GENOME SCAN IN COMMERCIAL ANGUS CATTLE FOR QUANTITATIVE TRAIT LOCI INFLUENCING GROWTH, CARCASS, AND REPRODUCTIVE TRAITS

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Doctor of Philosophy

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by

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JULY 2009

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And hereby certify that in their opinion it is worthy of acceptance.

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Dedication:

To my wife, mother, and father....without your support and encouragement this would have not have been possible.

Jen: While the journey through graduate school has had its ups and downs, dogs, horses, and a house there is no one else I would want to complete this journey with.

Mom and Dad: Thanks for always supporting my decisions and encouraging me to do my best. You were correct: Everything does work out in the end.

Love,

Matt

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CHAPTER 1

INTRODUCTION

Practically every economically important trait in the beef industry is quantitative and influenced by multiple genes as well as environmental factors. The genomic regions that contain genes which influence a trait's phenotypic variation are called quantitative trait loci (QTL) (Andersson 2001). The identification of QTL could lead to genetic improvement through the implementation of marker assisted selection (MAS) by producers to increase carcass quality and production efficiency (MacNeil & Grosz 2002). Genetic improvement by MAS may be substantially greater than selection based solely upon estimated breeding value for traits that are determined post-mortem, occur late in life, are lowly heritable, or are difficult and (or) expensive to measure (Davis & DeNise 1998). Considering the significant economic benefits from QTL discovery for traits deemed important to producers and consumers, multiple academic research groups have focused on the identification of QTL for quantitative trait variation in beef cattle.

While a number of QTL scans in cattle have been conducted with *Bos taurus* x *Bos indicus* crosses or with experimental *B. taurus* crosses the implementation of MAS using the detected QTL has been problematic. While the development of resource populations based upon crossbreeding does allow the detection of QTL, it hinders the identification of the underlying quantitative trait nucleotides (QTN) and thus the development of MAS programs. *B. indicus* and *B. taurus* diverged approximately 500,000 years ago (Miretti *et al.* 2002) and mutations with fixed allelic differences have accumulated about every 2 kb within these genomes (Taylor *et al.* 2006). Consequently, the confidence interval for any QTL trait found by

linkage analysis in such a crossbred population will contain thousands of mutations consistent with a *B. indicus* versus *B. taurus* QTL, which are statistically impossible to differentiate within the experimental design (Sellner *et al.* 2007). Our inability to identify the causal mutations underlying QTL makes it extremely difficult to implement MAS in commercial populations, since we do not know the marker-QTL allele phase relationships in these populations.

Furthermore, experimental designs that have historically been used for QTL mapping in cattle have captured a limited number of parental chromosomes and therefore have only detected the few QTL that were heterozygous within these parents (Casas *et al.* 2003; Mizoshita *et al.* 2004; Alexander *et al.* 2007). Typical genome scans for QTL in livestock use large, half-sib families from a few sires and 10-20 markers per chromosome, the resulting QTL confidence intervals are 5-20 cM with each family analyzed generating 3 to 5 QTL per trait studied (Chamberlain *et al.* 2007; Allan & Smith 2008). The QTL identified as segregating within a single sire half-sib family represent only a fraction of the total QTL segregating in a population (Mizoshita *et al.* 2005). With the large expense in collecting phenotypes on cattle many QTL scans have been underpowered and as a result underestimate the true number of QTL contributing to the phenotypic variance (Bogdan & Doerge 2005).

Since 1998, 1,375 bovine QTL for 110 traits have been identified and the number of unique QTL is likely to be considerably smaller because many of the published QTL have overlapping confidence intervals (http://www.animalgenome.org/cgi-bin/QTLdb/BT/summary) (Figure 1.1). Unfortunately among different populations the association between marker

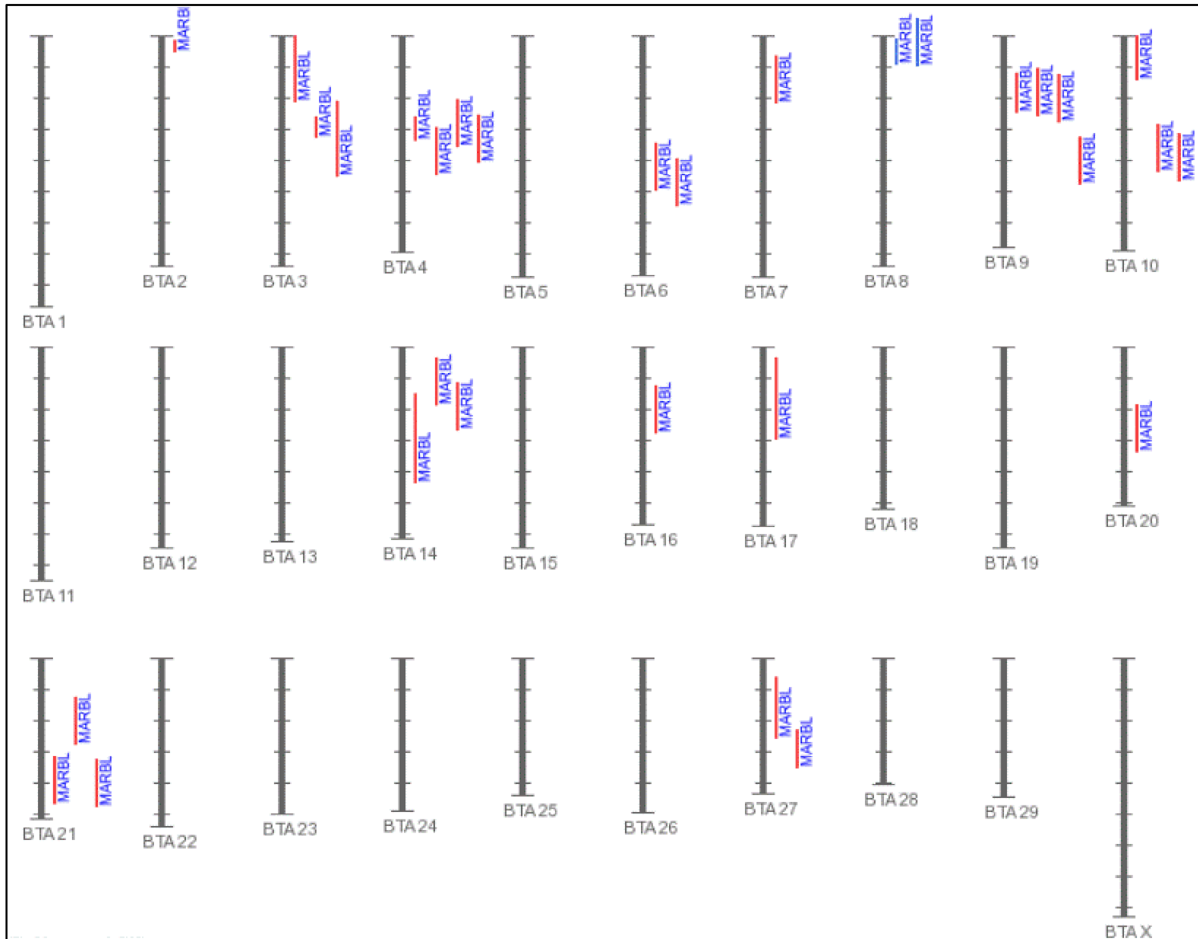

Figure 1.1. Graphical representation of locations of QTL for USDA marbling score reported in *Bos taurus*. Span of red lines represents confidence interval for QTL with significant statistical support, while blue lines represents confidence interval for QTL with suggestive statistical support. Image from: http://www.animalgenome.org/cgi-bin/QTLdb/BT/draw_traitmap?trait_ID=1027&QTLid=. Obtained June, 2009.

genotype and functional variation is unknown (Smith *et al.* 2003). As many of the populations used for QTL discovery are experimental crosses and do not represent commercial populations, discovered QTL need to be validated for marker phase relationship and magnitude of effect within each population in which the test is anticipated to have utility before it can be effectively commercialized (Van Eenennaam *et al.* 2007). This is necessary because diverse populations have different phase associations between the marker genotypes and the QTL alleles and the extent of linkage disequilibrium may differ due to dissimilar allele frequencies caused by drift or selection (Allan & Smith 2008). As a result of these issues, few of the discovered QTL have been commercialized as tests that can be used by producers for MAS.

To address many of these issues that have hampered the commercialization of previous research we have conducted a whole genome scan for carcass, growth, and reproductive QTL in a twenty-nine generation mapping population (N=1,769) comprised of registered American Angus sires born between 1955 and 2003 (Figure 1.2). This population represents the major commercial bloodlines in American Angus cattle and captures the majority of the chromosomes represented within the breed. By analyzing expected progeny differences (EPDs) for 14 traits: birth weight (BW), calving ease direct (CED), calving ease maternal (CEM), fat thickness (FAT), hot carcass weight (HCW), maternal milk (MILK), mature height (MH), USDA marbling score (MRB), mature weight (MW), ribeye muscle area (RIB), scrotal circumference (SC), weaning weight (WW), yearling

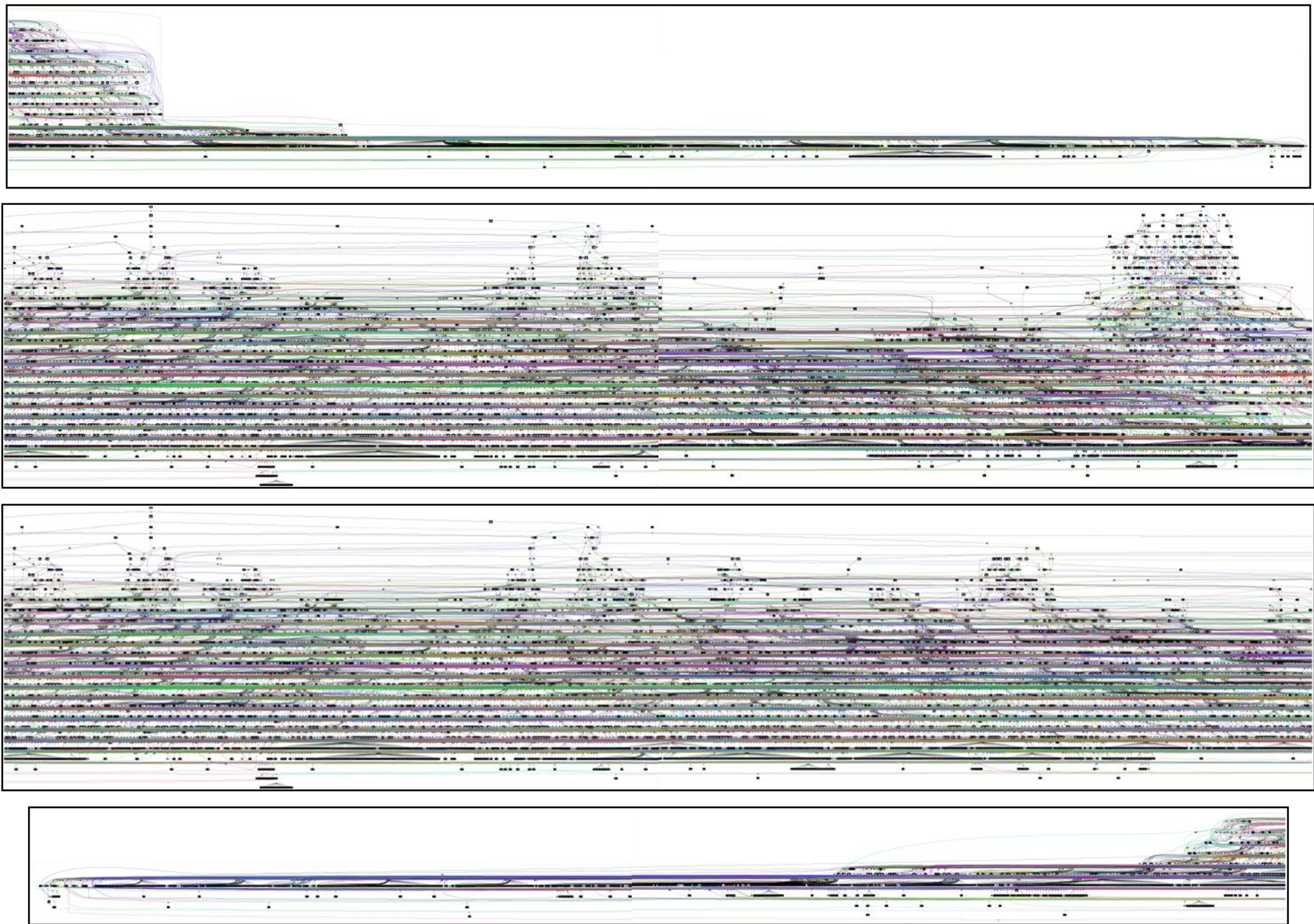

Figure 1.2. Graphical representation of the 29 generation Angus mapping population pedigree. Pedigree reads top to bottom, left to right.

height (YH), and yearling weight (YW) we were able to use the historic phenotypic data collected on each sire and its relatives, rather than having to generate phenotypic data in an experimental herd. Additionally each of the analyzed traits has a history of selection by Angus producers and measureable phenotypic change has resulted from this selection (Figure 1.3 and 1.4). EPD values, accuracies and pedigree information from the Spring, 2005 evaluation were obtained from the American Angus Association (St. Joseph, Missouri) and a statistical summary of the EPD values is in Table 1.1 and of the EPD accuracy values is in Table 1.2.

All sires were genotyped for 12 single nucleotide polymorphisms (SNP) and 417 microsatellite markers chosen from published genetic maps according to their numbers of alleles (Barendse *et al.* 1997; Kappes *et al.* 1997). Twenty-seven microsatellite markers worked poorly in multiplex PCR or were essentially monomorphic in our Angus population and were excluded from analysis. The remaining 402 genetic markers resulted in an average marker interval of 8.02 cM and a total genomic coverage of 2820.5 cM, representing a 93.5% coverage of the bovine genome. Genotype reactions that failed were not retried. GENOPROB (Thallman *et al.* 2001b, a) was used to assess genotype quality using map distances and locus order from the USMARC map (Kappes *et al.* 1997). Information linking all of the genotyped animals was assembled into a single pedigree to exploit the relationships between the genotyped sires and ungenotyped females. GENOPROB was also used to infer genotypes of other individuals in the pedigree. Individual genotypes with low quality (pGmx <0.98) were excluded from analysis. While only 1,769 males were genotyped 6,974 females and 4,458 additional males in the full pedigree had $\geq$1 estimated genotypes with a pGmx $\geq$ 0.98.

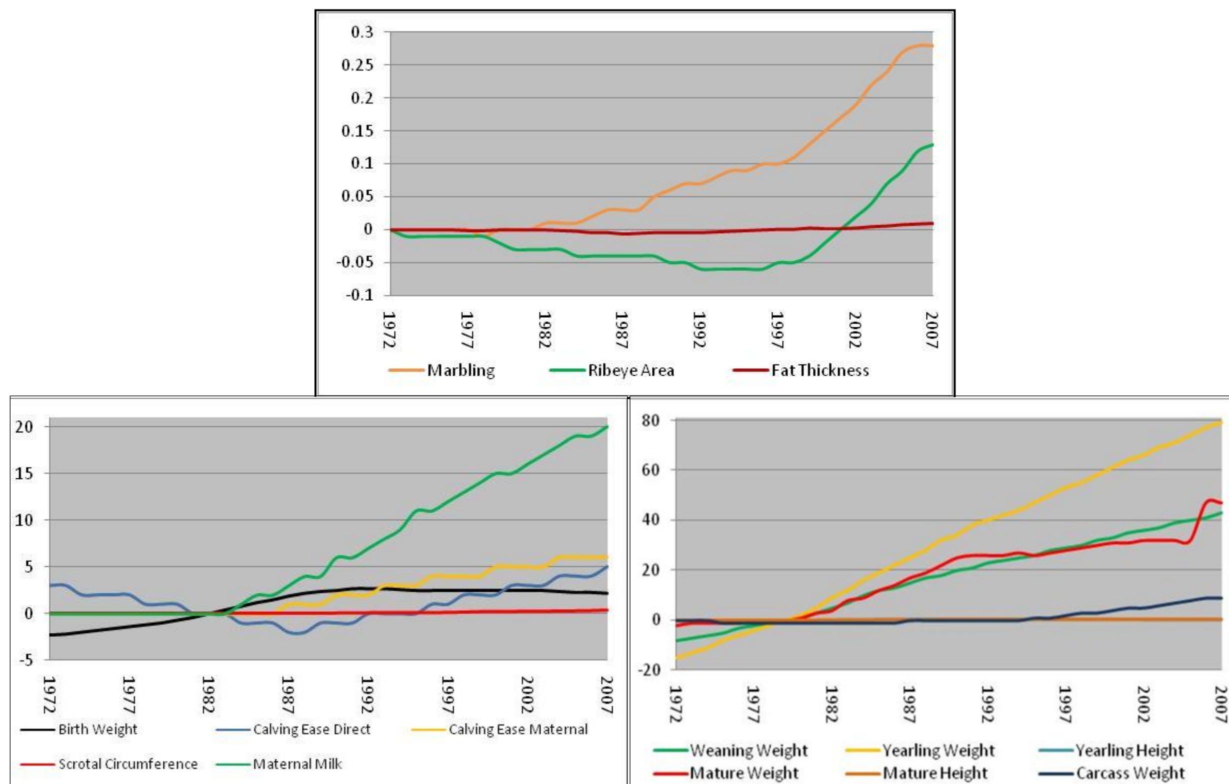

Figure 1.3. Average registered American Angus EPD from 1972 to 2007. X-axis unit is relative to EPD plotted. Data obtained from American Angus Association.

1953

1964

1972

1988

1994

2006

Figure 1.4. Photos of Grand Champion American Angus sires from the past 60 years. Date under each sire corresponds to year picture was taken . Photos from https://www.msu.edu/~ritchieh/historical/cattletype.html and http://holmescattlecompany.com/images/2007/aug8/HCC_BlackEagle.jpg

Table 1.1. Statistical summary of EPD values in the mapping population.

Trait	Unit	Variance	Kurtosis	Skewness	Average	Standard Deviation	Minimum	Maximum
BW	pounds	5.965	-0.127	0.021	2.254	2.442	-5.80	10.80
CED	% of unassisted births	30.233	1.167	-0.701	3.308	5.498	-29.00	16.00
CEM	% of unassisted births	22.691	2.129	-0.942	4.811	4.763	-21.00	16.00
CW	pounds	111.504	0.832	-0.148	3.100	10.56	-42.00	41.00
FAT	inches	0.001	0.934	-0.032	0.003	0.023	-0.11	0.10
MARB	% difference in USDA marbling score	0.032	1.009	0.525	0.103	0.179	-0.64	0.86
MH	inches	0.413	0.560	0.065	0.464	0.643	-1.60	3.00
MILK	pounds of weaning weight due to milk and mothering ability	91.210	0.142	-0.355	15.578	9.550	-17.00	46.00
MW	pounds	1393.834	0.568	-0.208	29.221	37.334	-106.00	166.00
RIB	square inches	0.034	0.789	0.363	0.087	0.184	-0.62	0.82
SC	centimeter	0.317	0.226	0.179	0.135	0.563	-1.84	2.21
WW	pounds	209.104	0.071	-0.496	33.34	14.46	-12.00	85.00
YH	inches	712.100	0.088	-0.557	61.552	26.685	-23.00	155.00
YW	pounds	0.180	1.078	0.297	0.306	0.425	-1.00	2.10

Table 1.2. Statistical summary of EPD accuracy values in the mapping population.

Trait	Variance	Kurtosis	Skewness	Average	Standard Deviation	Minimum	Maximum
BW	0.046	-0.634	-0.622	0.685	0.216	0.11	0.98
CED	0.031	-0.616	0.484	0.533	0.176	0.05	0.96
CEM	0.043	-0.494	0.735	0.427	0.206	0.05	0.95
CW	0.044	-0.278	0.955	0.219	0.211	0.05	0.88
FAT	0.038	0.075	1.065	0.202	0.195	0.05	0.86
MARB	0.050	-0.526	0.870	0.232	0.223	0.05	0.89
MH	0.062	-0.836	0.579	0.313	0.249	0.05	0.95
MW	0.061	-0.781	0.595	0.313	0.247	0.05	0.95
MILK	0.070	-1.314	-0.035	0.554	0.265	0.05	0.98
RIB	0.041	-0.103	1.011	0.210	0.202	0.05	0.87
SC	0.068	-1.036	0.039	0.450	0.261	0.05	0.97
WW	0.050	-0.723	-0.625	0.680	0.223	0.1	0.98
YH	0.055	-0.971	-0.388	0.626	0.234	0.05	0.98
YW	0.073	-1.088	-0.010	0.450	0.271	0.05	0.97

The percentage of the 402 genetic markers that were called with high support is shown for all animals (Figure 1.5 and separately for males and females (Figure 1.6).

The population-based design allows the flexibility of using multiple analytical methods to exploit both within family variation and the full pedigree information. Ten sires with 18 or more progeny that had $\geq$75% of their genotypes at pGmx>0.98 support were individually analyzed under a halfsib design model using QTL Express (Seaton *et al.* 2002) to determine the segregation status of each sire and to identify QTL. All animals analyzed had $\geq$75% of their genotypes at pGmx>0.98 support and individual EPDs were weighted by their accuracies. LOKI v2.4.5 (Heath 1997) was used to jointly analyze 2,854 animals that had >22% of their genotypes to estimate both the number and position of QTL within the full pedigree. As LOKI does not the use of weights reflecting heteroscedastic residual variances only EPDs with accuracies > 0.05 were used in the analysis. By combining the results of these analyses we are better able to estimate the number of QTL, their genomic positions, and their affects on trait variation.

Because the QTL scan was performed within a commercially relevant breed we can directly assess the extent of genetic variation currently found within the breed and explained by the discovered QTL. Further, because the discovery population is the .

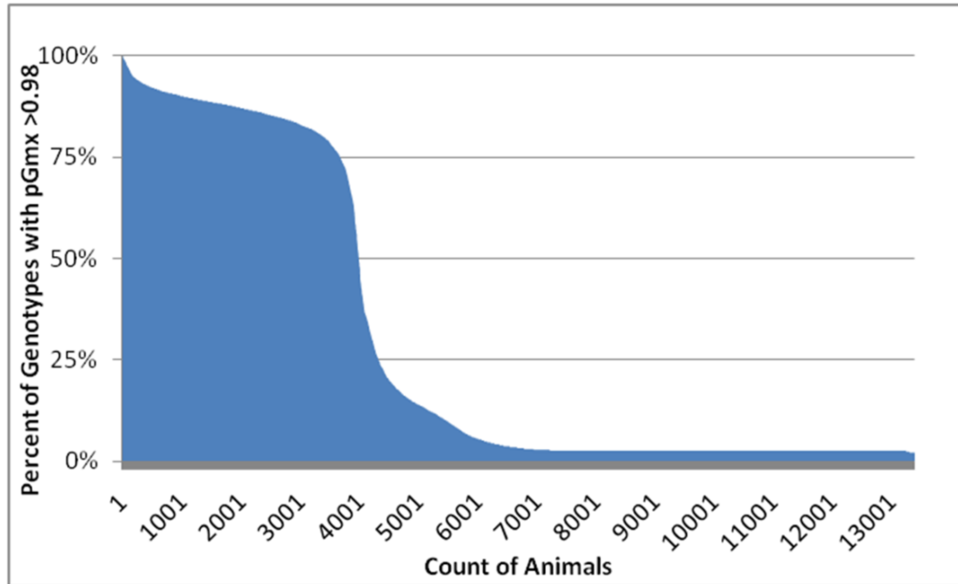

Figure 1.5. Cumulative count of animals according to their percentage of genotypes with high support (pGmx $\geq$ 0.98). 100% indicates that an animal had high support for 402 genotypes.

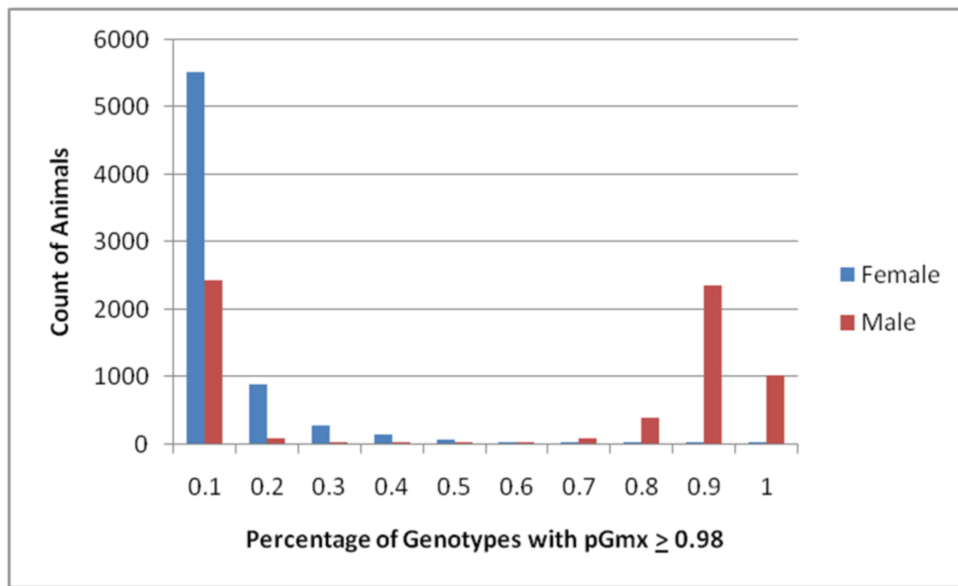

Figure 1.6. Count of males and females by percentage of genotypes with high support (pGmx $\geq$ 0.98).

same as the implementation population, MAS can rapidly be implemented using linked markers (Schnabel *et al.* 2003) and these may be continually refined as high density SNP chips, such as the BovineSNP50 BeadChip from Illumina Inc. (Matukumalli *et al*. 2009) become widely utilized

Producers who wish to use MAS within their herds need to collect a DNA sample on each potential breeding stock using a convenient sample collection process that allows simple and safe storage. To facilitate this, a separate study was performed to assess the potential of using blood and nasal swab samples collected on FTA cards as a source of DNA for the BovineSNP50 BeadChip.

