

A Whole-Genome Scan to Map Quantitative Trait Loci for Conformation and Functional Traits in Canadian Holstein Bulls

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ABSTRACT

Genetic improvement of livestock populations can be achieved through detection and mapping of genetic markers linked to quantitative trait loci (QTL). With the completion of the bovine genome sequence assembly, single nucleotide polymorphism (SNP) assays spanning the whole bovine genome and research work on large-scale identification, validation, and analysis of genotypic variation in cattle has become possible. A total of 462 Canadian Holstein Bulls were used to test the association between SNP and QTL. Single locus linkage disequilibrium regression model was implemented to perform a whole genome scan to identify and map QTL affecting conformation and functional traits. One thousand five hundred thirty-six SNP markers from introns and exons of potential QTL regions for economically important traits across the bovine genome were selected for association analysis. A total of 45 and 151 SNP were found to be associated with 17 conformation and functional traits at a genome- and chromosome-wise significance level, respectively. Among the 196 significant SNP, 169 of them are newly detected in this study, whereas 27 of them have been reported in previous literature and 161 of these were located in genes and are worth further investigating to potentially identify the causative mutations underlying the QTL. The single locus linkage disequilibrium regression method using SNP marker genotypes has proven to be a successful methodology for detecting and mapping QTL in dairy cattle populations.

Key words: genome scan, single nucleotide polymorphism, quantitative trait loci detection, linkage disequilibrium mapping

INTRODUCTION

Recent advances in molecular biotechnology that facilitate incorporation of molecular information into the

traditional genetic evaluation models have enabled the identification and characterization of genes that contribute to genetic variation in economically important quantitative traits, hence leading to improvements in selection accuracies in livestock populations. Fernando and Grossman (1989) presented methodology for the application of BLUP to marker-assisted selection in which QTL alleles are considered random in the context of the mixed model terminology. Because DNA extraction is not restricted by age or sex, molecular genetics can alleviate some of the limitations of quantitative genetic selection (Dekkers and Hospital, 2002).

Since the initiation of whole genome scans in dairy cattle by Georges et al. (1995), several genome scans and QTL mapping projects have been undertaken to identify the genomic regions harboring genes that underlie phenotypic variation of production and conformation traits in dairy cattle (Smaragdov et al., 2006). The QTL that mapped to regions containing likely candidate genes are of special interest. Several QTL and candidate genes for milk production, reproduction, functional, and conformation traits have been identified in previous studies on *Bos taurus* autosomes (BTA) 1, 2, 3, 4, 5, 6, 7, 9, 14, 19, 20, 23, 26, 27, and 29. Some of these QTL were detected and mapped in numerous studies (Boichard et al., 2003; Ashwell et al., 2005; Schnabel et al., 2005).

Single nucleotide polymorphisms are the most abundant form of DNA variation in the genome (Snelling et al., 2005), and their preference is growing over other types of genetic markers due to lower mutation rate and the ease of genotyping (Hinds et al., 2005). Single nucleotide polymorphisms have been used for the detection and localization of QTL for complex traits in many species (Daw et al., 2005). In addition, the availability of the bovine genome sequence assembly has accelerated the ability to associate specific genome variation with phenotypic variation across the bovine genome, which is the ultimate goal of many QTL identification and mapping projects. In cattle, a 7.1× sequence assembly has been produced with accompanying information on over 2,300,000 SNP genome-wide (Bovine Genome

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Project: <http://www.hgsc.bcm.tmc.edu/projects/bovine>). A set of SNP assays spanning the whole bovine genome becomes possible after mining this data, which helps accelerate the research work on large-scale identification, validation, and analysis of genotypic variation in cattle.

Several statistical approaches have been developed for whole genome scans and QTL mapping projects. The least squares model based on regression of phenotype on marker genotypes or haplotypes and the random effects models based on identity by descent approaches (George et al., 2000; Kolbehdari et al., 2005; Gautier et al., 2006) are commonly used. High-density SNP marker genotypes have increased the feasibility of QTL detection and mapping using historical population-wide linkage disequilibrium (LD), which requires a marker allele to be in LD with the QTL allele across the entire population. Linkage disequilibrium can be a result of migration, mutation, selection, small finite population size, or other genetic events that the population experiences. In livestock populations, finite population size is generally implicated as the key cause of LD, because effective population sizes for most livestock population are relatively small (Meuwissen and Goddard, 2000). Indeed, extensive LD has been observed in dairy cattle, sheep, and pig populations in previous studies (Farnir et al., 2000; Dekkers and Hospital, 2002).

The LD method regresses the phenotypes of the quantitative trait on the marker genotypes. Regression on single SNP marker genotypes does not require knowledge of SNP position and linkage phase and is therefore easier to implement. Studies have shown that a single marker test based on the LD regression model provided similar or greater power than a haplotype-based and an identity by descent-based model (Grapes et al., 2004; Zhao et al., 2007), and QTL could be detected and mapped by the LD regression method. Further, this method offers a greater flexibility to include dominance and epistatic effects. In addition, the random polygenic effects accounting for relationships among individuals could be added to this model. The objective of this study was to perform a whole genome scan to identify and map QTL affecting conformation and functional traits using the LD regression method and SNP genotype markers in the Canadian Holstein population.

MATERIALS AND METHODS

Genotyping Assay Design and Genotyping Platform

A total of 1,536 SNP markers were selected to represent introns and exons of potential candidate genes across the bovine genome sequence assembly (Btau_2.0). A subset of bovine SNP already characterized by the Alberta Bovine Genomics Laboratory was

combined into a single multiplex assay of 1,536 SNP for analysis on the Illumina Beadstation 500G SNP genotyping platform (Oliphant et al., 2002). Among these SNP, 139 poorly amplified and 56 monomorphic SNP during the genotyping were removed from the analysis. The genotyping assay was designed based on bovine genome sequence assembly version 2 (Btau_2.0). In the original design, these SNP were selected to be distributed as evenly as possible based on the physical locations on the bovine genome sequence assembly (Btau_2.0). The SNP known to be in putative candidate genes for milk production and confirmation traits were strategically added to the assay. However, after the assay was manufactured, an updated version of the bovine genome sequence assembly (Btau_3.1) was released. Chromosome assignments and SNP positions were recalculated based on the updated version of bovine genome sequence assembly.

A local database was developed that contains over 1.8 million bovine SNP and almost 30,000 genes gathered from the databases at the National Center for Biotechnology Information (<http://www.ncbi.nlm.nih.gov/genome/seq/BlastGen/BlastGen>). Querying the database provided details on each SNP, including its location and functional class. The SNP that are present in a gene locus can have one of the following National Center for Biotechnology Information-defined functional classes: locus-region, coding, coding-synonymous, coding-nonsynonymous, mRNA-UTR, intron, and splice-site. For SNP not located in a gene, the nearest gene was determined by querying the database for a list of genes on the same chromosome as the SNP, and the gene closest to the location of the SNP was identified.

