Identification and fine mapping of quantitative trait loci for growth traits on bovine chromosomes 2, 6, 14, 19, 21, and 23 within one commercial line of *Bos taurus*[1]

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ABSTRACT: We report the identification and fine mapping of QTL for birth weight (BWT), preweaning ADG (PWADG), and postweaning ADG on feed (ADGF) in a commercial line of *Bos taurus* using an identical-by-descent haplotype sharing method. One hundred seventy-six calves of 12 bulls (9 to 30 male calves from each sire) of the Beefbooster, Inc., M1 line were typed using 71 genetic markers from bovine chromosomes (BTA) 2, 6, 14, 19, 21, and 23 (8 to 16 markers from each chromosome). Sixteen haplotypes were found to have significant ($P < 0.05$) associations with BWT at the comparison-wise threshold. The 16 haplotypes span 13 chromosomal regions, two on BTA 2 (9.1 to 22.5 cM and 95.0 to 100.3 cM), three on BTA 6 (8.2 to 11.8 cM, 35.5 to 49.7 cM, and 83.0 to 86.2 cM), three on BTA 14 (26.0 to 26.7 cM, 36.2 to 46.2 cM, and 52.0 to 67.7 cM), one on BTA 19 (52.0 to 52.7 cM), two on BTA 21 (9.9 to 20.4 cM and 28.2 to 46.1 cM), and two on BTA 23 (23.9 to 36.0 cM and 45.1 to 50.9 cM). Thirteen haplotypes spanning seven chromosomal regions significantly affected ($P < 0.05$) PWADG at the comparison-wise threshold. The seven chromosomal regions include two regions on BTA 6 (11.8 to 44.2 cM and 83.0 to 86.2 cM), one on BTA 14 (26.7 to 50.8 cM), one on BTA 19 (4.8 to 15.9 cM), one on BTA 21 (9.9 to 20.4 cM), and two on BTA 23 (17.3 to 36.0 cM and 45.1 to 50.9 cM). For ADGF, 11 haplotypes were identified to have significant associations ($P < 0.05$) at the comparison-wise threshold. The 11 haplotypes represented eight chromosomal regions, one on BTA 2 (9.1 to 22.5 cM), two on BTA 6 (49.7 to 50.1 cM and 59.6 to 63.6 cM), two on BTA 14 (17.0 to 24.0 cM and 36.2 to 46.2 cM), two on BTA 19 (52.0 to 52.7 cM and 65.1 to 65.7 cM), and one on BTA 21 (46.1 to 53.1 cM). The QTL regions identified and fine mapped in this study will provide a reference for future positional candidate gene research and marker-assisted selection of various growth traits.

Key Words: Cattle, Growth, Haplotype Sharing Analysis, Quantitative Trait Loci

Introduction

A number of recent studies have reported the identification and mapping of QTL for growth and carcass traits in beef cattle (Davis et al., 1998; Stone et al., 1999; Casas et al., 2000). Some of these QTL, however, have been localized to large chromosomal segments (>30 cM) and are sometimes weakly supported. Fine mapping of those QTL is thus necessary to confirm and narrow down the chromosomal regions to provide a valuable reference for further positional candidate gene research.

Individuals within a semiclosed population, such as a commercial line of cattle, are expected to be derived from one or a limited number of founders. Thus, some common haplotypes originating from the common ancestors should carry on and segregate among the individuals of the breeding line, particularly when selection is applied. These common haplotypes may harbor QTL of interest and make it possible to locate QTL segregating in the line. Such an identical-by-descent haplotype-sharing QTL mapping strategy directly uses commercial herds and therefore avoids the generation of a well-designed mapping population. Obtaining such well-de-

signed mapping populations is costly and may be impractical in beef cattle. Fine mapping of QTL by analyzing identical-by-descent haplotypes has been successfully demonstrated in commercial populations of beef cattle (Li et al., 2002a,b; Moore et al., 2003), as well as in dairy cattle (Riquet et al., 1999). We report here the identification and fine mapping of QTL for growth traits in a commercial line of *Bos taurus* on bovine chromosomes (**BTA**) 2, 6, 14, 19, 21, and 23, chromosomes with previously identified growth QTL (Davis et al., 1998; Elo et al., 1999; Stone et al., 1999; Casas et al., 2000).

Materials and Methods

Animals, DNA Samples, and Phenotypic Data

In the spring of 1998, male calves were identified, and calf birth weights (**BWT**) at or near birth, as well as birth date, were recorded by Beefbooster, Inc. (Calgary, Canada), the company responsible for breeding the cattle. A 10-mL blood sample was collected by venipuncture from each male calf and potential sires. The DNA from each blood sample was extracted. Parentage identification of each male calf was carried out later by the Saskatchewan Research Council, Canada, using microsatellite markers. Meanwhile, cows and calves were placed on tame pastures from May through mid-September and October. In the fall of 1998, the calves were weaned and weighed between September 16 and October 20. The preweaning ADG (**PWADG**) was calculated as the difference between weaning weight and birth weight divided by days between weaning date and birth date. Over one-third (38.6%) of the bull calves with the lowest preweaning gain were then culled. The remaining male calves were placed in feedlot pens for postweaning performance testing. Briefly, animals were first placed in one of the feedlot pens, where they were adjusted to diet and environment over 21 to 29 d before the test. During the adjustment period, animals were fed a diet consisting of 50.5% barley silage, 15.0% chopped hay, 21.1% rolled barley grain, 10.0% wheat mill run pellets, and 3.4% calf supplement (as-fed basis). After the adjustment, animals were placed on a 120-d growth performance test. During the first 17-d test, the animals were fed the same diet as in the adjustment period, followed by a 22-d test, in which they were fed a diet consisting of 72.0% barley silage, 5.2% rolled barley grain, 20.0% wheat mill run pellets, and 2.8% calf supplement (as-fed basis). During the last 81-d test, the animals were fed a diet consisting of 87.5% barley silage, 10.1% wheat mill run pellets, and 2.4% calf supplement (as-fed basis). The postweaning ADG on feed (**ADGF**) was then calculated as the difference between weight when the test started and weight when the test ended divided by the days of test.

