Detection of Quantitative Trait Loci Affecting Milk Production, Health, and Reproductive Traits in Holstein Cattle

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ABSTRACT

We report putative quantitative trait loci affecting female fertility and milk production traits using the merged data from two research groups that conducted independent genome scans in Dairy Bull DNA Repository grandsire families to identify quantitative trait loci (QTL) affecting economically important traits. Six families used by both groups had been genotyped for 367 microsatellite markers covering 2713.5 cM of the cattle genome (90%), with an average spacing of 7.4 cM. Phenotypic traits included PTA for pregnancy rate and daughter deviations for milk, protein and fat yields, protein and fat percentages, somatic cell score, and productive life. Analysis of the merged dataset identified putative quantitative trait loci that were not detected in the separate studies, and the pregnancy rate PTA estimates that recently became available allowed detection of pregnancy rate QTL for the first time. Sixty-one putative significant marker effects were identified within families, and 13 were identified across families. Highly significant effects were found on chromosome 3 affecting fat percentage and protein yield, on chromosome 6 affecting protein and fat percentages, on chromosome 14 affecting fat percentage, on chromosome 18 affecting pregnancy rate, and on chromosome 20 affecting protein percentage. Within-family analysis detected putative QTL associated with pregnancy rate on six chromosomes, with the effect on chromosome 18 being the most significant statistically. These findings may help identify the most useful markers available for QTL detection and, eventually, for marker-assisted selection for improvement of these economically important traits.

(Key words: quantitative trait locus, pregnancy rate, milk production traits)

Abbreviation key: AIPL = Animal Improvement Programs Laboratory, BTA = *Bos taurus* autosome, DBDR = Dairy Bull DNA Repository, PL = productive life, DGAT1 = acylCoA:diacylglycerol acyltransferase gene, GHR = growth hormone receptor gene.

INTRODUCTION

Since the early 1990s with the development of cattle linkage maps (Bishop et al., 1994; Barendse et al., 1994; Ma et al., 1996; Barendse et al., 1997; Kappes et al., 1997), many groups around the world have conducted studies identifying QTL affecting economically important traits. Initially most groups focused on identifying QTL affecting milk production traits (Georges et al., 1995); however, traditional selection methods have been effective in improving milk production in dairy cattle without the need for DNA marker information. The same is not true for lowly heritable traits such as health and reproduction, which are becoming more important to producers because conception rates have declined as milk production has continued to increase (Pryce et al., 2002). In addition, infertility is the primary cause of involuntary culling in dairy herds (Bascom and Young, 1998). In terms of cost, infertility has a large impact on global competitiveness and the sustainability of the dairy industry, and these costs continue to increase each year.

In many species, especially livestock species, studies designed for identification of QTL are based on crosses of genetically distinct breeds or inbred lines. This approach has been less used in dairy cattle research because development of experimental populations is prohibitively expensive and the generation interval is long. In addition, the population structure that results from the use of elite AI bulls as sires is quite powerful and requires only modest amounts of genotyping for QTL identification. In 1991, the Dairy Bull DNA Repository (DBDR; Da et al., 1994) was initiated as a collection of semen from 35 dairy grandsire families that was available to collaborators for studies to identify QTL

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affecting economically important traits in Holstein cattle. Two genome-wide scans were conducted in DBDR families, focusing on identification of QTL affecting the milk production traits and SCS. Originally two groups conducted and reported independent research findings (Heyen et al. 1999; Ashwell et al. 2001). These datasets have now been merged for further analysis allowing a more thorough coverage of the bovine genome. Originally the independent genome scans were analyzed one marker at a time using analysis of variance methods, with interval regression analysis conducted only on specific chromosomes. Those studies lacked thorough grandsire-specific chromosomal coverage; the merged results presented here increased the coverage by combining genotypes from the different sets of DNA markers, such that interval regression analysis could be more thoroughly carried out on all 29 autosomes.