Animal Resource and Description of Phenotypic Data

A total of 462 Canadian Holstein bulls from Semex Canada (Guelph, Ontario, Canada), 319 of them originating from 10 core sire families, were used in the study. The DNA was extracted from bull semen and genotyped. Complete general pedigree information along with the most updated bull EBV (November 2006) were provided by the Canadian Dairy Network (Guelph, Ontario, Canada). The SNP genotypes were used to test the association with measured economically important traits including major type traits (overall conformation, mammary system, feet and legs, dairy strength, rump), 6 descriptive type traits (udder texture, median suspensory, foot angle, bone quality, stature, angularity), and 6 functional traits (herd life, daughter fertility, milking speed, milking temperament, calving ease, and maternal calving ease). Bull genotypes of the studied traits

Table 1. Descriptive statistics of the conformations and functional traits for the studied 462 bulls

Traits	Mean	SD	Minimum	Maximum
Conformation	3.04	5.56	-17	19
Mammary system	2.88	5.79	-18	19
Feet and leg	1.73	5.06	-17	18
Dairy strength	1.78	5.16	-14	17
Rump	0.99	4.93	-20	21
Udder texture	1.85	4.68	-16	27
Median suspensory	2.39	5.36	-17	16
Foot angle	0.39	5.21	-14	14
Bone quality	0.86	4.95	-19	18
Stature	1.49	5.23	-18	15
Angularity	2.51	4.99	-18	16
Herd life	3.08	0.24	2.49	3.65
Daughter fertility	65.56	3.37	57	74
Milking speed	85.51	4.14	70	95
Milking temperament	89.59	3.31	70	96
Calving ease	84.4	5.1	56	96
Maternal calving ease	86.11	5.37	62	96

are preferred for gene association studies over their raw phenotypic records, because the EBV of each bull is based on the records of many daughters and is therefore a much more accurate estimate of the genetic potential of each animal than a single cow phenotype. The descriptive statistics of these traits that were estimated from the 462 bulls that have been genotyped in current study are given in Table 1.

The definitions of the above traits are available at Canadian Dairy Network (<http://www.cdn.ca/articles.php>). Daughter fertility is a new fertility trait, which was provided by the Canadian Dairy Network for genetic evaluation of dairy sires and calculation of bull proofs for 4 different traits related to the fertility of dairy cattle. These include age at first insemination for heifers, 56-d nonreturn rate (**NRR**) in heifers, the interval from calving to first insemination within each lactation for cows, and the 56-d nonreturn rate in cows. The ability of an animal to remain productive in a dairy herd is of interest and is profitable for dairy cattle producers. Genetic evaluation values of herd life of bulls are calculated based on actual survival data of their daughters.

Statistical Analysis

To test the association between SNP and the QTL, a single locus LD regression model was implemented in this study. The markers were assumed to be in LD with the QTL over the entire genome. The simple regression model based on LD has been shown, using simulated data, to have an acceptable level of power and accuracy for fine mapping QTL (Grapes et al., 2004; Zhao et al., 2007). The following mixed linear LD regression model was fitted in this study by using the ASReml package (Gilmour et al., 2006):

$$\mathbf{y} = \mathbf{Xb} + \mathbf{Za} + \mathbf{e},$$

where \mathbf{y} = the vector of phenotypes (EBV); \mathbf{X} = the design matrix; \mathbf{b} = the vector of coefficients of the regression on recoded SNP genotypes; \mathbf{Z} = the incidence matrix for animal effects; \mathbf{a} = a vector of the polygenic animal effects; and \mathbf{e} = the vector of residuals.

The QTL allele substitution effects and additive genetic effects were evaluated in this model. The design matrix, \mathbf{X} , was coded as 2, 1, 0 for the SNP genotypes 1-1, 1-2, and 2-2, respectively. The F-statistic, type I error (P -value), and allele substitution effects were estimated for all SNP genotypes across the whole genome.

A major issue in multiple testing is the proper setting of significance thresholds. A useful statistic is false discovery rate (**FDR**), which is the expected proportion of falsely detected QTL (Benjamini and Hochberg, 1995). The FDR takes into account the number of tests that are performed as well as how significant one test is relative to the others in multiple comparison procedures. Family-wise error rate controls the probability of committing any type I error in families of comparisons. The FDR was used to establish the statistical significance critical value in this study. Two levels of significant controls were used in this study based on genome-wise and chromosome-wise type I errors, which were computed for all SNP (Benjamini and Hochberg, 1995; Fernando et al., 2004). The genome-wise level is a very conservative approach for a large number of markers in a whole genome scan study. Therefore, if SNP exceed the genome-wise type I error, they should be highly associated with the trait.

The FDR was calculated for a QTL on a genome or a chromosome-wise level by assuming n number of tests performed on a genome or a chromosome, and the P -

Table 2. Single nucleotide polymorphism (SNP) number and the average intervals between SNP (kbp¹) by chromosome

BTA ²	Frequency	Intervals (kbp)
1	64	2,193.3
2	64	1,935.3
3	78	1,492.4
4	75	1,424.5
5	59	1,828.6
6	40	2,749.2
7	71	1,392.8
8	36	2,788.1
9	33	2,656.7
10	44	2,058.6
11	56	1,722.1
12	14	5,530.7
13	54	1,452.9
14	27	2,690
15	67	1,115.6
16	48	1,432.7
17	39	1,809.7
18	44	1,380.9
19	64	991.7
20	29	2,223.1
21	32	1,950.3
22	42	1,425.7
23	44	1,075.7
24	19	2,877.4
25	40	1,058.5
26	41	1,142.9
27	16	2,123.7
28	34	1,135.6
29	67	668.9
Total	1,341	

¹kbp = kilobase pairs.

²BTA = *Bos taurus* autosome.

values were ranked from lowest to highest. The following equation was used to calculate the FDR:

$$FDR = \frac{n \times P(k)}{k}$$

where *k* = the individual relative test position.

RESULTS AND DISCUSSION

SNP Analysis

The SNP used in this study were distributed throughout the bovine genome. The total number of SNP on

each chromosome varied from 14 on BTA 12 to 78 on BTA 3. The average interval between SNP on different chromosomes varied from 668.9 kilobase pairs on BTA 29 to 5,530.7 kilobase pairs on BTA 12. The X chromosome was not included in this study. The average SNP polymorphism information content was 0.287 (0 to 0.375), and the average observed SNP heterozygosity was 0.389. The details of the number of SNP per chromosome and their average interval in kilobase pairs per chromosome are given in Table 2. The genotyping assay was originally designed based on Bovine Genome Sequence Assembly version 2 (Btau_2.0). New chromosome assignments and SNP positions were calculated based on the updated version of bovine genome sequence assembly (Btau_3.1). This recalculation resulted in a less even distribution of SNP than originally intended.

