IDENTIFICATION OF QTL FOR TWO MEASURES OF FEED EFFICIENCY IN NELLORE-ANGUS F_2 STEERS

An Honors Fellows Thesis

by

JOHN DAVID LUCK

Submitted to the Honors Programs Office
Texas A&M University
in partial fulfillment of the requirements for the designation as

HONORS UNDERGRADUATE RESEARCH FELLOW

April 2011

Majors: Animal Science
Genetics

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Associate Director of the Honors Programs Office: Dave A. Louis

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ABSTRACT

Identification of QTL for Two Measures of Feed Efficiency in Nellore-Angus F_2 Steers. (April 2011)

John David Luck
Department of Animal Science
Texas A&M University

Research Advisor: Dr. Clare Gill
Department of Animal Science

The objective of this study was to map quantitative trait loci for feed efficiency in *Bos taurus indicus* x *Bos taurus taurus* crossbred steers. Steers (n = 231) were from 13 full-sibling embryo transfer Nellore-Angus F_2 families raised in 9 contemporary groups in central Texas. Steers were fed in a Calan gate system beginning at 11 to 13 mo of age for a 129 to 152 d feeding period. Residual feed intake was calculated within contemporary group. A second measure of feed efficiency termed model predicted residual consumption used the NRC (2000) beef cattle model to predict expected daily dry matter intake. Both residual feed intake and model predicted residual consumption are deviations of observed from expected intake. We also investigated daily dry matter intake, average daily gain, and metabolic body weight, which are components traits for the two measures of efficiency. Residuals from analyses of variance with fixed factors of sire, family nested within sire, and with or without contemporary group as independent variables were used for QTL mapping. Steers were genotyped using the BovSNP50v1assay (Illumina Inc., San Diego, CA) and 34,980 SNP were used for single

marker association and interval analyses in PLINK and GridQTL software, respectively. Significance levels were established by permutation. Both single marker association and interval analyses identified suggestive quantitative trait loci ($P < 0.05$ chromosome-wise) on bovine chromosomes 11 and 21 for model predicted residual consumption and residual feed intake, respectively. There were significant clusters of single nucleotide polymorphisms for daily dry matter intake, average daily gain, and metabolic body weight on bovine chromsome 11 and 14 but not on bovine chromosome 21. Forkhead Box A1 was identified as a candidate gene for the quantitative trait locus on chromosome 21. Breed of origin of a 1 Mb region containing FoxA1 (near 48.6 Mb) accounted for 40% of variation in residual feed intake, 15% of the variation in model predicted residual consumption and 9% of the variation in daily dry matter intake in this crossbred population.

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This thesis would have been impossible without the instruction and guidance of many people.

First and foremost, Dr. Gill challenged me to write a thesis and guided me at every step. She taught me to think critically and to research answers to my questions. Colette Abbey patiently explained everything over and over again and kept lab work entertaining. Without Colette's encouragement, this project would have been impossible. Dr. Riley carefully explained multiple regression equations and analysis of variance - without his teaching, I would not understand this material.

Dr. Riggs gave a smile and a laugh whenever I needed one, which was often. Dr. Herring and Dr. Sanders gave expert advice frequently. Lauren Hulsman set an excellent example of diligent work and answered any question I threw at her.

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NOMENCLATURE

AA	Homozygous Angus
ADG	Average Daily Gain
BTA	*Bos taurus* Chromosome
CG	Contemporary Group
DDMI	Daily Dry Matter Intake
DMI	Dry Matter Intake
FCR	Feed Conversion Ratio
FoxA1	Forkhead Box A1
MBW	Metabolic Body Weight
MPRC	Model Predicted Residual Feed Intake
NA	Heterozygous Nellore-Angus
NN	Homozygous Nellore
QTL	Quantitative Trait Loci
RFI	Residual Feed Intake
SE	Standard Error

TABLE OF CONTENTS

CHAPTER Page

LIST OF FIGURES

LIST OF TABLES

CHAPTER I

INTRODUCTION

Increased efficiency in beef production yields greater profits for producers. Traditionally, selection in beef cattle has been primarily concerned with output, carcass, and reproductive traits, and recent improvements in the efficiency of beef production can be attributed to advances in technology and selection focused on output traits (Archer et al., 1999; Carstens and Kerley, 2009).

Differences in feed efficiency within and among beef cattle populations indicate that selection for increased feed efficiency may be possible; however, little progress has been made in genetic selection for feed efficiency. Limitations in genetic progress can be attributed to a focus on output traits, the complex nature of feed efficiency traits and the cost of measuring feed efficiency (Carstens and Kerley, 2009).The reasons behind variation in feed efficiency among animals are not well understood, and a better understanding of feed efficiency is required before producers will be able to exploit the variation for increased profit (Carstens and Kerley, 2009).

This thesis follows the style of the Journal of Animal Science.

Measures of feed efficiency

Feed conversion ratio

The ratio of dry matter intake (**DMI**) to gain (i.e. feed conversion ratio; **FCR**) is the most commonly used measure of feed efficiency (Koch et al., 1963; Archer et al., 1999; Nkrumah et al., 2006). Animals with less DMI and more gain (lower FCR) are more efficient. However, FCR is highly correlated with growth rate such that growing animals convert more of their food to body weight. Therefore, FCR is subject to change at different maturity levels. Additionally, selection of animals for growth rate results in a greater mature weight of animals, which is not always desirable (Dickerson, 1978; Archer et al., 1999). For this reason, alternative measures of feed efficiency that are not correlated to growth rate have been investigated.

Residual feed intake

Koch et al. (1963) suggested the use of partial regression equations to correct for body size and gain to predict feed intake in a group of growing calves. Expected feed intake is calculated within a contemporary group (**CG**) of animals by measurement of intake, gain, and body weight over a fixed period of time (Archer et al., 1997).The difference between the observed and predicted intake using such a model is now known as residual feed intake (**RFI**). Animals with a negative RFI require less feed for production than is predicted by the expected feed intake (Archer et al., 1999). Arthur et al. (2001a) reported heritability of RFI to be 0.39 ± 0.03 in a study of 1,180 Angus bulls and heifers.

Koch et al. (1963) suggested that selection for RFI would be selection for the variation attributable to differences in efficiency. Because RFI is a result of correction for gain and body weight, it is considered to be phenotypically independent of those production phenotypes, and selection pressure on RFI should affect neither gain nor body weight (Archer et al., 1999).Arthur et al. (2001a) showed that RFI was not correlated with average daily gain (**ADG**), longissimus muscle area, or rump fat depth. However, Kennedy et al. (1993) suggested that RFI is not independent of production genetics due to the inherent relationship between input of feed and output of body mass. Additionally, van der Werf (2004) asserts that RFI is fundamentally a mult-trait selection scheme, and that calculation of RFI, because it is dependent on production traits, adds no new information to selection choices.

Model predicted residual consumption

Because RFI is calculated within a CG, it is also difficult to compare the performance of animals across CG as would be found in a gene mapping study. This was the motivation for the development of model predicted residual consumption (**MPRC**) as a measure of feed efficiency (Amen et al., 2007). Amen et al. (2007) used the NRC (2000) beef cattle model to predict intake based on observed weight gain for each animal and standardized input for animal type, age, sex, condition, and breed. Like RFI, MPRC is the residual difference between observed and expected intake, but MPRC is not calculated within CG, allowing an entire CG to be more efficient than the rest of the experimental population.