Genotyping and Haplotype Identification

One hundred seventy-six calves and their 12 sires (nine to 30 calves of each sire) of the M1 line were
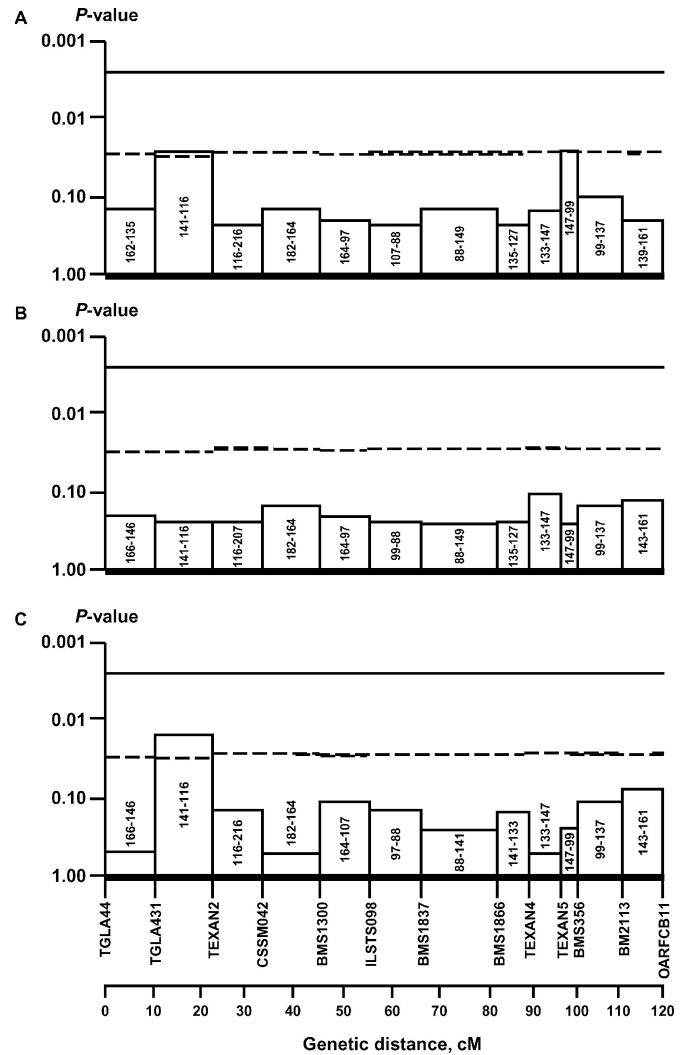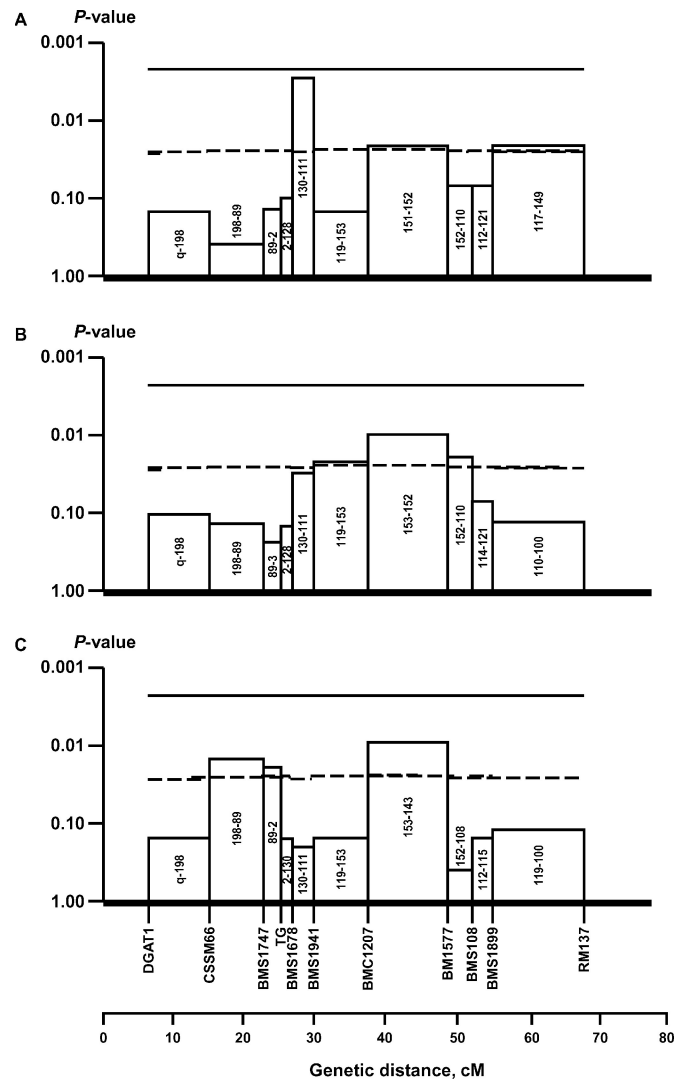

Figure 1. Haplotypes with the lowest *P*-values between adjacent loci along bovine chromosome 2 for birth weight (A), preweaning ADG (B), and ADG on feed (C) in the M1 commercial line of *Bos taurus* from Beefbooster, Inc. Haplotypes were defined by two alleles of a pair of loci. For example, haplotype TGLA431-141/TEXAN2-116 represents a segment of chromosome having allele 141 of TGLA431 and allele 116 of TEXAN2. The genetic map distance is indicated in cM. The dashed line represents the comparison-wise threshold *P*-value level, whereas the solid line represents the chromosome-wise *P*-value threshold level.

