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Selection for genetic markers in beef cattle reveals complex associations of thyroglobulin and casein1-S1 with carcass and meat traits

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Selection for genetic markers in beef cattle reveals complex associations of thyroglobulin and casein1-S1 with carcass and meat traits[1,2]

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ABSTRACT: Genetic markers in casein (*CSN1S1*) and thyroglobulin (*TG*) genes have previously been associated with fat distribution in cattle. Determining the nature of these genetic associations (additive, recessive, or dominant) has been difficult, because both markers have small minor allele frequencies in most beef cattle populations. This results in few animals homozygous for the minor alleles. Selection to increase the frequencies of the minor alleles for 2 SNP markers in these genes was undertaken in a composite population. The objective was to obtain better estimates of genetic effects associated with these markers and determine if there were epistatic interactions. Selection increased the frequencies of minor alleles for both SNP from <0.30 to 0.45. Bulls ($n = 24$) heterozygous for both SNP were used in 3 yr to produce 204 steer progeny harvested at an average age of 474 d. The combined effect of the 9 *CSN1S1* × *TG* genotypes was associated with carcass-adjusted fat thickness ($P < 0.06$) and meat tenderness predicted at the abattoir by visible and near-infrared reflectance spectroscopy ($P < 0.04$). Genotype did not affect BW from birth through harvest, ribeye area, marbling score, slice shear force, or image-based yield grade ($P > 0.10$). Additive, dominance, and epistatic SNP association effects were estimated from genotypic effects for adjusted fat thickness and predicted meat tenderness. Adjusted fat thickness showed a dominance association with *TG* SNP ($P < 0.06$) and an epistatic additive *CSN1S1* × additive *TG* association ($P < 0.03$). For predicted meat tenderness, heterozygous *TG* meat was more tender than meat from either homozygote ($P < 0.002$). Dominance and epistatic associations can result in different SNP allele substitution effects in populations where SNP have the same linkage disequilibrium with causal mutations but have different frequencies. Although the complex associations estimated in this study would contribute little to within-population selection response, they could be important for marker-assisted management or reciprocal selection schemes.

Key words: casein, cattle, epistasis, genotype, marker association, thyroglobulin

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INTRODUCTION

Marker allele effects can show simple, additive associations with traits, more complex dominance, or recessive associations, or even epistatic associations between alleles from different markers. Frequencies of many markers are closer to fixation than 0.5. When minor allele frequencies are far from 0.5, even simple additive associations may not be estimated well. One homozygous class will have few animals and in cattle will likely be sired by a few bulls and are more likely to have similar breed composition. When considering epistatic effects between 2 markers, animals homozygous for both minor alleles will be even rarer and more likely related.

Genetic markers in the thyroglobulin (**TG**; located on BTA14) and casein1-S1 (**CSN1S1**; located on *BTA 6*) genes have been associated with various measures of fatness (Barendse et al., 2004; White et al., 2007). Casas et al. (2007) and White et al. (2007) reported minor allele frequencies of 0.24 for a TG SNP and 0.08 for a CSN1S1 SNP, resulting in 31 and 4 minor allele homozygotes among 554 and 551steers

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from crosses of 7 widely used *Bos taurus* breeds, respectively. The *TG* SNP has been used in commercial genotyping, but associations with TG have varied and nonadditive effects have been suggested (Casas et al., 2005). The association of the CSN1S1 SNP with fat and retail product yield found by White et al. (2007) were strong but have not been validated.

The objective of this experiment was to estimate additive and nonadditive effects associated with 2 SNP in the TG and CSN1S1 genes, previously identified as being related to some aspect of fat in beef carcasses. However, TG has conflicting results in follow-up studies and CSN1S1 lacks confirmatory evidence. Estimated associations were enhanced by selection to increase frequencies of the minor SNP alleles and by using bulls heterozygous for both TG and CSN1S1 SNP to minimize background genetic differences.