The objective of this study was to map quantitative trait loci (**QTL**) for RFI and MPRC in steers from an F_2 Nellore-Angus beef cattle population.

CHAPTER II

MATERIALS AND METHODS

Experimental population

Steers (n = 213) from 13 full-sibling embryo transfer Nellore-Angus F_2 families of the McGregor Genomics Population were raised in 9 CG at McGregor, Texas. Steers were born in the spring and fall calving seasons from fall 2003 to spring 2007, and those born in the same year and season were managed as a single CG. Steers were weaned at 7 mo of age and placed on pasture for about 130 d. Steers were then fed in a Calan gate system for 129 to 152 d beginning at 11 to 13 mo of age. Steers were housed in partially covered pens of 4 and were weighed every 28 d. Feed was offered *ad libitum* and refused feed was weighed every 7 d. Dry matter content of feed was shown to average 90% (Amen et al., 2007). All procedures involving animals were approved by the Texas A&M Institutional Animal Care and Use Committee; AUP # 2002-116 and2005-147.

Measures of feed efficiency

Daily dry matter intake (**DDMI**) was calculated as 0.9 * total intake for the feeding period divided by the number of days on feed. Likewise, average daily gain (**ADG**) was calculated as total gain during the feeding period divided by the number of days on feed. Metabolic body weight (**MBW**) was average weight while on feed raised to the ¾ power. Expected feed intake was then calculated within a CG by regressing DDMI on ADG and MBW (Archer et al., 1997):

$$DDMI_{ij} = \beta_0 + \beta_1 ADG_i + \beta_2 MBW_i + CG_j + e_{ij}$$

whereβ_0 = regression intercept, β_1= partial regression coefficient of feed intake on ADG, β_2= partial regression coefficient of feed intake on MBW. The residual (e_{ij}) is the difference between observed and expected intake, which is RFI.

Model predicted residual consumption (Amen et al., 2007) was used as a second measure of feed efficiency. For this measure of efficiency, the NRC (2000) beef cattle model was used to predict intake based on observed weight gain for each animal and standardized input for animal type, age, sex, condition, and breed. The residual from this model is MPRC, which is the difference between observed and expected feed intake.

Genotyping

Steers and their parents and grandparents were genotyped for 54,001 single marker polymorphisms (SNP) using the BovSNP50v1 assay from Illumina (San Diego, CA). Single marker polymorphisms with low completion rate (< 90%), low minor allele frequency (< 5%), or deviation from Hardy-Weinberg equilibrium proportions (P<0.0001) were removed. In the final dataset there were 34,980 SNP for each animal.

Statistical analyses

Analysis of variance was performed for RFI and MPRC using the GLM procedure (SAS Inst., Cary, NC). Independent variables treated as fixed factors were sire, family nested within sire, and CG. Models with and without CG were examined:

$$RFI_{ijk} = \mu + sire_j + family(sire)_k + e_{ijk}$$

$$RFI\text{-}CG_{ijkl} = \mu + sire_j + family(sire)_k + CG_l + e_{ijkl}$$

$$MPRC_{ijk} = \mu + sire_j + family(sire)_k + e_{ijk}$$

$$MPRC\text{-}CG_{ijkl} = \mu + sire_j + family(sire)_k + CG_l + e_{ijkl}$$

Residuals from analysis of variance were used for QTL analysis.

Single marker association analysis

Genotypes were formatted for PLINK software (Purcell et al., 2007) using Perl scripts to produce output in long PLINK (lgen) format (Clare A. Gill, pers. comm.). Chromosomal coordinates for SNP were from build Btau4.0 of the bovine genome sequence. Single marker association analysis was performed using the 'assoc' option and overall significance levels were empirically determined by adaptive permutation (up to 1 million times). Associations were visualized by chromosome and coordinate as Manhattan plots in R.

QTL analysis

GridQTL software, supported by the UK National Grid service, was used to perform QTL analysis under an additive and dominance model with 1 cM steps. A distance of 1Mb was assumed to be equivalent to 1 cM. Significance thresholds were determined by 1000 permutations (which is randomly re-assigning the phenotypic data to the marker data in representation of the null hypothesis). Missing marker genotypes were not inferred for analysis. For each cM interval, the probability of an inherited genotype at a locus was inferred from the flanking marker genotypes (Coppieters et al., 1998). The inferred locus genotype was then posited as a QTL for the trait in question and the

likelihood that the data was explained by a QTL at that locus was compared with the likelihood that no QTL existed at that locus (Lander and Botstein, 1989).

Identification of a candidate region

We used the NCBI *Bos taurus* genome map viewer and results from PLINK and GridQTL to select a candidate gene for further investigation. By performing a PubMed search of gene names from the NCBI Btau 4.0 annotation, we were able to discover which of the genes near significant markers was likely to affect feed efficiency.

Primer design and sequencing

Primers for PCR (Table 1) were designed using Primer3Plus software from the www.bioinformatics.nl website. Design criteria included: optimal primer size (20bp), minimum primer size (18bp), maximum primer size (27bp), optimal melting temperature (60ºC), minimum melting temperature (57ºC), maximum melting temperature (63ºC), minimum GC content (20%), maximum GC content (80%), salt concentration (50nM), DNA concentration (50nM), maximum self complementarity (8bp), maximum 3' end self complementarity (3bp), GC clamp (0 bases), maximum repeat mispriming (12.00), pair maximum repeat mispriming (24), maximum template mispriming (12), pair maximum template mispriming (24), and product length ranges (400-1000bp). Primers were designed to amplify exons, introns, and both the 5' and 3' region of the *FoxA1* gene (accession number NW_001494047.2). Forward and reverse primers selected to

have similar melting temperatures were purchased from Integrated DNA technologies (Coralville, IA).

Each of the 50 μl PCR reactions included 2 units of TAQ polymerase, 0.1μM forward primer, 0.1 μM reverse primer, 1X Buffer (50mM KCl, 10mM Tris-HCl, pH 9.0, 0.1%Triton X-100), 1.5 mM $MgCl_2$, and 0.1mM dNTPs. For some reactions 50mM betaine or 1% v/v dimethylsulfoxide or both were required for amplification. Thermal cycling conditions were 95°C for 5 min, followed by 35 cycles of 95°C for 30 s, 30 s at the annealing temperature (Table 1), 72°C for 30 s, and a final extension of 7 min at 72°C.

Table 1. PCR primer sequences and conditions

Primer Set	Forward Primer Sequence 5'-3'	Reverse Primer Sequence 5'-3'	50mM Betaine[1]	1% DMSO[2]	T_A[3]
FoxA1_A	AGT AGA GCG GAT CGA GGT G	GTT CCC TTC CTA CGA CAG GA	+	-	63.2
FoxA1_D	GGA GCT CAG AAC ACT TCC TCA	CCG TCT TCC TTT TGC TTG AA	-	-	58.0
FoxA1_F	TTC AAC ATG TCC TAC GCA AA	GTG GCT GGA GTC TTC AAC TC	+	+	58.6
FoxA1_G	GCT CTC CTT CAA CGA CTG CT	GGC TTG GTA CGT GTG GTT TT	+	+	55.9
FoxA1_H	GCA GCA CAA GTT GGA CTT CA	AAC AGC AGC ACT GTC CTT CA	+	-	66.8
FoxA1_I	AAA TCC TCC TGC TTC CTT GT	CAC CAT GTC CAA CTG TGA AA	-	-	55.9
FoxA1_J	CAA TTG ATT GTG GCC ATT TT	CTG CCG TGA TGG TTA ATT TT	-	-	50.5

[1]+/- indicate whether betaine was added to the reaction or not.
[2]1% v/v dimethylsulfoxide where +/- indicates whether it was added to the reaction or not.
[3]Annealing temperature (ºC).