genotyped using 71 genetic markers: 13 from BTA 2, 16 from BTA 6, 11 from BTA 14, 14 from BTA 19, 8 from BTA 21, and 9 from BTA 23. The M1 line is an intermediate-framed strain developed from an Angus base and selected according to a selection index described by MacNeil and Newman (1994). The genetic markers genotyped on each chromosome (Figures 1 to 6) were chosen at an approximately even genetic distance and spanned, on average, 91.1% of the chromosomes, with a range of 70.0 (BTA 6) to 99.9% (BTA 23). Marker locations on BTA 2, 6, 19, 21, and 23, the primer
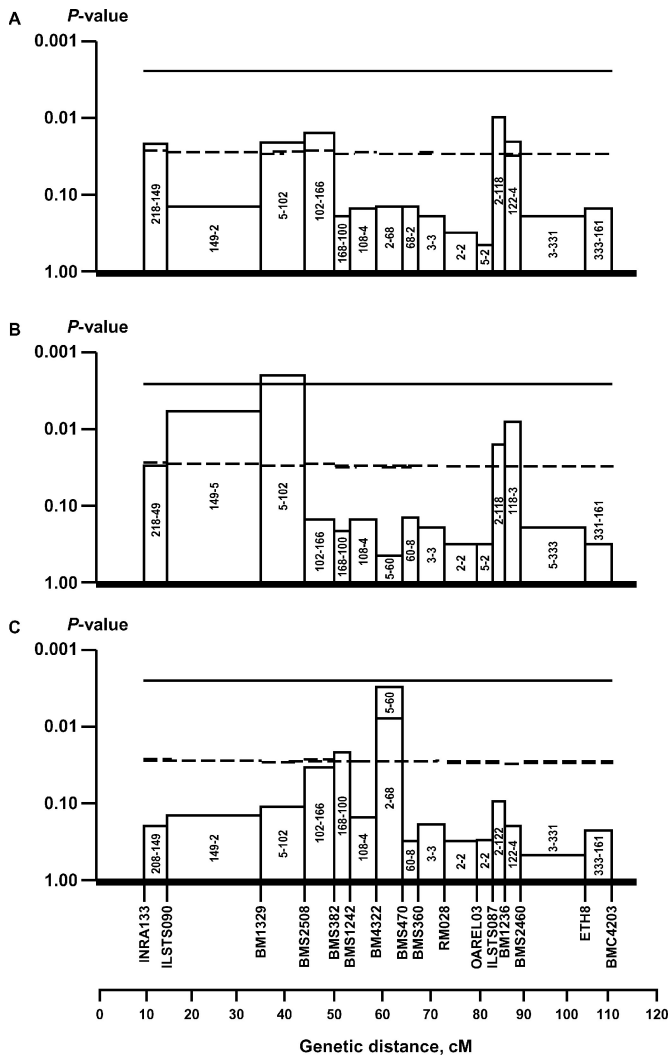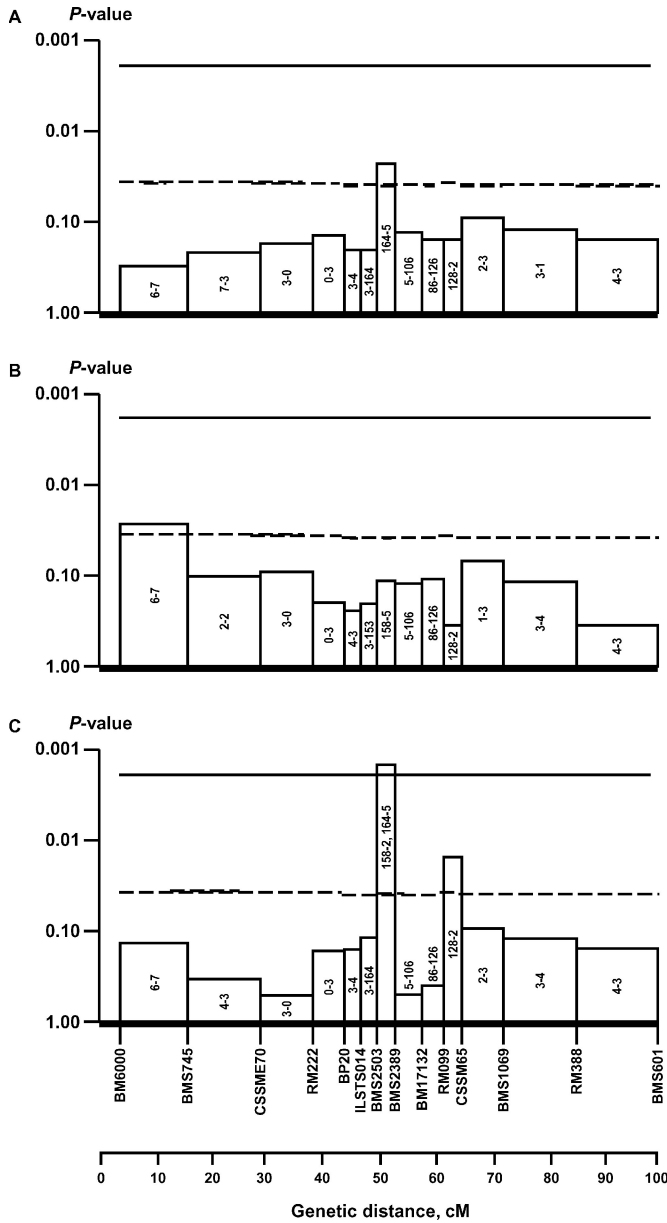
Figure 2. Haplotypes with the lowest *P*-values between adjacent loci along bovine chromosome 6 for birth weight (A), preweaning ADG (B), and ADG on feed (C) in the M1 commercial line of *Bos taurus* from Beefbooster, Inc. Haplotypes were defined by two alleles of a pair of loci. For example, haplotype INRA133-218/ILSTS090-149 represents a segment of chromosome having allele 218 of INRA133 and allele 149 of ILSTS090. The genetic map distance is indicated in centimorgans. The dashed line represents the comparison-wise threshold *P*-value level, whereas the solid line represents the chromosome-wise *P*-value threshold level.

Figure 3. Haplotypes with the lowest *P*-values between adjacent loci along bovine chromosome 14 for birth weight (A), preweaning ADG (B), and ADG on feed (C) in the M1 commercial line of *Bos taurus* from Beefbooster, Inc. Haplotypes were defined by two alleles of a pair of loci. For example, haplotype BMS1678-130/BMS1941-111 represents a segment of chromosome having allele 130 of BMS1678 and allele 111 of BMS1941. The genetic map distance is indicated in centimorgans. The dashed line represents the comparison-wise threshold *P*-value level, whereas the solid line represents the chromosome-wise *P*-value threshold level.

sequence, and other genetic marker information, including marker size and number of alleles, were obtained from the bovine genome maps on the USDA MARC Web site (http://www.marc.usda.gov/genome/genome.html), whereas consensus marker or gene locations on BTA 14 were determined using the bovine genome map on the USDA MARC Web site, bovine and human RH comparative maps (Band et al., 2000; http://bos.cvm.tamu.edu/htmls/rhbta.html), and the BTA 14 linkage map reported by Grisart et al. (2002).