MATERIALS AND METHODS

The U.S. Meat Animal Research Center (**USMARC**) Animal Care and Use Committee approved the procedures used in this experiment.

Composite Population

A composite cattle population known as MARC II was formed from 0.25 Angus, 0.25 Hereford, 0.25 Gelbvieh, and 0.25 Simmental, beginning in 1978 (Gregory et al., 1991). From 1992 through 1999, this population was divided into a calving ease selection line and smaller control line (Bennett, 2008). Subsequently, the calving ease selection and control line cows were bred to the same bulls and cows and their progeny treated as a single population. The MARC II population is an advanced generation, inter se mated composite. About 220 calves were born each year. Approximately 15 sires born within the herd were used each year by natural service and AI. Cattle born from 2004 through 2007 were progeny of 46 bulls.

Genetic Markers

Markers chosen for this experiment were SNP in promoter regions of casein1S1 and thyroglobulin. The casein1S1 SNP with C and G alleles (BTA 6; rs109757609) identified by Prinzenberg et al. (2003) and a thyroglobulin SNP with C and T alleles (BTA 14; rs135751032) identified as TG5 by Barendse (1999) will be abbreviated as CSN1S1 and TG. Their alleles will be abbreviated as **CSN1S1aC**, **CSN1S1aG**, **TGaC**, and **TCaT**. Both markers have been associated with fat deposition in meat and carcasses (Barendse et al., 2004; White et al., 2007), and frequencies of the minor alleles are typically <0.30 in *Bos taurus* beef populations.

Samples of DNA were extracted from blood or semen. Extraction of DNA was done using a Qiagen QIAamp DNA mini blood kit (Qiagen, Valencia, CA). Blood samples were collected in 10-mL syringes with 4% EDTA. Blood was frozen until DNA was extracted. Genotyping was performed using a primer extension method with mass spectrometry-based analysis of the extension products on a MassArray system, as suggested by the manufacturer (Sequenom, Inc., San Diego, CA), and described by Stone et al. (2002). When necessary, genotype assays were repeated to reduce missing genotypes.

Base, Selection, and Evaluation Phases

The experiment consisted of 3 phases: base, selection, and evaluation. In the base phase (birth years 2004 and 2005), DNA from live animals and some frozen semen from the Angus and 3 composite (**MARC I**, **MARC II**, and **MARC III**) populations completing the calving ease selection experiment (Bennett, 2008) were surveyed for CSN1S1aG and TGaT frequencies to determine which population would be selected for CSN1S1 and TG, beginning in 2006. Frequencies of CSN1S1aG and TGaT were 0.001 and 0.30 for Angus; 0.07 and 0.29 for MARC I; 0.25 and 0.28 for MARC II; and 0.10 and 0.18 for MARC III, respectively. The combination of greater frequencies for both CSN1S1aG and TGaT was the primary factor in choosing MARC II for this experiment.

In the selection phase (birth years 2006 and 2007), the goal was to increase frequencies of CSN1S1aG and TGaT toward 0.50. Calves were bled before weaning and genotyped so that replacement bulls and females could be selected soon after weaning. Replacements and USMARC-bred AI sires were selected to increase frequencies of CSN1S1aG and TGaT, based on their genotypes.

In the evaluation phase (birth years 2008, 2009, and 2010), sires, mostly heterozygous for both CSN1S1 and TG, were bred to heifers and cows whose frequencies were near 0.50. Twenty-four sires were used in this phase: 22 heterozygous for both CSN1S1 and TG, 1 homozygous CSN1S1aG and heterozygous TG, and 1 heterozygous CSN1S1 and homozygous TGaC. Resulting spring-born progeny were genotyped before weaning and those with incomplete genotypes removed from the experiment. Replacement bulls were randomly sampled within sire from among males heterozygous for both TG and CSN1S1. The remaining males were castrated soon after weaning and fed diets based on corn and corn silage, until harvest. Cattle were weighed at birth (mean date = April 17), weaning (mean age = 158 d, SD = 16 d), and as yearlings (mean age = 376 d, SD = 25 d).