The sequencing reaction was cleaned on a Sephadex G-50 column in a 300 μl filter plate (MPF-046 from Phenix research products). Sephadex (18.75 mg) was added to the plate with 300 μl of ddH_2O (with care taken not to introduce bubbles) and allowed to sit at room temperature for 3 h. The column was spun at 1000 *g* for 5 min before the sequencing reaction product was added and again spun at 1000 *g* for 5 minutes. Eluent was dried at 70°C for 20 min in an open PCR machine and the product was suspended in 10 μl deionized formamide. The formamide solution was denatured at 98°C for 2 min, snap cooled on ice for 2 min, and loaded into the ABI 3130XL Genetic Analyzer (Applied Biosystems by Life Technologies, Carlsbad, CA). Sequencing products were separated using POP7 polymer on a 50 cm capillary array. Sample was injected at 1.6 kV for 15 s and run at 8.5 kV for 6000 s.

Inclusion of *FoxA1* in the models of feed efficiency

Coordinates (Btau 4.0) of the investigated candidate gene (*FoxA1*) were used to extract SNP spanning a 1 Mb region centered on the gene. Haplotypes were obtained using FastPHASE (Scheet and Stephens, 2006) and then breed of origin (Nellore or Angus) of the haplotypes was determined by comparison of haplotypes in the steers to haplotypes of the parents and grandparents. The phase (breed of origin) of the region surrounding *FoxA1* was subsequently included as a fixed effect (homozygous Angus = 0, heterozygous = 1, or homozygous Nellore = 2) in the models for RFI and MPRC to estimate the effect of this gene on the traits.

CHAPTER III

RESULTS AND DISCUSSION

Summary statistics

Simple means for component traits (ADG, DDMI, and MBW) and feed efficiency traits (RFI and MPRC) are presented in Table 2. As expected, average RFI and MPRC for the population was 0.00. Large standard deviations were observed for each of the traits indicating that there is variation for the traits of interest in this F_2 Nellore-Angus population of steers. Thus, we would expect to be able to identify genes segregating between and within families for these traits.

Table 2. Simple means and standard deviations for intake, gain and efficiency traits

Variable[1]	N	Mean	Std. Dev.
MBW	231	74.48	6.15
ADG	231	1.06	0.27
DDMI	231	8.99	1.58
RFI	231	0.00	0.81
MPRC	231	0.00	1.37

[1]MBW = metabolic body weight (kg), ADG = average daily gain (kg), DDMI = daily dry matter intake (kgd^{-1}), RFI = residual feed intake (kgd^{-1}), MPRC = model predicted residual consumption (kgd^{-1})

The variation observed in our crossbred population is comparable to other studies. Archer et al. (1997) found DDMI to average 12.59 kgd^{-1}and11.5 kgd^{-1} in Angus bulls (n = 97) and heifers (n = 96), respectively. The standard deviation in DDMI was 1.08 kgd^{-1}

for each group. In this same population, ADG was 1.31 kgd^{-1} (0.10kgd^{-1}std.dev.)and 1.01 kgd^{-1} (0.10 kgd^{-1} std. dev.)for bulls and heifers, respectively. In Angus-Hereford crossbred steers (n = 30),Cruz et al. (2011) found DDMI to average 10.09 kgd^{-1}(1.1 kgd^{-1} std. dev.) and ADG was 2.09 kgd^{-1} (0.17 kgd^{-1} std. dev.). Reported standard deviations for RFI range from 0.59 to 1.2kgd^{-1} (Archer et al., 1997; Arthur et al., 2001; Bolormaa et al., 2011; Cruz et al., 2011).

Analysis of variance

Table 3. *P* values of fixed effects in analysis of variance

Dependent Variable[1]	Sire	Family(sire)	CG[2]	R^2
RFI (kgd^{-1})	0.0434	0.1978	-	0.08
MPRC (kgd^{-1})	0.0133	<0.0001	-	0.18
RFI (kgd^{-1})	0.0268	0.1419	0.8356	0.10
MPRC (kgd^{-1})	0.0056	0.0323	<0.0001	0.65

[1]RFI = residual feed intake; MPRC = model predicted residual consumption

[2]CG = contemporary group. Animals born in the same year and season were raised in a single CG.

Sire was a significant factor for both RFI and MPRC (Table 3). Although family nested within sire was not significant in the model for RFI, the fixed effect was left in the model for ease of comparison to MPRC. Contemporary group was not a significant fixed effect in the model for RFI, which was expected because RFI is calculated within CG. Contemporary group was a significant fixed effect in the model for MPRC. The tendency here would be to remove the variation due to CG from the model on the premise that the variation is due only to differences in the environment between seasons

and years (e.g. average temperature during the feeding period). We investigated models with and without the inclusion of CG in case there were underlying genetic differences that enabled animals to efficiently adapt to variation in the environment. We chose to do this because we had previously observed that the most efficient CG, fed in summer of 2006,experienced the hottest feeding period in our study, enduring 37 days over 37.8ºC and an average daily maximum temperature of 34.16ºC (Clare Gill, pers. comm.).When CG was omitted, the models for RFI and MPRC explained 8% and 18% of the variation in the traits, respectively. When CG was included in the models, the fixed factors accounted for 10% of the variation in RFI and 65% of the variation in MPRC (Table 3).

Single marker associations

There were clusters of SNP on bovine chromosomes (BTA) 3 and 21 that were associated ($P< 0.001$) with RFI (Figure 1). There were also single markers with $-\log_{10}(p)$ values above the significance threshold on BTA 2, 11 and 14. When CG was included in the model for MPRC (Figure 2), the profile of the single marker associations was similar to that observed for RFI. Among the 30 most significant SNP for RFI and MPRC, there were 12 SNP in common from BTA21, and 7 in common from BTA 3. The 3 significant SNP for MPRC on BTA3 were not among the 30 most significant SNP for RFI. When CG was omitted from the MPRC model, the profile was noticeably different (Figure 3). There were more significant SNP in the cluster on BTA 11 ($P< 0.001$) as well as several significant markers on BTA 5, 10 and 24, whereas the SNP on BTA 3 and 21 no longer reached the $P< 0.001$ significance threshold.

QTL analysis

Results from the single marker association analyses were confirmed by interval analysis. There was a significant QTL on BTA 11for RFI and MPRC (Figure 4) and a QTL on BTA 21 for RFI (Figure 5).The QTL for RFI on BTA 21 was chosen for more detailed investigation.