Haplotype identification was carried out along all the chromosomes as described elsewhere (Li et al., 2002a,b). Briefly, genotypes of each of the 176 male calves were checked against the sire's genotype to verify sire inheritance. For each calf, alleles of each locus contributed by the sire and by the dam were identified. The haplotypes (allele linkage phases) of each individual male calf were then established along all chromosomes. For example, the haplotype TGLA431-141/TEXAN2-116 represents a section of the chromosome
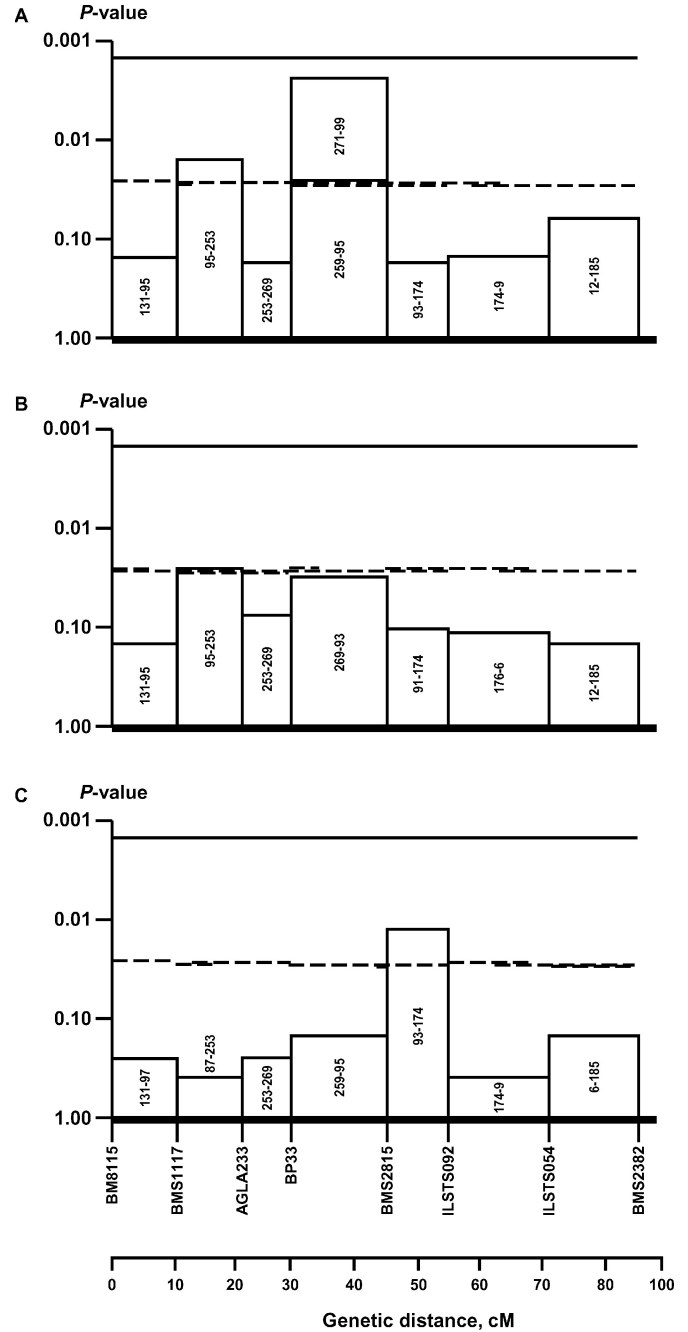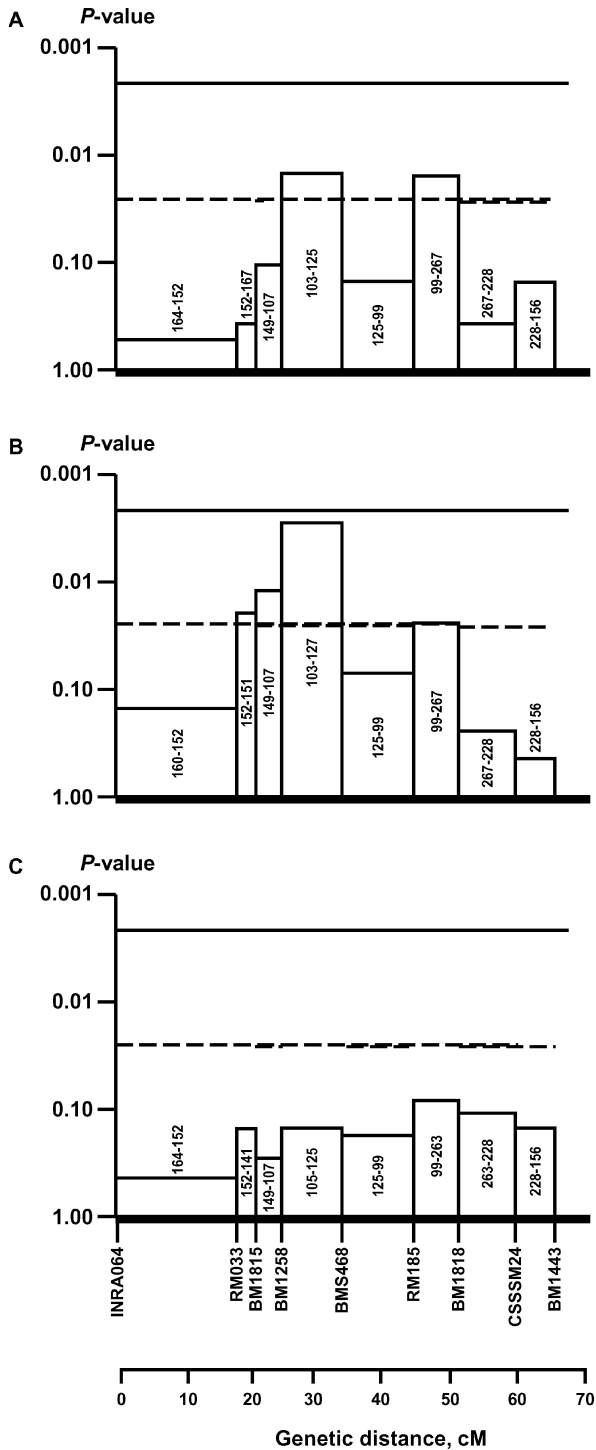
Figure 4. Haplotypes with the lowest *P*-values between adjacent loci along bovine chromosome 19 for birth weight (A), preweaning ADG (B), and ADG on feed (C) in the M1 commercial line of *Bos taurus* from Beefbooster, Inc. Haplotypes were defined by two alleles of a pair of loci. For example, haplotype BMS2503-164/BM2839-5 represents a segment of chromosome having allele 164 of BMS2503 and allele 5 of BM2839. The genetic map distance is indicated in centimorgans. The dashed line represents the comparison-wise threshold *P*-value level, whereas the solid line represents the chromosome-wise *P*-value threshold level.