Major Type Traits

The whole genome scan to map QTL for major type traits including overall conformation, mammary system, feet and legs, dairy strength, and overall rump identified 24 SNP significantly associated with these traits at the genome-wise level and 36 at the chromosome-wise level (*P* < 0.05). The details of the SNP showing association with these traits at the genome and chromosome significance level, including their heterozygosity, position, F-test statistic value, allele substitution effects, and *P*-value are shown in Tables 3 to 7.

Five SNP had significant effects on overall conformation at the chromosome-wise level (*P* < 0.05) on BTA 4, 18, 21, 23, and 29 (Table 3). A larger F-test statistic showed strong evidence of association between these chromosome regions of the bovine genome with overall conformation. For instance, SNP rs41634501 on BTA 23 (23,107,013 bp) had a F-test statistic of 14.59 and showed significant association with overall conformation at the chromosome-wise level (*P* < 0.01) with allele substitution effects of 1.58. These 5 significant regions may contain QTL responsible for overall conformation, which have not been reported previously. Of the 5 sig-

Table 3. Significant genome- and chromosome-wise single nucleotide polymorphisms (SNP) with conformation

SNP NCBI ¹ ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	<i>P</i> -value	Functional class	Gene name
rs41591551	4	96,244,404	0.36	11.25	1.38	0.00045*	nearest_gene	KIAA1549
rs41636734	18	53,743,293	0.48	11.62	1.24	0.00037*	intron	CD37
rs41565403	21	33,224,592	0.28	7.78	1.54	0.003*	coding-synonymous	STRA6
rs41634501	23	23,107,013	0.45	14.59	1.58	0.000078**	nearest_gene	LOC537895
rs29024010	29	30,954,390	0.31	10.67	1.84	0.00062*	intron	HNT

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome-wise (*P* < 0.05); **significant chromosome-wise (*P* < 0.01).

Table 4. Significant chromosome-wise single nucleotide polymorphisms (SNP) with mammary system

SNP NCBI ² ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	P-value	Functional class	Gene name
rs41652648	5	81,674,580	0.47	11.50	-1.46	0.0004*	intron	ITPR2
rs41636734	18	53,743,293	0.48	12.95	1.41	0.00018**	intron	CD37
rs41653440	28	25,280,138	0.47	9.45	1.33	0.0012*	intron	PSAP

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome-wise ($P < 0.05$); **significant chromosome-wise ($P < 0.01$).

nificant SNP, SNP rs41636734 and SNP rs29024010 are located in the introns of predicted genes (CD37 and HNT), SNP rs41565403 is a synonymous coding SNP, whereas the remaining 2 SNP are not located in genes (Table 3). It has been found that SNP rs41591551 also shows significant association with median suspensory, whereas SNP rs41636734 also shows significant association with rump and mammary system.

Two SNP had significant effects on the mammary system at the chromosome-wise level at $P < 0.05$ on BTA 5 and 28 (Table 4), whereas SNP rs41636734 on BTA 18 (53,743,293 bp) had a significant effect at the genome-wise level at $P < 0.01$. These SNP are located in introns of predicted genes (ITPR2, CD37, and PSAP). Of the 3 significant regions found in the current study, 2 of them (53,743,293 and 25,280,138 bp on BTA 18 and BTA 28) are in regions reported in a previous study by Ashwell et al. (2005). It has been found that SNP rs41636734 also shows significant association with conformation and rump.

Ten SNP were found to have a significant association with feet and legs at the genome-wise and 9 at the chromosome-wise level ($P < 0.05$) on BTA 1, 2, 4, 10, 13, 14, 21, 22, 23, and 27 (Table 5). Ten of these significant SNP are located in the introns of predicted genes, 3 of them are synonymous coding SNP, and 6 of them are not located in genes (Table 5). Two of the 19 regions, BTA 13 (64,863,304 bp) and BTA 14 (40,196,763 bp), have been reported in a previous study to be associated with feet and legs by Ashwell et al. (2005). Two of these SNP (rs41645645 and rs43710950) show significant association with foot angle. Five of these SNP (rs41645645, rs41632254, rs41603160, rs41645547, rs41643866) also show significant association with bone quality. Three of these SNP (rs41636945, rs41632254, rs41634501) also shows significant association with median suspensory. It has been found that SNP rs41643866 also shows significant association with herd life, whereas SNP rs41647383 also shows significant association with milking speed.

Table 5. Significant genome- and chromosome-wise single nucleotide polymorphisms (SNP) with feet and legs

SNP NCBI ¹ ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	P-value	Functional class	Gene name
rs41584408	1	63,350,131	0.17	10.76	-1.89	0.00059*	intron	ITGB5
rs41634489	1	74,380,472	0.51	14.60	-1.23	0.000078**G	intron	KNG
rs41634488	1	74,402,543	0.45	10.78	-1.08	0.00058*	intron	LOC786403
rs41605475	1	111,160,100	0.14	10.65	1.98	0.00062*	coding-synonymous	AGTR1
rs41636945	2	20,762,669	0.43	12.04	-1.14	0.0003**	nearest_gene	LOC540561
rs41567487	4	82,138,210	0.45	16.00	-1.53	0.000038**G	intron	WASL
rs41645645	10	26,616,376	0.46	8.10	0.96	0.0025*	intron	HH114
rs43710950	10	41,992,224	0.39	12.75	-1.46	0.0002**G	nearest_gene	TPM1
rs29026593	10	49,673,883	0.49	7.13	-0.94	0.0043*	coding-nonsynonymous	LOC507781
rs41632254	13	64,863,304	0.47	14.27	1.37	0.000092**G	intron	BPI
rs41603160	14	7,921,599	0.30	7.81	1.19	0.0029*	intron	TG
rs41587080	14	40,196,768	0.53	9.92	-1.01	0.00093*	nearest_gene	ZFHX4
rs41645547	21	52,902,193	0.47	9.80	-1.14	0.00099*	intron	LOC514011
rs41603503	22	39,937,030	0.32	14.07	1.48	0.0001**G	mrna-utr	MGC142526
rs41643866	22	40,066,742	0.20	12.89	-2.01	0.00019**G	intron	LOC613533
rs41634501	23	23,107,013	0.45	17.85	1.57	0.000015**G	nearest_gene	LOC537895
rs41642736	23	27,110,161	0.50	14.41	-1.32	0.000086**G	intron	TRIM10
rs41650218	27	12,597,543	0.26	13.27	-1.78	0.00015**G	nearest_gene	LOC535434
rs41647383	27	32,834,272	0.20	14.60	2.06	0.000078**G	coding-synonymous	FGFR1

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome-wise ($P < 0.05$); **significant chromosome-wise ($P < 0.01$).

^GSignificant genome-wise ($P < 0.05$).