All steers were harvested on a single day at a commercial abattoir within each year at an average age of 474 d. Carcasses were weighed hot, electrically stimulated, and chilled, using the proprietary system of the commercial facility. At 36 h postmortem, carcasses were ribbed between the 12th and 13th ribs, and an image analysis-based (VBG2000) grading system (Shackelford et al., 2003) assessed adjusted fat thickness, ribeye area, USDA marbling score, and calculated vision yield grade. Meat tenderness was predicted at the abattoir, using visible and near-infrared reflectance spectroscopy at 36 h postmortem (**VISNIR**; Shackelford et al., 2012a,b). A LM steak from the 13th rib region was returned to USMARC to evaluate slice shear force at 14 d postmortem (Shackelford et al., 1999).

Statistical Analysis

Either trait measurements or their base 10 logarithms (marbling score; slice and VISNIR shear forces) were analyzed with a mixed model, using MTDFREML (Boldman et al., 1995). The model was:

$$Y_{i,j,k,l} = \mu + Year_i + Aod5_j + Genotype_k + b \times Age_{i,j,k,l} + a_{i,j,k,l} + e_{i,j,k,l}$$

where $Y_{i,j,l,m}$ is the observation or its base 10 logarithm for the *i, j, k, l-th* animal, μ is the mean, $Year_i$ is birth year 2008, 2009, or 2010, $Aod5_j$ is age of dam (2, 3, 4, or ≥5 yr), b is a linear regression coefficient on the *i, j, k, l-th* age of the animal ($Age_{i,j,k,l}$) in days, $Genotype_k$ is 1 of the 9 combinations of 3 *CSN1S1* and 3 *TG* genotypes, $a_{i,j,k,l}$ is the additive polygenic animal effect, and $e_{i,j,k,l}$ is the residual effect of the *i, j, k, l-th* observation. The distribution of polygenic effects was assumed proportional to the pedigree relationship matrix and residual effects were assumed independent with constant variance. Calculation of polygenic relationships included >7,000 animals in the pedigree. Variance estimates for additive polygenic effects were expected to be imprecise because of the limited numbers of observations so heritability ($\mathbf{h^2}$) = $\sigma_a^2 \div \left(\sigma_a^2 + \sigma_e^2\right)$ was constrained to $0.20 \le h^2 \le 0.70$, similar to ranges in heritabilities estimated for these type traits in similar populations (Gregory et al., 1994; Bennett and Gregory, 1996). Distributions of marbling scores and meat tenderness traits were highly skewed, and base 10 logarithms of values were analyzed for those traits.

Linear contrasts were estimated for additive, dominance, and epistasis effects associated with *CSN1S1* and *TG* SNP if $P < 0.10$ for genotypes. Linear contrast coefficients are shown in Table 1. Estimated contrasts were divided by their SE and compared with a *t*-distribution with 190 df to determine significance. Testing contrasts only when variance due to the 9 SNP genotypes reaches suggestive levels ($P < 0.10$) protects against probability inflation due to multiple testing.

Table 1. Linear contrast coefficients used to estimate additive, dominance, and epistasis effects for *casein1-S1* and *thyroglobulin* SNP markers

Genotype mean		*CSN1S1*[1]		*TG*[1]		*CSN1S1 × TG*[2]			
CSN1S1	*TG*	A	D	A	D	AA	DA	AD	DD
CC	CC	–1	–1	–1	–1	1	1	1	1
CC	CT	–1	–1	0	2	0	0	–2	–2
CC	TT	–1	–1	1	–1	–1	–1	1	1
CG	CC	0	2	–1	–1	0	–2	0	–2
CG	CT	0	2	0	2	0	0	0	4
CG	TT	0	2	1	–1	0	2	0	–2
GG	CC	1	–1	–1	–1	–1	1	–1	1
GG	CT	1	–1	0	2	0	0	2	–2
GG	TT	1	–1	1	–1	1	–1	–1	1
Divisor[3]		3	6	3	6	1	2	2	4

[1]Linear contrast coefficients multiplied by genotype means to estimate *casein1S1* (*CSN1S1*) and *thyroglobulin* (*TG*) additive (A) and dominance (D) effects.