PUBLICATION OUTLINE

These studies represent the major focus of this thesis and results are presented in the following four publications, which will be referred to by their corresponding roman numerals:

I. McClure, MC, NS Morsci, JW Kim, MM Rolf, SD McKay, RD Schnabel, and JF Taylor. 2009. Genome Scan in Commercial Angus Cattle for Quantitative Trait Loci Influencing Carcass Traits. (Manuscript).

II. McClure, MC, NS Morsci, JW Kim, MM Rolf, RD Schnabel, and JF Taylor. 2009. Genome Scan in Commercial Angus Cattle for Quantitative Trait Loci Influencing Growth Traits. (Manuscript).

III. McClure, MC, NS Morsci, JW Kim, MM Rolf, JE Decker, RD Schnabel, and JF Taylor. 2009. Genome Scan in Commercial Angus Cattle for Quantitative Trait Loci Influencing Reproductive Traits. (Manuscript)

IV. McClure, MC, SD McKay, RD Schnabel, and JF Taylor. 2009. Assessment of DNA extracted from FTA® cards for use on the Illumina iSelect BeadChip. (*Published:* BMC Research Notes 2009, 2:107).

Paper I focuses on QTL results from the analysis of four traits that impact carcass quality: adjusted subcutaneous fat thickness between the 12th and 13th rib, final trimmed carcass weight, ribeye muscle area, and USDA marbling score. Paper II focuses on traits that determine the overall postnatal growth of an animal: weaning weight, yearling height, yearling weight, mature height, and mature weight. Traits that impact reproductive and maternal abilities are the focus of paper III: birth weight, calving ease direct, calving ease maternal, maternal milk, and scrotal circumference.

Paper IV considers the genotype call and concordance rates achieved between genomic DNA samples harvested from tissues collected on FTA filter paper and samples derived from whole blood. As FTA paper provides an ideal medium for the field collection of tissues from livestock, this paper analyzed bovine DNA extracted from tissues collected and stored on FTA paper to determine if the medium would provide DNA samples which yielded reliable genotypes when assayed using high-throughput and high-density SNP genotyping platforms, specifically the Illumina BovineSNP50 BeadChip.

While each paper is presented in the style required by the journal to which it was intended to be submitted to (Journal of Animal Genetics for papers I, II, and III and BMC Research Notes for paper IV), the reference style for all manuscripts in this thesis is that of the Journal of Animal Genetics. Each paper's figures and tables, including those submitted as supplemental information, are included after each corresponding manuscript. The numbering of figures and tables is sequential as each appears within the thesis.

CHAPTER 2

Genome Scan in Commercial Angus Cattle for Quantitative Trait Loci Influencing Carcass Traits.

Abstract

A genome-wide quantitative trait loci (QTL) scan for carcass traits was performed in a registered Angus sire mapping population. Three hundred and ninety microsatellite loci and 12 single nucleotide polymorphisms were scored in 1,769 registered Angus sires from a twenty-nine generation pedigree in which the earliest animal was born in 1955. Data analyzed for each sire were expected progeny differences (EPD) provided by the American Angus Association for the Spring 2005 evaluation. Statistical analysis was performed using two different analytical methods: half-sib least squares regression and Bayesian Monte Carlo Markov Chain linkage analysis. Each analyzed trait resulted in the identification of multiple QTL with high levels of statistical support distributed throughout the genome: carcass weight (36 QTL), fat thickness (30 QTL), USDA marbling score (29 QTL), and ribeye muscle area (40 QTL). In total 115 QTL regions were detected with 16 of these being pleiotropic. In total, 55 to 75% of the genetic variance in each trait was explained by these QTL. These results provide insight into the large number of QTL effecting carcass quality within an important beef breed.

Introduction

Over the past 30 years producers have made enormous changes in beef cattle through evolving management practices and the use of expected progeny differences (EPDs) to improve economically important traits. Genomic research in livestock species has identified multiple QTL for numerous traits in an effort to identify genetic variation that can be selected to improve animals. Ideally, QTL for economically important traits will be selected in breeding programs via marker assisted selection (MAS) schemes in which the contributions of multiple QTL are simultaneously considered. MAS is especially beneficial when used to improve traits that are determined post-mortem, occur late in life, or that are difficult and (or) expensive to accurately measure.

Many of the beef cattle QTL mapping populations created in the 1990s were based upon *Bos taurus* x *Bos indicus* experimental crosses (Stone *et al.* 1999; Kim *et al.* 2003). The logic behind these crosses was that the large genetic and phenotypic divergence between these subspecies for meat quality traits would maximize the probability of detecting QTL of large effect. While the crossbreeding strategy did allow the detection of QTL it also hindered the identification of the underlying quantitative trait nucleotides (QTN) and the development of MAS programs. *B. indicus* and *B. taurus* diverged approximately 500,000 years ago (Miretti *et al.* 2002) and mutations with fixed allelic differences have accumulated about every 2 kb within these genomes (Taylor *et al.* 2006). Consequently, the confidence interval for any QTL found in such a crossbred population contains thousands of mutations with fixed differences between *B. indicus*

and *B. taurus* alleles, which are statistically impossible to differentiate from the causal QTL alleles within the experimental design (Sellner *et al.* 2007).

Furthermore, historical experimental designs used for QTL mapping in cattle have sampled a limited number of parental chromosomes and therefore have only detected the few QTL that were heterozygous within these parents (Casas *et al.* 2003; Mizoshita *et al.* 2004; Alexander *et al.* 2007). On average, each analyzed sire's half-sib family generated only 3 to 5 QTL per trait (Chamberlain *et al.* 2007; Allan & Smith 2008) and the QTL identified from a single sire will represent only a fraction of the total number of QTL segregating within a population (Mizoshita *et al.* 2005). While multiple carcass trait QTL have been identified in cattle, as of June 2009, less than 11% of all reported bovine QTL influence a meat production trait (143 of 1375; http://www.animalgenome.org/QTLdb/cattle.html). According to a recent review (Allan & Smith 2008), only 24 QTL for USDA marbling score (MARB), 24 for adjusted subcutaneous fat thickness between the 12th and 13th rib (FAT), 6 for ribeye muscle area (REA), and 27 for final weight of trimmed carcass (CW) have been reported. As previous genome scans have found only a limited number of QTL segregating in commercial populations that influence any one trait, genetic improvement by MAS in cattle has been hindered by the inability to test for sufficient QTL to economically justify the cost of testing.

By using the largest commercial cattle mapping population assembled to date and by using sires that represent the major bloodlines within American Angus, we have

captured the majority of the chromosomes represented within the US breed. Mapping within commercial populations offers the advantage that experimental crosses are not needed and consequently pedigrees and phenotypes can quickly be collected. Additionally, any QTL identified within a commercial population may immediately be incorporated in the breeding program for that population (Schnabel *et al.* 2003). This experimental design also allows the flexibility of using multiple analytical approaches, to exploit both within family variation and the full pedigree information. Finally, it also maximizes the potential for identifying QTL of large effect that segregate within commercially relevant cattle populations.

Materials & Methods

Animals and Traits

The mapping population consisted of a 29 generation pedigree comprised of 1,769 registered American Angus sires born between 1955 and 2003, which represents the major sire lines within the breed. All sires, except family founders, have DNA on their sire represented in the mapping population and 77.9% also have DNA represented for their maternal grandsire. Cryopreserved semen straws were obtained from multiple semen companies and registered Angus breeders as sources of DNA. Genomic DNA was isolated by proteinase K digestion followed by Phenol:Chloroform:Isoamyl alcohol extraction, and ethanol precipitation (Sambrook 1989). The population is comprised of 10 male lineages; however, all of these lineages were interrelated through the bulls'

maternal pedigrees. Pedigree data, EPDs, and their accuracies (Spring, 2005 evaluation) were obtained from the American Angus Association.

Markers

Microsatellite markers that possess a large number of alleles and were easy to score were chosen (N=417) from published genetic maps (Barendse *et al.* 1997; Kappes *et al.* 1997) and twelve SNPs representing candidate genes and commercialized tests were selected for genotyping (Table 2.1) (Barendse *et al.* 2001; Grisart *et al.* 2002; Grisart *et al.* 2004). The forward PCR primer for each microsatellite marker was synthesized with one of four fluorescent dye labels and multiplexed PCR were developed based on allele size distributions, fluorescent label and the empirically determined ability of each marker to co-amplify as described in Schnabel *et al.* (2003). Between two and nine markers were co-amplified in each reaction, with PCR conditions optimized to maximize the number of loci per reaction. PCRs were performed in 5 µl reactions on an ABI GeneAmp 9700 thermocycler (Applied Biosystems, Foster City, CA, USA). Microsatellite markers were multiplexed in 69 assays; PCR annealing temperatures and multiplex setup are described in Table 2.2.

SNPs were amplified by allele-specific PCR and co-amplified with a 16S rRNA gene fragment which was used as a positive control for the PCR. Each primer ending at an SNP locus was designed with a mismatched third base at the 3' end, as compared to the bovine genomic sequence (Table 2.2). Weakening the primer by providing a partial

primer mismatch minimizes error in SNP genotyping by PCR amplification. PCR annealing temperatures and setup for SNPs are described in Table 2.3 and 2.4.

Genotypes

All 1,769 sires were genotyped for 417 microsatellite markers and 12 SNP. Alleles were seperated on an ABI 3730 Automated Sequencer or an ABI 3100 Automated Sequencer, with fragment sizes determined relative to the Gene Scan 500 LIZ internal size standard (Applied Biosystems). Fluorescent signals were detected using GENESCAN v3.1 (Applied Biosystems) and fragment sizes analyzed by GeneMapper v3.7 (Applied Biosystems). SNPs were primarily genotyped by allele-specific PCR with amplification products visualized on a 2% standard agarose gel. However the SNP in the Thyroglobulin (*TG5*) (Barendse *et al.* 2001) and Acyl-CoA:diacylglycerol acyltransferase (*DGAT1*) genes (Grisart *et al.* 2002; Grisart *et al.* 2004) were genotyped as PCR RFLPs and scored on agarose gels: 1.5% for *DGAT1* and 3% for *TG5* (50% standard agarose and 50% high resolution NuSieve 3:1 agarose (Cambrex Bioscience, Rockland, ME)).

Twenty-seven of the microsatellite markers either worked poorly in multiplex reactions or were essentially monomorphic in our mapping population. These were excluded from further analysis leaving 402 genetic markers to be analyzed, resulting in a 93.51% genome coverage (2820.49 cM) of the bovine autosomes, with an average marker interval of 8.02 cM (Table 2.5).

Data Analysis

GENOPROB (Thallman *et al.* 2001a, b) was used to verify generated microsatellite and SNP genotype scoring against the pedigree and to check genotype quality using published marker positions from the USDA MARC cattle mapping database (http://www.marc.usda.gov/genome/genome.html). GENOPROB was also used to identify misinheritances, genotyping errors, predict missing genotypes, and to estimate the probability that a genotype was scored correctly (pGmx). Complete pedigree information linking all of the genotyped animals was assembled into a single pedigree to capture relationships among the maternal lineages which were not genotyped. Consequently genotypes were inferred on 6,974 females and an additional 4,458 males by GENOPROB. Genotype and grand-parental origin probabilities were estimated for each of the genotyped animals using genotype, map, and pedigree information. Individual genotypes with low probability (pGmx < 0.98) were excluded from further analysis. Subsequently, 1,117,936 genotypes with pGmx $\geq$ 0.98 were generated, of which 224,708 genotypes were on females.

Two complementary approaches were used for QTL analysis to locate as many QTL as possible. Ten sires with 18 or more progeny (max 74) with at least $\geq$0.75% of their genotypes satisfying pGmx $\geq$ 0.98 from the GENOPROB analysis, were individually analyzed by half-sib least squares regression using the program QTL Express (Seaton *et al.* 2002) to identify QTL and determine the segregation status for each sire and trait combination. Chromosome and genome-wide significance levels were determined by

genome-wide permutations performed using 1,000 data permutations for each sire and each trait (Churchill & Doerge 1994). Since the number of offspring varied per sire, F statistic results were transformed to $-\log_{10}(P_{nominal})$ values to allow comparisons between sires. LOKI v.2.4.5 (Heath 1997) was used to perform multipoint QTL interval analysis on the AI sires using a Bayesian Markov chain Monte Carlo approach which analyzes all families jointly to simultaneously estimate the total number and position of QTL within the pedigree. This analysis was performed using 2,854 animals that had at least 22% of their genotypes satisfying pGmx $\geq$ 0.98 from the GENOPROB analysis. LOKI does not allow the use of weights reflecting heteroscedastic residual variances, consequently, only EPDs with accuracies >0.05 were used. An initial burn-in of 1,000 iterations was followed by 500,000 iterations, with parameter estimates collected at each iterate. LOKI reports statistical support as a L factor which were converted to Bayes Factor using a PERL script, QTL significance levels were chosen according to Jefferys (1961), where a Bayes Factor of $\geq$10 indicates strong support for the presence of a QTL

A chromosome was considered to harbor multiple segregating QTL for a trait if each detected QTL was separated by at least one marker and the QTL were at least 8 cM apart, which is the average marker interval. Statically significant QTL within 8 cM for the same trait were considered to be one QTL detected to be segregating in several families or by both analytical approaches The reported map location was chosen to correspond to the QTL with the highest statistical support. QTL were identified as being pleiotropic if separate trait QTL peaks were within 8 cM of each other, if both QTL were identified

by the same analytical approach, possess the same directional effect, visual support could be determined from the QTL graphs (Figure 2.1), and strong genetic correlations between the traits were demonstrated in the literature. For consistency, all analyses used a sex-averaged genetic map calibrated in Haldane cM units.

Analysis of variance (ANOVA) was performed using the PROC GLM function in SAS version 9.1 (SAS Institute, Cary, NC) to estimate the amount of genetic variation (in EPDs) explained by the QTL identified in this population. Microsatellite markers that were closest to each QTL position were included in the multiple factor ANOVA as a categorical variable using the class option in GLM. The model used was:

$$Y_k = \mu + M_{j1} \ ...M_{jn}+ e_k$$

Where Y_k is the EPD for animal k, μ is the overall mean, M_j is the genotype effect of marker j, and e_k is the random residual for each animal's EPD. This analysis was performed using 1,951animals that had at least 22% of their genotypes satisfying pGmx $\geq$ 0.98 from the GENOPROB analysis. Additionally, 100% of these animals had EPD values for BW, CED, CEM, MILK, WW, and YW; 98% for SC and YH, 94% for CW, FAT, MRB, and REA; and 91% for MW and MH.

Results

At a chromosome-wide $P \leq 0.01$ significance level or Bayes Factor $\geq$10 (Jefferys 1961), every autosome was found to harbor multiple carcass related QTL (Table 2.6). In total, 36 QTL for carcass weight, 30 QTL for fat thickness, 29 QTL for marbling and 40

QTL for ribeye area were identified to be segregating within the Angus genome (Table 2.7). Twenty-four of these carcass QTL have previously been reported in the literature. Of the 135 possible distinct QTL, 16 appear to be pleiotropic (Table 2.8), indicating that 119 independent carcass trait QTL were identified in this study.

On average, each chromosome harbors 4 carcass related QTL, with 4 chromosomes each harboring 6 QTL. Each chromosome contained, on average, 1.07 QTL for each trait with a range from 0 to 4 QTL. While significant QTL for carcass traits were found on every chromosome, on average, 7 chromosomes were not detected to contain QTL for any given trait. The average allele substitution effect (on EPDs which are one half of the allele substitution effects based upon phenotypes) from QTL Express for CW was 16.63 lb, REA was 0.29 in^2, MRB was 0.21, and FAT was 0.03 in. Differences between alternate homozygotes which are estimates of twice the allele substitution effect produced by LOKI were 3.05 lb for CW, 0.03 in^2 for REA, and 0.05 for MRB (Table 2.9).

The GLM analysis revealed that the QTL reported here explain a substantial amount of the genetic variation in each trait within our population (Table 2.10). With all significant QTL detected for each trait included in the model, 68.66% of the genetic variance was explained for CW, 60.15% for FAT, 55.15% for MRB, and 75.71% for REA. While at least 55% of each trait's genetic variation was explained when all QTL-associated markers were included in the model, no single marker individually explained more than 8% of the genetic variation within a trait.

Discussion

The experimental designs historically used for QTL detection in livestock have analyzed only a limited number of parental chromosomes. Therefore, most genome scans performed in *B. taurus* have identified a small number of QTL influencing any one trait. In this study, by capturing the majority of chromosomes represented within American Angus the experimental design maximizes the probability that the vast majority of economically important QTL segregating within American Angus will be identified.

The analysis detected 115 carcass trait QTL over 29 chromosomes at the chromosome-wide $P \leq 0.01$ significance level for QTL Express and Bayes Factor ≥ 10 significance level for LOKI (Table 2.7), with many of these QTL appearing to be novel. Of the 115 detected QTL only 24 appear to have previously been reported, seven for FAT, three for REA, eight for MRB, and six for CW. LOKI did not detect any QTL with support ≥ 10 Bayes Factor for FAT, which may be due to the low variance among EPDs (0.00076 in^2) in this population possibly reflecting that progeny of these bulls were slaughtered at a fatness dependent end-point, and that less than 50% of the animals analyzed had an EPD accuracy for FAT >0.05 (Table 2.9).

The lack of FAT QTL being detected by LOKI and the discrepancies of QTL identified by both methods are likely due to the methodological differences between the two analytical methods used. Variance component (VC) models such as LOKI (Heath, 1997) assume that both the allelic QTL effects and the polygenic components

are normally distributed and segregate in both parental lineages. Additionally, the genetic variance explained by a QTL is estimated across all animals in the pedigree. If a QTL is segregating at low frequency it may not be detected by a VC analysis model as the power of detection depends on the amount of variance explained by the QTL across the population (de Koning *et al*. 2003), while half sib (HS) models like QTL Express estimate allele substitution effects as a fixed effect in each sire analyzed. Maternally inherited QTL alleles are assumed to be randomly distributed between half-sibs and used to increase the number of offspring that are informative for the sire's allele. A QTL will be missed by a HS model if the sires analyzed by QTL Express are not segregating for it, while a QTL segregating in sires but not dams will have its effect diluted in a VC analyses and therefore be missed (de Koning *et al*. 2003).

As with other studies, discrepancies between the magnitude of significance between QTL detected by both LOKI and QTL Express are likely due to the differences in each models' ability to represent the true architecture of QTL in a population (de Koning *et al* 2003; Schnabel *et al*. 2005). Comparing the data to published results suggests that the majority of these QTL segregate within all *B. taurus* breeds of cattle. These results support population-based approaches to QTL mapping within commercially relevant populations.

This study reveals an abundant number of QTL with moderate to large effect influence carcass traits in American Angus. Even with selection for carcass improvement using EPDs over the past 30 years there remains variation in the frequency of carcass-

and-yield-enhancing alleles to high levels at many QTL, with an average estimated allele frequency of 0.441 for CW, 0.856 for MRB, and 0.542 for RIB (Tables 2.7 and 2.9). This allele frequency for highly selected, economically important traits is in agreement with what has been found for milk production QTL in dairy cattle (Chamberlain *et al.* 2007).

While we have identified 16 putative pleiotropic QTL (Table 2.8), the resolution of our scan is not sufficient to determine if a single quantitative trait nucleotide (QTN) influences both traits or if each trait has a separate QTN under the QTL peak. As the phase relationship between potentially distinct QTN cannot be identified from our analysis and LD extends for 500 kb (McKay *et al.* 2007) it is possible that use of these QTL in a MAS program could result in divergent selection in each of the traits. Additionally if a single QTN underlies the pleiotropic QTL, further work is required to determine the contribution of QTL to a rational selection objective. It makes little sense to apply strong selection pressure on a QTL that will slightly increase marbling score but that also strongly increases fat thickness as the economic gain from increased marbling may be offset by the loss from increasing fat thickness.

While including all detected QTL in a GLM analysis explains 60% to 70% of the traits genetic variation, on average a single marker explained only 1.9% of the total genetic variation for a trait (Tables 2.10, 2.11, 2.12, and 2.13). These estimates of genetic variation were determined by using the same animals used for QTL discovery, therefore the true amount of variation explained is likely to be smaller (Lou *et* al. 2003; Xu, 1998). Additionally the larger allele substitution effects estimated by QTL Express

could be due to the smaller half-sib family size of each sire versus the larger size of the entire mapping population (Lou *et* al. 2003). Beavis (1998) observed that as the number of progeny decreases there is an increase in the overestimation of the average estimated variances associated with identified QTL. Even with this known probability of overestimation of the amount of true genetic variation explained by these QTL, one can note that most of a trait's genetic variation is influenced by a large number of QTL.

Consequently, for a MAS program to have a significant impact on even a single trait information from multiple QTL must simultaneously be used. Genetic improvement programs that implement information from one, or even a few economically important QTL will have little value in beef cattle. Strategies must be devised that simultaneously test for multiple QTL for MAS to be economically viable. The identification of multiple QTL underlying variation in carcass traits in this study will assist in the development of multiple QTL tests. Estimating EPDs in cattle by integrating QTL information with available phenotypic data will allow producers to select for genetically superior animals.

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Table 2.1. Summary of microsatellite (MS) and SNP marker information. Markers were analyzed by both QTL Express and LOKI if an X is present, L=only LOKI analysis was performed, N=marker was not analyzed. Markers with the same multiplex ID were simultaneously assayed in a multiplex PCR. PCR set up refers to conditions in Table 2.3.