Table 6. Significant genome- and chromosome-wise single nucleotide polymorphisms (SNP) with dairy strength

SNP NCBI ¹ ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	P-value	Functional class	Gene name
rs43709927	3	25,148,574	0.43	11.18	1.22	0.00047*	coding-synonymous	LOC514870
rs41601701	3	98,500,067	0.08	11.03	2.69	0.00051**	coding-synonymous	MGC139728
rs41604534	5	29,067,052	0.55	7.32	1.00	0.0039*	intron	KRT5
rs41656703	5	32,429,000	0.52	6.20	-0.95	0.0073*	nearest_gene	MGC127063
rs29012216	5	40,289,953	0.46	12.18	1.38	0.00028**G	intron	BSM
rs41604564	5	58,756,658	0.33	12.61	-1.38	0.00022**G	nearest_gene	LTA4H
rs29014633	5	74,016,631	0.44	16.91	1.58	0.00024**G	intron	CACNG2
rs41590827	5	75,905,624	0.42	12.83	1.47	0.00019**G	intron	RAC2
rs41591892	5	81,801,975	0.52	8.56	-0.98	0.0019*	intron	ITPR2
rs41592948	5	99,016,571	0.47	5.80	0.92	0.0092*	coding-synonymous	GABARAPL1
rs41609478	7	37,343,116	0.50	16.77	1.48	0.00025**G	nearest_gene	LOC538639
rs41591943	7	39,956,874	0.37	13.39	1.51	0.00015**G	nearest_gene	LOC527275
rs41661265	7	50,312,323	0.46	15.93	-1.36	0.00039**G	coding-synonymous	MGC155209
rs41653025	10	49,942,146	0.23	10.11	-1.68	0.00084*	coding-synonymous	LOC540856
rs41566192	13	43,058,415	0.52	13.26	-1.27	0.00016**G	coding-nonsynonymous	MGC127374
rs41602212	19	37,837,691	0.46	16.91	1.53	0.00024**G	intron	CACNA1G
rs41645568	21	54,841,435	0.39	15.57	1.52	0.00047**G	nearest_gene	DICER1
rs41638600	21	62,412,401	0.50	8.01	-1.15	0.0026*	intron	AKT1
rs41651862	25	38,569,864	0.39	10.12	-1.22	0.00083*	coding-nonsynonymous	ZDHHC4
rs41650577	26	9,289,354	0.46	12.18	1.38	0.00028**G	intron	TNFRSF6

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome-wise ($P < 0.05$); **significant chromosome-wise ($P < 0.01$).

^GSignificant genome-wise ($P < 0.05$).

Eleven SNP were found to have a significant effect on dairy strength at the genome-wise and 9 at the chromosome-wise level ($P < 0.05$) on BTA 3, 5, 7, 10, 13, 19, 21, 25, and 26 (Table 6). Eight of these significant SNP are located in the introns of predicted genes, 7 of them are synonymous coding SNP, whereas 5 are not located in genes (Table 6). It has been found that SNP rs41604564 on BTA 5 (58,756,658 bp) corresponds to a QTL that has been previously reported to have an effect on dairy strength by Ashwell et al. (2005), who also detected several QTL regions affecting dairy strength.

Only 1 of these regions on BTA 5 was in a similar region to those found in the current study (SNP rs41604564). There are several potential reasons for this inconsistency between the 2 studies. One cause could be the presence of different QTL in the 2 animal populations (1,404 bulls from 10 families of the North American Holstein-Friesian). Another could be a lack of informative markers in this study for the regions found by Ashwell et al. (2005). Four of these SNP (rs41601701, rs41609478, rs41661265, rs41566192) also show significant association with angularity. It has been found

Table 7. Significant genome- and chromosome-wise single nucleotide polymorphisms (SNP) with overall rump

SNP NCBI ¹ ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	P-value	Functional class	Gene name
rs41578133	2	105,103,554	0.09	10.25	-2.50	0.00077*	coding-synonymous	LOC540098
rs43709845	3	17,701,057	0.51	20.11	1.51	0.00004**G	nearest_gene	CTSK
rs41609100	6	98,240,306	0.35	11.23	1.35	0.00046*	intron	FGF2
rs41656894	7	12,651,489	0.52	12.68	-1.18	0.00021*	nearest_gene	TSPAN16
rs41634707	8	50,183,175	0.44	8.38	1.04	0.0021*	intron	GNA14
rs41656444	8	57,171,946	0.32	10.28	-1.48	0.00076*	nearest_gene	MGC128728
rs41660431	11	29,041,552	0.44	9.35	1.19	0.0013*	intron	PPM1B
rs41636734	18	53,743,293	0.48	11.76	1.14	0.00034*	intron	CD37
rs41587258	25	22,580,988	0.35	8.32	1.11	0.0022*	nearest_gene	LOC617718
rs41649672	25	27,692,196	0.49	19.76	1.50	0.000055**G	mrna-utr	SUMF2
rs41587287	25	27,700,022	0.51	20.11	-1.51	0.000046**G	intron	SUMF2
rs29020548	25	38,121,530	0.46	6.83	-0.92	0.0051*	coding-synonymous	LOC527039
rs41647955	27	33,989,945	0.50	8.47	0.95	0.002*	intron	ANK1

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome-wise ($P < 0.05$); **significant chromosome-wise ($P < 0.01$).

^GSignificant genome-wise ($P < 0.05$).

Table 8. Significant genome- and chromosome-wise single nucleotide polymorphisms (SNP) with udder texture

SNP NCBI ¹ ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	P-value	Functional class	Gene name
rs41572038	3	57,607,378	0.27	22.85	2.37	0.000012** ^G	intron	LEC2
rs41604605	5	9,208,135	0.51	7.96	1.04	0.0027*	intron	LOC780969
rs41655901	5	28,108,890	0.47	9.18	-1.09	0.0014*	intron	GALNT6
rs41656703	5	32,429,000	0.52	8.10	-1.15	0.0025*	nearest_gene	MGC127063
rs41591891	5	81,733,566	0.44	12.27	1.53	0.00026*	intron	ITPR2
rs41588786	25	3,434,609	0.48	9.88	1.22	0.00095*	nearest_gene	LOC505453
rs41650226	27	12,861,193	0.35	8.58	-1.32	0.0019*	intron	IRF2

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome-wise ($P < 0.05$); **significant chromosome-wise ($P < 0.01$).

^GSignificant genome-wise ($P < 0.05$).

that SNP rs29014633 also shows significant association with angularity and stature, and SNP rs41602212 also shows significant association with angularity and milking temperament.

Three SNP were detected to have a significant effect on overall rump at the genome-wise and 10 at the chromosome-wise level ($P < 0.05$) on BTA 3, 6, 7, 8, 11, 18, 25, and 27 (Table 7). Of these significant SNP, 6 are located in the introns of predicted genes, 2 are synonymous coding SNP, and 5 are not located in any genes (Table 7). These 13 significant regions have not been reported previously. Because there is no comparable result from the literature, further investigations are encouraged in the future. In addition, SNP rs41660431 also shows significant association with herd life and daughter fertility.