[2]Linear contrast coefficients for 2-marker epistatic effects. These are identified with 2 letters. The first letter is the *CSN1S1* effect and second letter is the *TG* effect; e.g., AD is additive *CSN1S1* × dominance *TG* epistatic effect.

[3]Actual coefficients used were the whole numbers in table divided by this number.

RESULTS

Figure 1 shows changes in frequencies of *CSN1S1aG* and *TGaT* in MARC II calves genotyped throughout the experiment after the initial selection of MARC II from among the 4 available populations. Selection increased frequencies substantially but did not reach 0.50. Frequencies in the 3-yr evaluation phase averaged 0.45 for minor alleles of both SNP.

After removing replacement bulls and animals with incomplete genotypes, 204 MARC II steers were

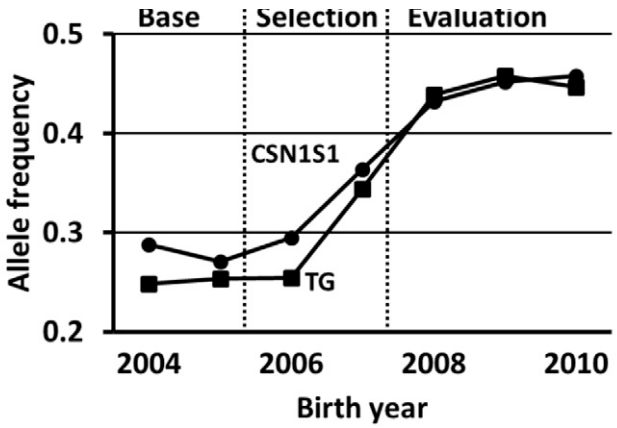

Figure 1. Frequencies of *casein1-S1* (*CSN1S1*) and *thyroglobulin* (*TG*) minor alleles by birth year and phase of the experiment.

Table 2. No. harvested Meat Animal Research Center II steers by genotype

CSN1S1 genotype[1]	TG genotype[2]			Total
	CC	CT	TT	
CC	18	30	14	62
CG	39	36	26	101
GG	13	19	9	41
Total	70	85	49	204

[1]Casein1-S1 genotypes.

[2]Thyroglobulin genotypes.

Table 3. Steer genotype distribution among 24 Meat Animal Research Center II sires

Item	Value
Sires with 3 progeny TG genotypes[1]	14
Average TG genotypes per sire	2.46
Sires with 3 progeny CSN1S1 genotypes[2]	17
Average CSN1S1 genotypes per sire	2.67
Sires with 7 to 9 CSN1S1 × TG genotypes	5
Sires with 1 to 3 CSN1S1 × TG genotypes	5
Average CSN1S1 × TG genotypes per sire	4.92

[1]Thyroglobulin (TG) genotypes were CC, CT, and TT.

[2]Casein1-S1 (CSN1S1) genotypes were CC, CG, and GG.

fed and evaluated for carcass traits. The steers were distributed among the 9 SNP genotypes, as shown in Table 2. Steers with different genotypes were distributed within and among sires (Table 3). Of the 24 sires, 14 had all 3 TG genotypes among their progeny and 17 had all 3 CSN1S1 genotypes. Nineteen sires had 4 or more of the 9 possible genotypes among their progeny and 1 sire had progeny with all 9 genotypes. Four sires had progeny with 7 or 8 of the 9 genotypes.