Marker Name	Analyzed	BTA	Position cM	Allele Count	Type	Dye Label	Multiplex	PCR set up	Nanomolar of primer
AGLA17	N	1	0.00		MS	FAM	1_3	6	2.6
BM6438_29	X	1	1.78	2	MS	FAM	1_2	1	1.8
BM8139	X	1	10.01	6	MS	FAM	1_3	3	1.4
BMS574	X	1	15.43	7	MS	VIC	1_3	3	1.8
BMS4017	X	1	38.08	5	MS	FAM	1_1	3	3.0
TGLA57	X	1	51.02	6	MS	FAM	1_1	3	3.0
BMS527	X	1	62.45	8	MS	FAM	PRTG A	7	1.8
INRA119	X	1	76.50	4	MS	FAM	28_1	4	1.4
BM6506	X	1	77.68	7	MS	FAM	1_2	1	1.2
BM7145	X	1	77.69	2	MS	NED	PURITY_A	7	4.0
BMS4008	X	1	80.38	9	MS	NED	1_1	3	1.6
APM_1431	X	1	81.00	2	SNP		APM_1431	1	4.0
APM_INDEL	X	1	81.00	2	SNP		APM_Indel	6	4.0
APM_1596	X	1	81.00	2	SNP		APM_1596	1	4.0
APM_MS	X	1	81.00	4	MS	FAM	1_1	3	2.8
APM_11867	X	1	81.01	3	SNP		SST_467_APM_11867	8/9	4.0
SST_467	X	1	82.00	2	SNP		SST_467_APM_11867	8/9	4.0
BMS4031	X	1	87.12	4	MS	PET	1_3	3	3.4
BM864	X	1	99.71	9	MS	FAM	1_1	3	4.8
BMS4040	X	1	111.35	6	MS	FAM	PURITY_B	6	3.0
BM1824	X	1	122.39	5	MS	FAM	1_3	3	2.0
BMS599	X	1	139.32	8	MS	PET	1_3	3	0.7
BMS4014	X	1	148.21	8	MS	PET	28_1	4	2.0
URB014	X	1	154.67	5	MS	VIC	1_2	1	1.6
BMC9007	X	2	2.78	6	MS	VIC	205	1	0.5
TGLA44	X	2	3.86	11	MS	VIC	2_1	1	1.8
ILSTS026	X	2	10.77	6	MS	NED	14_1	1	1.1
DIK2111	X	2	13.48	5	MS	NED	2_1	1	2.8
DIK1172	X	2	18.13	6	MS	FAM	14_1	1	2.0
CSSM50	X	2	20.54	6	MS	VIC	14_1	1	3.0
TGLA61	X	2	23.11	9	MS	FAM	206	1	2.0
TEXAN2	X	2	25.97	4	MS	PET	2_1	1	4.0

Marker Name	Analyzed	BTA	Position cM	Allele Count	Type	Dye Label	Multiplex	PCR set up	Nanograms of primer
TGLA377	X	2	30.74	6	MS	FAM	205	1	1.0
SRC23	X	2	33.84	9	MS	PET	26_2	1	8.0
URB042	X	2	37.56	8	MS	NED	204	1	1.6
CSSM42	X	2	38.01	9	MS	PET	PURITY_B	6	2.2
ETH121	X	2	38.10	9	MS	FAM	202	1	2.8
BM3010	X	2	38.90	3	MS	PET	203	1	1.4
ILSTS030	X	2	38.99	5	MS	FAM	204	1	2.0
BMC9002	X	2	40.19	4	MS	VIC	203	1	2.0
BMS803	X	2	44.51	7	MS	NED	202	1	1.8
BL1001	X	2	46.26	4	MS	PET	201	1	1.2
BMS1300	X	2	50.59	3	MS	VIC	204	1	2.0
RM356	X	2	56.91	5	MS	VIC	14_1	1	0.9
BM4440	X	2	60.26	12	MS	NED	PRTG B	6	2.8
BY32	X	2	67.26	10	MS	PET	2_1	1	3.4
RM041	X	2	74.84	7	MS	FAM	2_1	1	4.2
TGLA226	X	2	85.85	5	MS	FAM	205	1	1.8
BM1223	X	2	100.18	6	MS	NED	203	1	2.2
BMS2519	X	2	110.25	7	MS	PET	201	1	1.6
BL1028	X	2	114.21	6	MS	VIC	2_1	1	0.7
BM2113	X	2	115.44	11	MS	FAM	PRTG B	6	2.8
IDVGA37	X	2	117.18	5	MS	FAM	203	1	2.0
DIK1155	X	2	117.96	4	MS	VIC	204	1	2.0
DIK2084	X	2	125.62	2	MS	NED	205	1	0.9
IDVGA2	X	2	126.35	8	MS	FAM	202	1	1.0
FCB11	X	2	128.88	9	MS	NED	206	1	3.0
BMS871	X	3	0.00	3	MS	VIC	3_1	1	2.0
URB006	X	3	9.34	5	MS	VIC	3_1	1	5.0
BMS2904	X	3	26.05	4	MS	FAM	30_1	1	1.4
BMS482	X	3	34.04	11	MS	NED	3_2	1	3.0
BM723	X	3	46.04	7	MS	FAM	3_2	1	3.0
INRA003	X	3	59.36	7	MS	NED	7_1_M	1	2.0
HUJ246	X	3	67.98	5	MS	FAM	4_5	1	3.0
BMS1266	X	3	77.61	5	MS	NED	5_6	3	3.0
HUJII77	X	3	87.33	5	MS	FAM	3_2	1	5.0
BMS2145	X	3	93.83	8	MS	FAM	13_1	1	2.0
BM7225	X	3	101.75	8	MS	FAM	3_1	1	1.4
BMS896	X	3	116.54	3	MS	FAM	4_4	1	2.0
BMC4214	X	3	125.80	7	MS	FAM	4_2	1	4.0
RM309	X	3	127.91	5	MS	PET	13_1	1	2.4
BMC1410	X	4	4.16	7	MS	FAM	4_4	1	5.0

Marker Name	Analyzed	BTA	Position cM	Allele Count	Type	Dye Label	Multiplex	PCR set up	Nanograms of primer
BL1024	X	4	7.87	7	MS	VIC	4_2	1	2.0
BMS1788	X	4	12.54	8	MS	FAM	4_3	1	5.0
BMS827	X	4	28.45	7	MS	FAM	4_5	1	2.4
BMS1172	X	4	30.79	5	MS	PET	PRTG A	7	2.2
DIK2956	X	4	35.52	10	MS	FAM	4_6	1	3.0
BMS1840	X	4	46.54	7	MS	FAM	4_3	1	3.0
BMS885	X	4	53.89	10	MS	NED	4_5	1	5.0
INRA072	X	4	62.95	8	MS	FAM	30_1	1	2.4
BMS2571	X	4	69.73	7	MS	FAM	4_4	1	2.4
BMS2809	X	4	76.01	7	MS	FAM	4_1	1	5.0
UASMS2	X	4	87.33	2	SNP		UASMS2	1	4.0
UASMS3	X	4	87.33	3	SNP		UASMS3	1	4.0
LEP_EX2	X	4	87.33	2	SNP		GHR_LEP1	1	4.0
RM088	X	4	99.70	8	MS	NED	4_2	1	4.0
BR6303	X	4	104.91	4	MS	VIC	4_2	1	5.0
AGLA227	X	4	107.15	3	MS	PET	30_1	1	4.0
DIK4542	X	4	119.93	4	MS	NED	4_6	1	1.6
BMS695	X	5	1.17	4	MS	FAM	5_2	3	2.0
BM6026	X	5	6.05	9	MS	FAM	10_1	3	4.2
BMS610	X	5	12.02	12	MS	NED	5_1	3	2.0
BP1	X	5	17.29	12	MS	PET	5_1	3	4.6
RM103	X	5	29.43	8	MS	NED	10_1	3	2.6
DIK4759	X	5	40.29	4	MS	PET	5_6	3	6.0
BL37	X	5	52.09	7	MS	FAM	5_1	3	4.2
RM500	X	5	56.30	4	MS	FAM	PURITY_A	7	3.0
CA084	X	5	56.63	6	MS	VIC	5_3	3	1.7
BR2936	X	5	65.17	5	MS	PET	5_4	3	1.4
CSSM22	X	5	74.20	7	MS	FAM	5_1	3	4.2
BMS1216	X	5	78.21	9	MS	PET	5_3	3	4.0
RM029	X	5	81.92	5	MS	PET	5_2	3	4.0
BMS1248	X	5	90.85	5	MS	FAM	25_1	3	2.0
BM315	X	5	103.17	12	MS	PET	5_6	3	6.0
BMS1658	X	5	105.68	6	MS	FAM	11_2	5	8.0
BM2830	X	5	116.91	11	MS	FAM	5_2	3	2.4
ETH152	X	5	121.75	7	MS	FAM	5_1	3	1.8
BMS597	X	5	125.05	3	MS	NED	5_2	3	0.7
ILSTS093	X	6	0.00	6	MS	NED	6_2	2	2.4
INRA133	X	6	8.05	6	MS	VIC	6_2	2	2.0
BMS5006	X	6	17.00	3	MS	PET	6_1	2	2.4
URB016	X	6	34.45	9	MS	PET	6_2	2	4.6

Marker Name	Analyzed	BTA	Position cM	Allele Count	Type	Dye Label	Multiplex	PCR set up	Nanograms of primer
BM1329	N	6	35.40		MS	VIC	6_1	2	1.2
BMS2508	X	6	43.94	9	MS	FAM	6_2	2	4.6
ABCG2	X	6	46.70	3	SNP		ABCG2	10	2.0
OPN3907	X	6	46.86	2	MS	VIC	6_1	2	4.4
BM143	X	6	53.72	10	MS	PET	6_1	c	2.4
DIK082	X	6	57.57	6	MS	VIC	6_2	2	2.0
BMS360	X	6	72.88	9	MS	FAM	4_1	1	1.8
BM4621	X	6	77.61	3	MS	NED	6_1	2	1.6
CSNA	X	6	88.78	4	MS	FAM	6_1	2	4.0
CSN3	X	6	89.35	4	MS	FAM	6_1	2	1.0
BM8124	X	6	101.41	4	MS	NED	6_2	2	1.0
BMS5029	X	6	118.08	7	MS	VIC	6_1	2	1.8
BMC4203	X	6	119.05	7	MS	FAM	6_2	2	2.4
BM7160	X	7	0.00	6	MS	FAM	7_1	2	3.6
RM012	X	7	8.41	3	MS	VIC	15_3	2	1.0
DIK4378	X	7	16.76	8	MS	VIC	4_5	1	4.0
RM006	X	7	25.39	4	MS	VIC	30_1	1	2.2
IL4	X	7	32.04	5	MS	FAM	16_3	2	2.4
BM6105	X	7	36.95	9	MS	NED	17_2	1	3.0
DIK2819	X	7	47.91	8	MS	VIC	26_1	1	3.0
UWCA20	X	7	58.55	6	MS	FAM	15_4	1	2.0
BMS2840	X	7	65.31	11	MS	PET	7_1_M	1	3.4
BMS2258	X	7	77.19	7	MS	FAM	7_1	2	2.0
BM1853	X	7	85.32	4	MS	NED	4_2	1	3.0
BMS1331	X	7	90.70	4	MS	PET	30_1	1	2.4
BM9065	X	7	101.12	7	MS	PET	3_2	1	5.0
ILSTS006	X	7	116.63	7	MS	VIC	7_1_M	1	4.0
BMS1979	X	7	126.25	8	MS	NED	7_1_M	1	3.4
BMS1247	X	7	133.81	5	MS	PET	3_2	1	4.0
BL1043	X	7	135.56	9	MS	FAM	7_1	2	3.0
BMS1864	N	8	2.68		MS	NED	16_3	2	5.0
IDVGA11	X	8	11.34	7	MS	VIC	7_1	2	2.4
RM372	X	8	21.15	8	MS	VIC	PRTG A	7	4.4
BP2	X	8	30.52	5	MS	FAM	4_3	1	5.0
BMS678	X	8	41.60	6	MS	VIC	4_3	1	1.6
BM4006	X	8	50.11	6	MS	NED	3_1	1	5.0
BMS2072	X	8	66.03	5	MS	NED	7_1	2	3.0
MCM64	X	8	71.07	6	MS	NED	4_3	1	4.0
DIK2868	X	8	83.98	4	MS	FAM	30_3	1	4.0
BM711	X	8	92.73	9	MS	FAM	8_1	1	3.6

Marker Name	Analyzed	BTA	Position cM	Allele Count	Type	Dye Label	Multiplex	PCR set up	Nanograms of primer
CSSM047	X	8	118.72	5	MS	NED	8_1	1	2.0
BMS2847	X	8	120.86	8	MS	FAM	4_1	1	3.6
BMS836	X	8	122.91	6	MS	VIC	3_2	1	1.8
BMS2151	X	9	4.89	6	MS	PET	1_2	1	1.8
BM757	X	9	5.38	7	MS	NED	29_5	4	1.8
ETH225	X	9	12.75	5	MS	NED	29_5	4	1.6
BM1227	X	9	24.14	3	MS	NED	1_2	1	1.4
BMS817	X	9	42.49	8	MS	NED	1_3	3	2.0
BMS434	X	9	57.09	6	MS	FAM	22_1	3	6.0
BMC701	X	9	62.35	9	MS	FAM	1_3	3	3.6
BMS2377	X	9	71.45	3	MS	VIC	1_1	3	0.8
BMS1724	X	9	80.26	5	MS	VIC	9_4	3	0.6
BM4208	X	9	90.69	6	MS	NED	9_4	3	1.6
BMS2295	X	9	98.65	5	MS	FAM	9_4	3	1.4
BMS1967	X	9	109.29	12	MS	PET	9_4	3	1.6
BMS2094	X	9	116.17	5	MS	VIC	9_4	3	1.0
BM3033	X	10	1.86	3	MS	PET	10_1	3	1.8
BM6418	X	10	14.30	6	MS	PET	10_2	1	2.4
BMS528	X	10	24.01	10	MS	FAM	22_1	3	2.6
BRN	X	10	35.07	9	MS	VIC	10_1	3	1.0
SPS113	X	10	35.07	9	MS	NED	PURITY_A	7	4.0
BMS2742	X	10	44.25	12	MS	FAM	12_1	4	3.0
BMS419	X	10	59.52	11	MS	FAM	5_3	3	3.0
INRA071	X	10	68.10	8	MS	PET	10_1	3	2.0
INRA037	X	10	79.01	9	MS	NED	5_3	3	2.4
BMS2641	X	10	87.46	4	MS	VIC	10_2	1	1.0
BMS614	X	10	100.01	6	MS	FAM	10_3	3	2.0
BMS2614	X	10	109.39	6	MS	FAM	5_1	3	1.8
BL1134	X	10	111.91	6	MS	VIC	10_1	3	0.8
BM827	N	11	10.58		MS	FAM	5_2	3	0.6
INRA044	X	11	12.08	8	MS	FAM	23_1	3	2.0
BMS2325	X	11	21.08	7	MS	PET	PRTG B	6	2.2
BM2818	X	11	30.01	4	MS	VIC	10_2	1	1.8
RM096	X	11	40.48	6	MS	FAM	10_1	3	1.0
BM7169	X	11	50.31	8	MS	FAM	5_3	3	3.2
BMS1716	X	11	54.58	10	MS	FAM	5_4	3	2.8
ILSTS036	X	11	61.57	6	MS	FAM	5_6	3	2.8
RM150	X	11	70.14	9	MS	FAM	11_1	3	1.4
IDVGA3	X	11	81.80	6	MS	NED	10_1	3	1.0
BMS989	X	11	92.18	6	MS	PET	11_2	5	3.4

Marker Name	Analyzed	BTA	Position cM	Allele Count	Type	Dye Label	Multiplex	PCR set up	Nanograms of primer
BL1103	X	11	97.57	5	MS	FAM	5_3	3	2.0
BMS460	X	11	109.44	7	MS	FAM	10_2	1	1.2
HEL13	X	11	122.37	6	MS	VIC	11_2	5	11.0
DIK2571	X	11	126.09	3	MS	NED	12_1	4	6.0
BMS410	X	12	0.00	13	MS	NED	PRTG A	7	1.2
TGLA36	X	12	6.04	6	MS	FAM	5_4	3	0.6
BMS2252	X	12	14.36	8	MS	FAM	5_4	3	1.4
BMS2057	X	12	20.84	10	MS	FAM	25_1	3	2.0
BY10	X	12	27.42	2	MS	PET	12_1	4	4.0
INRA138	X	12	37.24	7	MS	VIC	5_4	3	0.7
BM1827	X	12	46.30	7	MS	NED	10_2	1	1.0
BMS975	X	12	63.84	5	MS	FAM	5_3	3	2.2
SRC97	L	12	73.60	2	MS	VIC	5_2	3	4.0
BM4028	X	12	83.56	9	MS	FAM	5_6	3	1.6
INRA5	X	12	86.85	3	MS	FAM	12_1	4	10.0
BMS1316	X	12	101.97	8	MS	NED	11_2	5	5.0
BMS2724	X	12	108.98	5	MS	NED	5_4	3	3.6
TGLA23	X	13	8.99	8	MS	VIC	4_4	1	1.2
BMC1222	X	13	27.60	11	MS	FAM	30_3	1	4.0
BMS1352	X	13	38.66	6	MS	PET	3_1	1	2.4
BM720	X	13	46.63	12	MS	VIC	PRTG B	6	3.0
BM9248	X	13	62.81	8	MS	NED	13_1	1	3.0
RM327	X	13	73.64	10	MS	FAM	13_1	1	2.0
BL1071	X	13	80.98	8	MS	FAM	13_1	1	2.0
AGLA232	X	13	91.38	10	MS	FAM	16_3	2	2.0
BMS2319	X	13	97.26	7	MS	FAM	26_2	1	1.6
BM6548	X	13	99.38	4	MS	PET	3_1	1	5.0
DGAT	X	14	0.00	2	SNP		DGAT1	1	4.0
CSSM66	X	14	5.13	8	MS	NED	206	1	0.7
DIK4015	X	14	10.03	7	MS	PET	201	1	2.0
BMS1747	X	14	10.50	7	MS	VIC	203	1	1.0
TG	X	14	11.95	2	SNP		TG	1	4.0
DIK4438	X	14	14.09	3	MS	FAM	202	1	2.0
BM1508	X	14	17.85	6	MS	FAM	17_2	1	4.0
RM180	X	14	33.31	5	MS	PET	204	1	2.0
RM011	X	14	43.63	8	MS	NED	14_1	1	2.6
BMC1207	X	14	51.94	9	MS	PET	14_1	1	1.4
BL1029	X	14	59.44	8	MS	FAM	14_1	1	1.4
BM1577	X	14	63.16	8	MS	FAM	2_1	1	1.8
BMS108	X	14	67.67	7	MS	PET	14_1	1	2.0

Marker Name	Analyzed	BTA	Position cM	Allele Count	Type	Dye Label	Multiplex	PCR set up	Nanograms of primer
BMS1304	X	14	67.70	3	MS	VIC	204	1	1.0
BMS1899	X	14	69.01	9	MS	FAM	14_1	1	1.6
BMS2513	X	14	69.10	4	MS	PET	206	1	2.4
BMS947	X	14	69.79	11	MS	NED	201	1	4.4
NRKM020	X	14	74.09	3	MS	FAM	203	1	3.6
DIK2648	N	14	75.03		MS	FAM	15_4	1	4.0
DIK2742	X	14	76.56	8	MS	PET	205	1	3.6
BM4513	X	14	79.79	9	MS	VIC	PURITY_A	7	2.4
RM66	X	14	81.25	2	MS	VIC	205	1	1.2
BM4305	X	14	83.31	6	MS	NED	204	1	2.0
BM2934	X	14	83.93	7	MS	NED	202	1	2.4
BMS2055	X	14	93.70	8	MS	VIC	202	1	2.8
BM6425	X	14	95.14	8	MS	FAM	201	1	2.8
BL1036	X	14	100.02	8	MS	VIC	201	1	2.4
DIK2777	X	15	0.00	15	MS	PET	30_2	1	5.0
MGTG13B	X	15	8.25	5	MS	PET	15_3	2	4.4
BR3510	X	15	9.41	7	MS	NED	15_1	2	2.4
BMS2533	X	15	13.92	12	MS	FAM	15_2	2	3.6
ADCY2	X	15	22.67	8	MS	FAM	15_2	2	3.6
JAB8	X	15	31.21	4	MS	NED	15_2	2	3.6
HEL1	X	15	37.96	4	MS	NED	4_1	1	4.0
MBO76	X	15	54.29	6	MS	NED	15_1	2	2.4
INRA046	X	15	59.28	4	MS	VIC	15_2	2	2.0
DIK2768	X	15	77.95	9	MS	VIC	15_4	1	5.0
BMS812	X	15	84.89	10	MS	FAM	15_1	2	1.6
BL1095	X	15	94.78	4	MS	VIC	30_2	1	4.0
BMS927	X	15	105.00	7	MS	PET	16_3	2	5.4
TGLA245	X	16	0.91	12	MS	NED	16_2	2	2.2
BMS1348	X	16	14.77	6	MS	FAM	16_2	2	1.2
BY22	X	16	34.72	5	MS	FAM	16_2	2	2.0
TGLA53	X	16	38.55	11	MS	PET	19_2	2	4.6
BMS1907	X	16	43.74	5	MS	VIC	26_1	1	5.0
IDVGA49	X	16	54.10	6	MS	FAM	15_1	2	5.4
IDVGA69	X	16	65.20	3	MS	FAM	15_1	2	5.4
INRA048	X	16	72.20	8	MS	FAM	20_1	2	5.4
BM1706	X	16	80.00	8	MS	FAM	PRTG B	6	4.4
BM3509	X	16	84.00	18	MS	FAM	16_1	2	1.0
DIK4437	X	16	93.50	8	MS	PET	17_1	2	4.0
BMS462	X	16	94.46	5	MS	PET	16_1	2	1.2
IDGVA49	N	16			MS	FAM	16_2	2	2.0

Marker Name	Analyzed	BTA	Position cM	Allele Count	Type	Dye Label	Multiplex	PCR set up	Nanograms of primer
BB718	X	17	0.00	4	MS	PET	15_1	2	3.0
BMS1825	X	17	5.50	15	MS	FAM	17_1	2	2.2
DIK5379	X	17	13.94	9	MS	NED	17_2	1	3.0
DIK4665	X	17	21.41	5	MS	PET	17_2	1	3.6
INRA193	N	17	33.38		MS	PET	17_1	2	1.2
BMS941	X	17	37.01	12	MS	NED	20_2	2	2.0
OARFCB48	X	17	41.70	3	MS	VIC	17_1	2	2.0
BM305	X	17	44.45	15	MS	NED	17_1	2	1.0
DIK2668	X	17	57.09	8	MS	VIC	4_6	1	6.0
BM8125	X	17	66.48	5	MS	FAM	17_1	2	1.0
BM1862	X	17	80.86	8	MS	FAM	19_2	2	1.0
BM1233	X	17	92.07	6	MS	VIC	17_1	2	1.8
BMS3004	N	18	1.71		MS	NED	18_1	2	0.5
BMS1355	X	18	2.86	5	MS	FAM	16_1	2	3.0
BMS1322	X	18	13.48	5	MS	FAM	19_2	2	1.4
TEXAN10	X	18	20.70	7	MS	VIC	18_1	2	1.6
BMS2213	X	18	24.49	7	MS	FAM	18_1	2	4.0
BR4406	X	18	33.40	4	MS	VIC	18_1	2	2.4
BM8151	X	18	40.21	7	MS	PET	21_2	2	1.6
BM7109	X	18	46.98	6	MS	FAM	18_1	2	5.0
BMS2639	X	18	55.53	9	MS	PET	PRTG A	7	4.0
IDVGA55	X	18	67.72	3	MS	NED	16_1	2	4.0
BM2078	X	18	76.78	8	MS	NED	18_1	2	1.0
TGLA227	X	18	84.09	7	MS	FAM	PURITY_B	6	4.4
DIK4013	X	18	84.38	9	MS	VIC	16_2	2	4.0
BM9202	X	19	0.00	7	MS	FAM	19_1	2	3.6
BM6000	X	19	5.35	3	MS	PET	19_1	2	1.4
BMS745	X	19	16.04	7	MS	VIC	19_1	2	0.6
X82261	X	19	18.80	5	MS	PET	19_2	2	3.2
BMS2142	X	19	43.32	12	MS	NED	19_1	2	1.0
BMS650	X	19	56.52	13	MS	NED	19_1	2	1.4
BM17132	X	19	59.20	10	MS	FAM	PRTG A	7	2.8
CSSM065	X	19	69.83	4	MS	FAM	19_1	2	1.4
IDVGA44	X	19	86.01	9	MS	VIC	19_1	2	2.2
RM388	X	19	95.04	6	MS	NED	20_1	2	1.1
BMC1013	X	19	106.83	4	MS	NED	19_2	2	3.2
BMS601	X	19	107.95	7	MS	FAM	20_1	2	1.0
BM3517	X	20	0.00	9	MS	PET	20_2	2	1.6
RM106	X	20	2.69	5	MS	PET	20_1	2	1.6
BM1225	X	20	8.24	8	MS	NED	PRTG B	6	3.0

Marker Name	Analyzed	BTA	Position cM	Allele Count	Type	Dye Label	Multiplex	PCR set up	Nanograms of primer
BMS1282	X	20	19.14	6	MS	FAM	20_2	2	2.0
DIK2467	X	20	26.28	4	MS	PET	30_3	1	3.0
DIK5354	X	20	37.12	8	MS	FAM	15_4	1	2.4
GHR	X	20	42.00	2	SNP		GHR_LEP1	1	4.0
BMS2361	X	20	49.73	5	MS	FAM	20_1	2	1.8
BMS703	X	20	60.08	10	MS	PET	20_2	2	5.0
BM5004	X	20	71.81	8	MS	VIC	20_2	2	3.0
UWCA26	X	20	77.09	9	MS	NED	20_1	2	1.1
DIK553	X	20	82.94	2	MS	NED	20_2	2	1.8
BM8115	X	21	0.00	6	MS	VIC	19_2	2	4.0
BMS1117	X	21	10.97	6	MS	PET	21_2	2	2.0
BM3413	X	21	14.99	8	MS	PET	21_1	2	2.4
ILSTS095	X	21	23.74	4	MS	FAM	21_2	2	1.0
BM103	X	21	29.77	7	MS	VIC	21_1	2	0.7
BMS2557	X	21	35.90	4	MS	NED	16_1	2	3.0
RM222	X	21	41.56	7	MS	VIC	21_1	2	2.0
BMS868	X	21	43.13	7	MS	FAM	21_1	2	6.0
TGLA337	X	21	52.14	8	MS	NED	21_2	2	2.4
BM846	X	21	61.25	6	MS	FAM	17_2	1	3.0
ILSTS054	X	21	65.85	7	MS	PET	21_1	2	2.8
BMS743	X	21	75.31	9	MS	NED	21_1	2	1.0
BMS2382	X	21	80.28	3	MS	VIC	21_1	2	1.1
DIK3023	X	21	83.79	7	MS	VIC	21_2	2	1.6
CSSM026	X	22	0.00	11	MS	FAM	15_3	2	4.4
INRA026	X	22	2.86	5	MS	VIC	22_1	3	2.8
BMS672	X	22	5.79	6	MS	PET	22_1	3	2.6
BM1558	X	22	19.05	4	MS	FAM	30_4	1	3.0
DIK2694	X	22	31.53	6	MS	NED	26_1	1	5.0
BMS2573	X	22	42.38	7	MS	FAM	15_4	1	2.0
BM3628	X	22	47.07	9	MS	PET	PRTG B	6	3.0
BM2613	X	22	54.05	6	MS	NED	22_1	3	2.4
BMS875	X	22	64.09	4	MS	FAM	15_3	2	0.5
OARFCB304	X	22	70.74	6	MS	VIC	23_1	3	1.8
BM4102	X	22	82.93	4	MS	FAM	7_1_M	1	0.8
DIK115	X	22	85.37	9	MS	PET	10_3	3	6.0
INRA132	X	23	4.70	7	MS	PET	28_1	4	4.0
SRC119	X	23	10.71	8	MS	VIC	23_1	3	4.0
BM47	X	23	13.77	14	MS	FAM	4_6	1	4.0
UWCA1	X	23	26.52	13	MS	PET	23_1	3	5.0
BOLADRB1	X	23	37.72	10	MS	FAM	30_2	1	2.0