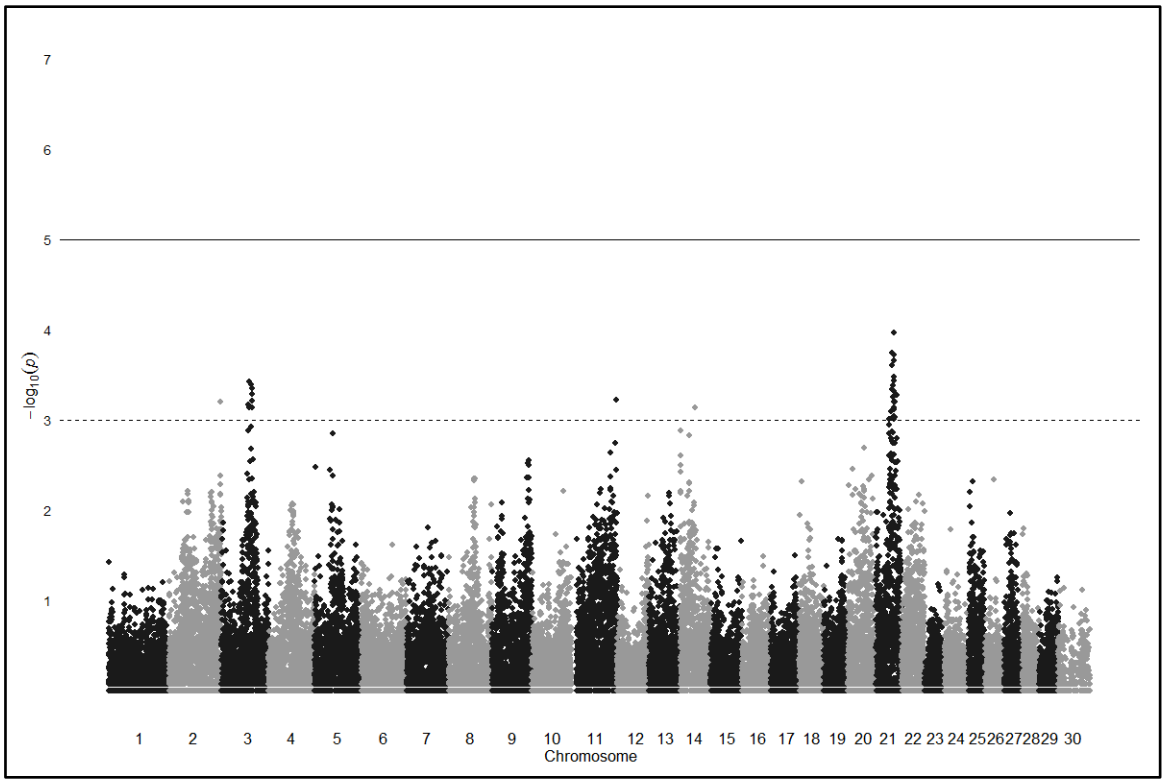

Figure 1. Single marker associations for RFI using a model that omitted CG. Each point represents the probability of association (on a -$\log_{10}$(p) scale) established by adaptive permutation of a SNP with RFI. Horizontal lines are arbitrary significance thresholds. Markers are arranged by position according to build Btau4.0 of the bovine genome sequence.

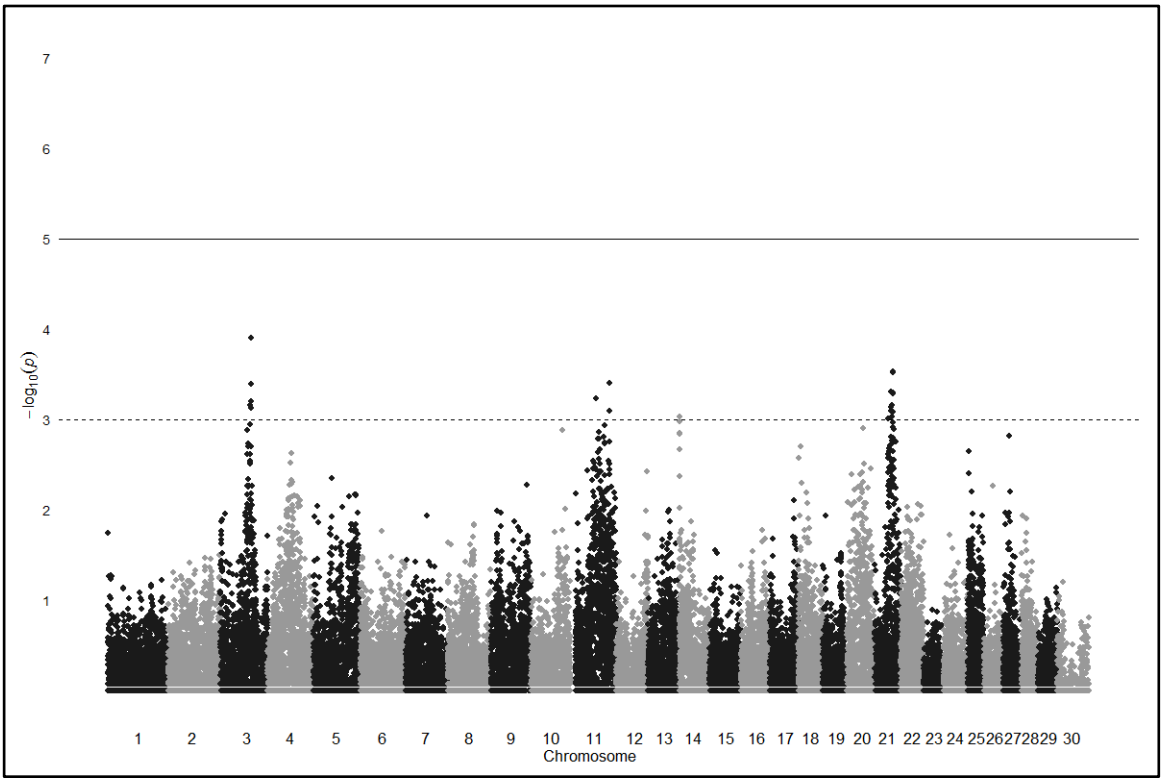

Figure 2. Single marker associations for MPRC using a model that included CG. Each point represents the probability of association (on a -$\log_{10}$(p) scale) established by adaptive permutation of a SNP with MPRC. Horizontal lines are arbitrary significance thresholds. Markers are arranged by position according to build Btau4.0 of the bovine genome sequence.