Averages and SD of analyzed steer traits are shown in Table 4, and sources of variation are shown in Table 5. Calf age was significant for postnatal weight traits, carcass traits other than ribeye area, and slice shear force. Age of dam was significant for BW traits. Birth year was significant for carcass weight, marbling score, ribeye area, and slice shear force. Initial heritability estimates were outside the 0.20 to 0.70 range for birth weight, 3 carcass yield traits (ribeye area, adjusted fat thickness, and instrument Yield Grade), and both measures of meat tenderness. Genotype was suggestive or significant for VISNIR-predicted shear force and adjusted fat thickness.

Tables 6 shows estimated means for the 3 CSN1S1 and 3 TG genotypes. Table 7 shows the 9 estimated genotype means for the 2 traits with $P < 0.10$: adjusted fat thickness and VISNIR-predicted shear force. Linear contrasts among genotype means (Table 8) identify *TG* dominance ($P = 0.06$) and CSN1S1 additive × TG additive effects ($P = 0.03$), causing the overall $P = 0.06$ for adjusted fat thickness genotype and TG dominance ($P = 0.002$), causing the overall $P = 0.04$ for VISNIR-predicted tenderness genotype. For adjusted fat thickness, heterozygous *TG* animals exceed those with either homozygous genotype, resulting in overdominance. The additive × additive effect results from animals homozygous for both minor alleles or for both major alleles having less fat thickness than those homozygous for both a minor allele and a major allele. For VISNIR-predicted tenderness and TG genotypes, CT animals were more tender than either CC or TT, resulting in heterozygote advantage for tenderness. Although TG dominance was significant for VISNIR-predicted shear force and not slice shear force, the TG means (Table 6) for both VISNIR and slice shear force showed a similar trend.

Table 4. Steer trait means and SD ($n = 204$)

Trait	Avg	SD
Birth weight, kg	39.7	5.6
Weaning weight, kg	194	25
Yearling weight, kg	460	52
HCW, kg	357	34
Marbling score[1]	382	58
Ribeye area, cm^2	85.1	9.0
Adjusted fat thickness, mm	11.3	4.0
Vision Yield Grade[2]	2.81	0.71
Slice shear force, kg	16.1	5.2
VISNIR shear force[3], kg	14.7	1.4

[1]300 = $Slight^{00}$; 400 = $Small^{00}$ (USDA, 1997).

[2]Prediction of USDA Yield Grade. Smaller numbers indicate greater yield of boneless, closely trimmed, retail cuts.

[3]VISNIR = visible and near-infrared reflectance spectroscopy prediction (Shackelford et al., 2012a).

Table 5. *P*-values for sources of variation and heritability estimates (h^2) used in analyses

Trait	Year	Dam age	Calf age[1]	Genotype	h^2 [2]
Birth weight	0.10	0.01	0.35	0.37	0.70[3]
Weaning weight	0.77	<0.001	<0.001	0.86	0.30
Yearling weight	0.35	0.03	<0.001	0.87	0.63
HCW	0.001	0.06	<0.001	0.74	0.24
Marbling score[4,5]	0.02	0.25	0.004	0.72	0.50
Ribeye area	<0.001	0.37	0.28	0.53	0.70[3]
Adjusted fat thickness	0.38	0.39	0.004	0.06	0.70[3]
Vision Yield Grade[6]	0.24	0.11	0.001	0.14	0.70[3]
Slice shear force[4]	<0.001	0.27	0.003	0.68	0.20[3]
VISNIR shear force[4,5]	0.29	0.94	0.30	0.04	0.20[3]

[1]Julian birthday linear covariate was used for birth weight; linear age covariate used for other traits.

[2]Heritabilities are reported for completeness; median SE was 0.23.

[3]Constrained to $0.20 \leq h^2 \leq 0.70$.

[4]Logarithm (base 10) values of traits were analyzed.

[5]VISNIR = visible and near-infrared reflectance spectroscopy prediction (Shackelford et al., 2012a).