Figure 5. Haplotypes with the lowest *P*-values between adjacent loci along bovine chromosome 21 for birth weight (A), preweaning ADG (B), and ADG on feed (C) in the M1 commercial line of *Bos taurus* from Beefbooster Inc. Haplotypes were defined by two alleles of a pair of loci. For example, haplotype BMS1117-95/AGLA233-253 represents a segment of chromosome having allele 95 of BMS1117 and allele 253 of AGLA233. The genetic map distance is indicated in centimorgans. The dashed line represents the comparison-wise threshold *P*-value level, whereas the solid line represents the chromosome-wise *P*-value threshold level.

having allele 141 at TGLA431 (TGLA431-141) and allele 116 at TEXAN2 (TEXAN2-116). Haplotypes of adjacent loci occurring at a frequency of more than 8% were used in further analysis of associations between a haplotype and the growth traits. Haplotypes that extended

Figure 6. Haplotypes with the lowest *P*-values between adjacent loci along bovine chromosome 23 for birth weight (A), preweaning ADG (B), and ADG on feed (C) in the M1 commercial line of *Bos taurus* from Beefbooster, Inc. Haplotypes were defined by two alleles of a pair of loci. For example, haplotype BM1258-103/BMS468-125 represents a segment of chromosome having allele 103 of BM1258 and allele 125 of BMS468. The genetic map distance is indicated in centimorgans. The dashed line represents the comparison-wise threshold *P*-value level, whereas the solid line represents the chromosome-wise *P*-value threshold level.

more than two loci were not included in the final analysis because of their relatively lower frequencies in the data set.

Statistical Analyses

Data were analyzed using the GLM procedure of SAS (Version 8; SAS Inst., Inc., Cary, NC). The GLM procedure was used to test the association between a given haplotype and the various growth traits. The linear model was as follows:

$$Y_{ijk} = \mu + T_i + H_j + (TH)_{ij} + \beta(A_{ijk} - \overline{A}...) + E_{ijk}$$

where Y_{ijk} = the observation of animal k for haplotype i under herd j, μ = overall experimental mean, T_i = haplotype effect, equal to 1 when the individual has the haplotype and 0 when the individual is without the haplotype, H_j = herd effect, equal to 1 or 2 (two herds were used), TH_{ij} = the interaction between the haplotype effect and the herd effect, $\beta(A_{ijk} - \overline{A}...)$ = dam age effect as a covariate, and E_{ijk} = residual error. The uncertain haplotypes (22.6%, on average) were considered missing values and were deleted from the analysis. Individuals carrying two copies of the haplotype were combined with individuals carrying one copy of the haplotype as class "1" because of the small number of individuals carrying two copies of the haplotype in the data set.

Type III sums of squares were used in all *F*-tests. Haplotype effect and herd effect were treated as fixed effects. Haplotype effect in standard deviations was estimated by dividing the difference of the growth trait least squares means between haplotype classes "1" and "0" by the standard deviation of the trait. The relevant statistics for the three growth traits analyzed were summarized in Table 1 of Li et al. (2002b).

The comparison-wise and chromosome-wise threshold *P*-values were generated empirically from a modified version of the permutation method outlined by Churchill and Doerge (1994) and as described by Li et al. (2002b) for the three growth traits in the M1 line. Briefly, individuals were indexed from 1 to *n*. Their phenotypic data was then randomly shuffled and also indexed from 1 to *n*; it was then assigned back to the individual with the same index. Randomly shuffled data were analyzed again for haplotype association along each of BTA 2, 6, 14, 19, 21, and 23. The process of shuffling was repeated 1,000 times and the corresponding lowest *P*-value for the three traits was recorded at the haplotype level and at the chromosome level. The comparison-wise threshold of *P*-value for a given haplotype was calculated by choosing the 100(1−α) percentile (α is the type I error) of its *P*-value distribution at the haplotype level for each trait. The 100(1−α) percentile of the 1000 lowest *P*-values at the chromosome level for the three growth traits was selected as the empirical chromosome-wise threshold for these traits. Type I error rates of 0.05 and 0.10 were used for calculating comparison-wise and chromosome-wise *P*-value thresholds, respectively.

Results

On average, 6.6 alleles were detected for each locus on the chromosomes, with a range of two to 14 alleles per locus. The frequencies of the most common haplotypes analyzed in this study ranged from 8.5 to 46.0%, with an average of 18.5%. In total, 34 haplotypes were found to have significant associations with the three growth traits at the comparison-wise threshold level and six of them had significant effects on more than one growth trait. Among the 34 haplotypes, three haplotypes, BM1329-5/BMS2508-102, BMS 2503-158/ BMS 2389-2, and BMS 2503-164/BMS 2389-5, reached the chromosome-wise threshold level (Table 1).

On BTA 2, two haplotypes showed significant associations with BWT and one haplotype with ADGF at the comparison-wise threshold (Table 1). The two haplotypes, TGLA431-141/TEXAN2-116 and TEXAN5-147/BMS356-99, that affected BWT spanned two chromosomal regions located at 9.1 to 22.5 cM and 95.0 to 100.3 cM (Figure 1). Haplotype TGLA431-141/TEXAN2-116 in the first chromosomal region and haplotype TEXAN5-147/BMS356-99 in the second chromosomal region both had significant negative effects on BWT, decreasing it by 0.36 SD and 0.32 SD, respectively. In the chromosomal region of 9.1 to 22.5 cM, haplotype TGLA431-141/TEXAN2-116, which affected BWT, also had a significant effect on ADGF at the comparison-wise threshold, but increased ADGF by 0.39 SD. No haplotypes were found to have significant effects on PWADG on BTA 2.

On BTA 6, five haplotypes were identified to have significant associations with BWT, four with PWADG, and three with ADGF at the comparison-wise threshold (Table 1). The five haplotypes that affected BWT represented three chromosomal regions, 8.2 to 11.8 cM, 35.5 to 49.7 cM, and 83.0 to 86.2 cM (Figure 2). Haplotypes INRA133-218/ILSTS090-149 in the first chromosomal region and haplotypes BM1329-5/BMS2508-102 and BMS2508-102/BMS382-166 in the second chromosomal region all had significant positive effects on BWT, increasing BWT by 0.67, 0.69, and 0.53 SD, respectively. In the third chromosomal region, haplotype ILSTS087-2/BM1236-118 had a significant positive effect of 0.36 SD on BWT, whereas haplotype BM1326-122/BMS2460-4 showed a significant negative effect of 0.55 SD on BWT. The four haplotypes that were significantly associated with PWADG spanned two chromosomal regions, 11.8 to 44.2 cM and 83.0 to 86.2 cM. The four haplotypes, ILSTS090-149/BM1329-5, BM1329-5/BMS2508-102 in the first chromosomal region, and ILSTS087-2/BM1236-118 and BM1236-118/BMS2460-3 in the second chromosomal region, all had significant positive effects on PWADG, increasing it by 0.37 to 0.70 SD, with an average of 0.51 SD. The significant association between haplotype BM1329-5/BMS2508-102 and PWADG reached the chromosome-wise threshold level. The three haplotypes that showed significant effects on ADGF represented two chromosomal regions,

49.7 to 50.1 cM and 59.6 to 63.6 cM. In the first chromosomal region, haplotype BMS382-168/BMS1242-100 had a significant negative effect of 0.70 SD on ADGF. In the second chromosomal region, haplotype BM4322-5/BMS470-60 had a significant negative effect on ADGF, decreasing ADGF by 0.99 SD, whereas an alternative haplotype, BM4322-2/BMS470-68, of the same chromosomal location showed a significant positive effect on ADGF, increasing it by 1.37 SD.