Since the two datasets were generated and merged, researchers with the USDA-ARS Animal Improvement Programs Laboratory (AIPL) have calculated genetic evaluations for female fertility (VanRaden et al., 2003). The female fertility evaluations are expressed as the pregnancy rate, which is defined as the percentage of nonpregnant cows that become pregnant during each 21-d period. Heritability for this trait has been estimated at 4% (VanRaden et al., 2003), making this an ideal candidate trait for a marker-assisted selection program.

The objective of this study was to identify QTL affecting milk production traits using the merged set of DBDR genotypes as well as provide the first report of putative QTL affecting the pregnancy rate trait.

MATERIALS AND METHODS

Resource Population

Semen samples from 10 large Holstein families (families 1 to 9, 12), consisting of 1415 bulls, were selected from the DBDR (Da et al., 1994) as previously described (Ashwell et al., 1996; Heyen et al., 1999). This collection consists of semen from sons of 35 elite, progeny-tested, sires. This semen was contributed by nine North American AI organizations for the purpose of identifying QTL affecting economically important traits using the granddaughter design (Weller et al., 1990).

Originally the two research groups (University of Illinois, Urbana/ARO, Israel and USDA-ARS, Beltsville) conducted independent genome scans. Each group selected eight families for study, six that were common across both studies (families 1 to 5, 8) and four families that were studied by only one of the two groups (families 6 and 7 by University of Illinois/ARO; families 9 and 12 by USDA-ARS).

Genotyping

DNA was extracted from semen as previously described (Ashwell et al., 1996; Heyen et al., 1999). The PCR was carried out using either fluorescently-labeled primers or by [α - 32 P] incorporation into PCR products as previously described (Ashwell et al., 1996; Heyen et al., 1999). For each individual genome scan, microsatellite markers were selected at approximately 20-cM intervals from published bovine maps (Bishop et al., 1994; Barendse et al., 1994; Ma et al., 1996; Barendse et al., 1997; Kappes et al., 1997). Heyen et al. (1999) selected 174 markers; Ashwell et al. (2001) selected 232 markers, 38 of which were genotyped by both groups. Duplicate markers were treated as separate loci because allele-calling methods were not consistent across both datasets. When the two datasets were merged, genome coverage was estimated to be 2713.5 cM (90%), assuming a 3000-cM genome. The average number of markers per chromosome was 12.5, with an average spacing of 7.4 cM.

Phenotypic Data

Data for milk yield and composition, SCS, and productive life (PL) collected through November 2001 were processed as part of the routine USDA/DHIA genetic evaluation procedure by the AIPL of USDA-ARS. The female fertility trait, pregnancy rate, is a new genetic evaluation being calculated by AIPL. Evaluations are expressed as the pregnancy rate, which is defined as the percentage of nonpregnant cows that become pregnant during each 21-d period (VanRaden and Tooker, 2003; VanRaden et al., 2003). The PTA values for pregnancy rate trait ranged from -4.9 to 3.3%, with an average of -0.4% and a standard deviation of 1.1 for the sires used in this study. Pregnancy status is determined from the date of last breeding and is verified using the next calving date or veterinary diagnosis when available. Cows that are sold for reproductive problems are assumed not pregnant. Pregnancy status is determined only within the first 250 d of lactation because many cows not pregnant by 250 d are not bred again but instead are culled. Mean pregnancy rate for Holsteins in 1995 was 23% and SD of sire evaluations was 1%. These evaluations for pregnancy rate are obtained from data on days open, and an increase of 4 d open equals a 1% decrease in pregnancy rate. Data since 1960 from the first 5 lactations are included, for a total of 40 million records. Data are adjusted for month of calving, age at first calf, and lactation number and are computed using the same animal model evaluation programs used for yield traits, productive life, and SCS (VanRaden and Tooker, 2003; VanRaden et al., 2003). The present study

included 3 mo less data than the first official evaluations that were released in February 2003.