[6]Prediction of USDA Yield Grade. Smaller numbers indicate greater yield of boneless, closely trimmed, retail cuts.

Table 6. Means of traits by casein1-S1 and thyroglobulin genotypes

	CSN1S1[1]			TG[2]			
Trait	CC	CG	GG	CC	CT	TT	SEM[3]
Birth weight, kg	39.5	40.2	39.4	39.7	40.3	39.2	1.6
Weaning weight, kg	195.6	193.4	194.3	195.9	195.6	191.9	4.4
Yearling weight, kg	467.0	457.1	457.2	461.9	462.9	456.6	13.7
HCW, kg	361.5	353.6	355.7	356.0	360.5	354.2	6.8
Marbling score[4,5]	385	375	377	382	377	377	15
Ribeye area, cm^2	85.2	85.5	84.7	85.2	85.7	84.5	2.4
Adjusted fat thickness, mm	11.4	10.9	11.6	10.7	12.0	11.2	1.2
Vision Yield Grade[6]	2.86	2.73	2.84	2.73	2.87	2.83	0.19
Slice shear force[5], kg	15.89	15.09	15.64	15.75	15.07	15.80	0.82
VISNIR shear force[5,7], kg	14.61	14.65	14.32	14.96	14.09	14.53	0.30

[1]Casein1-S1 genotypes with alleles C and G. The heterozygous genotype is CG.

[2]Thyroglobulin genotypes with alleles C and T. The heterozygous genotype is CT.

[3]Average SEM across 6 means. Individual SEM varied from 0.91 to 1.09 of the mean.

[4]300 = $Slight^{00}$; 400 = $Small^{00}$ (USDA, 1997).

[5]Base 10 logarithms of trait were analyzed and converted back to the original unit.

[6]Prediction of USDA Yield Grade. Smaller numbers indicate greater yield of boneless, closely trimmed, retail cuts.

[7]VISNIR = visible and near-infrared reflectance spectroscopy prediction (Shackelford et al., 2012a).

DISCUSSION

The thyroglobulin marker TG has been widely studied because of its early discovery (Barendse, 1999) and adoption in commercial genetic marker tests. Tests of its associations with marbling and other traits have been done in several countries, populations, and management systems, and results were inconsistent for marbling traits. For example, Barendse et al. (2004), Wood et al. (2006), and Bonilla et al. (2010) found significant increases in marbling associated with the T allele, and Rincker et al. (2006), Johnston and Graser (2010), McClure et al. (2010), and Pannier et al. (2010) found no evidence of association. Other studies found inconclusive, population-specific, or suggestive evidence for associations of TG with marbling or found associations with other measures of fatness (Casas et al., 2005, 2007; Van Eenennaam et al., 2007). Also, results from this study are marginal evidence for an effect on a fat-related trait other than marbling but do not support an effect on marbling. Several of the cited studies also suggest that the *T* allele has a recessive mode of inheritance for marbling or other traits. Results from this study show heterozygotes outside the intervals spanned by the homozygotes for adjusted fat thickness and VISNIR-predicted tenderness, supporting a nonadditive genetic effect of TG.

White et al. (2007) found that CSN1S1 had moderate to highly significant associations with growth, fat-related, and retail product traits in a *Bos taurus* crossbred population. However, in a second crossbred population with some *Bos indicus* influence only bone yield and KPH were significant. In both populations, only the differences between GG homozygotes and CG heterozygotes were meaningful because <0.75% were homozygous CC. Our results showed little overall effect of CSN1S1, except as it interacted with TG for adjusted fat thickness.