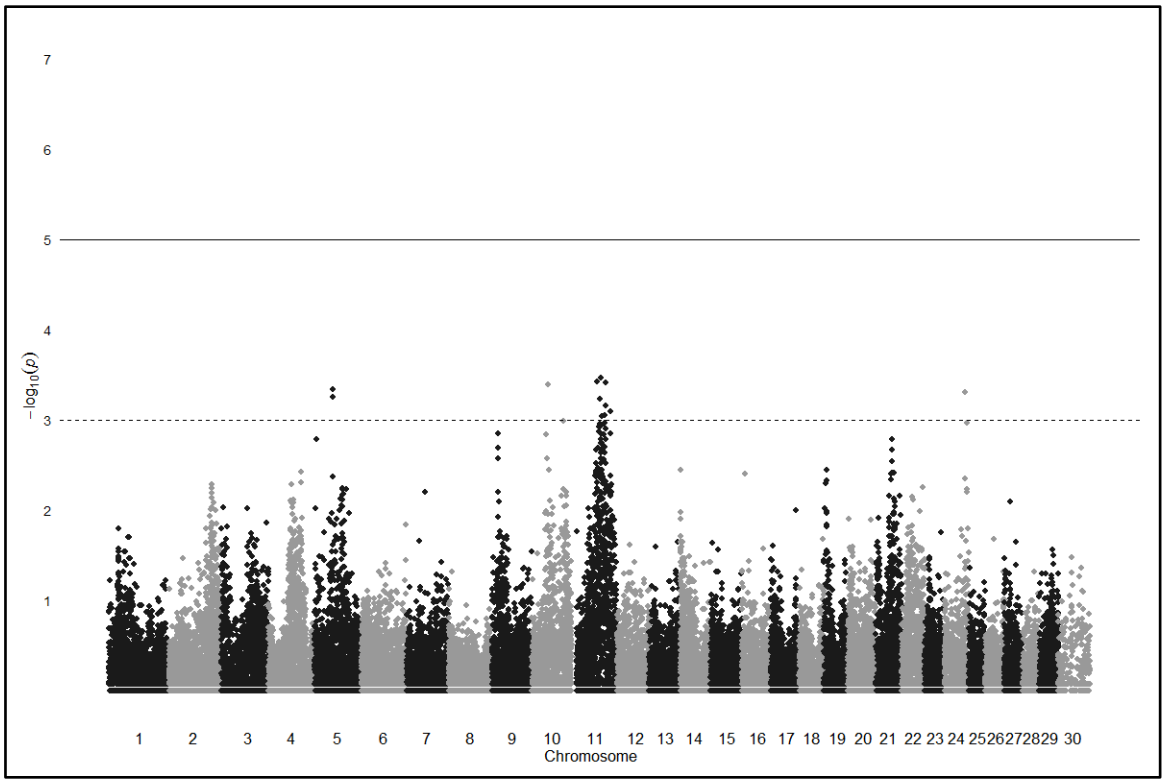

Figure 3. Single marker associations for MPRC using a model that omitted CG. Each point represents the probability of association (on a $-\log_{10}(p)$ scale) established by adaptive permutation of a SNP with MPRC. Horizontal lines are arbitrary significance thresholds. Markers are arranged by position according to build Btau4.0 of the bovine genome sequence.

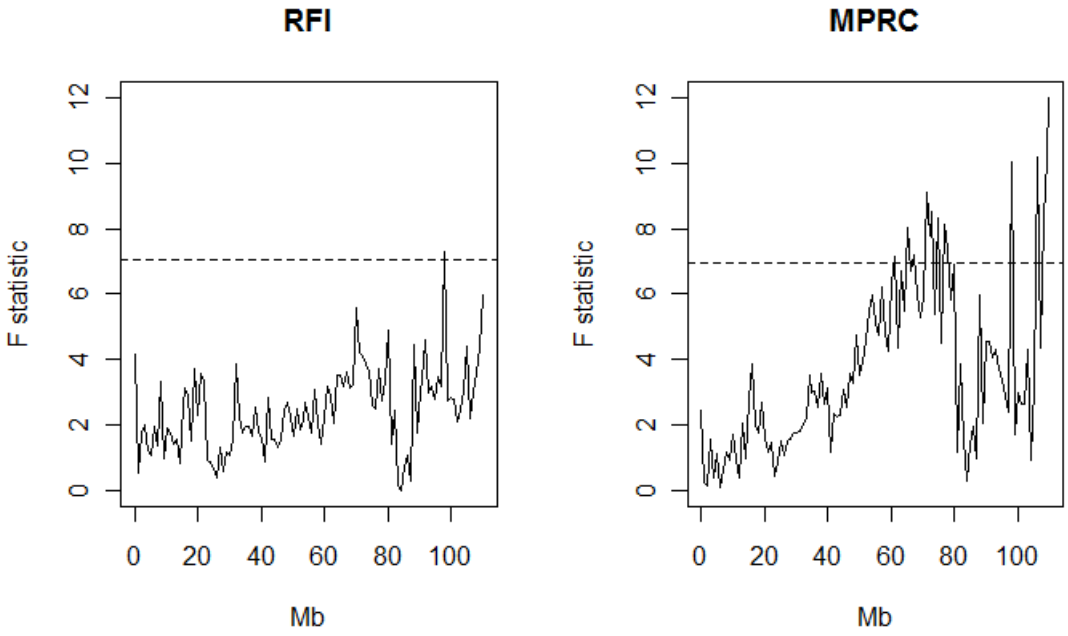

Figure 4. Interval analysis on BTA 11 for RFI and MPRC. Horizontal dashed line indicates the F statistic threshold for chromosome-wise significance established by permutation.

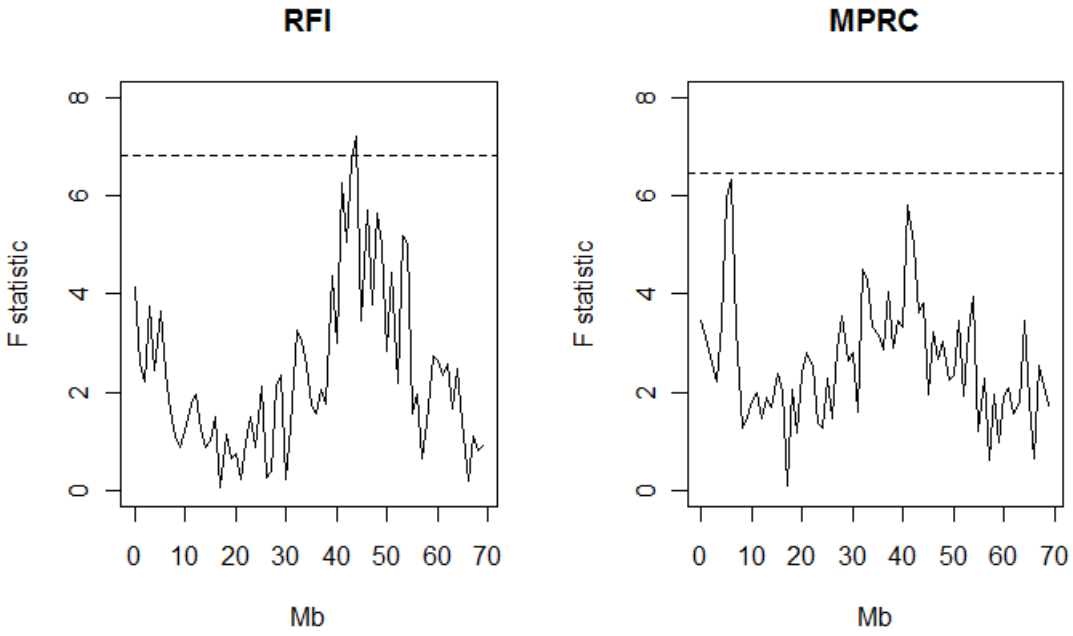

Figure 5. Interval analysis on BTA 21 for RFI and MPRC. Horizontal dashed line indicates the F statistic threshold for chromosome-wise significance established by permutation.

Numerous suggestive QTL for DMI have been reported in the literature, including 2 suggestive QTL on BTA 21 at 2.0 cM and 53.5 cM (Nkrumah et al., 2007; Banos et al., 2008; Sherman et al., 2008; Marquez et al., 2009; Rincon et al., 2009). Suggestive QTL for RFI have been reported, including 4 suggestive QTL on BTA 21 at 2.0, 3.3, 38.6, and 73.3 cM (Nkrumah et al., 2007; Marquez et al., 2009). Additionally, significant QTL for ADG have been reported on 16 chromosomes (Li et al., 2004; Mizoshita et al., 2004; Nkrumah et al., 2007; Sherman et al., 2008; Marquez et al., 2009; Huang et al., 2010).

Identification of a candidate region

Examination of the 8 Mb region of BTA21 (Figure 6) that contained the 8markers with the lowest *P*-values from the single marker association analysis showed that the first and fourth lowest P-values were located near 48.6 Mb, adjacent to Forkhead box A1 (*FoxA1*). Forkhead box A1, also known as hepatocyte nuclear factor 3 alpha (HNF-3a), was selected as a candidate gene for feed efficiency due to its role in the regulation of development and differentiation (Gao et al., 2005). Forkhead box A1 binds to genes expressed in liver, intestine, lung, and pancreas (Liu et al., 2002; Hughes et al., 2003; Wan et al., 2005). Additionally, *FoxA1* is required for estrogen receptor binding (Carroll et al., 2005).