Statistical Analysis

Data from a total of eight traits were analyzed using a regression approach originally described by Haley and Knott (1992). A web-based version of this regression interval mapping method is now available (Seaton et al., 2001). The software, QTL Express (<http://qtl.cap.ed.ac.uk>), analyzes data from F_2 , half-sib, and sib-pair families to detect QTL. The software allows the user to fit one or two QTL in the model and includes tools for permutation and bootstrap analyses to calculate chromosome-wise significance thresholds and 95% confidence intervals, respectively. For this study, 1000 permutations were studied for each trait to determine the $P < 0.05$ and $P < 0.01$ chromosome-wise significance thresholds, and the regression interval analysis was conducted at 1-cM intervals along the chromosome. Both within- and across-family analyses were conducted, fitting one and two QTL in the model. Data included daughter deviations for milk, fat, and protein yield, fat and protein percentage, SCS, and PL, weighted by their respective reliabilities. At the time this analysis was conducted, no daughter deviations were available for pregnancy rate, therefore, PTA for pregnancy rate were used. Within family analyses correspond to a contrast of two sire marker alleles with one degree of freedom, while the across-family analysis tests for the evidence of different marker effects across families. Marker effects are nested within sire family so that no assumptions are made regarding the phase of QTL allelic effects in the across-family analysis.

RESULTS AND DISCUSSION

Marker Effects on Milk Production Traits

Five traits were evaluated to identify QTL affecting milk production and composition (Table 1). Only effects with a chromosome-wise P value of <0.01 are reported. Forty-five significant effects modeling one QTL were identified within families on 16 of the 29 autosomes. However, caution should be used when considering QTL identified in family 12 due to the limited number of informative sons from this family. Nine significant effects found on five chromosomes were identified in the across-family analysis (Table 2). No evidence was found favoring the two QTL model over the one QTL model in the within and across-family analyses. If the number of significant tests expected under the null hypothesis is compared to the number observed, evidence exists for QTL affecting milk production traits in this population. For these traits, a total of 1450 trait-chromosome-fam-

ily combinations were tested, with 15 significant tests expected by chance at $P < 0.01$, and 45 were observed. Similarly, for across-family analyses, a total of 145 chromosome-trait combinations were tested. With this many tests, two significant tests are expected by chance and nine were observed. The most significant effects (F statistics > 15) were located on *Bos taurus* autosome (BTA) 3, BTA6, BTA14 and BTA20. Heyen et al. (1999) detected a significant effect on BTA3, Ashwell et al. (2001) detected effects on BTA6 and BTA20, and both studies detected an effect on BTA14. To date, the genes responsible for the effects observed on BTA3 and BTA6 have not been identified. However, many groups are currently working to fine map these QTL.

Grisart et al. (2002) identified a mutation in the bovine acylCoA:diacylglycerol acyltransferase (*DGAT1*) gene on BTA14, which is associated with a major effect on milk fat content, thus implicating this gene as a strong candidate for this QTL. *DGAT1* maps to the centromeric end of BTA14. Results from our merged data analysis support this finding, placing QTL affecting fat percentage at the centromere of BTA14 in several families (Table 1).

Recently, the same group (Blott et al., 2003) identified a mutation in the growth hormone receptor (*GHR*) gene that is associated with an effect on milk yield and milk composition. *GHR* mapped to BTA20 at 43 cM on their map and is associated with a major effect on milk protein percentage. Results from the DBDR merged dataset identified a QTL affecting milk protein percentage at 51 cM, based on the MARC map (Kappes et al., 1997). The QTL identified in our DBDR study most likely corresponds to the QTL identified by Blott et al. (2003).