The importance of epistasis in livestock and other realms of genetics is controversial. Hill et al. (2008) concluded from summaries of within-population genetic variance estimates and theoretical predictions that dominance and epistasis contributions to variance must be small. There are examples of dominance and epistasis estimates, such as found for mouse weight and fatness by Leamy et al. (2011), and in this study for adjusted fat thickness of cattle. Further examples in livestock are reviewed by Carlborg and Haley (2004). However, analyses by Hill et al. (2008) and Crow (2010) suggested that these are of little importance for selection within populations. These analyses do not

Table 7. Means and SE of adjusted fat thickness and visible and near-infrared reflectance predicted slice shear force at 14 d postmortem for casein1-S1 and thyroglobulin genotypes

	CSN1S1	TG genotype[3]		
Trait[1]	Genotype[2]	CC	CT	TT
Fat thickness, mm	CC	9.7 ± 1.4	11.6 ± 1.2	12.9 ± 1.5
	CG	10.6 ± 1.2	12.1 ± 1.2	10.2 ± 1.3
	GG	11.9 ± 1.4	12.3 ± 1.4	10.6 ± 1.6
VISNIR shear force, kg	CC	15.06 ± 0.41	14.17 ± 0.34	14.61 ± 0.45
	CG	14.94 ± 0.33	14.25 ± 0.33	14.76 ± 0.35
	GG	14.89 ± 0.45	13.84 ± 0.39	14.22 ± 0.52

[1]Fat thickness is image analysis-based adjusted fat thickness (Shackelford et al., 2003). VISNIR shear force is visible and near-infrared reflectance spectroscopy prediction of meat tenderness (Shackelford et al., 2012a). Base 10 logarithms of VISNIR shear force were analyzed and converted back to the original scale.

[2]Casein1-S1 genotypes with alleles C and G. The heterozygous genotype is CG.

[3]Thyroglobulin genotypes with alleles C and T. The heterozygous genotype is CT.

Table 8. Estimated marker-associated additive and nonadditive effects for traits with $P < 0.10$ for genotype

	Adjusted fat thickness, mm			VISNIR shear force[2], kg		
Marker effect[1]	Value	SE	*P*-value	Value	SE	*P*-value
CSN1S1 additive	0.19	0.74	0.79	–0.30	0.25	0.30
CSN1S1 dominance	–0.58	0.53	0.27	0.16	0.17	0.35
TG additive	0.52	0.73	0.48	–0.42	0.25	0.13
TG dominance	1.03	0.54	0.06	–0.65	0.18	0.002
Additive × additive	–4.59	2.03	0.03	–0.23	0.71	0.77
Dominance × additive	–1.39	1.33	0.30	0.34	0.47	0.46
Additive × dominance	0.74	1.42	0.60	–0.07	0.51	0.92
Dominance × dominance	1.04	1.02	0.31	0.08	0.36	0.80

[1]Epistatic effects are listed as casein-S1 (CSN1S1) effect × thyroglobulin (TG) effect. Linear contrast coefficient used to estimate additive, dominance, and epistatic effects are shown in Table 1.

[2]VISNIR = visible and near-infrared reflectance. Base 10 logarithms of VISNIR shear force were analyzed and converted back to the original scale.

directly address whether nonadditive variance might be important for individual animal management decisions, mate selection, or reciprocal recurrent selection programs (Comstock et al., 1949; Li et al., 2008). Although these SNP were chosen because they both had been associated with aspects of fat deposition, we are not aware of specific pathways that involve both genes.

Hill et al. (2008) noted that epistasis could cause estimates of gene substitution effects to differ widely among populations differing in allele frequencies, thus making attempts to replicate findings difficult even when linkage disequilibrium with a causative polymorphism is the same. Allele substitution effects were calculated as linear regressions, using genotypic means for adjusted fat thickness from Table 7 and Hardy-Weinberg equilibrium genotypic frequencies. Figures 2 and 3 show how substitution effects would vary at different CSN1S1aG and TGaT frequencies. At frequencies of CSN1S1aG and TGaT near 0.5, as in this experiment, substitution effects are near 0. In other populations, substitution effects could range from large positive to large negative values, depending on average CSN1S1 and TG frequencies. In most populations, TGaT frequencies will be on the left side of the graphs and CSN1S1 frequencies will fall between the top 2 lines, resulting in positive substitution effects for both. Figure 2 also shows that the substitution effect of TGaT would decrease if selection increased its frequency and CSN1S1 was <0.5.