Descriptive Type Traits

The whole genome scan to map QTL for 6 descriptive type traits identified 13 SNP significantly associated with these traits at the genome-wise level and 57 at the chromosome-wise level ($P < 0.05$). The details of the SNP are shown in Tables 8 to 13, for udder texture, median suspensory, foot angle, bone quality, stature, and angularity, respectively.

One SNP had significant effects on udder texture at the genome-wise and 6 at the chromosome-wise levels ($P < 0.05$) on BTA 3, 5, 25, and 27 (Table 8). It was found that SNP rs41572038 on BTA 3 (57,607,378 bp) had a significant effect on udder texture at the genome-wise level with an F-test statistic of 22.85 and allele substitution effects of 2.37. Of these significant SNP, 5 are located in the introns of predicted genes, and 2 of them are not located in genes (Table 8). The regions around SNP rs41591891 on BTA 5 (81,733,566 bp) has also been reported by Ashwell et al. (2005) for udder index at 119 cM. Two SNP (rs41588786, rs41650226) also show significant association with bone quality, whereas SNP rs41588786 was also significant with median suspensory. It has been found that SNP rs41656703 also shows significant association with dairy strength, whereas SNP rs41572038 also shows significant association with 2 traits stature, and herd life.

Nine SNP had significant effects on the median suspensory at the chromosome-wise level ($P < 0.05$) on BTA 2, 4, 5, 13, 22, 23, and 25 (Table 9). Two of these SNP (rs41655901 and rs41634501) on BTA 5 and BTA 23, respectively, have a significant effect on median suspensory at the chromosome-wise level ($P < 0.01$). Of the significant median suspensory SNP, 4 are located in

Table 9. Significant genome- and chromosome-wise single nucleotide polymorphisms (SNP) with median suspensory

SNP NCBI ¹ ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	P-value	Functional class	Gene name
rs41637504	2	555,621	0.45	8.98	1.01	0.0015*	nearest_gene	LOC512912
rs41636945	2	20,762,669	0.43	7.96	-0.99	0.0027*	nearest_gene	LOC540561
rs41591551	4	96,244,404	0.36	11.22	1.31	0.00046*	nearest_gene	KIAA1549
rs41655901	5	28,108,890	0.47	13.8	-1.27	0.00012**	intron	GALNT6
rs41632254	13	64,863,304	0.47	9.95	1.21	0.00091**	intron	BPI
rs41644471	22	46,449,737	0.46	8.32	-1.13	0.0022*	intron	CACNA1D
rs41634501	23	23,107,013	0.45	13.22	1.43	0.00015**	nearest_gene	LOC537895
rs41588808	25	2,521,355	0.45	8.42	-1.19	0.0021*	intron	LOC789778
rs41588786	25	3,434,609	0.48	9.89	1.14	0.00094**	nearest_gene	LOC505453

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome-wise ($P < 0.05$); **significant chromosome-wise ($P < 0.01$).

Table 10. Significant genome- and chromosome-wise single nucleotide polymorphisms (SNP) with foot angle

SNP NCBI ¹ ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	P-value	Functional class	Gene name
rs41584408	1	63,350,131	0.17	7.40	-1.56	0.0037*	intron	ITGB5
rs41567487	4	82,138,210	0.45	14.67	-1.46	0.000075** ^G	intron	WASL
rs41642656	5	102,927,637	0.45	20.05	-1.79	0.0000047** ^G	intron	VWF
rs41655488	5	107,896,631	0.19	9.64	-1.29	0.0011*	intron	ATP6V1E1
rs41595440	7	57,368,652	0.55	10.63	-1.20	0.00063*	coding-nonsynonymous	LOC509419
rs41645645	10	26,616,376	0.46	7.99	0.94	0.0027*	intron	HH114
rs43710950	10	41,992,224	0.39	12.08	-1.41	0.00029*	nearest_gene	TPM1
rs41653025	10	49,942,146	0.23	11.73	1.73	0.00035**	coding-synonymous	LOC540856
rs41593881	10	69,314,163	0.46	7.95	-1.01	0.0027*	intron	HIF1A
rs41588884	10	87,182,581	0.50	9.98	1.17	0.00089*	intron	TSHR
rs41634818	16	65,875,535	0.46	15.45	1.42	0.00005** ^G	intron	KCNH1

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome-wise ($P < 0.05$); **significant chromosome-wise ($P < 0.01$).

^GSignificant genome-wise ($P < 0.05$).

the introns of predicted genes, and 5 of them are not located in genes (Table 9). Two of these regions (555,621 and 64,863,304 bp) on BTA 2 and BTA 13 have been reported for front udder attachment and udder index by Ashwell et al. (2005). These 2 regions on BTA 2 and BTA 13 are good candidate regions for further investigation of candidate QTL affecting median suspensory and udder attachment in dairy cattle. It has been found that SNP rs41632254 also shows significant association with feet and leg and bone quality, whereas SNP rs41634501 also shows significant association with overall conformation and feet and leg.

Three SNP had significant effects on foot angle at the genome-wise and 8 at the chromosome-wise levels ($P < 0.05$) on BTA 1, 4, 5, 7, 10, and 16 (Table 10). Eight of these SNP are located in the introns of predicted genes, 2 of these SNP are synonymous coding SNP, whereas 1 is not located in any gene (Table 10). One of these regions, (57,368,652 bp) on BTA 7, has been reported for this trait at 83 cM of this chromosome by Ashwell et al. (2005). This region of the bovine genome showed strong evidence of harboring QTL affecting foot angle in cattle. It has been found that SNP rs41653025 also shows significant association with dairy strength.

Table 11. Significant genome- and chromosome-wise single nucleotide polymorphisms (SNP) with bone quality

SNP NCBI ¹ ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	P-value	Functional class	Gene name
rs41639301	1	114,963,599	0.34	12.01	1.53	0.00031*	coding-synonymous	LOC533642
rs29023607	3	1,043,852	0.32	9.71	1.46	0.0011*	intron	CD3Z
rs41650242	5	74,090,417	0.17	14.11	2.28	0.0001** ^G	intron	CACNG2
rs41658748	7	10,183,570	0.28	8.85	-1.45	0.0016*	intron	CACNA1A
rs41658737	7	10,335,915	0.30	8.68	1.38	0.0018*	intron	CACNA1A
rs41588239	7	12,077,407	0.45	9.92	-1.24	0.00092*	coding-synonymous	GADD45GIP1
rs41658022	7	35,844,869	0.43	14.66	1.44	0.000075** ^G	intron	SLC34A1
rs41645645	10	26,616,376	0.46	13.01	1.27	0.00018**	intron	HH114
rs29020608	11	95,980,305	0.13	10.92	-2.41	0.00054**	coding-synonymous	LOC617309
rs41632254	13	64,863,304	0.47	14.63	1.44	0.000076** ^G	intron	BPI
rs41603160	14	7,921,599	0.30	12.85	1.58	0.00019** ^G	intron	TG
rs29010770	19	21,530,439	0.49	10.79	-1.08	0.00057**	coding-synonymous	RPA1
rs41600178	19	41,647,314	0.13	10.00	-2.03	0.00088*	nearest_gene	GAS
rs41581582	20	51,741,640	0.20	7.81	1.53	0.0029*	intron	FLJ20152
rs41643786	21	45,669,248	0.36	7.76	-1.19	0.003*	coding-synonymous	MGC133693
rs41645547	21	52,902,193	0.47	9.28	-1.16	0.0013*	intron	LOC514011
rs41643866	22	40,066,742	0.20	13.54	-2.19	0.00013**	intron	LOC613533
rs41583038	23	5,098,037	0.10	10.55	2.54	0.00065*	coding-synonymous	LOC524959
rs41588786	25	3,434,609	0.48	11.23	1.22	0.00046*	nearest_gene	LOC505453
rs41650614	26	15,147,925	0.46	9.82	1.03	0.00098**	intron	DNTT
rs41650227	27	12,860,998	0.22	5.32	-1.24	0.012*	intron	IRF2