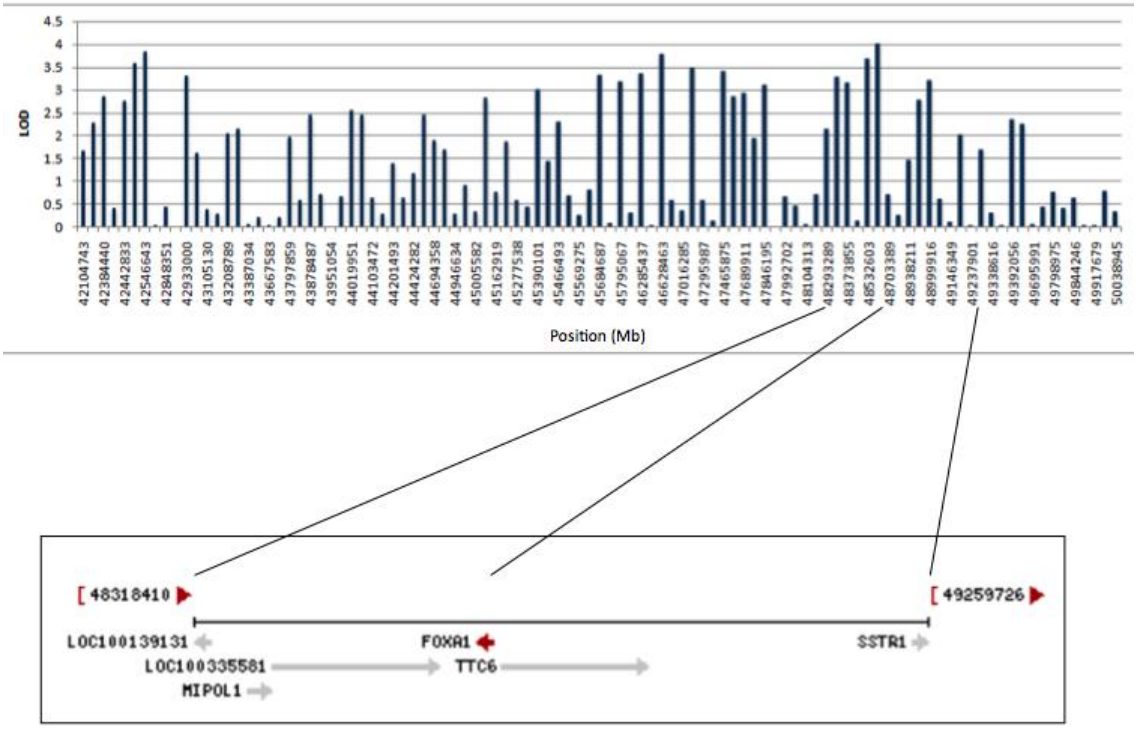

Figure 6. Region from 42 to 50 Mb of BTA 21 containing 8 significant markers for RFI. Markers were aligned to genes using the NCBI genome viewer.

Discovery of SNP in *FoxA1*

Because none of the SNP on the BovSNP50v1 chip fell in *FoxA1*, we sequenced several regions of the gene using the Nellore and Angus grandparents as templates for SNP discovery. Three sets of primers produced amplicons but no usable sequence (FoxA1_A, FoxA1_D, and FoxA1_F). The remaining 4 sets of primers were used to generate sequence for overlapping amplicons spanning exon 2 of *FoxA1* and the 3'UTR. A C/T SNP was discovered at 48678229 of BTA21 in the 3'UTR of *FoxA1*. We subsequently amplified and sequenced this region in 22 steers from family 80. We showed that this SNP was in complete disequilibrium with the flanking SNP from the BovSNP50v1 chip and so we inferred breed of origin of *FoxA1* using the flanking SNP for all steers in the population rather than performing additional sequencing.

Effect of region containing *FoxA1* on feed efficiency

We used breed of origin of the region of BTA21 that includes *FoxA1*as a fixed factor in models for RFI and MPRC to evaluate the extent to which the region explains variation in these traits:

$$RFI_{ijkl} = \mu + sire_j + family(sire)_k + FoxA1_l + e_{ijkl}$$

$$MPRC_{ijkl} = \mu + sire_j + family(sire)_k + FoxA1_l + e_{ijkl}$$

Breed of origin of *FoxA1* was a significant factor in both models ($P< 0.001$). Interval analysis (Figure 7) using residuals from these models showed that inclusion of *FoxA1* accounted for the variation in RFI and MPRC such that no markers on BTA21 were

above the significance threshold. Thus, *FoxA1* or a gene in complete disequilibrium with *FoxA1* causes the variation in feed efficiency on BTA 21.

Table 4. Least squares means and SE for feed efficiency by breed of origin of *FoxA1*[1]

Dependent Variable[2]	Vp[3]	AA	NA	NN	$\left\|\frac{a}{Vp}\right\|$[4]
RFI (kgd^{-1})	0.65	-0.14 ± 0.13^{a}	0.14 ± 0.09^{b}	0.38 ± 0.14^{b}	0.40
MPRC (kgd^{-1})	1.88	-0.05 ± 0.13^{a}	0.28 ± 0.10^{b}	0.50 ± 0.50^{b}	0.15
DDMI (kgd^{-1})	2.50	8.81 ± 0.22^{a}	9.14 ± 0.17^{b}	9.23 ± 0.25^{b}	0.09

[1]Within a row, values with different superscripts differ ($P < 0.05$). AA = homozygous Angus, NA = heterozygous Nellore-Angus, NN = homozygous Nellore.
[2]RFI = residual feed intake; MPRC = model predicted residual consumption; DDMI = daily dry matter intake
[3]Vp = Phenotypic variance
[4]Proportion of phenotypic variation due to *FoxA1*