Marker Name	Analyzed	BTA	Position cM	Allele Count	Type	Dye Label	Multiplex	PCR set up	Nanograms of primer
RM185	X	23	52.29	8	MS	FAM	8_1	1	3.6
BM1818	X	23	58.19	7	MS	FAM	7_1_M	1	4.0
BMS2269	X	23	67.93	13	MS	NED	11_2	5	2.0
BM1905	X	23	71.65	9	MS	NED	PRTG B	6	2.4
BM1443	X	23	73.78	7	MS	NED	25_1	3	3.6
DIK4203	X	23	73.80	9	MS	PET	23_1	3	6.0
BL6-1	N	24	2.87		MS	VIC	8_1	1	2.4
BMS2526	X	24	8.15	8	MS	VIC	22_1	3	3.0
DIK2662	X	24	16.34	7	MS	FAM	26_2	1	1.6
BMS2270	X	24	23.69	12	MS	VIC	PURITY_A	7	1.0
AGLA269	X	24	30.53	11	MS	FAM	10_3	3	4.0
BMS1862	X	24	35.50	12	MS	VIC	PRTG A	7	2.0
BMS1743	X	24	43.85	11	MS	FAM	4_5	1	2.0
BMS466	X	24	48.80	8	MS	NED	25_1	3	1.8
BMS1926	X	24	61.20	6	MS	NED	23_1	3	6.0
BMS3024	X	24	65.93	5	MS	FAM	30_2	1	2.0
BMC4216	X	25	0.59	3	MS	PET	25_1	3	5.0
RM074	X	25	2.24	3	MS	VIC	25_1	3	3.2
BMS130	X	25	14.45	5	MS	NED	11_1	3	3.2
BMS2843	X	25	22.64	6	MS	VIC	11_2	5	5.0
BM737	X	25	31.60	8	MS	PET	11_1	3	4.0
BMS1353	X	25	46.44	7	MS	FAM	30_3	1	2.0
MB063	N	25	57.65		MS	NED	12_1	4	2.0
AF5	X	25	61.67	11	MS	FAM	17_2	1	3.6
BM1864	X	25	68.42	5	MS	NED	12_1	4	1.2
RM169	X	26	0.00	6	MS	PET	26_1	1	3.6
BMS651	X	26	2.84	10	MS	VIC	5_6	3	7.0
FASMC2	X	26	15.46	8	MS	NED	28_1	4	1.8
BM1314	X	26	26.90	4	MS	PET	PURITY_B	6	3.0
INRA081	X	26	29.62	8	MS	FAM	4_6	1	1.4
BM188	X	26	42.48	9	MS	FAM	26_1	1	3.0
BMS2567	X	26	52.46	7	MS	FAM	26_2	1	5.0
BM804	X	26	60.48	6	MS	PET	11_1	3	1.0
ILSTS091	N	26	71.51		MS	VIC	12_1	4	0.5
BM3507	X	27	0.00	9	MS	FAM	15_3	2	3.0
BMS2168	X	27	3.00	8	MS	VIC	11_1	3	2.4
BM6526	X	27	10.06	8	MS	PET	10_3	3	1.6
BMS2137	X	27	20.78	4	MS	PET	4_2	1	3.0
CSSM043	X	27	34.53	6	MS	FAM	4_6	1	4.0
CSSM36	X	27	43.00	8	MS	FAM	PURITY_A	7	4.0

Marker Name	Analyzed	BTA	Position cM	Allele Count	Type	Dye Label	Multiplex	PCR set up	Nanograms of primer
INRA134	X	27	45.25	5	MS	VIC	4_1	1	3.4
BMS2116	X	27	54.39	8	MS	FAM	28_1	4	3.2
BMS1675	X	27	64.10	6	MS	FAM	4_2	1	3.2
BM203	X	27	64.10	9	MS	VIC	15_1	2	3.6
BMS2060	X	28	6.04	4	MS	NED	28_1	4	2.2
DIK2451	X	28	7.64	7	MS	VIC	15_3	2	3.0
IDVGA29	X	28	16.06	6	MS	VIC	13_1	1	3.0
BL25	X	28	24.77	7	MS	FAM	28_1	4	2.0
BMS510	X	28	29.16	9	MS	VIC	PRTG A	7	1.0
BMS2608	X	28	38.48	8	MS	PET	4_4	1	2.0
BMS1714	X	28	49.40	6	MS	PET	4_3	1	4.0
MB023	L	28	59.56	3	MS	VIC	28_1	4	4.0
BM4602	X	29	0.92	11	MS	FAM	29_5	4	4.0
BMS764	X	29	11.29	7	MS	FAM	11_1	3	1.8
BMS1787	X	29	19.58	9	MS	FAM	9_4	3	1.6
BMS1600	X	29	29.20	4	MS	PET	29_5	4	2.4
RM040	X	29	40.16	2	MS	VIC	29_5	4	0.8
BMC3224	X	29	46.67	3	MS	VIC	PURITY_B	6	2.4
BL1100	X	29	50.41	6	MS	VIC	9_4	3	1.1
BMS1948	X	29	65.64	6	MS	NED	29_5	4	4.0
ILSTS081	X	29	69.01	6	MS	PET	29_5	4	2.0
BMS631	N	X	0.00		MS	VIC	8_1	1	2.4
BM6017	N	X	6.50		MS	NED	30_1	1	3.6
ACC40	N	X	24.70		MS	PET	30_4	1	8.0
BMS811	N	X	42.10		MS	PET	7_1_M	1	4.0
BMS2227	N	X	53.30		MS	FAM	30_3	1	8.0
XBM111	N	X	61		MS	NED	8_1	1	2.4
BMS417	N	X	69.50		MS	VIC	4_4	1	5.0
BR215	N	X	79.10		MS	VIC	16_3	2	2.4
BMC6021	N	X	90.40		MS	PET	8_1	1	2.4
BMS2798	N	X	101.60		MS	VIC	15_2	2	5.0
BMS397	N	X	106.50		MS	VIC	7_1_M	1	1.6
INRA120	N	X	120.60		MS	NED	15_4	1	2.8
BMS911	N	X	130.10		MS	FAM	30_2	1	2.0
TGLA325	N	X	135.80		MS	PET	4_1	1	1.8
INRA30	N	X	140.90		MS	NED	30_2	1	3.6
XBM451	N	X	142.1		MS	NED	4_4	1	3.0

Table 2.2. Single nucleotide polymorphism primer sequences.

Primer Name[1]	Primer Sequence* 5'-3'	Polymorphism	Size (bp)[1]
16S_F	CCCCGCCTGTTTACCAAAAACAT		
16S_R1	TACTCCGGTTTGAACTCAGATC		594
16S_R2	GAGGTCGTAAACCCTATTGTCG		500
ABCG2_AF	AGCATTCCTCGATACGGATA	ABCG2	
ABCG2_AR	TCAACTTGACCCAAGGCTTA	Allele A	171
ABCG2_CF	GAGCATTCCTCGATACGGTTC	ABCG2	
ABCG2_CR	TATGAGTTATCTCCCAATCCTTCA	Allele C	240
APM_11867_CF	GACAGAAAAGTCCCCTATGCAC	APM1 SNP 11867	
APM_11867_CR	CTCCAGGTTCTCCCTTTCTG	Allele C	397
APM_11867_TF	GACAGAAAAGTCCCCTATGCAT	APM1 SNP 11867	
APM_11867_TR	TTCCCTCCAACTTTATCTCCA	Allele T	102
APM_1431_CF	GACCACCAGGCAATTCATTT	APM1 SNP 1431	
APM_1431_CR	GGGAACCTGGTGCAACCTAG	Allele C	186
APM_1431_TF	GGCCAGAGAGGAAAGGATGT	APM1 SNP 1431	
APM_1431_TR	GGGAACCTGGTGCAACCTAA	Allele T	281
APM_1596_AF	AGTGGGAGCTGATGGTGGTA	APM1 SNP 1596	
APM_1596_AR	CAGTCAGGGTGGAAGTAGGAAGT	Allele A	386
APM_1596_GF	CCTTGGTCCCGTCTTCTGT	APM1 SNP 1596	
APM_1596_GR	TCAGGGTGGAAGTAGGAAGC	Allele G	290
APM_5UE1_F3	GCCAAAGCCTGGAGACATAA	APM1 Promoter	
APM_5UE1_R4	CTCGGTACTCATGGGGACAA	insertion/deletion	280/200
DGAT_F	CCATCCTCTTCCTCAAGCTG	*	
DGAT_R	GGGAAGTTGACCTCGTAGCA	Digested with Eae1	
GHR_FF	TGGGCTAGCAGTGACATTGTT	GHR	
GHR_FR	GTAGTCACTAGCCTCACCCTC	Allele G	178
GHR_YF	TGGGCTAGCAGTGACATTGTA	GHR	
GHR_YR	ACGTTTCACTGGGTTGATGA	Allele T	238
LEP_EX2_CR	CCAGGGAGTGCCTTTCATTA	LEP Exon2	
LEP_EX2_CR	GGTGTCATCCTGGACCTTACG	Allele C	305
LEP_EX2_TF	GGACCCCTGTATCGATTCCT	LEP Exon2	
LEP_EX2_TR	GGTGTCATCCTGGACCTTACA	Allele T	86
SST_467_A	ATGCTGGATAGAGTGGTCTGATG	SST SNP 467	
SST_467_C	ATCTCACCAGCGGTTTTAC	Allele G	317
SST_467_GF	ATGCTGGATAGAGTGGTCTGATA	SST SNP 467	
SST_467_GR	GATGCCACATATGTCACTCCAT	Allele A	164
TG_F	GGGGATGACTACGAGTATGACTG	*	
TG_R	GTGAAAATCTTGTGGAGGCTGTA	Digested with Dpn1	
UASMS2_CF	ACTCAGCGGTTGCAACATAC	UASMS2	
UASMS2_CR	GCCTTCCTTGGTGGTACAGT	Allele C	160
UASMS2_TF	ACTCAGCGGTTGCAACATAT	UASMS2	
UASMS2_TR	CTCAGTCTCTCCCCAGTCCTT	Allele T	286
UASMS3_CF	GTGAGAGTGTGTGTATTGATCGC	UASMS3	
UASMS3_CR	CACAAGACCATTACCACACAAGA	Allele C	437
UASMS3_GF	GTGAGAGTGTGTGTATTGATCGG	UASMS3	
UASMS3_GR	GAGCCTGGTTGTTTTGCTTT	Allele G	332

[1] DGAT and TG PCR products scored as cut or uncut by their respective restriction enzyme.

Table 2.3. Multiplex PCR reagent concentrations and annealing temperature for 5 µl total volume.

PCR ID	DNA (ng)	Buffer[1] (µl)	MA[2] (µl)	dNTP (mM)	$MgCl_2$ (mM)	Taq (U)	Annealing Temp (°C)
1	20	0.50	0.50	0.25	2.75	0.5	56
2	20	0.50	0.50	0.25	3.00	0.5	56
3	20	0.63	0.50	0.25	2.99	0.5	56
4	20	0.50	0.50	0.25	2.60	0.5	56
5	20	0.50	0.50	0.25	2.60	0.5	56
6	20	0.50	0.50	0.25	2.75	0.5	54
7	20	0.63	0.50	0.25	2.99	0.5	54
8	20	0.50	0.50	0.25	2.75	0.5	58
9	20	0.50	0.50	0.25	2.75	0.5	60
10	20	0.63	0.50	0.25	2.99	0.4	56

[1] Buffer is 10X Buffer (Promega, Madison, WI, USA).
[2] MA is MasterAmp (Epicentre Biotechnologies, Madison, WI, USA).

Table 2.4. Multiplex PCR conditions.

Temperature	Time (min)	
94°	1.00	
94°	0.20	4 cycles
A	0.30	–1.0°/cycle
65°	0.30	
94°	0.20	
B	0.30	30cycles
65°	0.30	
65°	5.00	

A is the annealing temperature from Table 2.3 plus 4°.
B is the annealing temperature from Table 2.3.

Table 2.5. Marker coverage information for each autosome.

BTA	# of markers	Average interval (cM)	Centromeric Marker (cM)	Telomeric Marker (cM)	Genome Coverage (cM)
1	23	6.95	1.78	154.67	152.89
2	33	3.94	2.78	128.88	126.10
3	14	9.84	0.00	127.91	127.91
4	18	6.81	4.16	119.93	115.77
5	19	6.88	1.17	125.05	123.88
6	17	7.94	0.00	119.05	119.05
7	17	8.47	0.00	135.56	135.56
8	13	10.14	11.34	122.91	111.57
9	13	9.27	4.89	116.17	111.28
10	13	9.17	1.86	111.91	110.05
11	15	8.77	12.08	126.09	114.01
12	13	9.08	0.00	108.98	108.98
13	10	10.04	8.99	99.38	90.38
14	27	4.00	0.00	100.02	100.02
15	13	8.75	0.00	105.00	105.00
16	13	8.50	0.91	94.46	93.55
17	12	9.21	0.00	92.07	92.07
18	13	7.41	2.86	84.38	81.52
19	12	9.81	0.00	107.95	107.95
20	12	7.54	0.00	82.94	82.94
21	14	6.45	0.00	83.79	83.79
22	12	7.76	0.00	85.37	85.37
23	11	6.91	4.70	73.80	69.10
24	10	7.22	8.15	65.93	57.78
25	9	9.69	0.59	68.42	67.82
26	9	8.64	0.00	60.48	60.48
27	10	7.12	0.00	64.10	64.10
28	8	7.65	6.04	59.56	53.52
29	9	8.51	0.92	69.01	68.09
Average	14.21	8.02		Total	2820.49

Table 2.6. Count of carcass QTL by chromosome

Trait	*Bos taurus* autosome																												
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
Carcass Weight	2	4	4		1	2	2	3	1	2	1			1	2	1	2				2	1	1			1	1	1	1
Fat Thickness	1		1	1	1	2	1	1			2	1	2	1	1	3		1			1	1	2	2			1	2	2
Marbling	1	1			1	4		1	1	2	2		2	1		1	1		2	1	1			1	1		2	1	2
Ribeye Area	2		2			1	2	2	4	1	4	2	2	1	2	3	1	1	1	2	1	1	1	1		1	1	1	
Pleiotropic	1		2			1		2			2		1		1	1	1				1		1				1		1
Total	5	5	5	1	3	8	5	5	6	5	7	3	5	4	4	7	3	2	3	3	4	3	3	4	1	2	4	5	4

Table 2.7. Carcass QTL data summary.

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	QTL Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
MRB	1	2.78	*BM6438_29*	*BM8139*	2.731*	0.255					
REA	1	79.78	*BM7145*	*BMS4008*	2.602*	0.314					
CW	1	138.78	*BM1824*	*BMS599*	2.802*	17.202					
FAT	1	138.78	*BM1824*	*BMS599*	5.575***	0.03					
REA	1	149.78	*BMS599*	*URB014*	2.412*	0.299					
CW	1	152.78	*BMS4014*	*URB014*	4.685***	29.512					
CW	2	44.78	*BMS803*	*BL1001*	4.264***	13.23					
MRB	2	63.5	*BM4440*	*BY32*	2.71*	0.146					MRB (4)
CW	2	74.78	*BY32*	*RM041*	3.612**	18.967					SW (8)
CW	2	93.5	*TGLA226*	*BM1223*	3.409**	16.494	38.22	0.877	-0.016	4.607	
CW	2	125.5	*DIK1155*	*DIK2084*	4.893***	19.976	14.46	0.672	-0.006	-4.482	HCW (10)
CW	3	0.5	*BMS871*	*URB006*			10.78	0.843	-0.064	3.061	
REA	3	1.5	*BMS871*	*URB006*			20.27	0.88	-0.008	0.052	
CW	3	17	*URB006*	*BMS2904*	2.057*	20.38					
REA	3	19	*URB006*	*BMS2904*	3.891**	0.328					
CW	3	79.5	*BMS1266*	*HUJII77*			13.36	0.842	-0.04	2.869	
CW	3	102.5	*HUJII77*	*BMS896*	3.606*	14.206					
FAT	3	117	*BMS896*	*BMC4214*	2.713*	0.021					
FAT	4	93.16	*LepEx2*	*RM088*	3.183*	0.04					
MRB	5	41.17	*DIK4759*	*BL37*	3.752**	0.206					MRB (11)
CW	5	123.17	*ETH152*	*BMS597*	2.328*	17.769					
FAT	5	124.17	*ETH152*	*BMS597*	3.538*	0.015					

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	QTL Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
MRB	6	36	*URB016*	*BMS2508*	3.089*	0.232					
FAT	6	89	*CSNA*	*CSN3*	3.442**	0.035					FAT (9)
CW	6	93.5	*BM4621*	*BM8124*	5.981***	20.716					
REA	6	101	*CSN3*	*BM8124*	3.115*	0.263					
MRB	6	108.5	*BM8124*	*BMS5029*			17.89	0.893	-0.004	0.054	
FAT	6	112	*BM8124*	*BMS5029*	2.923*	0.038					
CW	6	119	*BMS5029*	*BMC4203*	3.036*	11.543					
MRB	6	134.25	*BMC4203*	Telomeric			14.77	0.895	-0.006	0.054	
CW	7	21	*DIK4378*	*RM006*	4.653***	19.461					
REA	7	79	*BMS2258*	*BM1853*	2.93*	0.137					
FAT	7	95	*BMS1331*	*BM9065*	4.473***	0.044					
REA	7	105	*BM9065*	*ILSTS006*	3.94***	0.714					
CW	7	119.5	*ILSTS006*	*BMS1979*			27.35	0.812	0.011	-4.559	
CW	8	11.34	*BL1043*	*IDVGA11*	3.014*	9.859					
FAT	8	11.34	*BL1043*	*IDVGA11*	3.46**	0.033					FAT (3)
REA	8	16.34	*IDVGA11*	*RM372*	4.162***	0.248					
MRB	8	18.34	*IDVGA11*	*RM372*	5.96***	0.274					MRB (3)
CW	8	53.34	*BM4006*	*BMS2072*	2.735*	8.711					
REA	8	67.34	*BMS2072*	*MCM64*	3.599**	0.511					
CW	8	101.34	*BM711*	*CSSM047*	3.779**	19.932					

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	QTL Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
CW	9	0.5	Centromeric	*BMS2151*			11.31	0.83	0.239	-3.487	
REA	9	21.5	*ETH225*	*BM1227*			15.92	0.852	0.005	-0.047	
REA	9	32.89	*BM1227*	*BMS817*	6.417***	0.445					
REA	9	61.89	*BMS434*	*BMC701*	2.872*	0.227					
REA	9	77.89	*BMS2377*	*BMS1724*	2.782*	0.212					
MRB	9	99.89	*BMS2295*	*BMS1967*	2.486*	0.112					
CW	10	36.86	*SPS113*	*BMS2742*	2.052*	20.557					CW (5)
MRB	10	55.86	*BMS2742*	*BMS419*	2.555*	0.153					
MRB	10	88.86	*BMS2641*	*BMS614*	2.341*	0.159					
CW	10	111.86	*BMS2641*	*BL1134*	3.207**	15.541					
MRB	11	50.08	*RM096*	*BM7169*	3.482**	0.209					
FAT	11	54.08	*BM7169*	*BMS1716*	2.538*	0.027					
REA	11	54.08	*BM7169*	*BMS1716*	4.396***	0.396					
CW	11	58.08	*BMS1716*	*ILSTS036*	3.407**	8.223					
REA	11	70.08	*ILSTS036*	*RM150*	2.787*	0.152					
FAT	11	98.08	*BL1103*	*BMS460*	2.95*	0.034					%KPH (13)
REA	11	102.5	*BL1103*	*BMS460*			12.76	0.821	0	0.009	
MRB	11	109.08	*BL1103*	*BMS460*	4.591***	0.161					
REA	11	129.5	*HEL13*	Telomeric	3.722**	0.329	23.09	0.86	0.007	-0.046	
REA	12	0.5	*BMS410*	*TGLA36*			11.43	0.845	0.005	-0.038	
FAT	12	1	*BMS410*	*TGLA36*	2.993*	0.023					
REA	12	46	*INRA138*	*BM1827*	3.081**	0.359					REA (10)

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	QTL Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
REA	13	18.99	*TGLA23*	*BMC1222*	2.825*	0.284					
FAT	13	32.99	*BMC1222*	*BMS1352*	2.685*	0.021					
MRB	13	50.99	*BM720*	*BM9248*	3.565**	0.269					
FAT	13	57.99	*BM720*	*BM9248*	2.795*	0.049					RF (13)
REA	13	82	*BL1071*	*AGLA232*			16.76	0.872	-0.007	0.045	
MRB	13	90.99	*BL1071*	*AGLA232*	2.471*	0.278					MRB (11)
MRB	14	5	*DGAT*	*CSSM66*	3.735***	0.219					
CW	14	38.5	*RM180*	*RM011*			14.6	0.818	0.013	3.026	CW (8,12)
REA	14	45	*RM011*	*BMC1207*	3.877**	0.34					
FAT	14	99	*BM6425*	*BL1036*	3.165**	0.021					
CW	15	14	*BMS2533*	*ADCY2*	2.607*	13.075					
FAT	15	15	*BMS2533*	*ADCY2*	2.625*	0.03					%KPH (8)
REA	15	53.5	*HEL1*	*MBO76*			17.87	0.835	-0.002	0.011	
CW	15	101	*BL1095*	*BMS927*	4.168***	19.214					
REA	15	101	*BL1095*	*BMS927*	3.882**	0.371					
MRB	16	0.91	*BMS927*	*TGLA245*	3.106**	0.146					
FAT	16	19.91	*BMS1348*	*BY22*	3.818**	0.04					
CW	16	31.5	*BMS1348*	*BY22*	3.02*	22.522					
REA	16	37.5	*BMS1348*	*TGLA53*	2.356*	0.207					
REA	16	58.91	*IDVGA49*	*IDVGA69*	3.166*	0.424					
FAT	16	83.91	*BM1706*	*BM3509*	4.355**	0.016					FAT (10)
REA	16	83.91	*BM1706*	*BM3509*	3.155**	0.123					
FAT	16	93.91	*DIK4437*	*BMS462*	2.95*	0.026					

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	QTL Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
REA	17	13.5	*BB718*	*TEXAN10*	4.207***	0.156					
CW	17	14	*DIK5379*	*DIK4665*	4.409***	10.546					
CW	17	59	*DIK2668*	*BM8125*	3.802**	17.551					
MRB	17	63	*DIK2668*	*BM8125*	3.388**	0.222					
FAT	18	9.86	*BMS1355*	*BMS1322*	2.572*	0.03					
REA	18	27.86	*BMS2213*	*BR4406*	3.743**	0.341					
MRB	19	43	*X82261*	*BMS2142*	2.461*	0.171					
REA	19	75	*CSSM065*	*IDVGA44*	4.159**	0.384					REA (14)
MRB	19	78.5	*CSSM065*	*IDVGA44*	3.94***	0.274					
REA	20	60	*BMS2361*	*BMS703*	2.803*	0.202					
MRB	20	69	*BMS703*	*BM5004*	2.323*	0.236					
REA	20	70	*BMS703*	*BM5004*	3.337*	0.249					
FAT	21	1	*BM8115*	*BMS1117*	2.197*	0.024					
CW	21	43.5	*BMS868*	*TGLA337*			17.44	0.872	0.058	-5.115	
MRB	21	66.5	*ILSTS054*	*BMS743*			10.47	0.871	-0.004	0.039	
REA	21	74	*ILSTS054*	*BMS743*	2.597*	0.152					
CW	21	81	*BMS2382*	*DIK3023*	2.337*	15.9446					
CW	22	33	*DIK2694*	*BMS2573*	4.234*	20.6455					
FAT	22	82	*OARFCB304*	*BM4102*	3.476**	0.0302					
REA	22	83	*BM4102*	*DIK115*	2.49*	0.1157					
CW	23	26.7	*UWCA1*	*BOLADRB1*	2.557*	12.8922					SW (7), HCW (8)
REA	23	26.7	*UWCA1*	*BOLADRB1*	2.419*	0.1981					
FAT	23	47.7	*BOLADRB1*	*RM185*	2.169*	0.0182					
FAT	23	62.7	*BM1818*	*BMS2269*	2.608*	0.0283					FAT (9)

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	QTL Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
REA	24	8.15	*BMS2526*	*DIK2662*	2.924*	0.3274					
FAT	24	31.15	*AGLA269*	*BMS1862*	3.447**	0.0189					
FAT	24	43.15	*BMS1862*	*BMS1743*	3.374*	0.0145					
MRB	24	77.5	*BMS3024*	Telomeric			33.27	0.892	-0.007	0.062	
MRB	25	6.59	*RM074*	*BMS130*	3.037*	0.2643					
REA	26	0	*RM169*	*BMS651*	3.492*	0.3052					REA (13)
CW	26	2.5	*RM169*	*BMS651*	2.56*	13.068					
FAT	27	32	*BMS2137*	*CSSM043*	2.419*	0.0254					
MRB	27	34.5	*BMS2137*	*CSSM043*			13.78	0.824	-0.003	0.042	MRB (5)
REA	27	40	*CSSM043*	*CSSM36*	3.685**	0.2338					
CW	27	44	*CSSM36*	*INRA134*	3.332*	16.0926					
MRB	27	51.5	*INRA134*	*BMS1675*	2.283*	0.2283					MRB (2,6)
REA	28	9.04	*DIK2451*	*IDVGA29*	3.862**	0.232					
FAT	28	17.04	*IDVGA29*	*BL25*	3.138*	0.0381					
CW	28	25.5	*BL25*	*BMS510*			15.58	0.788	0.054	-2.451	
FAT	28	28.04	*BL25*	*BMS510*	4.204***	0.0382					
MRB	28	30.04	*BMS510*	*BMS2608*	2.613*	0.1855					
CW	29	1.5	*BM4602*	*BMS764*			13.08	0.792	0.007	-3.035	HCW (1,8)
FAT	29	18.92	*BMS764*	*BMS1787*	2.990*	0.0257					
MRB	29	19.92	*BMS1787*	*BMS1600*	2.828*	0.1695					MRB (10)
FAT	29	29.92	*BMS1600*	*RM040*	2.897*	0.0234					
MRB	29	66.92	*BMS1948*	*ILSTS081*	2.524*	0.1949					MRB (10)

[1] Listed is each QTL's most likely location in cM, flanking markers, associated information from QTL Express and LOKI, and whether the QTL has previously been identified.