On BTA 14, three haplotypes were found to have significant associations with each of the three growth traits at the comparison-wise threshold (Table 1). Haplotypes BMS1678-130/BMS1941-111, BMC1207-151/BM1577-152, and BMS1899-117/RM137-149 all had significant positive effects on BWT, increasing it by 0.56, 0.37, and 0.49 SD, respectively. The three haplotypes spanned three chromosomal regions, 26.0 to 26.7 cM, 36.2 to 46.2 cM, and 52.0 to 67.7 cM (Figure 3). For PWADG, the three haplotypes that showed significant associations covered one chromosomal region, 26.7 to 50.8 cM. The three haplotypes were all positively associated with PWADG, increasing it by 0.67, 0.42, and 0.68 SD, respectively. On the same chromosome, two regions, 17.0 to 24.0 cM and 36.2 to 46.2 cM, represented by haplotypes CSSM66-198/BMS1747-89, BMS1747-89/TG-2, and BMC1207-153/BM1577-143 were found to have significant associations with ADGF at the comparison-wise threshold. Haplotypes CSSM66-198/BMS1747-89 and BMS1747-89/TG-2 in the first chromosomal region had significant positive effects on ADGF, increasing it by 0.89 and 0.50 SD, respectively. In the second chromosomal region, haplotype BMC1207-153/BM1577-143, however, showed a significant negative effect on ADGF, decreasing it by 0.73 SD.

On BTA 19, we found one haplotype that was significantly associated with BWT, one haplotype that had a significant association with PWADG and three haplotypes having significant associations with ADGF at the comparison-wise threshold (Table 1). Haplotype BMS2503-164/ BMS2389-5 in the chromosomal region of 52.0 to 52.7 cM showed a significant positive effect of 0.55 SD on BWT. Haplotype BM6000-6/BMS745-7 at chromosomal region of 4.8 to 15.9 cM had a significant negative effect on PWADG, decreasing it by 0.45 SD. For ADGF, the three haplotypes that had significant associations spanned two chromosomal regions, 52.0 to 52.7 cM and 65.1 to 65.7 cM (Figure 4). In the first chromosomal region, haplotype BMS2503-158/BMS2389-2 and an alternative haplotype, BMS2503-164/ BMS2389-5, both had significant positive effects on ADGF. The two haplotypes increased ADGF by 0.91 and 0.86 SD, respectively, and they both reached the chromosome-wise threshold level. In the second chromosomal region, however, haplotype RM099-128 CSSM65-2 was found to have a significant negative effect on ADGF, decreasing it by 0.54 SD.

On BTA 21, three haplotypes were found to have significant effects on BWT, and one haplotype showed

Table 1. Association between haplotypes and growth traits in the M1 line of *Bos taurus* on BTA 2, 6, 14, 19, 21, and 23[a]

Haplotype[b]	Chromosome	Location, cM	Trait[c]	*P*-value[d]	Haplotype effect[e]
TGLA431-141, TEXAN2-116	2	9.1–22.5	BWT	0.050*	−0.36 SD (1.61)
TEXAN5-147, BMS356-99	2	95.0–100.3	BWT	0.049*	−0.32 SD (1.43)
TGLA431-141, TEXAN2-116	2	9.1–22.5	ADGF	0.032*	+0.39 SD (0.07)
INRA133-218, ILSTS090-149	6	8.2–11.8	BWT	0.041*	+0.67 SD (3.00)
BM1329-5, BMS2508-102	6	35.5–44.2	BWT	0.039*	+0.69 SD (3.09)
BMS2508-102, BMS382-166	6	44.2–49.7	BWT	0.031*	+0.53 SD (2.37)
ILSTS087-2, BM1236-118	6	83.0–83.9	BWT	0.015*	+0.36 SD (1.61)
BM1236-122, BMS2460-4	6	83.9–86.2	BWT	0.025*	−0.55 SD (2.46)
ILSTS090-149, BM1329-5	6	11.8–35.5	PWADG	0.009*	+0.46 SD (0.05)
BM1329-5, BMS2508-102	6	35.5–44.2	PWADG	0.004**	+0.70 SD (0.08)
ILSTS087-2, BM1236-118	6	83.0–83.9	PWADG	0.034*	+0.37 SD (0.04)
BM1236-118, BMS2460-3	6	83.9–86.2	PWADG	0.019*	+0.52 SD (0.06)
BMS382-168, BMS1242-100	6	49.7–50.1	ADGF	0.034*	−0.70 SD (0.13)
BM4322-5, BMS470-60	6	59.6–63.6	ADGF	0.004*	−0.99 SD (0.18)
BM4322-2, BMS470-68	6	59.6–63.6	ADGF	0.008*	+1.37 SD (0.25)
BMS1678-130, BMS1941-111	14	26.0–26.7	BWT	0.006*	+0.56 SD (2.51)
BMC1207-151, BM1577-152	14	36.2–46.2	BWT	0.049*	+0.37 SD (1.66)
BMS1899-117, RM137-149	14	52.0–67.7	BWT	0.031*	+0.49 SD (2.20)
BMS1941-119, BMC1207-153	14	26.7–36.2	PWADG	0.046*	+0.67 SD (0.07)
BMC1207-153, BM1577-152	14	36.2–46.2	PWADG	0.023*	+0.42 SD (0.05)
BM1577-152, BMS108-110	14	46.2–50.8	PWADG	0.041*	+0.68 SD (0.07)
CSSM66-198, BMS1747-89	14	17.0–22.0	ADGF	0.025*	+0.89 SD (0.16)
BMS1747-89, TG-2	14	22.0–24.0	ADGF	0.026*	+0.50 SD (0.09)
BMC1207-153, BM1577-143	14	36.2–46.2	ADGF	0.039*	−0.73 SD (0.13)
BMS2503-164, BM2389-5	19	52.0–52.7	BWT	0.035*	+0.55 SD (2.46)
BM6000-6, BMS745-7	19	4.8–15.9	PWADG	0.049*	−0.45 SD (0.05)
BMS2503-158, BM2389-2	19	52.0–52.7	ADGF	0.004**	+0.91 SD (0.16)
BMS2503-164, BM2389-5	19	52.0–52.7	ADGF	0.001**	+0.86 SD (0.15)
RM099-128, CSSM65-2	19	65.1–65.7	ADGF	0.014*	−0.54 SD (0.10)
BMS1117-95, AGLA233-253	21	9.9–20.4	BWT	0.019*	+0.65 SD (2.91)
BP33-259, BMS2815-95	21	28.2–46.1	BWT	0.044*	+0.55 SD (2.46)
BP33-271, BMS2815-99	21	28.2–46.1	BWT	0.007*	+1.42 SD (6.36)
BMS1117-95, AGLA233-253	21	9.9–20.4	PWADG	0.045*	+0.70 SD (0.08)
BMS2815-93, ILSTS092-174	21	46.1–53.1	ADGF	0.013*	+0.88 SD (0.16)
BM1258-103, BMS468-125	23	23.9–36.0	BWT	0.021*	−0.58 SD (2.60)
RM185-99, BM1818-267	23	45.1–50.9	BWT	0.034*	+0.50 SD (2.24)
RM033-152, BM1815-151	23	17.3–19.8	PWADG	0.038*	−0.72 SD (0.08)
BM1815-149, BM1258-107	23	19.8–23.9	PWADG	0.014*	−0.57 SD (0.06)
BM1258-103, BMS468-127	23	23.9–36.0	PWADG	0.006*	−0.80 SD (0.09)
RM185-99, BM1818-267	23	45.1–50.9	PWADG	0.049*	+0.40 SD (0.04)