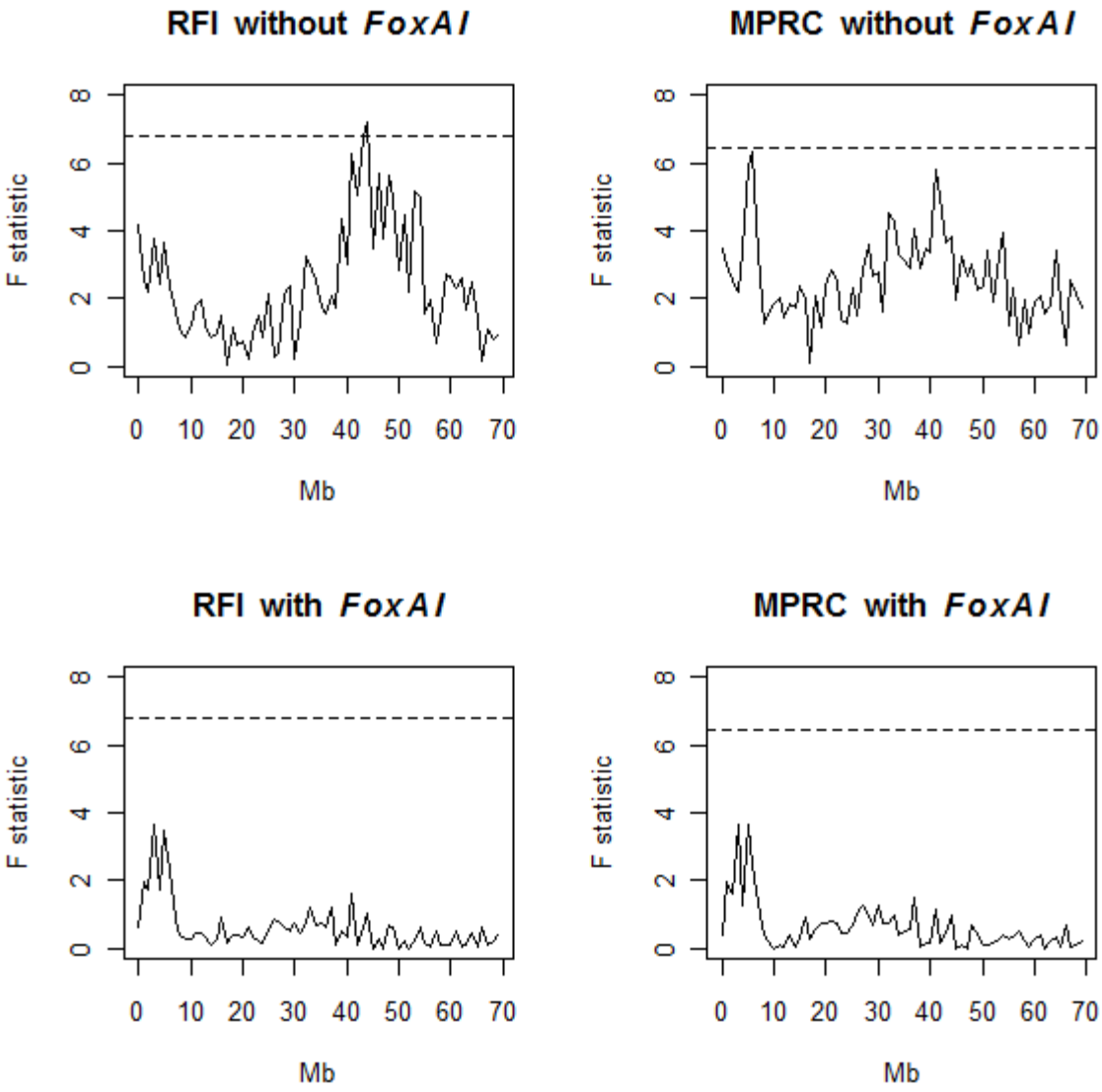

Figure 7. Interval analysis on BTA 21 for RFI and MPRC with and without breed of origin of *FoxA1* in the model used to produce residuals for mapping. Horizontal dashed line is the chromosome-wise significance threshold established by permutation.

Angus homozygotes for *FoxA1*were 0.52 kgd^{-1}more efficient than Nellore homozygotes using RFI as a measure of efficiency (Table 4). For MPRC, Angus homozygotes were estimated to be 0.55 kgd^{-1}more efficient than Nellore homozygotes. Breed of origin of *FoxA1* was also a significant factor ($P< 0.001$) in the model for DDMI and Angus homozygotes were estimated to consume 0.42 kgd^{-1}less than Nellore homozygotes. Thus, the breed of origin of *FoxA1* accounted for 40% of the variation in RFI, 15% of the variation in MPRC and 9% of the variation in DDMI.

Investigation of component traits

Examination of the QQ plots for single marker associations for RFI and MPRC suggested that we have low power for the 2 traits (data not shown). We expect a factor contributing to low power is that both traits are, after analysis of variance, residuals of residuals. For this reason, we decided to examine the association of SNP with DDMI, ADG and MBW that are the component traits of RFI and MPRC.

Although *FoxA1* accounts for 9% of the variation in DDMI, no SNP on BTA 21 reached the $P< 0.001$ significance threshold (Figure 8). Instead, there was a cluster of SNP on BTA 11 that dominated the Manhattan plot. Chromosomes 11 and 14 were also significant for ADG and MBW (Figures 9 and 10).

Given the very large effect that the QTL on BTA 21 has on RFI and the moderate effect it has on MPRC, we were surprised there were no significant SNP for any of the

component traits. Recent work in our laboratory suggests that genetic variation RFI and MPRC due to the QTL on BTA 21 may be due to variation in feeding behavior because a QTL for temperament has been mapped to the same region (Lauren Hulsman, pers. comm.).

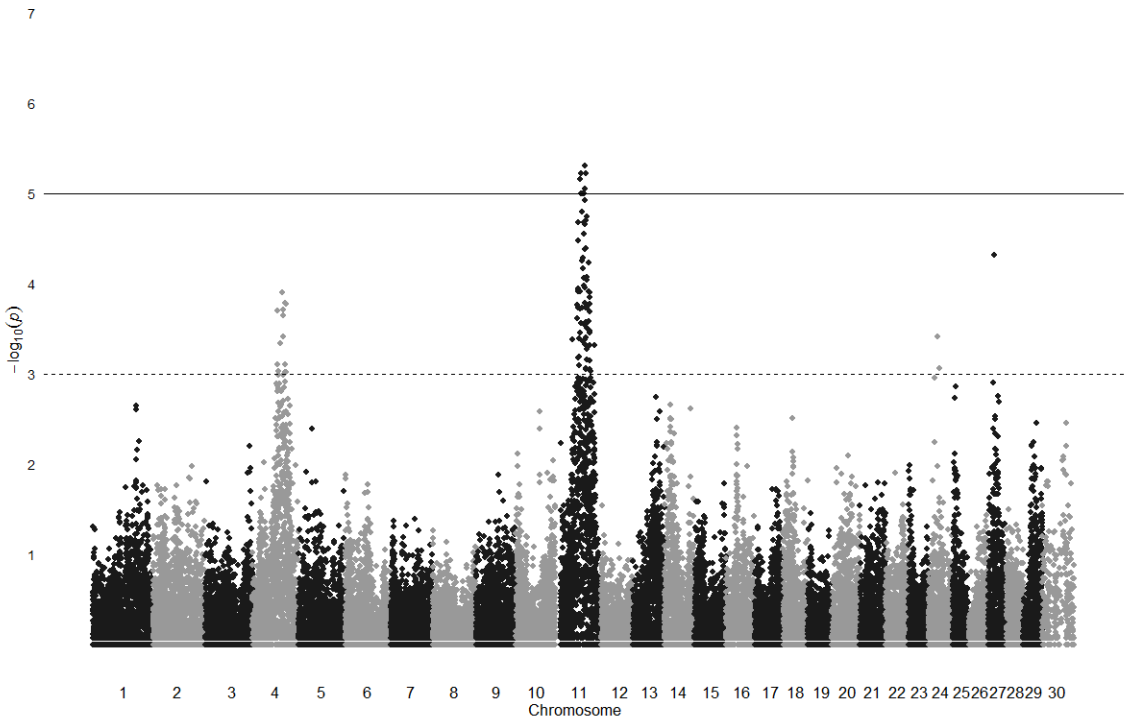

Figure 8. Single marker associations for DDMI using a model that included CG. Each point represents the probability of association (on a $-\log_{10}(p)$ scale) established by adaptive permutation of a SNP with DDMI. Horizontal lines are arbitrary significance thresholds. Markers are arranged by position according to build Btau4.0 of the bovine genome sequence.

