identifying and locating QTL for milk production in sheep. Using multiple phenotypic measurements for milk production allowed us to identify the maximum number of QTL. Nevertheless, the marker coverage on some of these chromosomes was not sufficiently dense for optimum screening. Fine-mapping within this pedigree, other pedigrees, and across breeds, to further refine the map locations of these QTL, will be a necessary next step to validate these results. The fine-mapping strategy will be based partly on chromosomal regions in which we have mapped QTL with high F -statistics. Other criteria will include corroborating evidence of QTL for milk production based on ovine-bovine synteny. Fine-mapping is an important step and may help direct the search for genetic variants and genes controlling milk production to be incorporated in marker assisted selection programmes.

Conclusions

Dairy sheep production is a relatively new but growing industry in North America. This QTL mapping experiment identified ovine chromosomes 2, 12, 18, 20 and 24 as harbouring putative QTL for milk yield-related traits. Additional analyses to confirm and fine-map these QTL will be essential to narrow these chromosomal regions and will facilitate identification of positional candidate genes for further investigation. This will lead not only to a better understanding of the genetic mechanisms underlying milk production, but more importantly, should provide dairy sheep farmers with molecular markers that could be used in selection programmes.

Acknowledgements

This project was supported by National Research Initiative Grant no. 2005-35205-17680 from the USDA Cooperative State Research, Education, and Extension Service; by the Oklahoma Agricultural Experiment Station; and by New York Agricultural Experiment Station Hatch Project 470. We appreciate the help of Old Chatham Shepherding Company in collecting blood samples and providing milking records.

References

- Alipanah M., Kalashnikova L. & Rodionov G. (2007) Association of *prolactin* gene variants with milk production traits in Russian Red Pied cattle. *Iranian Journal of Biotechnology* **5**, 158–61.
- Ashwell M.S., Da Y., Van Tassell C.P., VanRaden P.M., Miller R.H. & Rexroad C.E., Jr (1998) Detection of putative loci affecting milk production and composition, health, and type traits in a United States Holstein population. *Journal of Dairy Science* **81**, 3309–14.
- Barillet F., Arranz J.J. & Carta A. (2005) Mapping quantitative trait loci for milk production and genetic polymorphisms of milk proteins in dairy sheep. *Genetics Selection Evolution* **37**(Suppl. 1), S109–23.
- Brym P., Kaminski S. & Wojcik E. (2005) Nucleotide sequence polymorphism within exon 4 of the bovine *prolactin* gene and its associations with milk performance traits. *Journal of Applied Genetics* **46**, 179–85.
- Cappio-Borlino A., Portolano B., Todaro M., Macciotta N.P., Giaccone P. & Pulina G. (1997) Lactation curves of Valle del Belice dairy ewes for yields of milk, fat, and protein estimated with test day models. *Journal of Dairy Science* **80**, 3023–9.
- Carta A., Sanna S.R. & Casu S. (1995) Estimating lactation curves and seasonal effects for milk, fat and protein in Sarda dairy sheep with a test day model. *Livestock Production Science* **44**, 37–44.
- Carvalho J.G., Blake R.W., Pollak E.J., Quaas R.L. & Duran-Castro C.V. (1998) Application of an autoregressive process to estimate genetic parameters and breeding values for daily milk yield in a tropical herd of Lucerna cattle and in United States Holstein herds. *Journal of Dairy Science* **81**, 2738–51.
- Casas E., Shackelford S.D., Keele J.W., Koohmaraie M., Smith T.P. & Stone R.T. (2003) Detection of quantitative trait loci for growth and carcass composition in cattle. *Journal of Animal Science* **81**, 2976–83.
- Churchill G.A. & Doerge R.W. (1994) Empirical threshold values for quantitative trait mapping. *Genetics* **138**, 963–71.
- Dario C., Carnicella D., Dario M. & Bufano G. (2008) Genetic polymorphism of *B-lactoglobulin* gene and effect on milk composition in Leccese sheep. *Small Ruminant Research* **74**, 270–3.
- Diez-Tascon C., Bayon Y., Arranz J.J., De La F.F. & San Primitivo F. (2001) Mapping quantitative trait loci for milk production traits on ovine chromosome 6. *Journal of Dairy Research* **68**, 389–97.
- FAO (2006) *FAO STAT Database Collections*. Available at: <http://faostat.fao.org> (Accessed 30 July 2009).
- Gutierrez-Gil B., El-Zarei M.F., Alvarez L., Bayon Y., De La Fuente L.F., San P.F. & Arranz J.J. (2009) Quantitative trait loci underlying milk production traits in sheep. *Animal Genetics* **40**, 423–34.
- Haley C.S., Knott S.A. & Elsen J.M. (1994) Mapping quantitative trait loci in crosses between outbred lines using least squares. *Genetics* **136**, 1195–207.
- Hu Z. & Xu S. (2008) A simple method for calculating the statistical power for detecting a QTL located in a marker interval. *Heredity* **101**, 48–52.
- Pietrola E., Carta A., Fraghi A., Piredda G. & Pilla F. (2000) Effect of *β -lactoglobulin* locus on milk yield in Sarda ewes. *Zoot. Nutr. Anim.* **26**, 131–5.
- Ramos A.M., Matos C., Bettencourt C., Pinheiro C. & Rangel-Figueiredo T. (2002) *Influence of as1-Casein, B-Lactoglobulin and Prolactin Genotypes on Milk Production Traits in Two Portuguese Sheep Breeds*. Montpellier, France: Proceedings 7th World Congress of Genetics Applied to Livestock Production.
- Ramos A.M., Matos C.A.P., Russo-Almeida P.A., Bettencourt C.M.V., Matos J., Martins A., Pinheiro C. & Rangel-Figueiredo T. (2009) Candidate genes for milk production traits in Portuguese dairy sheep. *Small Ruminant Research* **82**, 117–21.
- Seaton G., Hernandez J., Grunchev J.A., White I., Allen J., DeKoning D.J., Wei W., Berry D., Haley C.S. & Knott S.A. (2006) *GRIDQTL: a grid portal for QTL mapping of compute intensive datasets*. Proceedings of 8th World Congress of Genetics Applied to Livestock Production, pp. 16–18.
- Staiger E.A., Thonney M.L., Buchanan J.W., Rogers E.R., Oltenacu P.A. & Mateescu R.G. (2009) Effect of *prolactin*, *β -lactoglobulin* and *κ -casein* genotype on estimated breeding values for milk production in East Friesian sheep. *Journal of Dairy Science*, doi:10.3168/jds.2009-2630.
- Stanton T.L., Jones L.R., Everett R.W. & Kachman S.D. (1992) Estimating milk, fat, and protein lactation curves with a test day model. *Journal of Dairy Science* **75**, 1691–700.
- Viitala S.M., Schulman N.F., de Koning D.J., Elo K., Kinoshita R., Virta A., Virta J., Maki-Tanila A. & Vilkkii J.H. (2003) Quantitative trait loci affecting milk production traits in Finnish Ayrshire dairy cattle. *Journal of Dairy Science* **86**, 1828–36.
- Visscher P.M., Thompson R. & Haley C.S. (1996) Confidence intervals in QTL mapping by bootstrapping. *Genetics* **143**, 1013–20.
- Zhang Q., Boichard D., Hoeschele I. *et al.* (1998) Mapping quantitative trait loci for milk production and health of dairy cattle in a large outbred pedigree. *Genetics* **149**, 1959–73.