[a]Beefbooster, Inc., Calgary, Alberta, Canada.

[b]The haplotypes were named by two alleles of a pair of loci. For example, haplotype TGLA431-141/TEXAN2-116 represents a segment of chromosome having allele 141 of TGLA431 and allele 116 of TEXAN2.

[c]BWT = birth weight, PWADG = preweaning ADG, ADGF = ADG on feed.

[d]* and ** indicate the *P*-values above the comparison-wise and chromosome-wise thresholds, respectively.

[e]SD = standard deviation, "−" represents the negative effect, whereas "+" represents the positive effect. The actual haplotype effects in kilograms were shown in parentheses.

significant associations with each PWADG and ADGF at the comparison-wise threshold (Table 1). The three haplotypes, BMS1117-95/AGLA233-253, BP33-259/BMS2815-95, and BP33-271/BMS2815-99, that showed significant effects on BWT spanned two chromosomal regions, 9.9 to 20.4 cM and 28.2 to 46.1 cM (Figure 5), and all three haplotypes had significant positive effects on BWT, increasing it by 0.65, 0.55, and 1.42 SD, respectively. Haplotype BMS1117-95/AGLA233-253 at the chromosomal region of 9.9 to 20.4 cM had a significant positive effect on PWADG and increased it by 0.70 SD. At the chromosomal region of 46.1 to 53.1 cM, haplotype

BMS2815-93/ILSTS092-174 had a significant positive effect on ADGF, increasing it by 0.88 SD.

On BTA 23, two haplotypes were found to have significant associations with BWT and four haplotypes with PWADG, whereas no haplotypes were found to have significant effects on ADGF at the comparison-wise threshold level (Table 1). The two haplotypes that significantly affected BWT spanned two chromosomal regions, 23.9 to 36.0 cM and 45.1 to 50.9 cM (Figure 6). Haplotype BM1258-103/BMS468-125 in the first chromosomal region had a significant negative effect of 0.58 SD on BWT. Haplotype RM185-99/BM1818-267 in the

second chromosomal region, however, had a significant positive effect on BWT, increasing it by 0.50 SD. The five haplotypes that showed significant associations with PWADG represented two chromosomal regions, 17.3 to 36.0 cM and 45.1 to 50.9 cM. Three haplotypes, RM033-152/BM1815-151, BM1815-149/BM1258-107, and BM1258-103/BMS468-127, in the first chromosomal region all had negative effects on PWADG, decreasing it by 0.72, 0.57, and 0.80 SD, respectively. In the second chromosomal region, RM185-99/BM1818-267 had a significant positive effect on PWADG, increasing it by 0.40 SD.

Discussion

Identification and fine mapping of a QTL region is a key step toward successful positional candidate gene studies and marker-assisted selection. In cattle, linkage disequilibrium is commonly observed and can extend for several tens of centimorgans (Farnir et al., 2000), making the identical-by-descent haplotype sharing analysis a feasible approach for identifying and fine mapping QTL. In a previous study, Li et al. (2002b) mapped QTL for BWT, PWADG, and ADGF on BTA 5 in both the M1 and M3 commercial lines of Beefbooster, Inc., using the identical-by-descent haplotype sharing analysis. The identical-by-descent haplotype sharing analysis detected the same, but better defined, QTL regions in comparison to the interval mapping method (Li et al., 2002a), and was able to narrow down some of the QTL regions to less than 10 cM. Moore et al. (2003) also mapped a QTL region for backfat on BTA 14 in the M1 commercial line of Beefbooster, Inc., using the same approach and found that the QTL region was consistent with other studies, indicating the effectiveness of QTL mapping using the identical-by-descent haplotype sharing analysis in commercial lines of *Bos taurus*.

In this study, we used the same identical-by-descent haplotype sharing analysis that was described by Li et al. (2002b), and identified 13 regions that were significantly associated with BWT, seven regions with PWADG and eight regions with ADGF on BTA 2, 6, 14, 19, 21, and 23 at the comparison-wise threshold level. Some of these QTL regions were in agreement with other studies, whereas new QTL regions were also detected. On BTA 2, QTL for BWT have been mapped in the region of 108 to 122 cM by Grosz and MacNeil (2001) and in the region of 117 to 129 cM by Kim et al. (2003). We identified a similar region, 95.0 to 100.3 cM, which had a significant effect on BWT. Our results seem to confirm the QTL regions reported on BTA 2 by Grosz and MacNeil (2001) and Kim et al. (2003), even though the QTL regions were distal to each other by several centimorgans. In addition, we also detected the chromosomal region of 9.1 to 22.5 cM on BTA 2, which showed significant associations with both BWT and ADGF.