[2] Significance levels for QTL Express: *=P≤chromosome-wide 0.01, **=P≤genome-wide 0.05, ***=P≤genome-wide 0.01. Freq_1 is the frequency of the 1 allele; effect values estimated in LOKI assume that 11 genotype has an effect of 0.

[3] Abbreviations: carcass weight (CW); fat thickness (FAT); hot carcass weight (HCW); kidney, pelvic, heart percent fat (%KPH); rib fat (RF); ribeye area (REA); slaughter weight (SW).

[4] References: 1=(Alexander *et al.* 2007); 2= (Casas *et al.* 2000); 3=(Casas *et al.* 2001); 4=(Casas *et al.* 2003); 5=(Casas *et al.* 2004b); 6=(Elo *et al.* 1999); 7=(Kim *et al.* 2003); 8=(Li *et al.* 2004); 9=(MacNeil & Grosz 2002); 10=(Mizoshita *et al.* 2004); 11=(Mizoshita *et al.* 2005); 12=(Stone *et al.* 1999); 13=(Taylor *et al.* 1998).

Table 2.8. Summary of carcass QTL identified as pleiotropic.

BTA	Position	Trait 1	Trait 2	Express 1	LOKI 1	Express 2	LOKI 2
1	150	CW	REA	17.202		0.299	
3	1	CW	REA		3.061		0.052
3	18	CW	REA	20.380		0.328	
6	97	CW	REA	20.716		0.263	
8	14	CW	REA	9.859		0.248	
8	14	MRB	FAT	0.248		0.033	
11	52	MRB	FAT	0.209		0.027	
11	56	CW	REA	8.223		0.396	
13	54	MRB	FAT	0.269		0.049	
15	101	CW	REA	19.214		0.371	
16	34	CW	REA	22.522		0.207	
17	14	CW	REA	10.546		0.156	
21	77	CW	REA	15.945		0.152	
23	27	CW	REA	12.892		0.198	
27	42	CW	REA	16.093		0.234	
29	19	MRB	FAT	0.026		0.170	

Express 1,2 and LOKI 1,2 are the allele substitution effect from QTL Express and the alternative homozygote effect for trait 1 and 2 respectively.

Table 2.9. Statistical summary of carcass QTL.

	Count		LOKI		QTL Express	EPD					Acc >0.05
Trait	QTL	Reference	Freq [1]	Effect [2]	Effect [3]	StDev	Var	Kurt	Skew	Count [4]	Count [5]
Carcass Weight	36	6	0.44	3.05	16.625	12.08	145.90	0.5	-0.2	1873	904
Fat Thickness	30	7			0.029	0.03	0.0008	0.2	0.0	1873	899
Marbling	29	8	0.86	0.47	0.206	0.21	0.04	0.4	0.3	1873	895
Ribeye Area	40	3	0.54	0.33	0.292	0.22	0.05	0.2	0.0	1873	894

[1] The average frequency of the economically desirable allele as determined by LOKI.
[2] The average effect of the economically desirable homozygote as determined by LOKI.
[3] The allele substitution effect economically desirable allele as determined by QTL Express.
[4] Count of animals with an EPD value recorded.
[5] Count of animals with an EPD accuracy value >0.05.
Statistical information is based the EPDs from the mapping population.

Table 2.10. Analysis of variance results for carcass weight QTL.

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1191	951831.5	799.187	1.4	<.0001
Error	759	434416.5	572.354		
Corrected Total	1950	1386247.9			

R-Square	0.6866
Coeff Var	-736.5561
Root MSE	23.9239
Mean	-3.2481

Table 2.11. Analysis of variance results for fat thickness QTL.

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1102	669147.9	607.212	1.16	0.0105
Error	848	443278.4	522.734		
Corrected Total	1950	1112426.2			

R-Square	0.6015
Coeff Var	-372.5101
Root MSE	22.8634
Mean	-6.1377

Table 2.12. Analysis of variance results for marbling score QTL.

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	904	614824.0	680.115	1.42	<.0001
Error	1046	499904.3	477.920		
Corrected Total	1950	1114728.4			

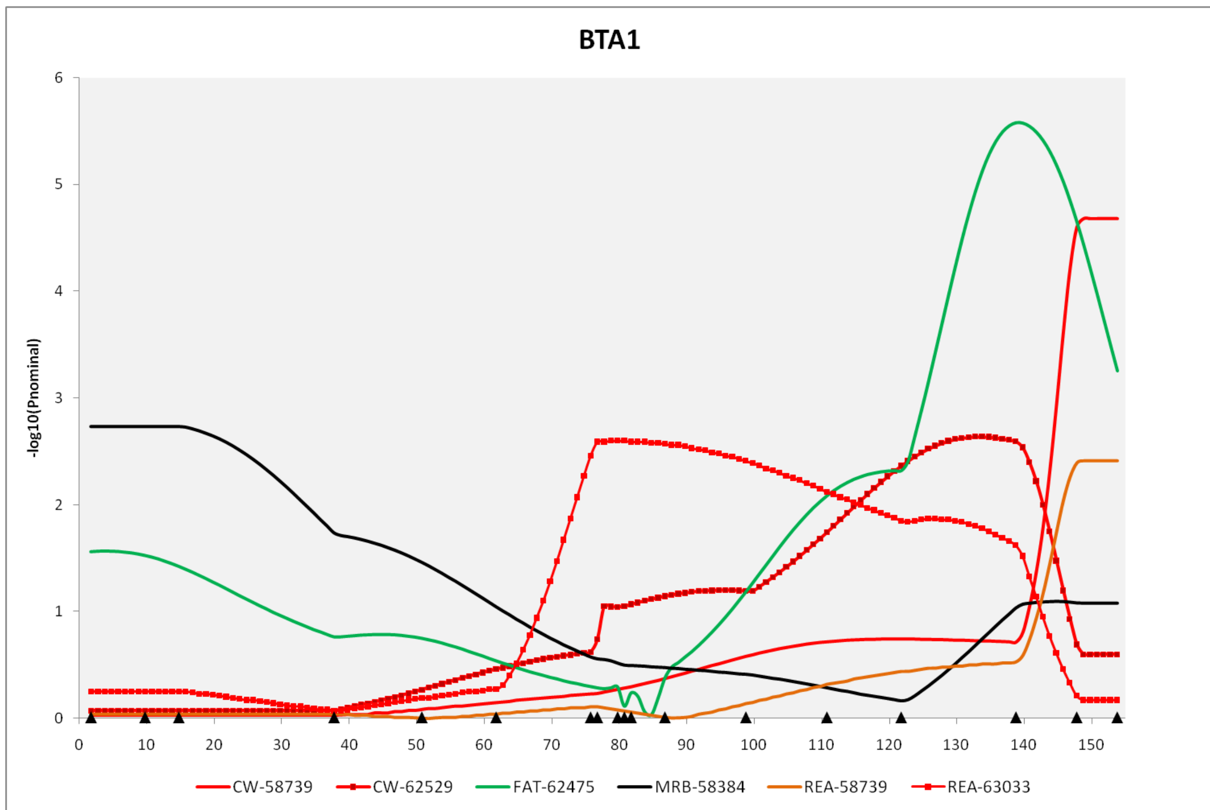
R-Square	0.5515
Coeff Var	-361.7042
Root MSE	21.8614
Mean	-6.0440

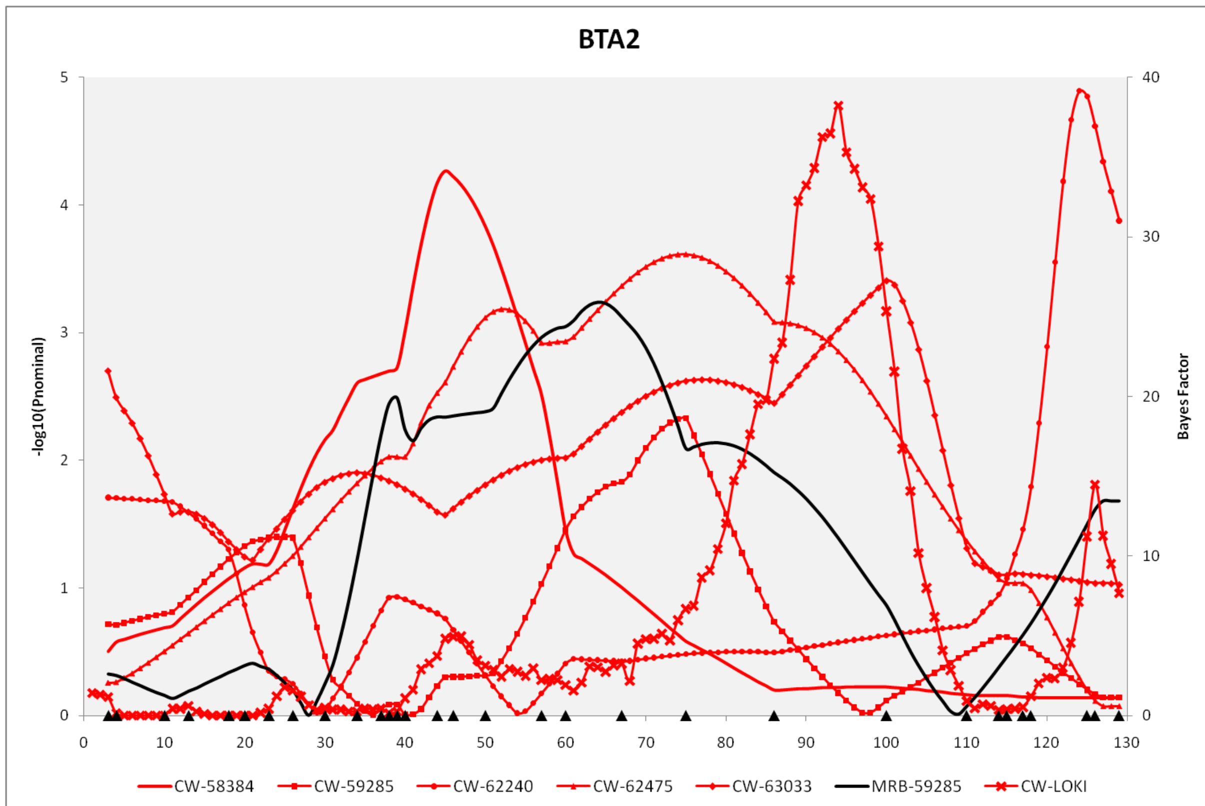
Table 2.13. Analysis of variance results for ribeye area QTL.

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1438	843684	586.707	1.11	0.0798
Error	512	270692.3	528.696		
Corrected Total	1950	1114376			

R-Square	0.757091
Coeff Var	-379.502
Root MSE	22.99339
Mean	-6.05884

Figure 2.1. Carcass QTL graphs for each *B. taurus* autosome. Plots are for half-sib data analyzed from American Angus sire linage by QTL Express, unless indicated from LOKI. QTL Express data are expressed in $-\log_{10}P_{nominal}$ values units while LOKI data are express as Bayes Factors. Colored lines represent different traits as follows: red=CW; green=FAT; black=MRB; and gold=REA. Significance levels for QTL Express are as follows: chromosome-wide P≤0.01 = 2.8, genome-wide P≤0.05 = 3.3, genome-wide P≤0.01 =4.1. Significance levels for LOKI are ≥10. All X-axis values are in cM, ▲ represent genomic markers