Marker Effects on SCS and Productive Life

No evidence favoring the two QTL models over the one QTL model was found in the within and across-family analyses for SCS and productive life. Eight significant effects on SCS were identified within families on eight chromosomes when one QTL was modeled (Table 1). Four significant effects on SCS were identified in the across-family analysis (Table 2). For SCS, a total of 290 chromosome-family combinations were tested, with three significant tests expected by chance at $P < 0.01$ and eight were observed. In the across-family analysis, 29 tests were conducted, with less than one significant test expected by chance, and four were observed. All significant effects on this trait were detected in the independent DBDR studies, except for the within-family associations on BTA15 and BTA20. Boichard and Bishop (1997) also detected an association on BTA15 at 36 cM, close to the same location reported here. Al-

Table 1. Significant chromosome-wise ($P < 0.01$) effects from within family analysis for milk production, SCS, and PL.

BTA ¹	DBDR Family#	Trait ²	Location (cM)	F statistic	Estimated allelic difference ³	SE	Marker interval
2	1	FAT %	29	12.2	6.1	1.7	ETH121-BM4440
2	3	PRO %	16	10.6	3.6	1.1	TGLA431-TGLA377
3	1	FAT %	49	22.0	7.6	1.6	HUJ246-TGLA263
3	1	MILK	32	13.7	350	95	BL41-ILSTS29
3	1	PRO %	29	15.0	2.9	0.7	BL41-ILSTS29
3	5	FAT YLD	10	10.9	14.9	4.5	RM19-ILSTS96
3	5	PRO %	10	9.5	3.1	1.0	RM19-ILSTS96
3	5	PRO YLD	39	20.7	16.1	3.5	BL41-ILSTS29
3	12	PRO %	97	10.0	4.9	1.5	BM2924-Telomere
5	2	FAT %	87	9.1	6.7	2.2	BM1819-BMS1248
5	2	SCS	54	9.1	15.9	5.3	BL37-BM1819
6	3	PRO YLD	24	13.1	14.0	3.9	BMS5006-URB016
6	4	PRO %	106	16.9	3.4	0.8	AFR227-BM4311
6	9	FAT %	49	21.7	9.3	2.0	BMS2508-BMS5037
6	9	PRO %	51	46.6	7.0	1.0	BMS5037-BM143
7	1	MILK	30	11.0	288	3.3	BM2607-BM6015
7	1	PL	71	9.9	9.8	3.1	BMS2258-INRA192
7	1	PRO YLD	30	10.6	7.7	2.4	BM2607-BM6105
7	1	SCS	61	8.8	9.2	3.1	BM6117-BMS2258
10	8	MILK	98	11.9	531	154	CSSM46-BMS2614
11	2	PRO YLD	83	12.6	9.2	2.6	BMS1716-URB057
11	12	FAT YLD	90	11.9	19.6	5.7	HUJV174-BL1103
13	1	MILK	84	11.0	298	90	BMS1226-BMS995
13	1	PRO YLD	77	10.7	8.7	2.7	BMS1226-BMS995
13	8	PRO %	34	7.8	3.4	1.2	BMC1222-ILSTS59
14	1	FAT %	4	23.1	8.6	1.8	ILSTS39-BMS1678
14	1	FAT YLD	4	12.1	13.2	3.8	ILSTS39-BMS1678
14	1	PRO %	9	9.5	2.3	0.7	BMS1678-ILSTS11
14	3	FAT %	3	17.9	7.2	1.7	ILSTS39-BMS1678
14	3	FAT YLD	5	12.0	12.3	3.5	ILSTS39-BMS1678
14	4	FAT %	1	28.5	10.3	1.9	ILSTS39-BMS1678
14	4	FAT YLD	2	14.0	17.1	4.6	ILSTS39-BMS1678
14	5	FAT %	3	21.2	9.2	2.0	ILSTS39-BMS1678
14	6	FAT YLD	33	10.5	24.7	7.6	BMS1941-BM8215
14	6	PRO YLD	74	14.7	14.5	3.8	BM4305-INRA100
15	4	SCS	34	9.8	11.4	3.7	BMS2684-HBB
17	3	PRO YLD	96	8.6	8.3	2.9	BM1862-BM1233
18	4	FAT YLD	84	12.3	17.3	4.9	BM6507-TGLA227
20	4	MILK	68	10.9	909	275	BM5004-AFR2215
20	5	PRO %	40	18.4	5.0	1.2	BM713-BMS2361
20	7	SCS	29	11.8	15.2	4.4	RM310-TGLA126
20	12	MILK	54	10.9	584	177	BM4107-BM5004
20	12	PRO %	63	15.3	5.6	1.4	BM4107-BM5004
22	2	PRO %	77	9.4	3.5	1.2	BMS875-BM4102
22	7	PRO YLD	30	9.6	13.8	4.4	BM1303-BM3628
23	4	SCS	50	12.7	13.5	3.8	BB705-BM1818
26	3	SCS	0	11.2	13.1	3.9	Centromere-BM1314
26	7	SCS	0	11.0	15.2	4.6	Centromere-BM1314
27	4	FAT YLD	5	11.7	17.9	5.2	BM3507-TGLA179
28	12	MILK	33	10.3	480	150	BL25-BM6466
29	1	FAT YLD	0	8.9	12.2	4.1	Centromere-BMS764
29	6	PRO YLD	10	13.2	23.0	6.3	ARO26-BMC8012
29	7	MILK	1	9.6	566	183	BMS764-ARO26
29	7	SCS	50	8.0	18.7	6.6	BMC1206-BMS1948