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome-wise ($P < 0.05$); **significant chromosome-wise ($P < 0.01$).

^GSignificant genome-wise ($P < 0.05$).

Table 12. Significant genome- and chromosome-wise single nucleotide polymorphisms (SNP) with stature

SNP NCBI ¹ ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	P-value	Functional class	Gene name
rs41581655	1	95,732,116	0.38	11.66	-1.42	0.00036*	coding-synonymous	LOC506307
rs41572038	3	57,607,378	0.27	13.98	1.79	0.0001**	intron	LEC2
rs29011323	4	56,130,854	0.48	11.61	-1.26	0.00037*	intron	CDC10
rs41592968	5	10,289,798	0.24	13.72	1.89	0.00012**	intron	C3F
rs29014633	5	74,016,631	0.44	11.44	1.33	0.00041*	intron	CACNG2
rs41591943	7	39,956,874	0.37	12.90	1.51	0.00019*	nearest_gene	LOC527275
rs29026038	11	63,320,525	0.44	13.00	1.30	0.00018*	intron	ANXA4
rs41640016	19	16,342,539	0.17	11.95	1.97	0.00031*	coding-nonsynonymous	LOC614984
rs41567447	24	39,886,746	0.22	8.26	1.57	0.0022*	nearest_gene	LOC781824

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome wise ($P < 0.05$); **significant chromosome-wise ($P < 0.01$).

We detected 4 SNP that had significant effects on bone quality at the genome-wise and 17 at the chromosome-wise levels ($P < 0.05$) on BTA 1, 3, 5, 7, 10, 11, 13, 14, 19, 20, 21, 22, 23, 25, 26, and 27 (Table 11). Of these 21 SNP, 13 are located in the introns of predicted genes, 6 of them are synonymous coding SNP, whereas 2 of them are not located in genes (Table 11). Five of these regions (10,335,915; 12,077,407; 51,741,640; 5,098,037; 15,147,925 bp) detected in the present study on BTA 7, 20, 23, and 26 have been reported in a previous study (Ashwell et al., 2005). The results of current and previous studies shown are strong evidence of QTL on BTA 7, 20, 23, and 26 for bone quality in dairy cattle.

Nine SNP have been detected that have a significant effect on stature at the chromosome-wise level ($P < 0.05$) on BTA 1, 3, 4, 5, 7, 11, 19, and 24 (Table 12). Two of these SNP (rs41572038 and rs41592968) on BTA 3 and BTA 5 had a significant effect on stature at the chromosome-wise level of $P < 0.01$. Among the 9 significant SNP, 5 of them are located in the introns of predicted genes, and 2 of them are synonymous coding SNP (Table

12). Three of these regions (56,130,854; 16,342,539; 39,886,746 bp) on BTA 4, 19, and 24 have been reported by Ashwell et al. (2005). These 9 regions of the bovine genome detected in this study should serve as candidate regions for further investigation. It has been found that SNP rs41591943 shows significant association with dairy strength, and SNP rs29014633 shows significant association with 2 other traits, dairy strength and angularity.

For angularity, 5 SNP were found to have a significant effect at the genome-wise and 8 at the chromosome-wise level ($P < 0.05$) on BTA 3, 5, 7, 13, 19, 26, 28, and 29 (Table 13). Of these significant SNP, 9 and 3 of them are located in the introns of predicted genes and synonymous coding SNP, respectively, and 1 of them is not located in a gene (Table 13). None of the 13 significant regions have been previously associated with angularity in dairy cattle. In addition, SNP rs41586983 also shows significant association with maternal calving ease.

Table 13. Significant genome- and chromosome-wise single nucleotide polymorphisms (SNP) with angularity

SNP NCBI ¹ ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	P-value	Functional class	Gene name
rs41601701	3	98,500,067	0.08	14.24	2.94	0.000093** ^G	coding-synonymous	MGC139728
rs41604534	5	29,067,052	0.55	8.36	1.03	0.0021*	intron	KRT5
rs29014633	5	74,016,631	0.44	10.37	1.20	0.00073*	intron	CACNG2
rs41590827	5	75,905,624	0.42	11.47	1.35	0.0004*	intron	RAC2
rs41591892	5	81,801,975	0.52	7.58	-0.89	0.0033*	intron	ITPR2
rs41578761	7	36,718,783	0.49	14.82	-1.31	0.000069** ^G	intron	LOC529633
rs41609478	7	37,343,116	0.50	15.77	1.39	0.000042** ^G	nearest_gene	LOC538639
rs41661265	7	50,312,323	0.46	15.46	-1.29	0.000049** ^G	coding-synonymous	MGC155209
rs41566192	13	43,058,415	0.52	15.03	-1.30	0.000062** ^G	coding-nonsynonymous	MGC127374
rs41602212	19	37,837,691	0.46	12.20	1.26	0.00027*	intron	CACNA1G
rs41648723	26	40,422,508	0.23	9.53	-1.45	0.0011*	intron	CTBP2
rs41606880	28	21,540,955	0.57	10.90	-1.11	0.00054*	intron	JDP1
rs41586983	29	7,579,883	0.23	10.59	1.66	0.00064*	intron	EED

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome-wise ($P < 0.05$); **significant chromosome-wise ($P < 0.01$).

^GSignificant genome-wise ($P < 0.05$).