Few, if any, similar experiments selecting for genetic markers in cattle exist. Results of this study show that SNP associations with cattle traits, such as fat thickness and meat tenderness, can be complex. This estimated complexity illustrates how SNP associations could differ among populations when the average frequencies differ. This is a potential explanation, in addition to differences in linkage disequilibrium, when SNP associations fail to

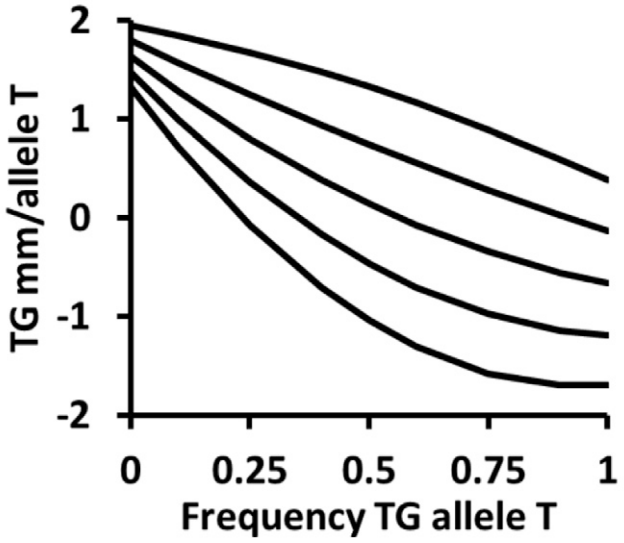

Figure 2. Calculated thyroglobulin (TG) allele T substitution effects, using estimated genotype means for adjusted fat thickness from Table 7 and different frequencies of casein1-S1 (CSN1S1) and TG. The 5 lines represent different CSN1S1 allele G frequencies of 0.01 (top line), 0.25, 0.5, 0.75, and 0.99 (bottom line).

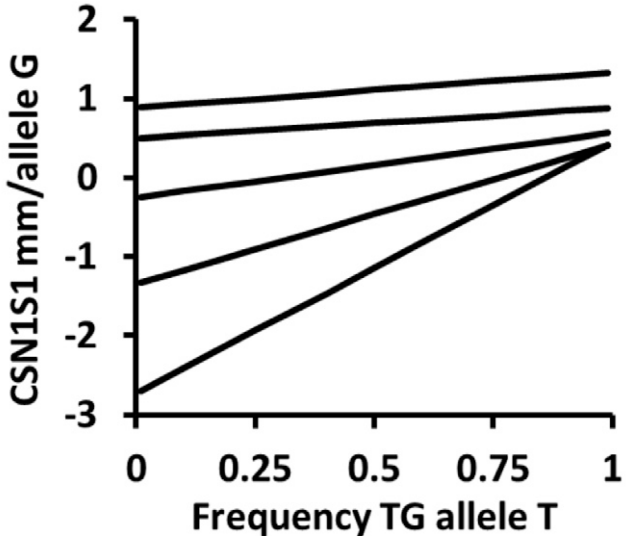

Figure 3. Calculated Casein1-S1 (CSN1S1) allele G substitution effects, using estimated genotype means for adjusted fat thickness from Table 7 and different frequencies of CSN1S1 and thyroglobulin (TG). The 5 lines represent different CSN1S1 allele G frequencies of 0.01 (top line), 0.25, 0.5, 0.75, and 0.99 (bottom line).

be verified in different populations. A second implication is that these markers will not contribute much to within-population selection but could contribute to selection response in reciprocal selection schemes. Also, marker-assisted management can use complex SNP associations if they can be estimated well.

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