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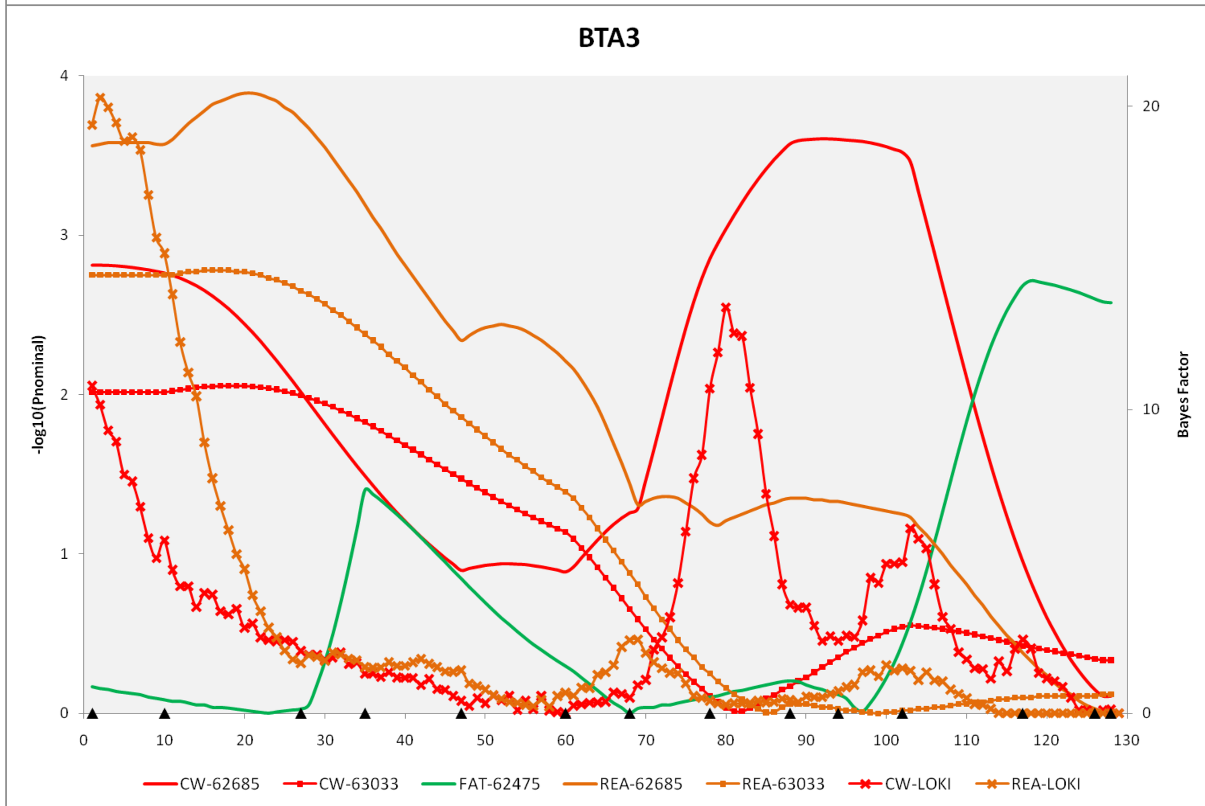
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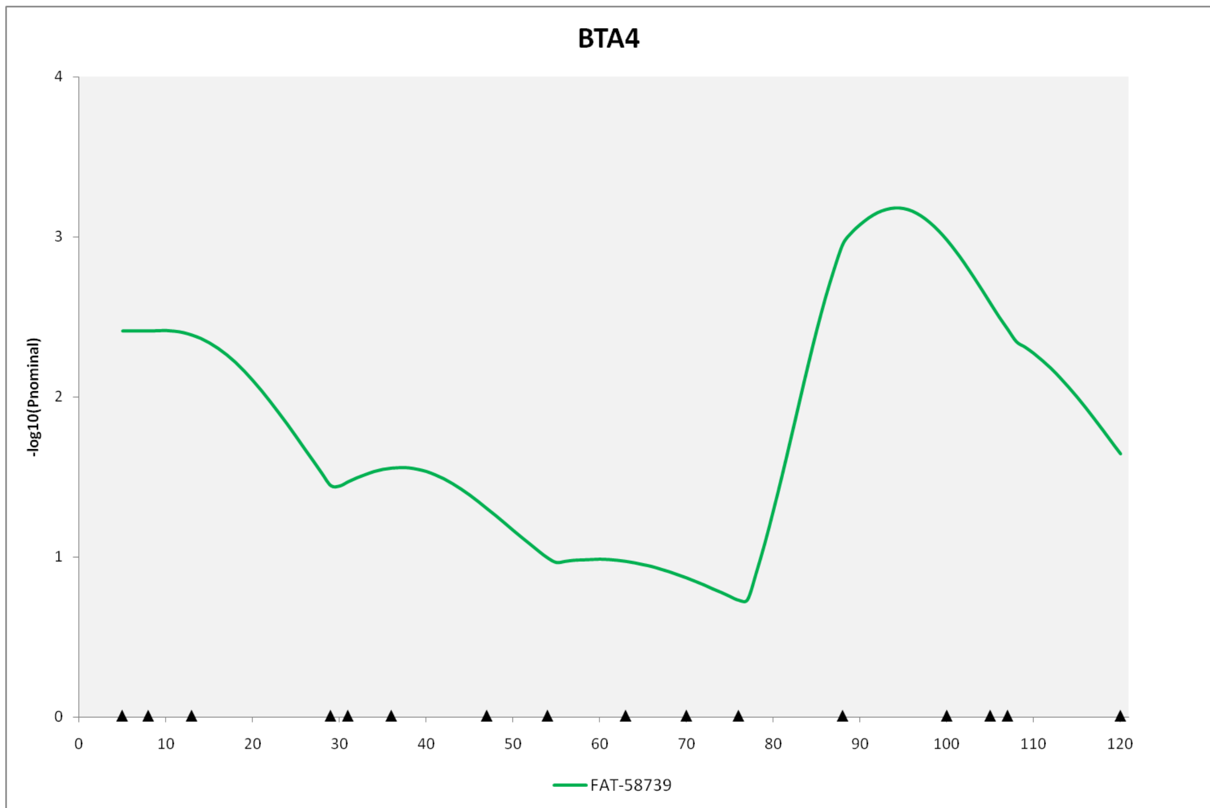
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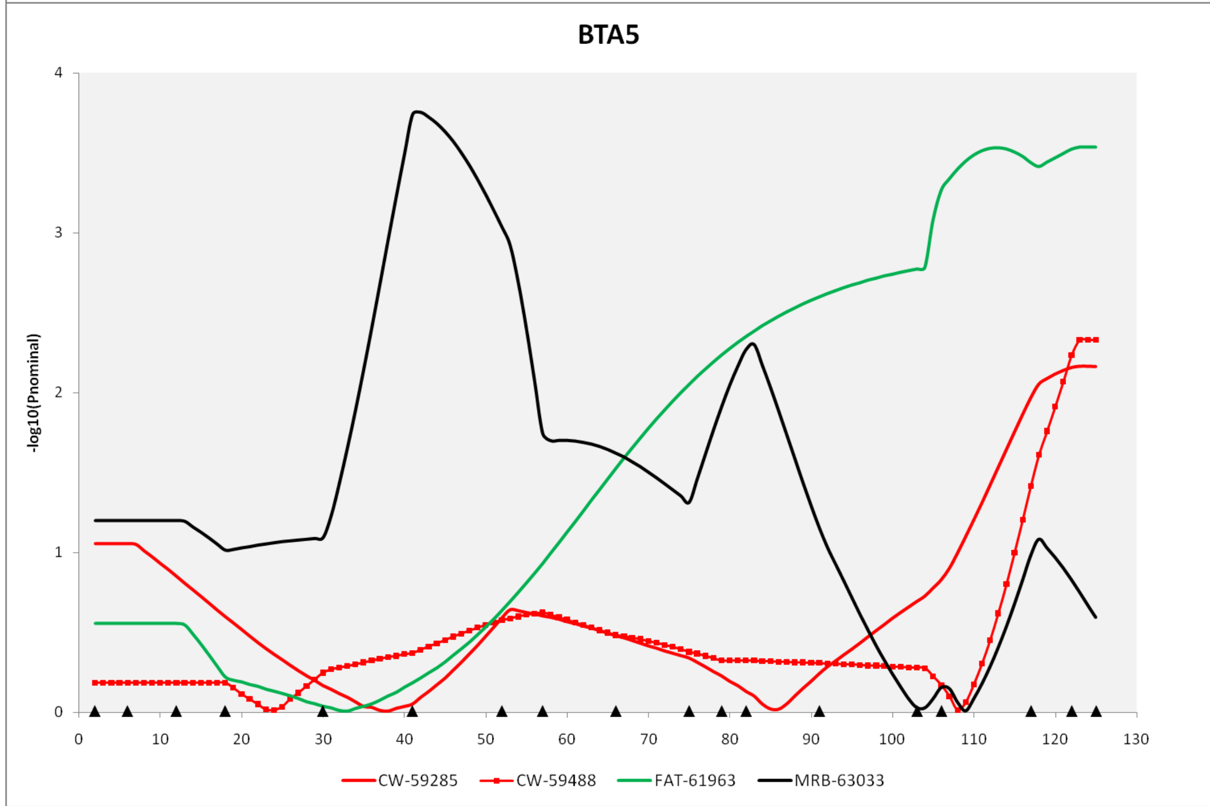
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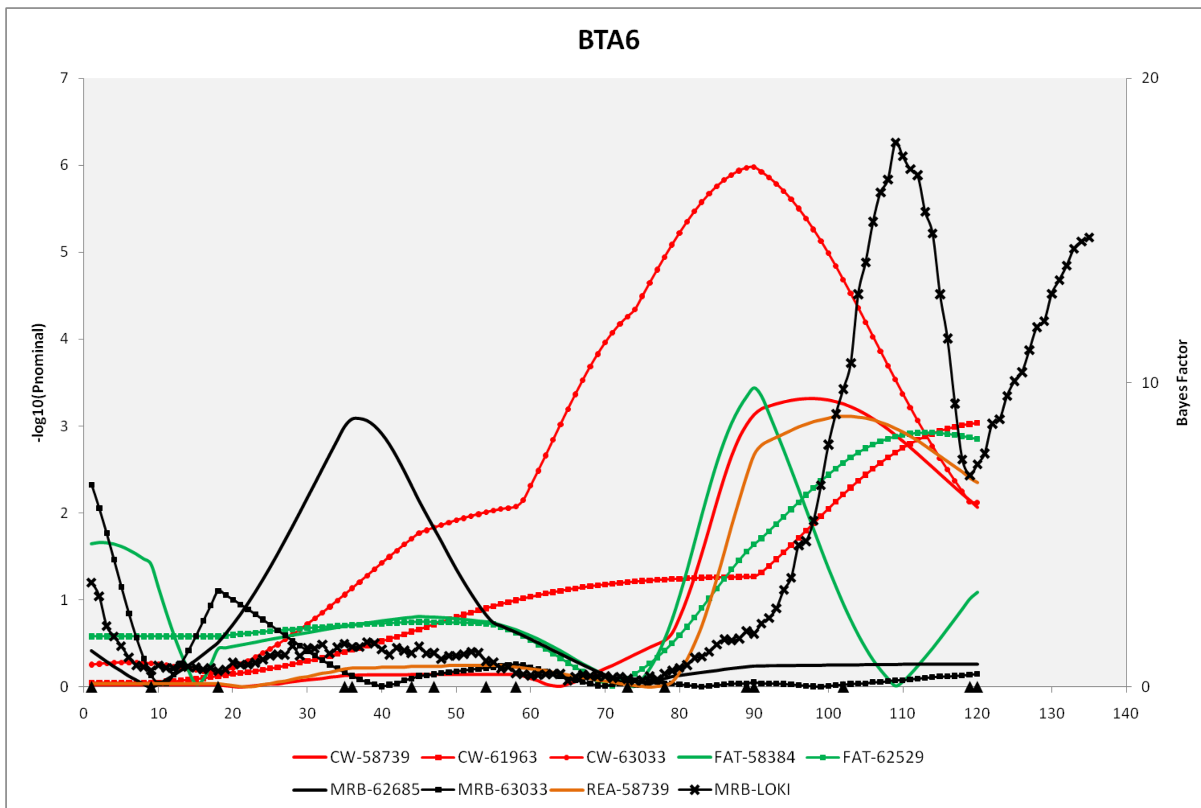
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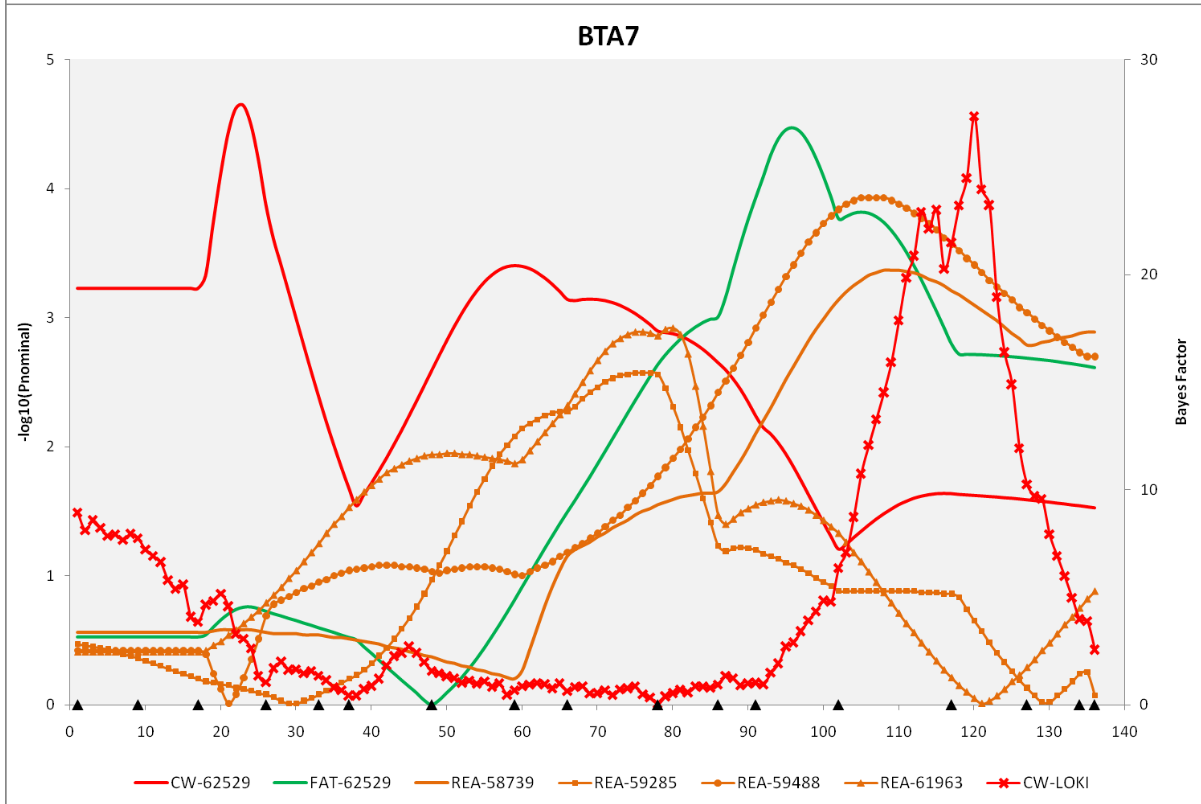
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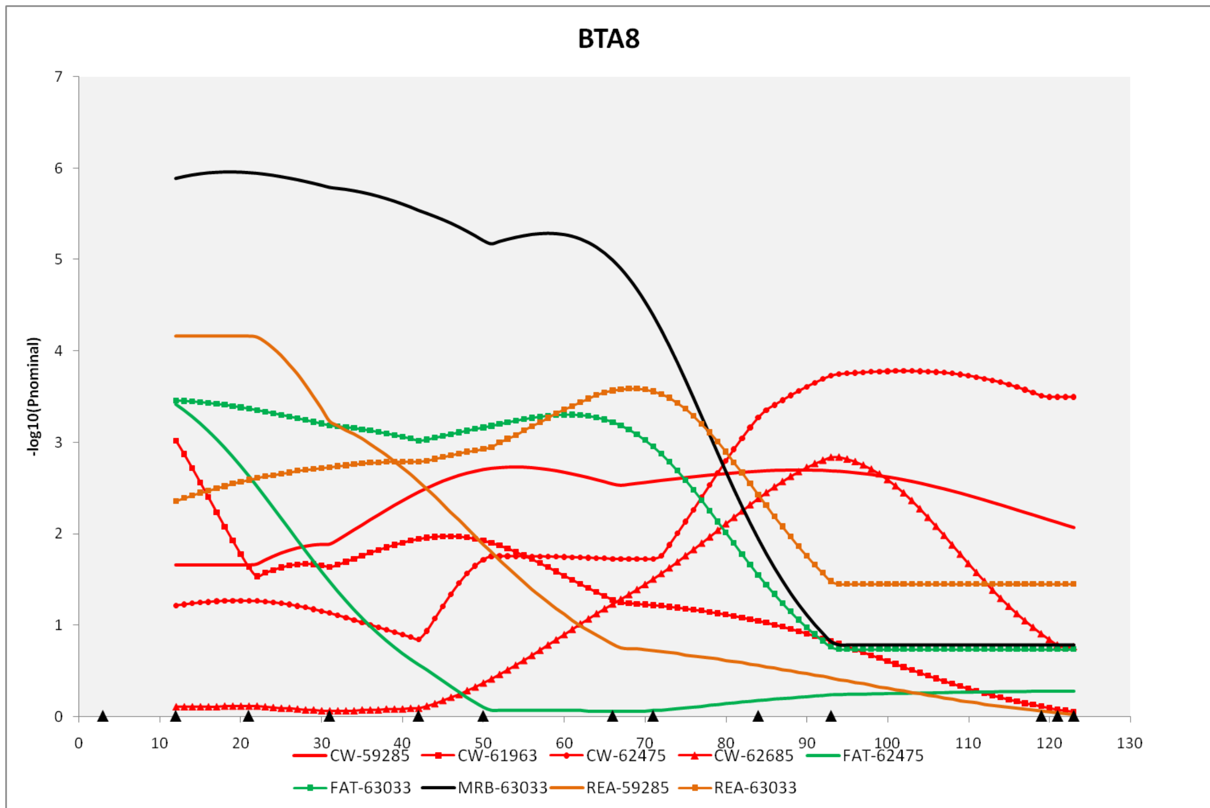
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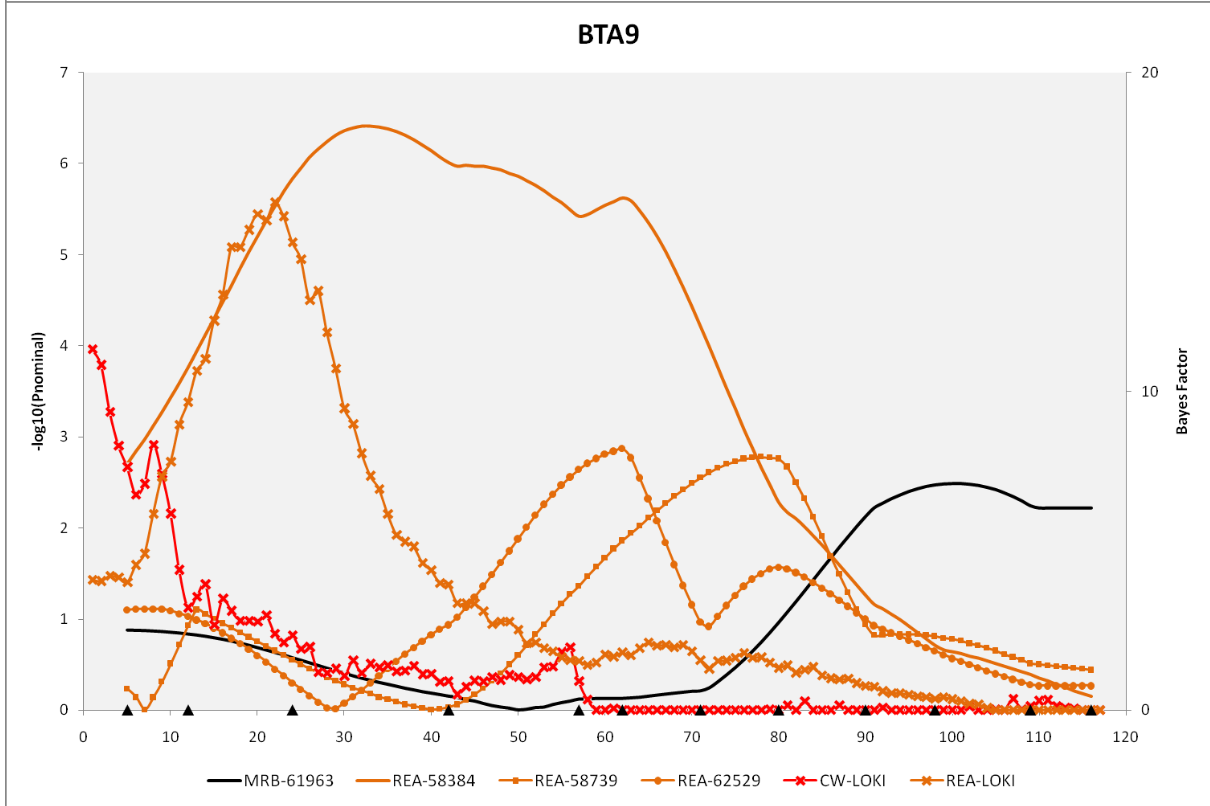
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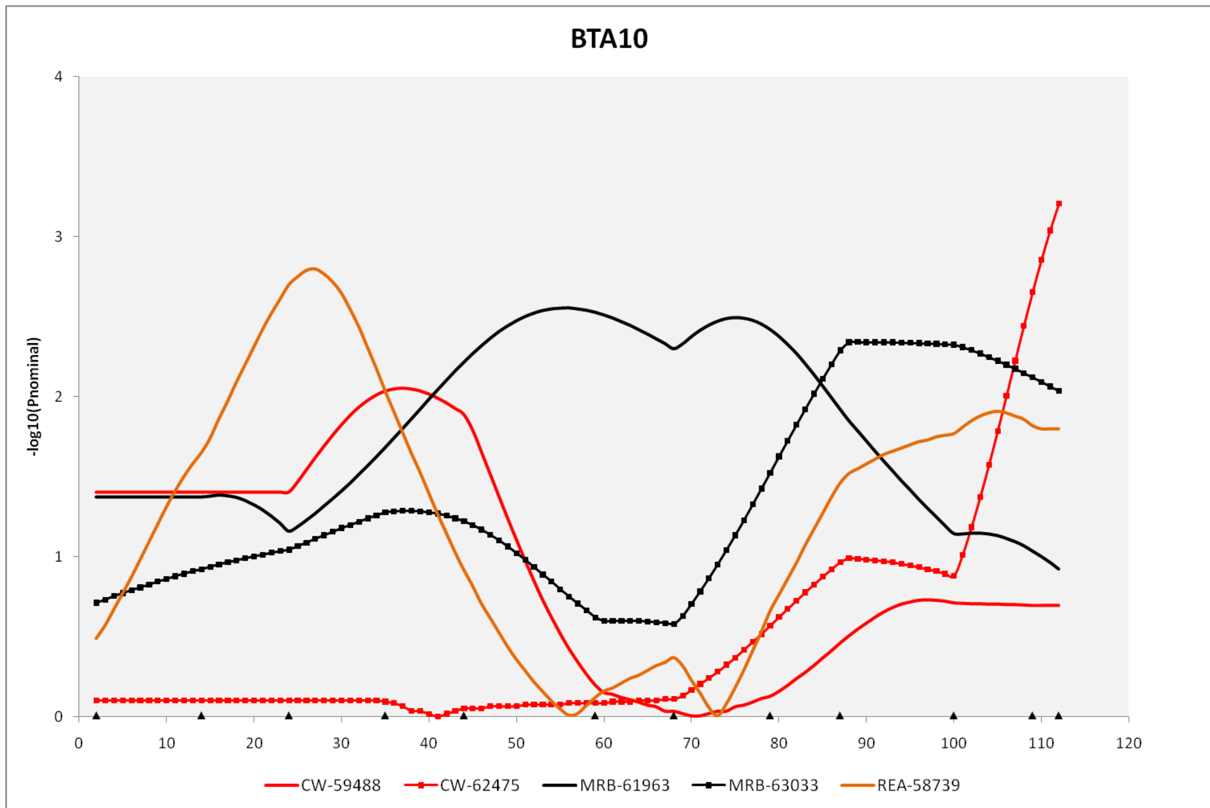

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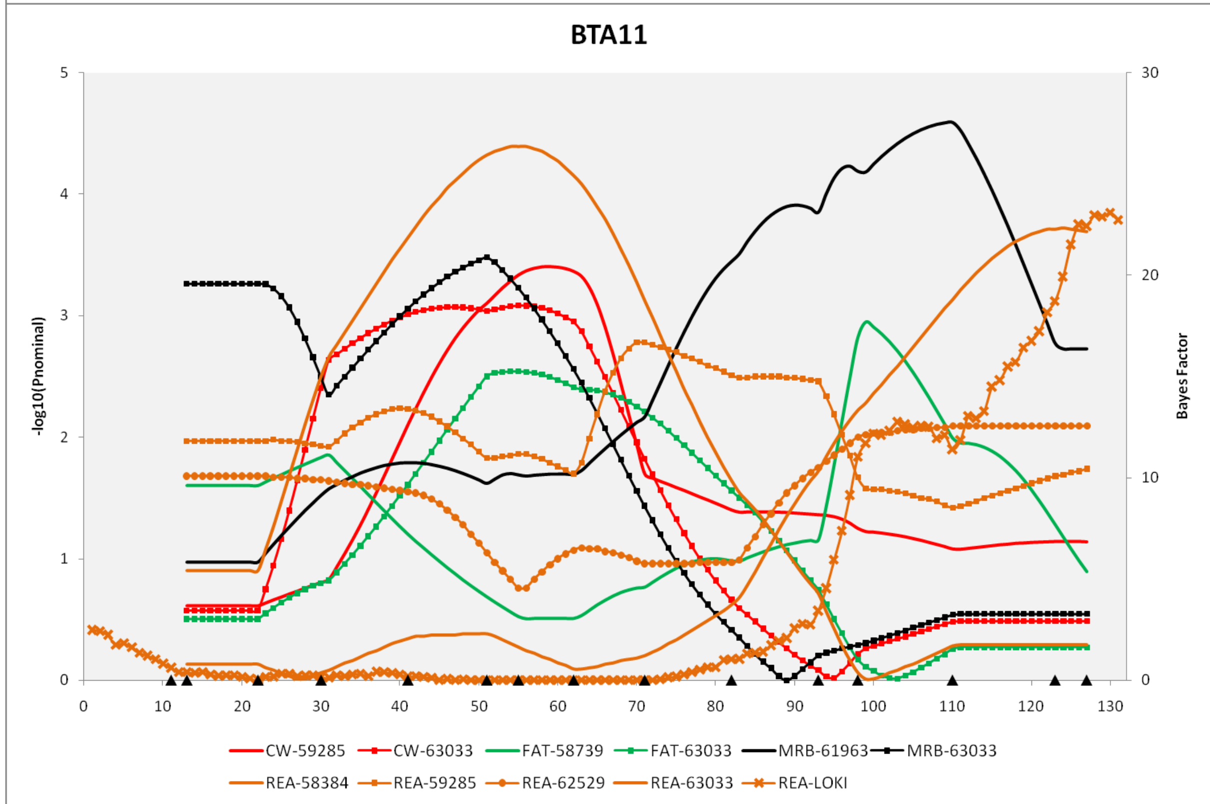