¹*Bos taurus* autosome.²Daughter deviations for fat percentage (FAT %), protein percentage (PRO %), milk yield (MILK), fat yield (FAT YLD), protein yield (PRO YLD), SCS, and productive life (PL).³Units of estimated allelic differences: daughter deviations for milk, fat, protein yield reported in kg; SCS adjusted to log base 2 of the concentration; % protein and fat reported as % of protein or fat yield/milk yield; productive life reported as months of life, limited to 7 yr 10 mo of life/lactation.

Table 2. Significant chromosome-wise ($P < 0.01$) effects from across-family analysis for milk production, SCS, and PL.

BTA ¹	Trait ²	Location (cM)	F statistic	Marker interval
3	PRO %	10	3.6	RM19–ILSTS96
6	PRO %	50	5.8	BMS5037–BM143
7	MILK	111	3.3	BM9065–ILSTS6
7	PRO YLD	111	2.9	BM9065–ILSTS6
7	SCS	67	3.2	BM6117–BMS2258
11	PRO YLD	83	3.0	BMS1716–URB057
14	FAT %	1	11.0	ILSTS39–BMS1678
14	FAT YLD	2	5.7	ILSTS39–BMS1678
14	PRO %	1	2.9	ILSTS39–BMS1678
20	PRO %	51	4.1	BMS2361–BM4107
22	SCS	80	3.3	BMS875–BM4102
23	SCS	41	3.0	BB705–BM1818
26	SCS	0	2.7	Centromere–BM1314

¹*Bos taurus* autosome.

²Daughter deviations for fat percentage (FAT %), protein percentage (PRO %), milk yield (MILK), fat yield (FAT YLD), protein yield (PRO YLD), SCS, and productive life (PL).

though many groups have detected QTL on BTA20, none have been reported affecting SCS.

A putative QTL affecting SCS was detected on BTA26 at 0 cM in families 3 and 7. A SCS QTL on BTA26 was reported by Zhang et al. (1998) and Boichard and Bishop (1997); however, they report the location to be toward the telomere, between TGLA429 and BM804. DBDR families were not genotyped for marker TGLA429; however, families 3 and 7, as well as 4, 5, and 6, were heterozygous at BM804 and all their sons were genotyped. Therefore, one explanation for these findings is that two QTL affecting SCS are located on BTA26 at opposite ends of the chromosome and were detected in different families.