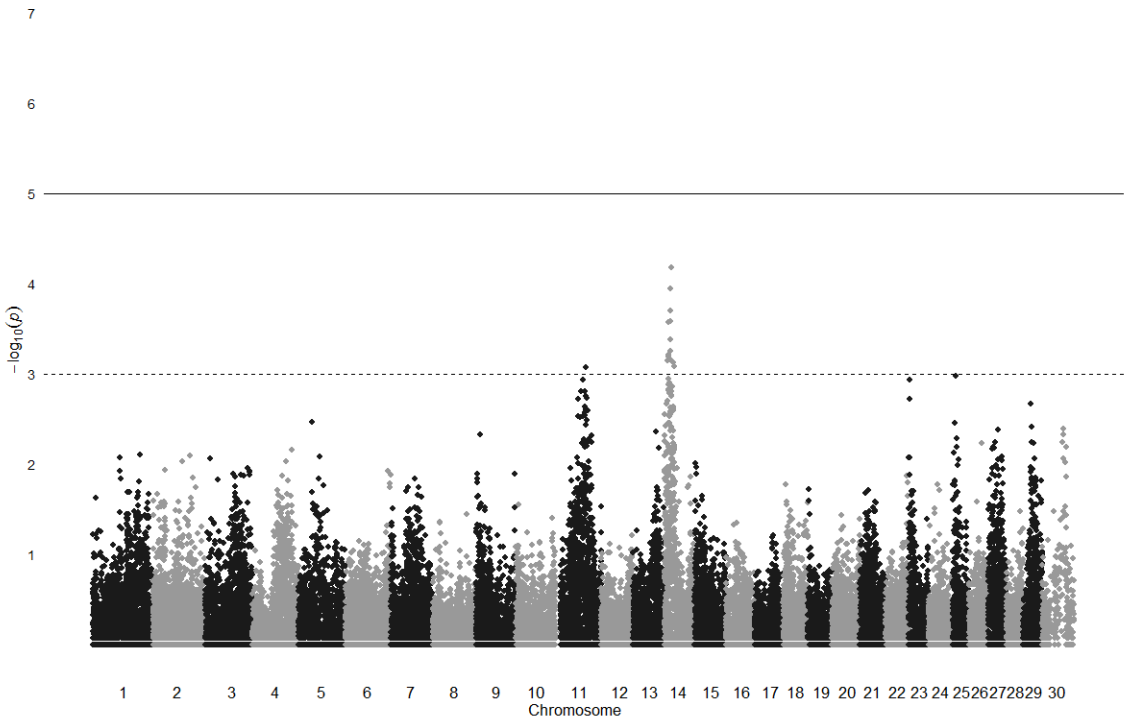

Figure 9. Single marker associations for ADG using a model that included CG. Each point represents the probability of association (on a $-\log_{10}(p)$ scale) established by adaptive permutation of a SNP with ADG. Horizontal lines are arbitrary significance thresholds. Markers are arranged by position according to build Btau4.0 of the bovine genome sequence.

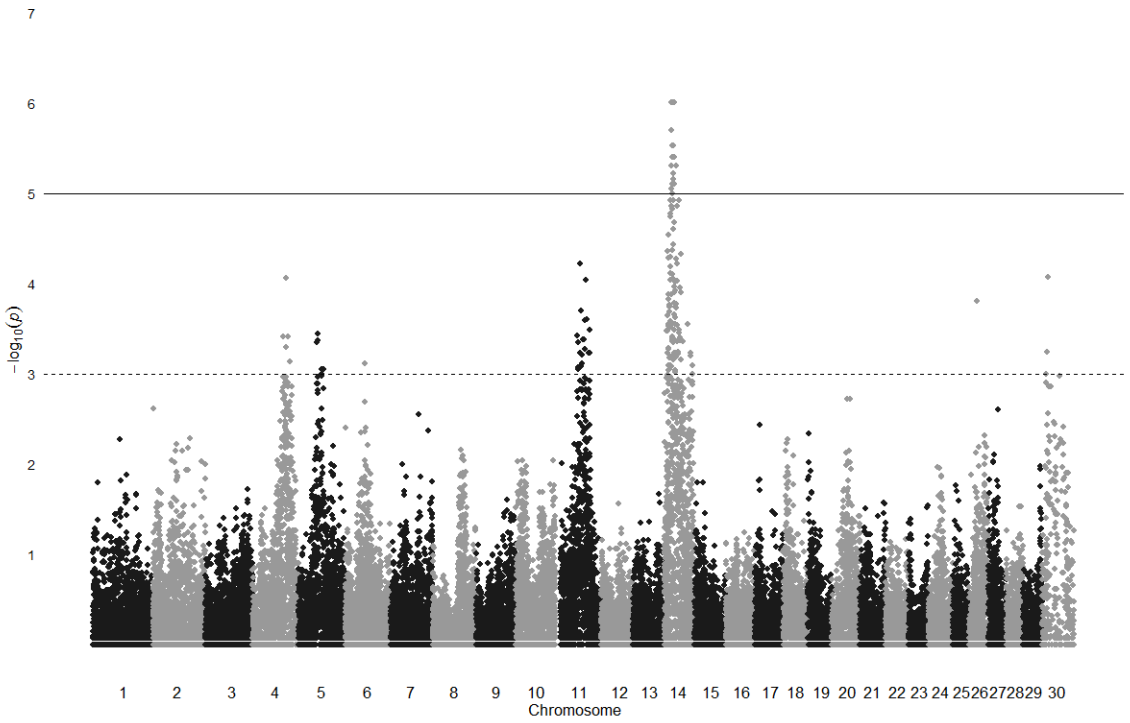

Figure 10. Single marker associations for MBW using a model that included CG. Each point represents the probability of association (on a $-\log_{10}(p)$ scale) established by adaptive permutation of a SNP with MBW. Horizontal lines are arbitrary significance thresholds. Markers are arranged by position according to build Btau4.0 of the bovine genome sequence.

CHAPTER IV

SUMMARY AND CONCLUSIONS

The objective of this study was to map QTL for feed efficiency in crossbred steers. Steers (n = 231) were from 13 full-sibling embryo transfer Nellore-Angus F_2 families raised in 9 contemporary groups in central Texas. Steers were fed in a Calan gate system beginning at 11 to 13 mo of age for a 129 to 152 d feeding period. Residual feed intake was calculated within contemporary group whereas MPRC was based on the NRC (2000) beef cattle model. Daily dry matter intake, ADG, and MBW were also investigated. Residuals from analyses of variance with fixed factors of sire, family nested within sire, and with or without contemporary group as independent variables were used for QTL mapping. Both single marker association and interval analyses, identified suggestive QTL ($P< 0.05$ chromosome-wise) on BTA 11 and 21 for MPRC and RFI, respectively. There were significant clusters of SNP for DDMI, ADG, and MBW on BTA 11 and 14 but not on BTA 21. Forkhead Box A1 was identified as a candidate gene for the QTL on BTA 21. Breed of origin of a 1 Mb region containing *FoxA1* (near 48.6 Mb) accounted for 40% of variation in RFI, 15% of the variation in MPRC and 9% of the variation in DDMI. Future work will involve integrating these association data with expression analyses to characterize the QTL identified in this study.

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CONTACT INFORMATION

Name:	John David Luck
Professional Address:	c/o Dr. Clare Gill Department of Animal Science MS 2471 Texas A&M University College Station, TX 77843
Email Address:	JohnDLuck@gmail.com
Education:	B.S., Animal Science and Genetics Texas A&M University, May 2011 Magna Cum Laude Honors Undergraduate Research Fellow University Honors