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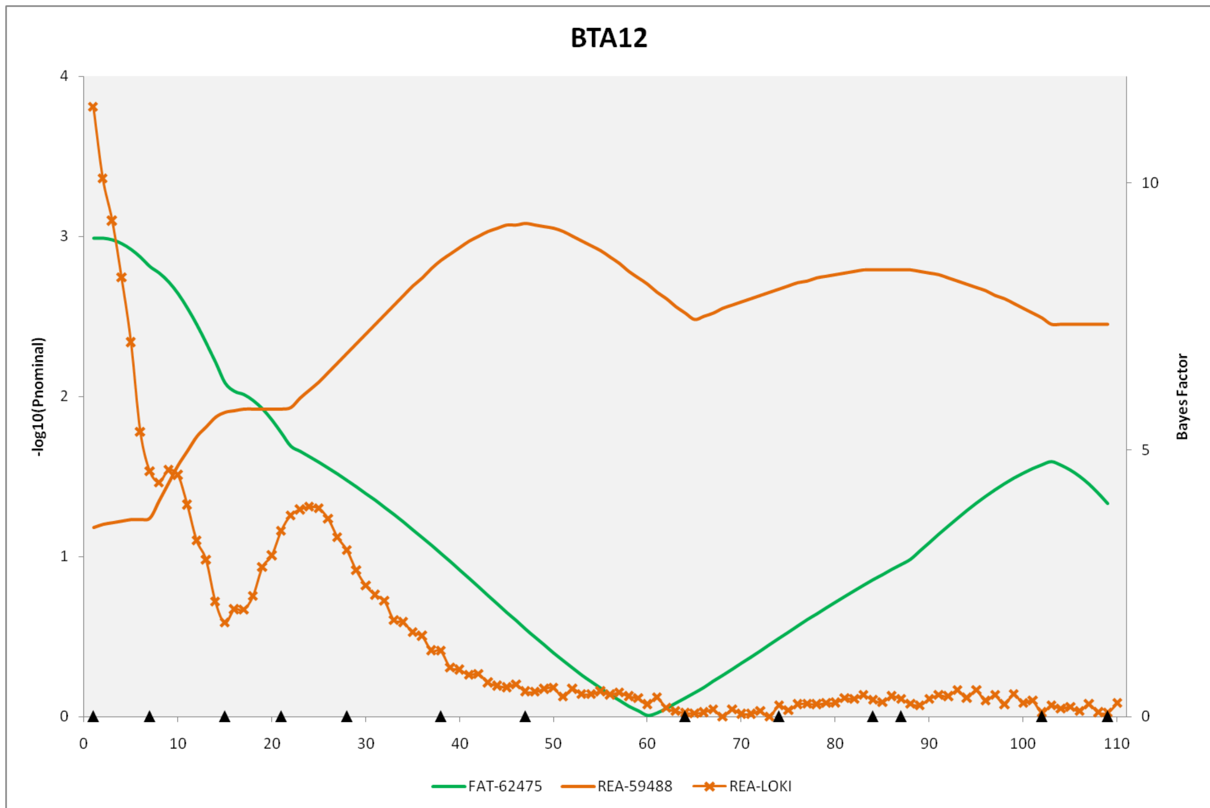
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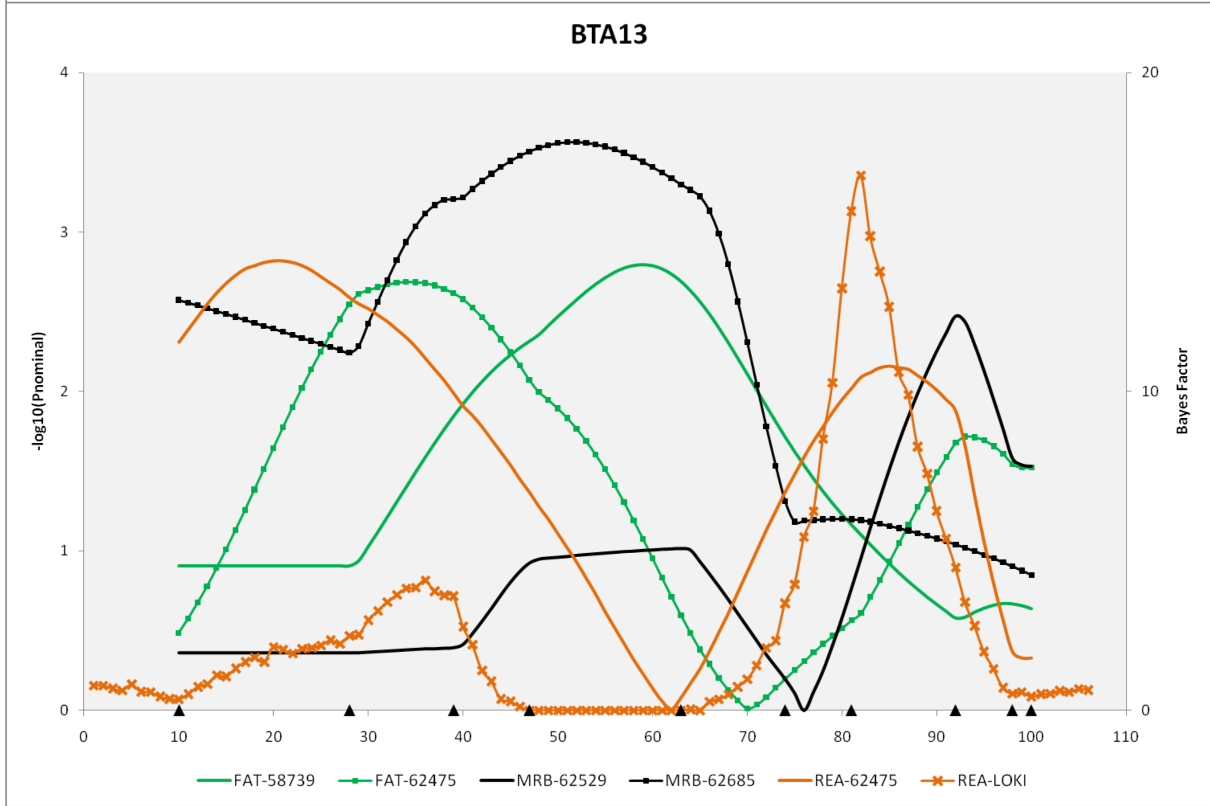
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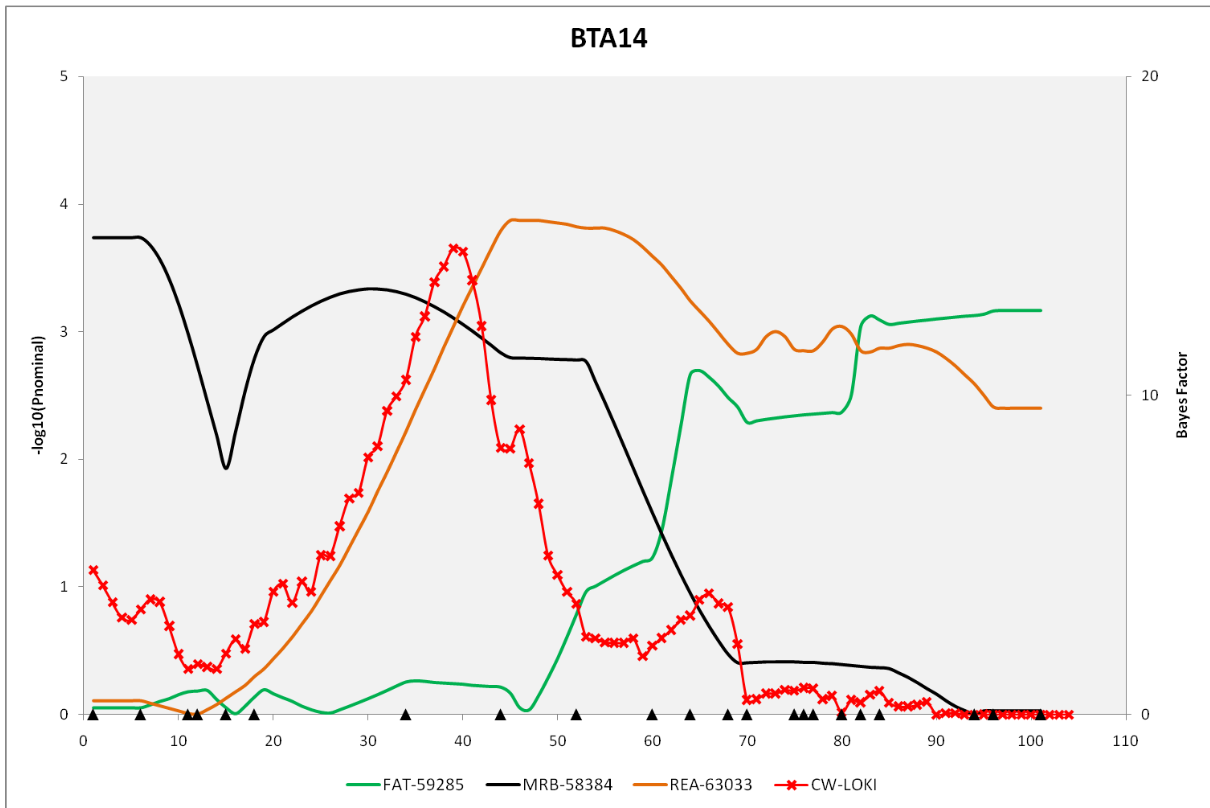
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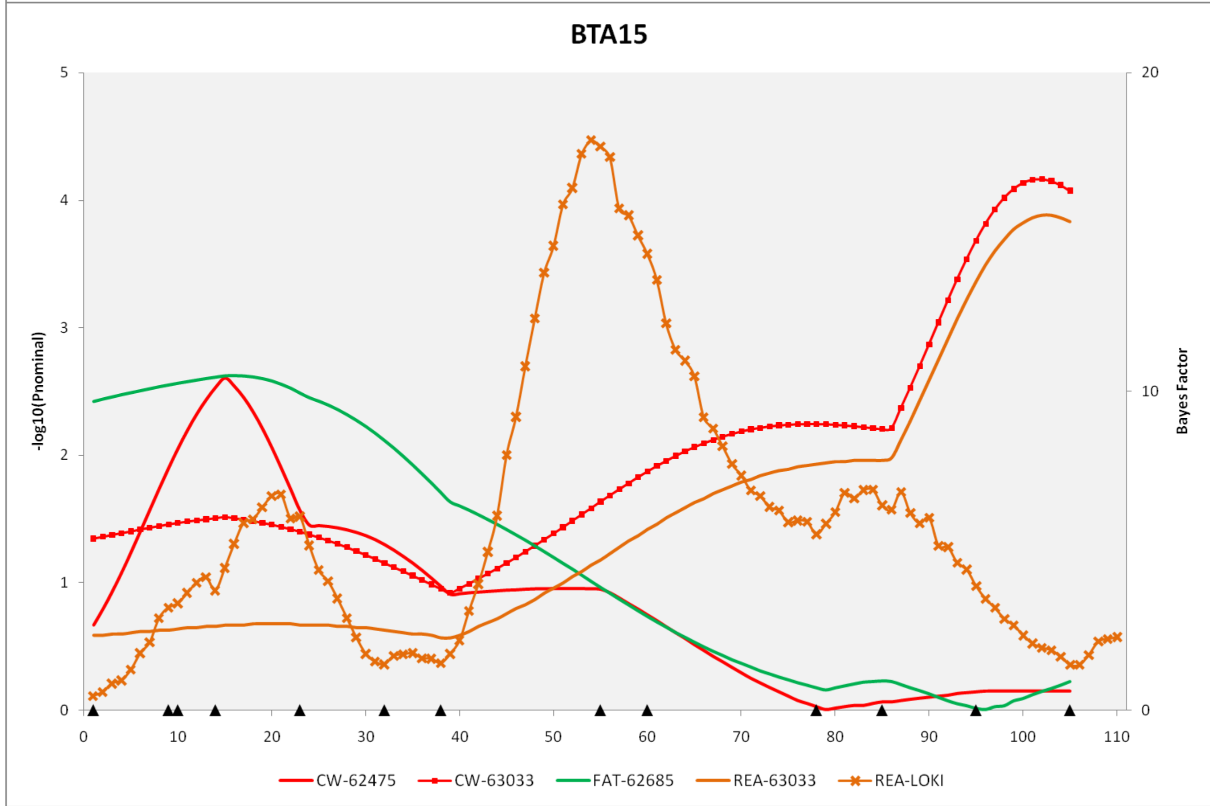
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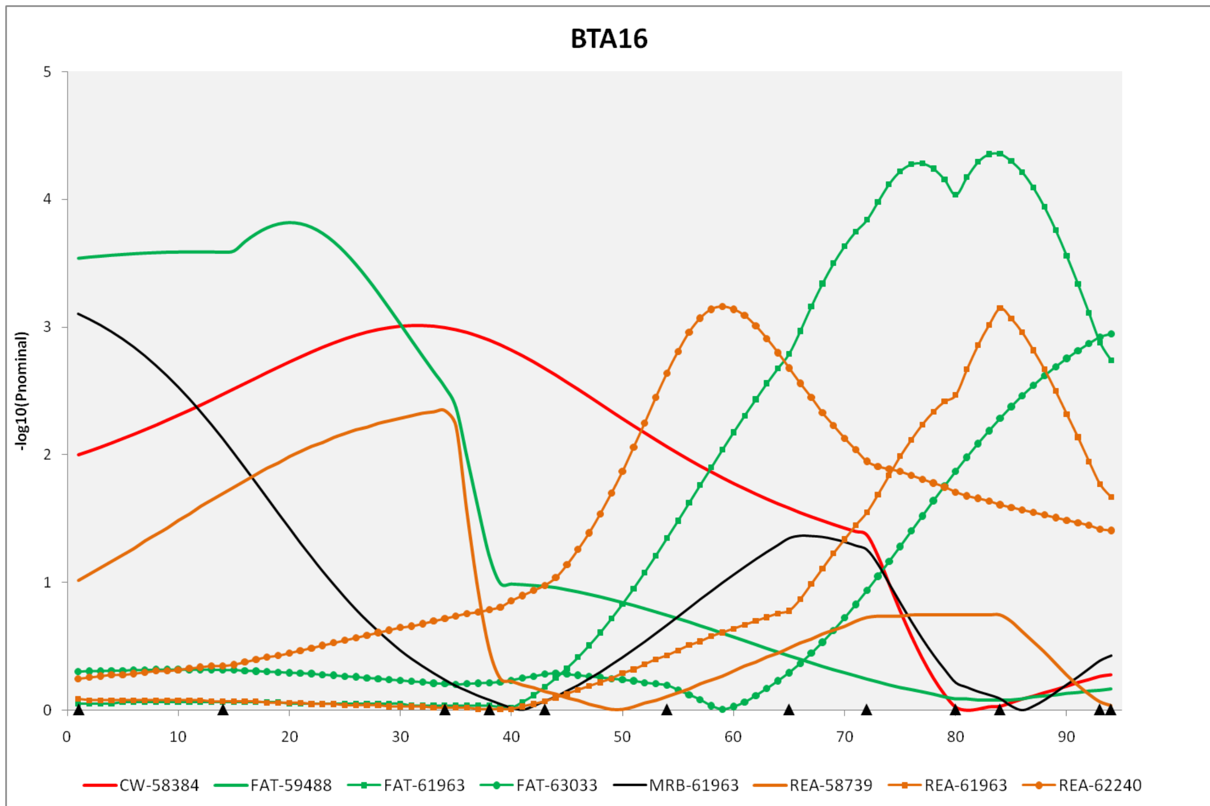
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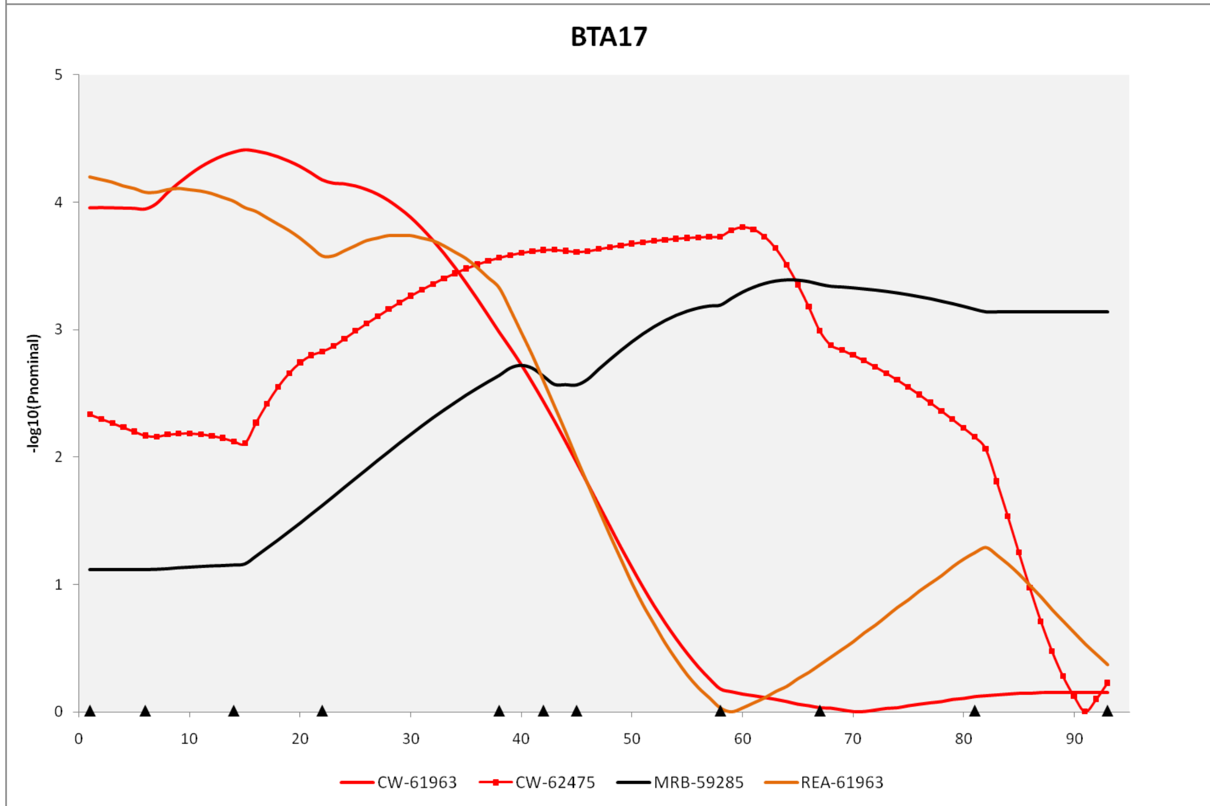
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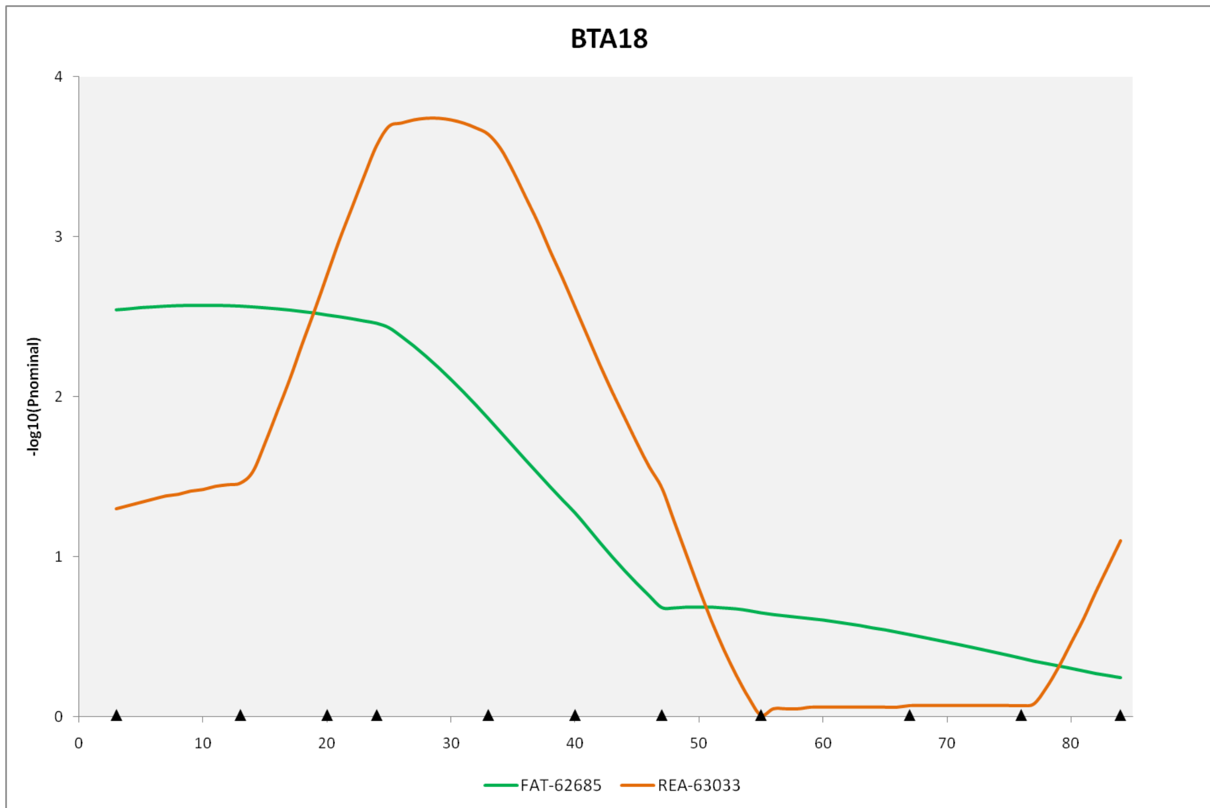
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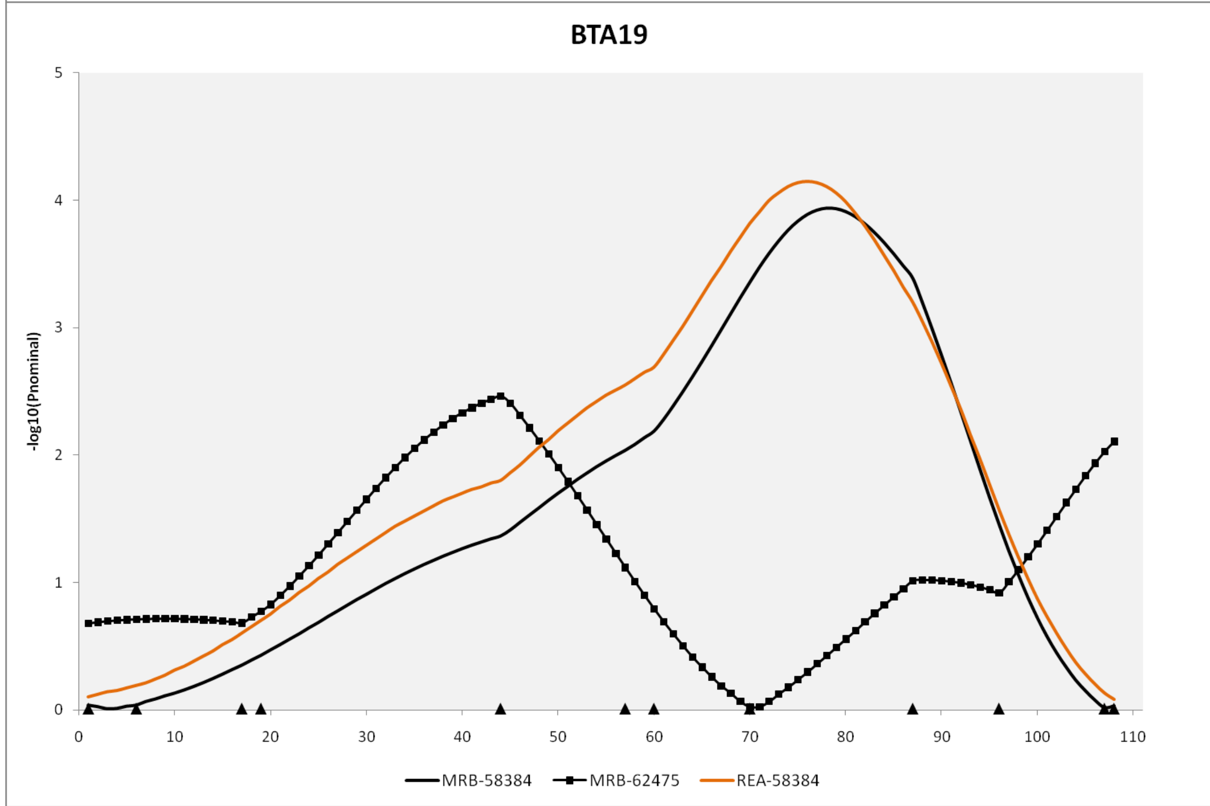
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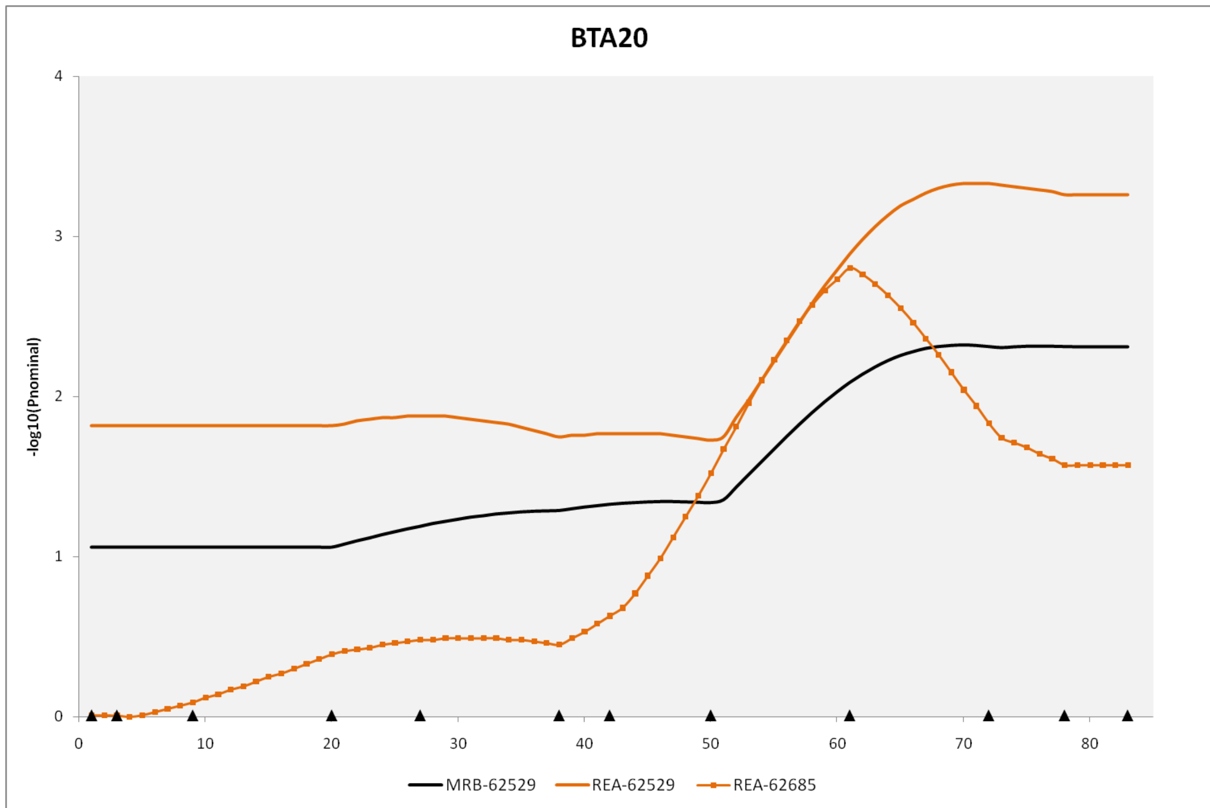
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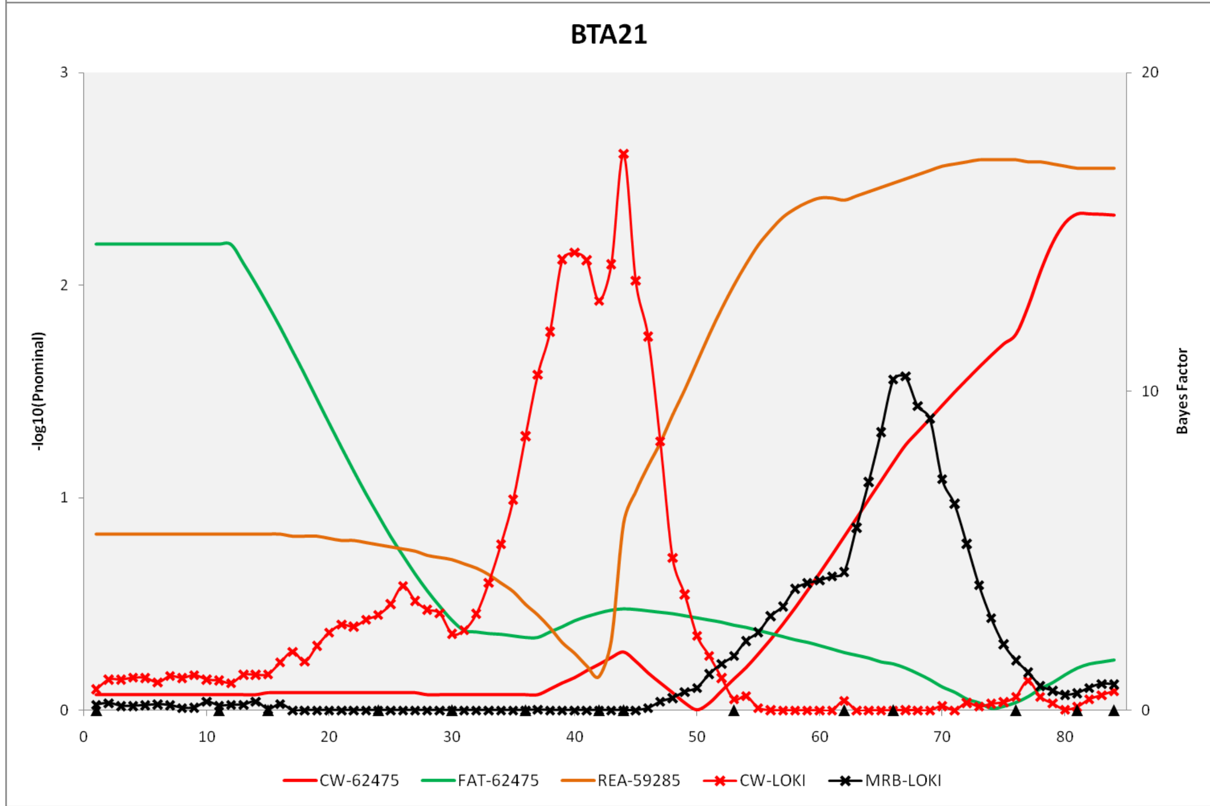
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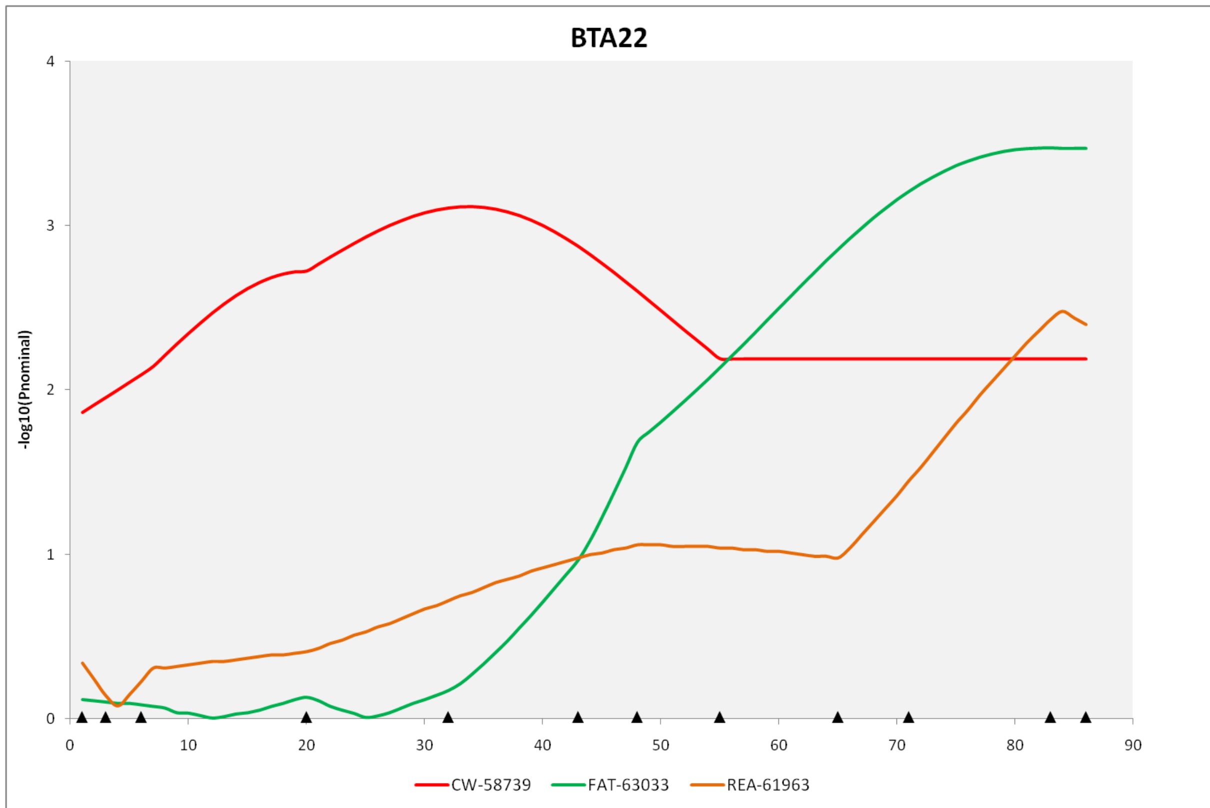
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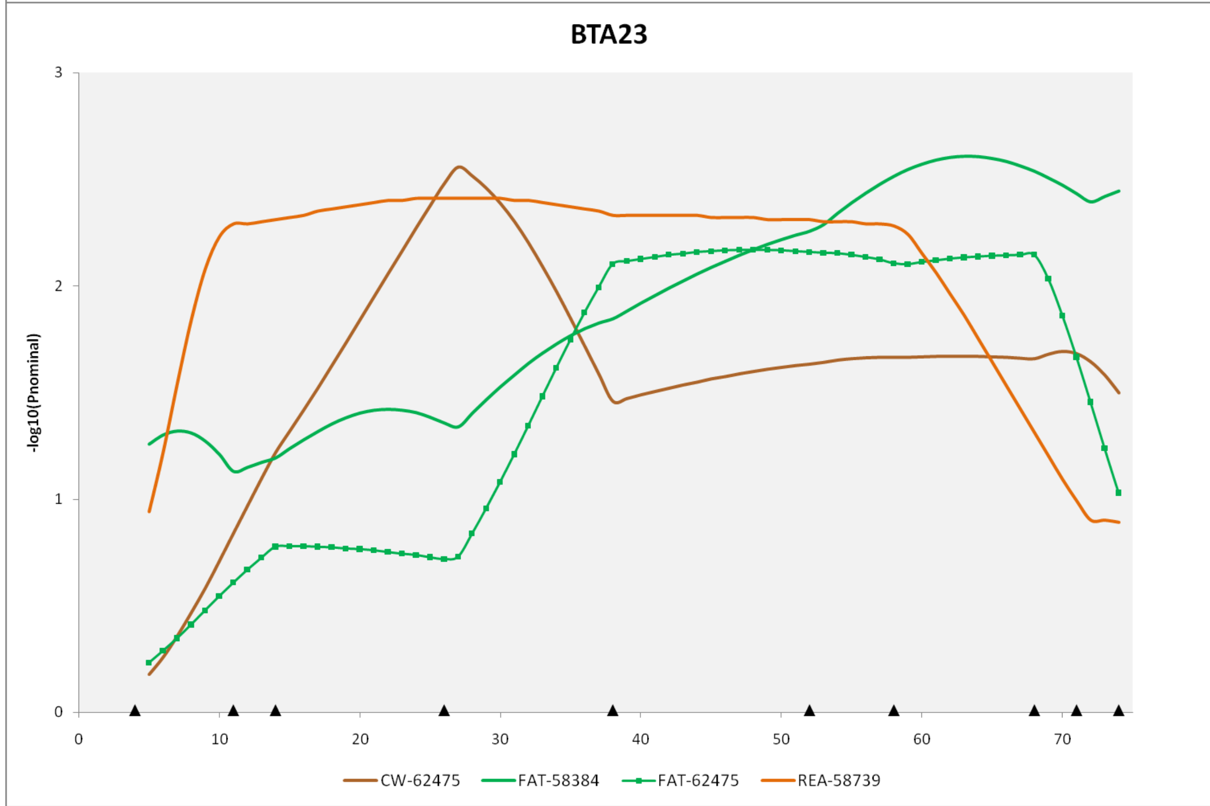
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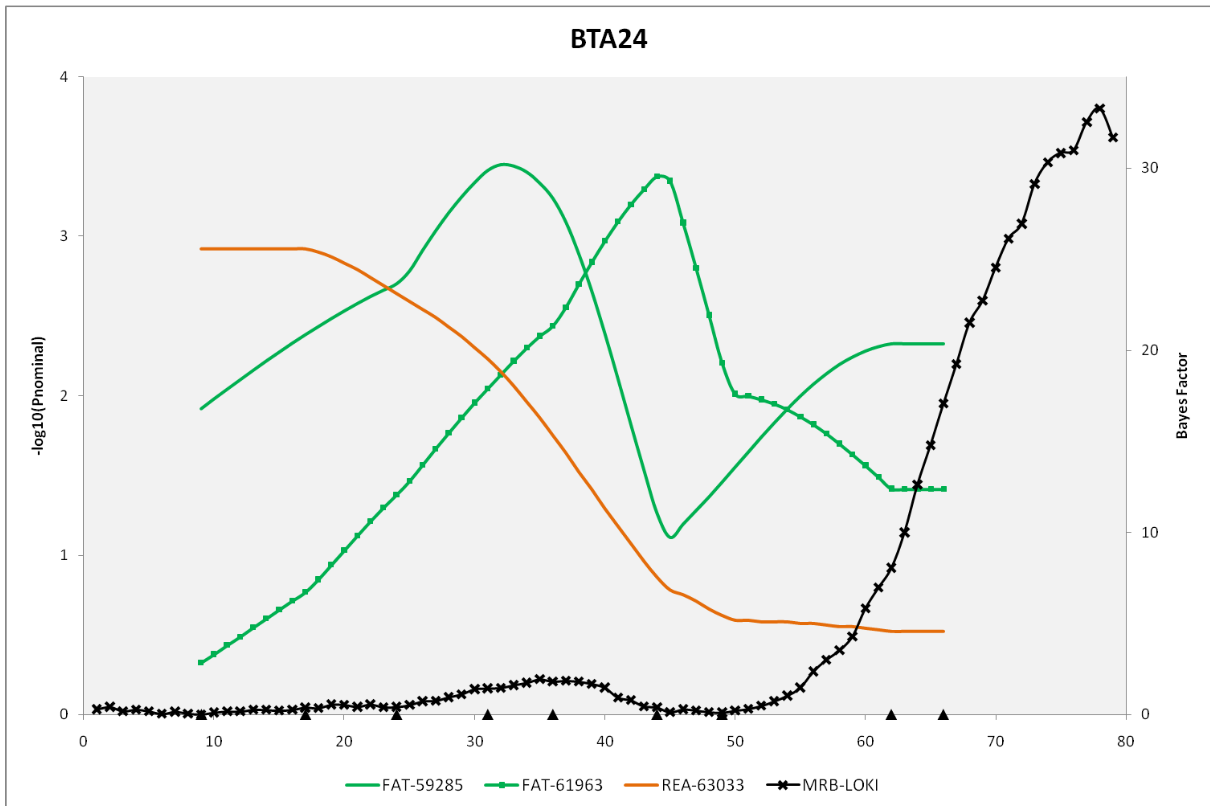
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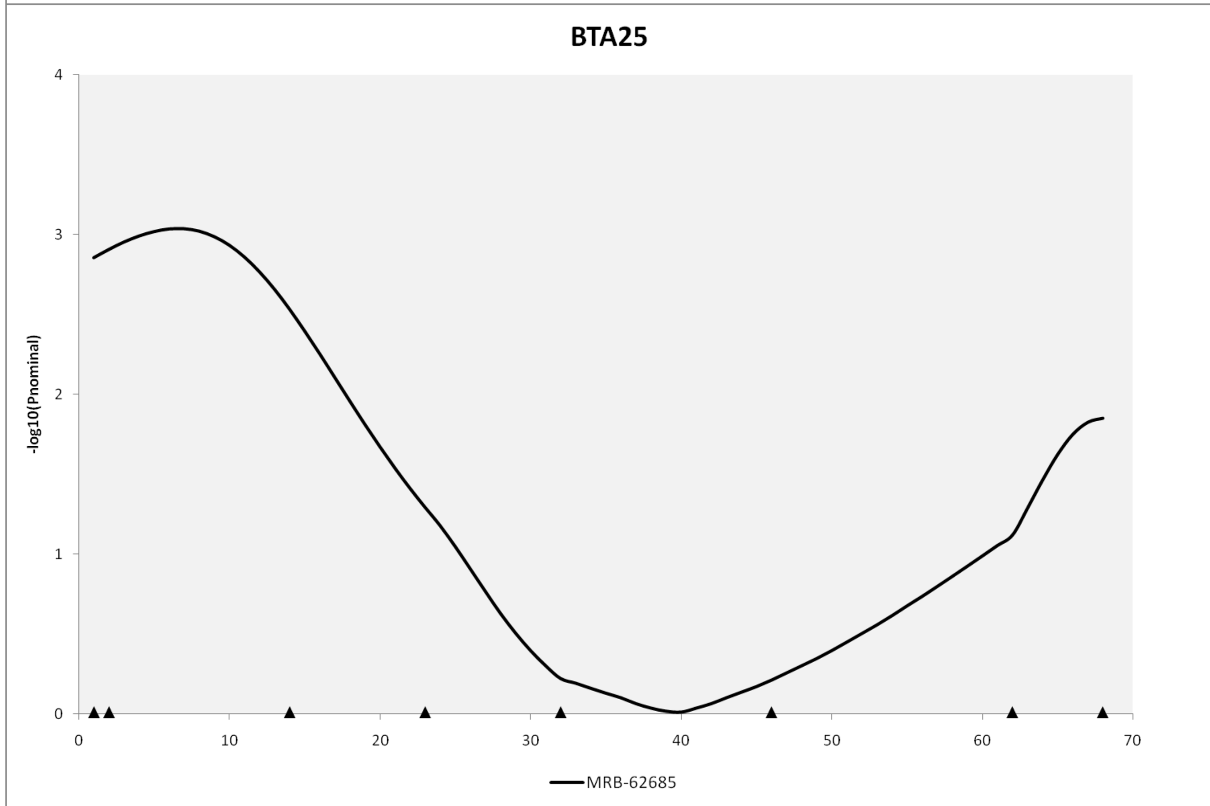
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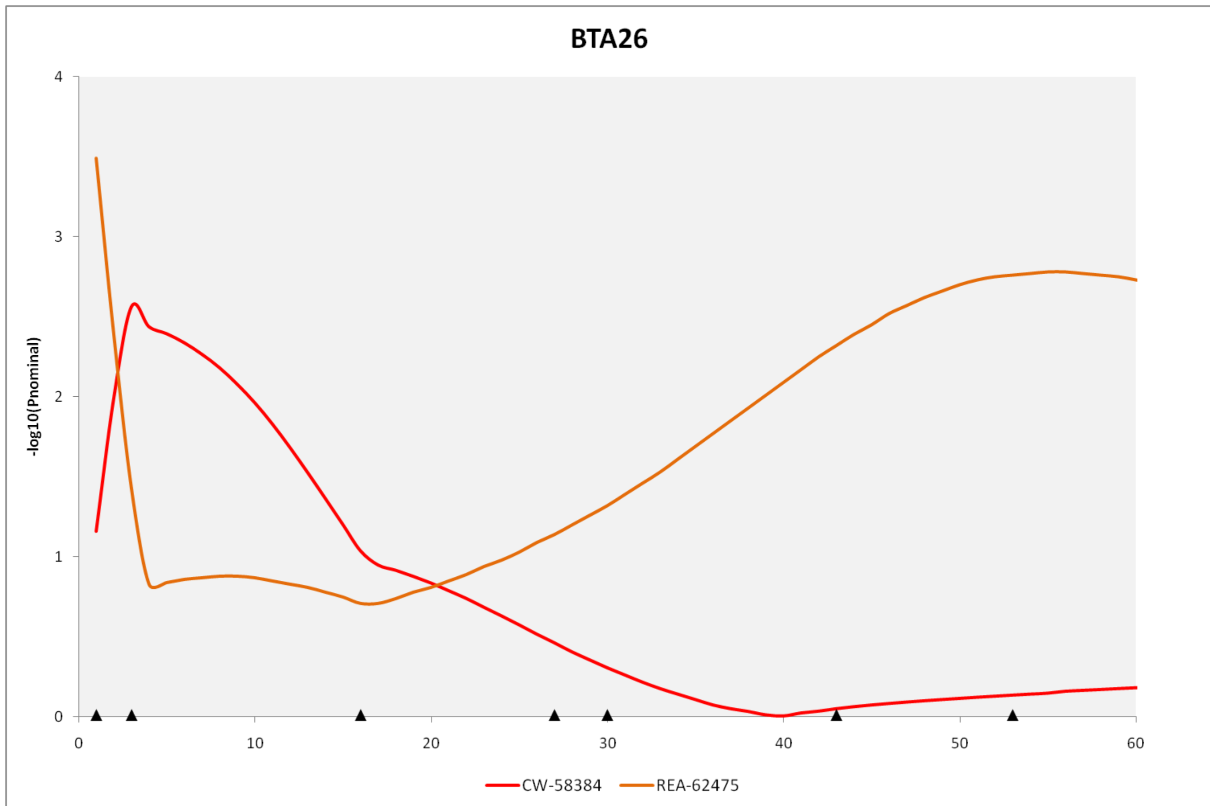
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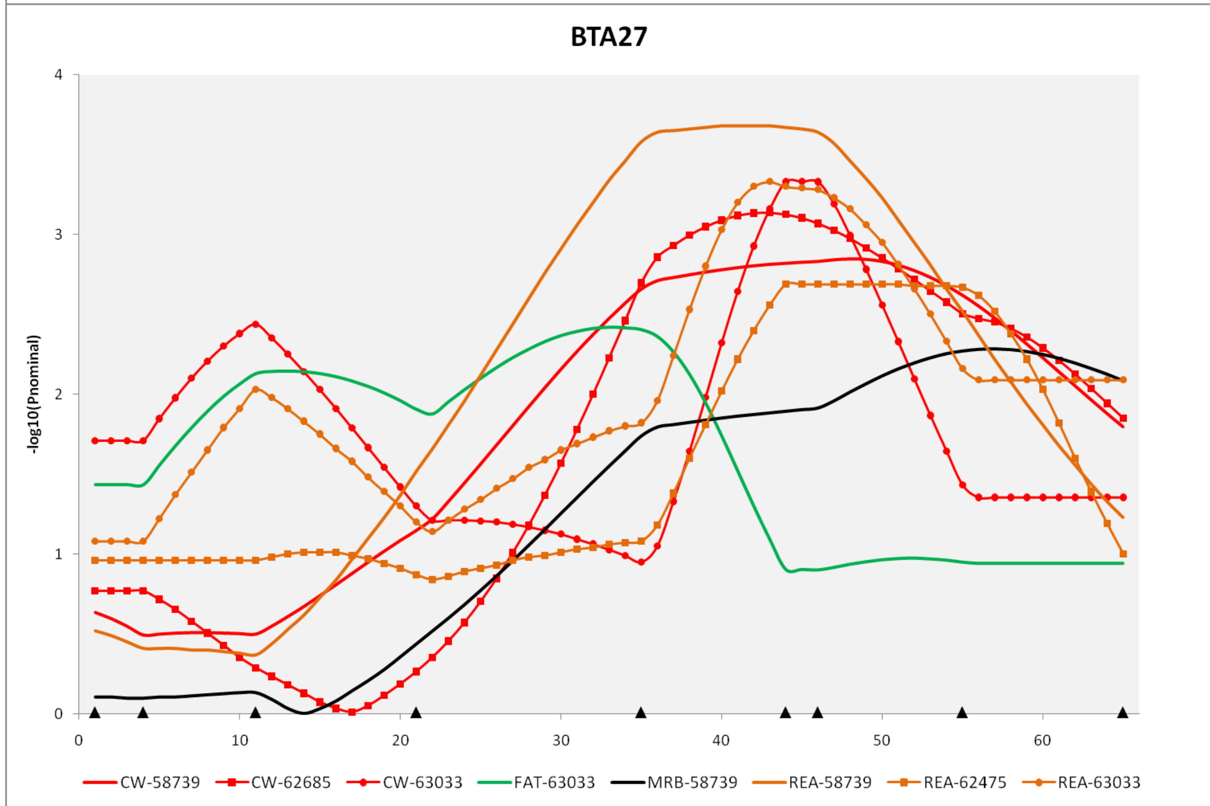
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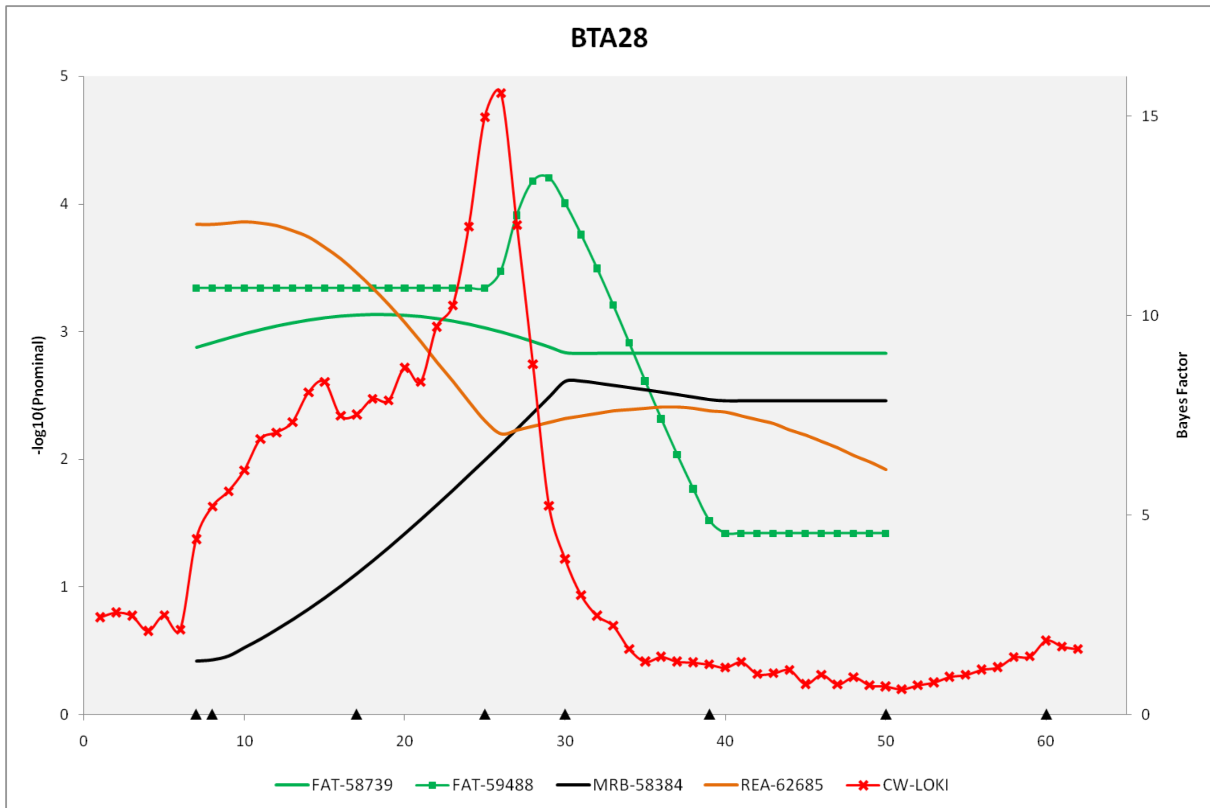
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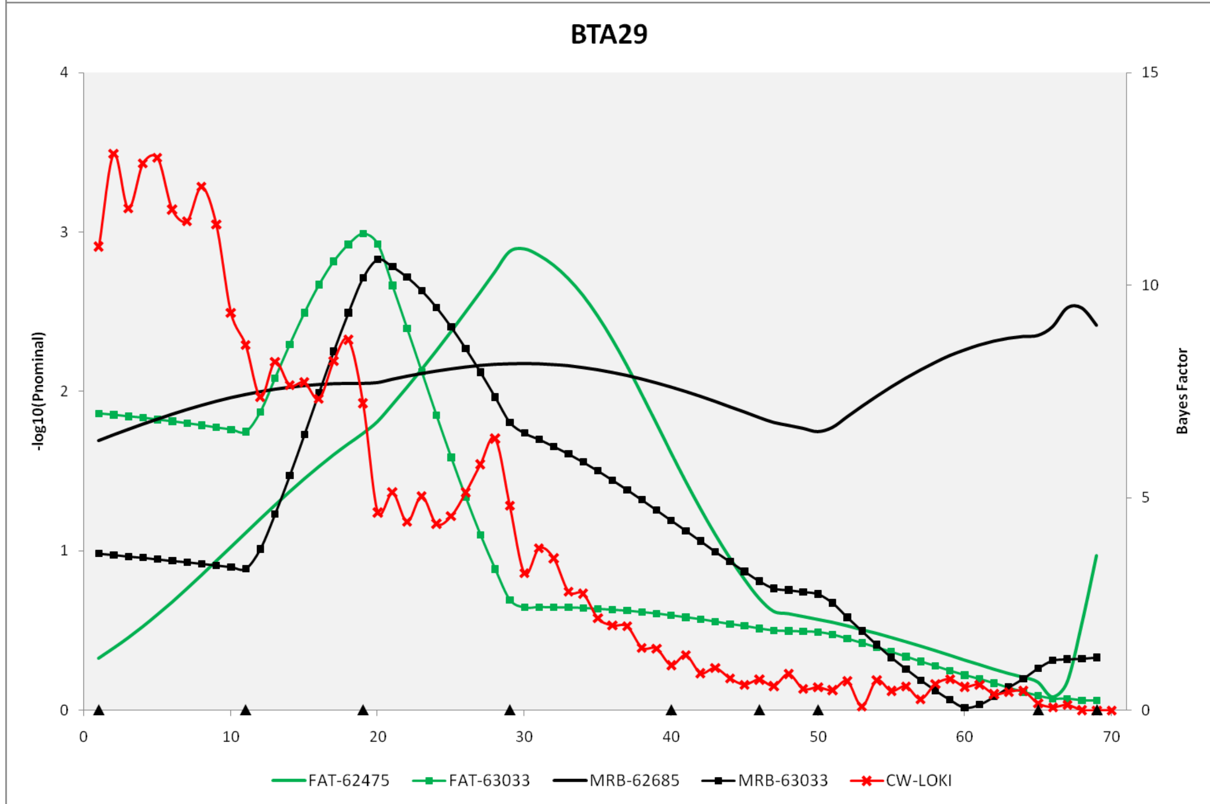
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CHAPTER 3