Only one significant effect on PL, modeling one QTL, was detected. The putative QTL was detected within family 1 on BTA7 (Table 1). Neither of the independent scans detected a significant association affecting PL, however the Heyen et al. (1999; see also <http://cagst.animal.uiuc.edu/genemap/WEB/Table1.html>) study detected a suggestive association ($P < 0.1$) in another family. Comparison of this finding with those from other groups is difficult because few groups have tried to identify PL QTL and the phenotype and genetic evaluation systems differ from country to country (van der Linde and de Jong, 2002). A total of 29 significance tests were conducted, with three significant tests expected by chance at $P < 0.01$; therefore the effect detected on BTA7 may be a false-positive association.

Marker Effects on Pregnancy Rate

The PTA for pregnancy rate (VanRaden et al., 2002) were recently computed, allowing, for the first time, identification of putative QTL affecting this trait. Seven significant effects were identified within families on six

chromosomes (Table 3). A total of 290 significant tests were conducted, with three significant tests expected by chance at $P < 0.01$ and seven observed. The most significant within-family effect (F statistic = 14.1) was located on BTA18 in DBDR family 4 (Figure 1). The estimate of the difference of the allelic effect for this QTL was $0.57 (\pm 0.15)$ units (Table 3). The only significant associations previously detected on this chromosome affected rump angle; however, this was in a different DBDR family (Ashwell et al., 2001). No significant effects were detected across families. This is likely if the heterozygosity at the QTL is low due to selection (Heyen et al., 1999) and QTL will only be detected within families and not across the families. No evidence was found favoring the two QTL model over the one QTL model in the within- and across-family analyses for this trait.

Few groups have identified QTL affecting fertility traits in cattle. Most QTL research affecting fertility has focused on identification of ovulation rate QTL in twinning populations (Kappes et al., 2000; Kirkpatrick et al., 2000; Lien et al., 2000). These three groups have identified QTL affecting ovulation rate on BTA5, BTA7, and BTA19. None of these QTL corresponds with any of the pregnancy rate QTL detected in this study, but this is to be expected, as ovulation rate and pregnancy rate are very different traits. Therefore the majority of the putative pregnancy rate QTL detected here on BTA16, BTA18, and BTA28 are novel and need validation. The remaining putative pregnancy rate QTL (BTA6, BTA14, and BTA27) are located on chromosomes already thought to carry QTL that may be related to fertility, as discussed below.

Schrooten et al. (2000) analyzed “nonreturn daughters” and “interval calving to first insemination” fertil-

Table 3. Significant chromosome-wise ($P < 0.01$) effects from within family analysis for pregnancy rate.

BTA	DBDR family#	Location (cM)	F statistic	Estimated allelic difference	SE	Marker interval
6	8	122	11.1	0.91	0.27	BMS5021–BMS5029
14	6	11	9.9	0.84	0.27	ILSTS11–CSSM66
16	8	81	9.4	0.66	0.21	BM1706–BM3509
18	4	54	14.1	0.57	0.15	BM7109–ILSTS2
18	7	14	7.9	0.60	0.21	ILSTS021–TEXAN10
27	9	62	8.4	0.95	0.33	INRA027–BM203
28	4	48	10.7	0.54	0.16	BM6466–BM2515

ity traits in their QTL study. Suggestive linkage was found on BTA2 and BTA9 affecting the nonreturn daughters trait. These locations cannot be confirmed with the pregnancy rate findings. Larsson and Andersson-Eklund (2002) analyzed "interval calving to first insemination," fertility treatments, and a combined fertility index in their partial genome scan to identify QTL affecting reproduction traits in Swedish dairy cattle. Putative QTL affecting the interval from calving to first insemination were identified on BTA3, BTA11, and BTA25 and cannot be confirmed by the pregnancy rate findings. They also detected QTL on BTA6 affecting fertility treatments and the combined fertility index. Schrooten et al. (2000) also identified suggestive link-