Table 14. Significant genome- and chromosome-wise single nucleotide polymorphisms (SNP) with herd life

SNP NCBI ¹ ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	P-value	Functional class	Gene name
rs29012920	2	3,605,592	0.43	11.07	-0.06	0.00049*	intron	PROC
rs41572038	3	57,607,378	0.27	13.74	0.09	0.00012** ^G	intron	LEC2
rs29013620	7	98,895,573	0.33	15.98	0.09	0.00038** ^G	coding-synonymous	LOC521539
rs41657163	9	12,369,884	0.46	8.13	-0.05	0.0025*	coding-synonymous	LOC535127
rs41656367	9	85,942,784	0.50	9.72	0.05	0.001*	intron	VIL2
rs41658400	11	24,918,752	0.50	8.77	0.05	0.0017*	intron	EPAS1
rs41660431	11	29,041,552	0.44	10.50	0.06	0.00068*	intron	PPM1B
rs41626908	12	32,355,128	0.26	11.29	0.08	0.00044**	coding-synonymous	MGC139047
rs41639261	20	30,876,706	0.43	10.98	-0.06	0.00052*	intron	GHR
rs41580285	20	32,099,693	0.36	10.90	-0.06	0.00054*	intron	NNT
rs41640212	20	36,431,884	0.40	8.55	0.05	0.0019*	intron	SLC1A3
rs41581582	20	51,741,640	0.20	5.26	0.06	0.012*	intron	FLJ20152
rs41584559	22	34,688,462	0.11	11.11	0.13	0.00048**	coding-synonymous	LOC780993
rs41643866	22	40,066,742	0.20	13.94	-0.11	0.00011** ^G	intron	LOC613533
rs29024274	22	46,425,659	0.31	18.80	-0.10	0.00009** ^G	intron	CACNA1D
rs41641232	23	19,093,160	0.44	9.87	-0.06	0.00095*	intron	RHAG

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome-wise ($P < 0.05$); **significant chromosome-wise ($P < 0.01$).

^GSignificant genome-wise ($P < 0.05$).

Functional Traits

The whole genome scan to map QTL for functional traits identified 8 SNP significantly associated with these traits at the genome-wise level and 58 SNP at the chromosome-wise level ($P < 0.05$). The details of the SNP showing association with these traits are given in Tables 14 to 19 for herd life, daughter fertility, milking speed, milking temperament, calving ease, and maternal calving ease, respectively.

Four SNP were detected to have a significant effect on herd life at the genome-wise and 12 at the chromosome-wise level ($P < 0.05$) on BTA 2, 3, 7, 9, 11, 12, 20, 22,

and 23 (Table 14). One of these regions (19,093,160 bp) on BTA 23 has been reported by Kuhn et al. (2003) at 24 ± 16 cM on this chromosome, whereas the remaining regions are new findings of the present study. The confirmed QTL on BTA 23 in the current study provides strong evidence for QTL affecting herd life, and the new findings for this trait in the current paper should provide a foundation for further investigations for the QTL affecting this trait. Twelve of these significant SNP are located in the introns of predicted genes, and 4 of them are synonymous coding SNP (Table 14). It has been found that SNP rs29013620 showed significant

Table 15. Significant genome- and chromosome-wise single nucleotide polymorphisms (SNP) with daughter fertility

SNP NCBI ¹ ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	P-value	Functional class	Gene name
rs41640518	2	87,002,903	0.52	10.40	1.09	0.00071*	nearest_gene	LOC521734
rs41636478	2	108,326,427	0.52	8.89	1.12	0.0016*	intron	PDE6D
rs41590152	4	67,936,574	0.53	10.67	1.16	0.00062*	intron	ADCY1
rs41657867	11	23,532,560	0.12	11.49	2.26	0.0004**	intron	SLC8A1
rs41660431	11	29,041,552	0.44	7.99	1.10	0.0027*	intron	PPM1B
rs29026844	11	57,582,523	0.48	8.91	-1.05	0.0016*	intron	SLC1A4
rs29010310	12	31,526,216	0.50	7.17	-0.95	0.0042*	coding-synonymous	LOC539378
rs41633631	14	7,969,609	0.49	9.02	-1.00	0.0015*	intron	TG
rs41584901	19	20,610,368	0.49	11.19	1.22	0.00047**	coding-synonymous	LOC512334
rs41640182	20	34,802,135	0.47	9.02	-1.00	0.0015*	nearest_gene	MGC155116
rs41584559	22	34,688,462	0.11	7.45	2.09	0.0036*	coding-synonymous	LOC780993
rs41643866	22	40,066,742	0.20	10.26	-1.86	0.00077*	intron	LOC613533
rs29024274	22	46,425,659	0.31	11.92	-1.57	0.00032**	intron	CACNA1D
rs41585938	22	51,240,319	0.22	7.77	-1.56	0.003*	coding-synonymous	LOC523793
rs41667511	23	13,897,540	0.08	10.70	-1.42	0.00061*	intron	BYSL
rs41607485	27	12,842,179	0.10	11.42	2.57	0.00041**	intron	IRF2
rs43706139	29	33,480,476	0.51	12.73	-1.34	0.00021**	mrna-utr	SLC3A2

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome-wise ($P < 0.05$); **significant chromosome-wise ($P < 0.01$).

Table 16. Significant genome- and chromosome-wise single nucleotide polymorphisms (SNP) with milking speed

SNP NCBI ¹ ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	P-value	Functional class	Gene name
rs29024165	1	8,164,917	0.08	11.33	3.58	0.00043*	intron	ADAMTS5
rs41571923	1	134,451,951	0.47	12.38	-1.53	0.00025**	nearest_gene	LSS
rs29020989	10	19,944,056	0.30	12.72	1.98	0.00021**	intron	TGM1
rs41600178	19	41,647,314	0.13	10.57	-2.50	0.00065*	nearest_gene	GAS
rs41644418	24	20,051,012	0.43	11.91	1.62	0.00032**	intron	HMCS
rs41606777	26	34,495,734	0.40	9.41	1.50	0.0012*	intron	SLC18A2
rs41647383	27	32,834,272	0.20	8.02	-1.88	0.0026*	coding-synonymous	FGFR1

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome-wise ($P < 0.05$); **significant chromosome-wise ($P < 0.01$).

association with calving ease, and SNP rs41584559 showed significant association with daughter fertility.

For daughter fertility, 17 SNP were found to have significant effects on this trait at the chromosome-wise level ($P < 0.05$) on BTA 2, 4, 11, 12, 14, 19, 20, 22, 23, 27, and 29 (Table 15). Five of these SNP (rs41657867, rs41584901, rs29024274, rs41607485, rs43706139) on BTA 11, 19, 22, 27, and 29 had significant effects on daughter fertility at the chromosome-wise level ($P < 0.01$). Ten of these SNP are located in the introns of predicted genes, 4 are synonymous coding SNP, and 3 are not located in genes (Table 15). Two of these regions (7,969,609; 12,842,179 bp) on BTA 14 and BTA 27 have been reported previously by Schnabel et al. (2005). Two of these SNP (rs41590152, rs41657867) also show significant association with calving ease. It has been found that SNP rs29024274 also shows significant association with milking temperament, whereas SNP rs41667511 also shows significant association with 3 more traits, maternal calving ease, calving ease, and milking temperament.