On BTA 6, Davis et al. (1998) reported a QTL for BWT in the chromosomal region of 15 to 75 cM. Casas et al. (2000) found a QTL for BWT at 25 to 60 cM and for yearling weight around 48 to 58 cM. In this study, we identified three chromosomal regions on BTA 6 (8.2 to 11.8 cM, 35.5 to 49.7 cM, and 83.0 to 86.2 cM) that affected BWT, two chromosomal regions (11.8 to 44.2 cM and 83.0 to 86.2 cM) that affected PWADG, and another two chromosomal regions (49.7 to 50.1 cM and 59.6 to 63.6 cM) that affected ADGF. For BWT, the second region of 35.5 to 49.7 cM identified in this study seems to be in agreement with those identified by Davis et al. (1998) and Casas et al. (2000). The QTL region of 49.7 to 50.1 cM on BTA 6 that affected ADGF in this study is also located very close to the QTL region of 48 to 58 cM for yearling weight detected by Casas et al. (2000); however, how these two QTL regions are related needs to be determined.

On BTA 19, the growth hormone 1 gene (GH1) has previously been mapped to the location of approximately 66 cM, making this chromosome a likely candidate for mapping growth QTL. Taylor et al. (1998) reported a QTL region for BWT near the region of 95 to 105 cM and a QTL for gain on feed in the region of 80 to 85 cM on BTA 19. In this study, we failed to detect any haplotypes in the regions of 95 to 105 cM and 80 to 85 cM of BTA 19 that showed significant associations with any of the three growth traits. Instead, we found one chromosomal region at 52.0 to 52.7 cM that affected BWT, one chromosomal region at 4.8 to 15.9 cM that affected PWADG, and two chromosomal regions at 52 to 52.7 cM and 65.1 to 65.7 cM that affected ADGF. None of the chromosomal locations identified in this study on BTA 19 confirms the QTL regions identified by Taylor et al. (1998). However, one of the QTL regions that affected ADGF (65.1 to 65.7 cM) in this study seems to be in close proximity to the *GH1* gene. Whether this gene is the gene or one of the causative genes underlying the QTL still remains to be determined.

On BTA 21, QTL for BWT were previously mapped in the area of 0 to 20 cM by Davis et al. (1998) and Casas et al. (2003), and in the chromosomal region of 52 to 73 cM by Kim et al. (2003). In this study, we detected two chromosomal regions of 9.9 to 20.4 cM and 28.2 to 46.1 cM that were significantly associated with BWT on BTA 21. Our first chromosomal region seems to confirm the QTL region identified by Davis et al. (1998) and Casas et al. (2003), whereas the second chromosomal region is located close to that detected by Kim et al. (2003).

On BTA 23, Elo et al. (1999) mapped a QTL for live weight to the region spanning 12 to 41 cM. We detected two chromosomal regions of 23.9 to 36.0 cM and 45.1 to 50.9 cM and two chromosomal regions of 17.3 to 36.0 cM and 45.1 to 50.9 cM that affected BWT and PWADG, respectively. The chromosomal region of 23.9 to 36.0 cM that affected BWT, and the chromosomal region of 17.3 to 36.0 cM that affected PWADG, are very close to the QTL region identified by Elo et al. (1999). Further study is needed to determine whether one or multiple causative genes underlie this QTL region.

The QTL regions for BWT, PWADG, and ADGF identified in this study often overlapped to some extent or were positioned next to each other. In some cases, one haplotype was significantly associated with more than one growth trait, suggesting genes underlying the QTL regions affect more than one growth trait. On BTA 2, haplotype TGLA431-141/TEXAN2-116 at the chromosomal region of 9.1 to 22.5 cM affected both BWT and ADGF. Animals with the haplotype tended to have lower BWT but higher ADGF. This tendency would prove very useful in beef cattle breeding as selection for small birth weight could be achieved without compromising ADGF. It is noteworthy that the *mh* gene locus associated with double muscling has been localized to a position near the COL3AI locus of BTA 2 (Charlier et al., 1995; Casas et al., 1997; Sonstegard et al. 1997), which is also in close proximity to TGLA431 at the location of 9.1 cM. Furthermore, myostatin, which causes muscular hypertrophy in mice (McPherron et al., 1997), has been mapped in the interval in which *mh* was mapped (Smith et al., 1997). It is known that double muscling plays a role in increasing the proficiency of converting feed to muscle. Studies show that calves homozygous for double muscling tend to have higher BWT and greater birth to weaning gain than calves with two normal alleles at the double muscling locus (Casas et al., 1997). Although double muscling has been strongly selected for and has been fixed in certain breeds, the gene is believed to still be segregating in other cattle populations such as Angus, the same breed used in the development of the M1 line of Beefbooster Inc. However, whether the myostatin/*mh* is a causative gene underlying the QTL region that is associated with both BWT and ADGF remains to be determined.

Haplotypes that affected both BWT and PWADG or ADGF were also found on BTA 6, BTA 19, BTA 21, and BTA 23, but they all had positive effects on both BWT and PWADG or ADGF. On BTA 6, haplotypes BM1329-5/BMS2508-102 and ILSTS087-2/BM1236-118 had positive effects on both BWT and PWADG. Animals with the haplotypes showed higher BWT as well as higher PWADG. On BTA 19, haplotype BMS2503-164/BM2389-5 was positively associated with both BWT and ADGF. Animals with the haplotype tended to have both higher BWT and higher ADGF. On BTA 21, haplotype BMS1117-95/AGLA233-253 had a significantly positive effect on both BWT and PWADG. Animals that carried the haplotype had higher BWT and higher PWADG. On BTA 23, haplotype RM185-99/BM1818-267 also had a significant positive effect on both BWT and PWADG. Animals with the haplotype showed higher BWT and higher PWADG. These general trends of haplotypes affecting BWT and PWADG or ADGF in the same direction not only reflect that the traits are genetically positively correlated, but also imply that genes affecting BWT may affect other growth traits.

The aim of this study was to identify and fine map QTL for growth on bovine chromosomes 2, 6, 14, 19, 21, and 23, chromosomes on which QTL for growth have been previously identified. We have confirmed and narrowed down some of the QTL regions to less than 10 cM, especially when the chromosome-wise threshold is applied, which will provide a valuable reference for further positional candidate gene research. Some of the QTL, however, still remain localized to fairly large chromosomal regions and most of the QTL regions barely reached a significance level of the comparison-wise threshold. Those QTL regions need to be further confirmed and narrowed down, possibly by using a larger sample of animals and more densely spaced genetic markers.

Implications

Quantitative trait loci affecting birth weight, preweaning average daily gain, and postweaning average daily gain on feed have been identified and fine mapped on bovine chromosomes 2, 6, 14, 19, 21, and 23 in this study. In total, 13 quantitative trait loci regions were identified to have significant associations with birth weight, seven quantitative trait loci regions with preweaning average daily gain, and eight quantitative trait loci regions with postweaning average daily gain on feed. Some of the quantitative trait loci regions have been confirmed and narrowed down to 10 cM or less. The results should provide a valuable reference for further positional candidate gene research and marker-assisted selection.

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