age on BTA6 and BTA17 affecting the interval from calving to first insemination. The putative QTL on BTA6 identified by Schrooten et al. (2000), located at 106 cM in their study, may be supported by the pregnancy rate QTL detected on this chromosome at 122 cM in our study. In addition, BTA6 is also known to harbor QTL effecting traits such as milk production (Kühn et al., 1999; Nadesalingam et al., 2001; Ron et al., 2001), clinical mastitis (Klungland et al., 2001) and calving ease (Schrooten et al., 2000; Larsson and Andersson-Eklund, 2002). Once the genes underlying these QTL are identified, researchers may be able to determine the pleiotropic effects on important traits in dairy breeding.

Figure 1. Interval map of BTA18 for DBDR family 4. Only traits with F-statistics higher than the chromosome-wise levels at $P < 0.05$ are shown. Traits include PTA for pregnancy rate (Preg rate; ♦), fat yield (■), protein yield (▲), and SCS (x). Diamonds at top of plot indicate location of genotyped markers.

The putative pregnancy rate QTL on BTA14 may be explained by effects of the *DGAT1* gene discussed above. *DGAT1* maps to the centromeric end of BTA14 and is included in the region where a pregnancy rate QTL was detected. *DGAT1* catalyzes the last step in triglyceride synthesis and Grisart et al. (2002) identified a mutation in this gene that is associated with a major effect on milk fat content. It has been shown that changes in the fat:protein ratio in milk during early lactation has a negative effect on fertility (de Vries and Veerkamp, 2000). Therefore mutations in the *DGAT1* gene may have pleiotropic effects on the pregnancy rate.

Previously, no fertility QTL were reported on BTA27. However, a previous study (Ashwell et al., 2001) detected a QTL affecting the conformation trait, dairy form, on the telomeric end of BTA27 in the same region as the pregnancy rate QTL. Casas et al. (2002) also identified a putative QTL affecting marbling in beef cattle in the same region of chromosome 27. Therefore, results suggest at least one gene affecting fat metabolism is located on this chromosome that may also affect fertility. Rogers et al. (1999) studied the genetic correlations between type traits and three groups of diseases: reproductive, foot and leg, and metabolic and digestive diseases. Results from this study showed that the genetic correlation between dairy form and the three disease categories were negative and moderate in magnitude. Metabolic disorders (such as milk fever and ketosis) are indicators of negative energy balance (Rogers et al., 1999), which is known to affect reproductive performance (de Vries and Veerkamp, 2000). Therefore, selection for increased dairy form may lead to cows that are more prone to reproductive and metabolic diseases (Rogers et al., 1999).

It should be emphasized that the results associated with pregnancy rate are preliminary and require validation. However, based on these results, one can speculate that identification of the genes underlying the pregnancy rate QTL may actually be genes affecting body condition and the metabolic state of dairy animals. In several cases there are effects on milk production traits in regions where putative pregnancy rate QTL have been detected, so it may be difficult to improve female fertility without sacrificing some milk production. However, it may be more economically advantageous to sacrifice some gains in milk production in order to be able to breed cows in a shorter period of time.

These data are just the first step in identifying and locating QTL. Work is underway to validate these QTL. Once these results are validated, fine-mapping studies will begin, so the genes responsible for the observed effects can be identified and incorporated into marker-assisted selection programs.

CONCLUSIONS

This study has identified putative QTL affecting female fertility, milk production, and SCS in DBDR Holstein grandsire families using genotypic data from 367 markers located throughout the genome. These results provide additional evidence of QTL on BTA3 (affecting protein and fat percentages), BTA6 (affecting protein and fat percentages), BTA14 (affecting fat percentage), and BTA20 (affecting protein percentage). This study is also the first to report putative QTL affecting pregnancy rate. Significant effects were detected on six chromosomes, with a highly significant effect detected on BTA18.

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