Seven SNP with significant effects on milking speed at the chromosome-wise level ($P < 0.05$) were detected on BTA 1, 10, 19, 24, 26, and 27 (Table 16), and 3 of

these SNP (rs41571923, rs29020989, rs41644418) on BTA 1, 10, and 24 had significant effects on milking speed at the chromosome-wise level ($P < 0.01$). Of these 7 significant SNP, 4 are located in the introns of predicted genes, 1 is a synonymous coding SNP, whereas 2 are not located in genes. The SNP rs41600178 on BTA 19 (41,647,314 bp) has been reported to affect milking speed by Schrooten et al. (2004) at 70 ± 15 cM, whereas the remaining 6 SNP are specific to the present study. In addition, SNP rs41606777 showed significant association with milking temperament.

One significant SNP affecting milking temperament at the genome-wise level ($P < 0.05$) and 9 SNP with a significant effect on milking temperament at the chromosome-wise level ($P < 0.05$) were detected on BTA 4, 13, 19, 22, 23, 26, and 29 (Table 17). It has been found that SNP rs41602212 on BTA 19, located at 37,837,691 bp, has an F-test value of 21.67 and allele substitution effects of 2.11. Six of these significant SNP are located in the introns of predicted genes, 3 of them are synonymous, and 1 of them is not located in a gene region (Table 17).

Two SNP had a genome-wise and 7 SNP had a chromosome-wise level of significant effects ($P < 0.05$) on

Table 17. Significant genome- and chromosome-wise single nucleotide polymorphisms (SNP) with milking temperament

SNP NCBI ¹ ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	P-value	Functional class	Gene name
rs41587635	4	40,499,442	0.11	12.97	-3.06	0.00018**	intron	NRCAM
rs41601522	13	60,045,226	0.43	12.29	-1.3	0.00026*	coding-synonymous	MGC142355
rs41602212	19	37,837,691	0.46	21.67	2.11	0.0000021** ^G	intron	CACNA1G
rs29024274	22	46,425,659	0.31	12.48	-2.03	0.00024*	intron	CACNA1D
rs41667511	23	13,897,540	0.08	10.71	-1.75	0.00061*	intron	BYSL
rs41606777	26	34,495,734	0.40	11.41	1.65	0.00041*	intron	SLC18A2
rs41584970	29	23,068,761	0.75	9.72	1.02	0.0011*	nearest_gene	LOC782544
rs29024010	29	30,954,390	0.31	10.07	-2.01	0.00085*	intron	HNT
rs41652321	29	36,737,805	0.25	13.31	2.33	0.00015**	coding-nonsynonymous	LOC510943
rs43706181	29	38,944,167	0.35	8.94	1.6	0.0016*	coding-synonymous	DPP3

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome-wise ($P < 0.05$); **significant chromosome-wise ($P < 0.01$).

^GSignificant genome-wise ($P < 0.05$).

Table 18. Significant genome- and chromosome-wise single nucleotide polymorphisms (SNP) with direct calving ease

SNP NCBI ¹ ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	P-value	Functional class	Gene name
rs41590152	4	67,936,574	0.53	10.84	1.60	0.00056*	intron	ADCY1
rs41655043	6	92,323,386	0.53	11.60	-1.57	0.00038*	intron	PTPN13
rs41591742	8	97,443,379	0.17	9.94	-2.43	0.00091*	intron	PAPPA
rs41657867	11	23,532,560	0.12	11.56	3.00	0.00038*	intron	SLC8A1
rs41636749	18	52,852,134	0.38	17.87	-2.39	0.000014*** ^G	coding-synonymous	LOC538513
rs41565419	21	54,857,317	0.52	7.90	1.30	0.0028*	nearest_gene	DICER1
rs41638600	21	62,412,401	0.50	10.15	1.71	0.00082*	intron	AKT1
rs41667511	23	13,897,540	0.08	30.81	-3.17	0.00000002*** ^G	intron	BYSL
rs41587540	23	22,135,294	0.40	8.79	1.55	0.0017*	coding-synonymous	LOC510825

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome-wise ($P < 0.05$); **significant chromosome-wise ($P < 0.01$).

^GSignificant genome-wise ($P < 0.05$).

direct calving ease on BTA 4, 6, 8, 11, 18, 21, and 23 (Table 18). Six of these significant SNP are located in the introns of predicted genes, and 2 of them are synonymous coding SNP (Table 18). Four of these regions (92,323,386; 97,443,379; 13,897,540; 22,135,294 bp) on BTA 6, 8, and 23 were previously associated with direct calving ease by Smaragdov et al. (2006).

One and 6 SNP had significant effects on maternal calving ease at the genome- and chromosome-wise levels ($P < 0.05$), respectively, on BTA 7, 9, 23, 24, 28, and 29. Of the 7 significant SNP, 5 are located in the introns of predicted genes, and 2 of them are synonymous coding SNP (Table 19). Two of these regions (85,942,784; 41,818,493 bp) on BTA 9 and BTA 24 were previously associated with maternal calving ease by Ashwell et al. (2005).

CONCLUSIONS

This study has used a medium-density genome-wide scan, using SNP markers located in or nearby known genes. Considering the marker density used, it is unlikely that any of the SNP found associated with conformational or functional traits represent causal muta-

tions. It does, however, provide a starting point for uncovering quantitative trait nucleotides, particularly where the results of this study are backed up by other independent studies. Among the 60 significant SNP for the 5 major type traits, 5 of these regions have been reported in previous studies by various authors. Of the 70 SNP that had significant associations with 6 descriptive type traits, 12 of the regions have been reported in previous studies. Of the 66 SNP associated with functional traits, 10 of these regions have been reported in previous studies. Use of much denser marker sets recently developed for cattle will no doubt aid in moving from the marker associations, such as those reported in this study, toward revealing the causal mutations underlying many of the economically important traits in dairy cattle.

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Table 19. Significant genome- and chromosome-wise single nucleotide polymorphisms (SNP) with maternal calving ease

SNP NCBI ¹ ID	BTA ²	Position (bp)	Heterozygosity	F-test	Effects	P-value	Functional class	Gene name
rs29013620	7	98,895,573	0.33	16.21	2.49	0.000034*** ^G	coding-synonymous	LOC521539
rs41656367	9	85,942,784	0.50	9.10	1.46	0.0014*	intron	VIL2
rs41667511	23	13,897,540	0.08	12.52	-2.2	0.00023*	intron	BYSL
rs41646680	24	41,818,493	0.52	8.87	-1.48	0.0016*	coding-synonymous	LOC511553
rs29023262	28	11,084,209	0.52	7.60	-1.37	0.0033*	intron	CHRM3
rs41652496	28	23,732,208	0.33	9.22	1.77	0.0013*	intron	PP
rs41586984	29	7,578,139	0.39	9.09	1.78	0.0014*	intron	EED

¹NCBI = National Center for Biotechnology Information.

²BTA = *Bos taurus* autosome.

*Significant chromosome-wise ($P < 0.05$); **significant chromosome-wise ($P < 0.01$).

^GSignificant genome-wise ($P < 0.05$).

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