Genome Scan in Commercial Angus Cattle for Quantitative Trait Loci Influencing Postnatal Growth Traits

Abstract

To gain insight into the number of quantitative trait loci (QTL) that impact an animal's growth potential, a genome-wide QTL scan was conducted on a twenty-nine generation commercial American Angus population. Expected progeny differences (EPD) for mature height (MH), mature weight (MW), weaning weight (WW), yearling height (YH), and yearling weight (YW) produced for the Spring 2005 evaluation by the American Angus Association were analyzed. Two separate analytical methods were employed: half-sib least squares regression and Bayesian Monte Carlo Markov Chain modeling linkage analysis, allowing EPDs to be analyzed for both across pedigree and within family genetic variation. These analyses resulted in the identification of 173 growth QTL.: 30 MH QTL, 44 MW QTL, 28 WW QTL, 19 YH QTL, and 52 YW QTL. For each trait, between 40 and 89% of the total genetic variance was explained by the QTL detected within this population.

Introduction

In the past 60 years producers have made striking changes in the physical size of American Angus cattle (Northcutt & Wilson 1993). The power of selection is especially evident when considering that the average height of the American grand champion Angus bull has ranged in height from 3 feet in the 1950's to 6 feet in the 1990's, with a rapid return to the

current moderate size (Figure 1.4). Through the use of evolving management practices and expected progeny differences (EPD), American Angus breeders continue to alter the growth potential of cattle. To aid livestock producers with selection of superior breeding stock, researchers have identified QTL for numerous economically important traits to identify the alleles responsible for creating genetic variation within a trait. Ideally, breeding stock possessing the most beneficial QTL alleles can be identified and utilized for breeding via marker assisted selection (MAS) programs.

While MAS can be a powerful management tool, it has been limited to date by the small number of QTL that have been identified for any one trait. Many experimental designs used for QTL mapping in cattle have analyzed a limited number of parental chromosomes and therefore have detected only the few QTL that were heterozygous within these parents (Casas *et al.* 2003; Mizoshita *et al.* 2004; Alexander *et al.* 2007). Consequently, most genome scans performed in cattle have identified only a small number of QTL as influencing any one trait (Allan & Smith 2008). While over 1,375 QTL have been identified in cattle, only 4 have been reported for hip height, 4 for weaning weight, 7 for yearling weight, 12 for slaughter weight, and 28 for carcass weight (http://www.animalgenome.org/QTLdb/cattle.html, last accessed June 13, 2009). Consequently, genetic improvement in the growth rate of cattle via MAS has been hindered by a lack of sufficient numbers of QTL to explain significant amounts of the genetic variation in growth. By assembling the largest commercial beef mapping population (N=1,769) to date and by using the major American Angus bloodlines, this study analyzed the majority of the chromosomes found in the US breed for QTL that affect growth traits used by the industry. The

study's design also maximized the potential for identifying QTL of large effect that segregate within American Angus cattle.

Material and Methods

Material and methods for this study were described in Chapter 2: Genome Scan in Commercial Angus Cattle for Quantitative Trait Loci Influencing Carcass Traits.

Results

By analyzing both the within-family and across-pedigree variations, 173 QTL influencing growth were discovered: 30 MH QTL, 44 MW QTL, 28 WW QTL, 19 YH QTL, and 52 YW QTL (Table 3.1). At a chromosome-wide $P \leq 0.01$ significance level or ≥ 10 Bayes Factor (Jefferys 1961), every autosome was found to harbor multiple growth QTL (Table 3.2). Fourteen of these QTL have previously been reported in the literature: two for MH, six for MW, one for WW, one for YH, and four for YW (Table 3.1). Of the 173 possible QTL, 20 appear to be pleiotropic (Table 3.3), indicating that 153 independent growth trait QTL were identified in this study.

Each chromosome contained an average of 5 QTL, and approximately 1.2 QTL for each trait (range of 0 to 6). While an average of 9 chromosomes did not contain a QTL for an individual trait, 25 chromosomes harbored multiple QTL for a trait (Figure 3.1 and Table 3.3). The average allele substitution effect from QTL Express for MH was 0.58 in, 36.63 lb for MW, 11.11 lb for WW, 0.34 in for YH, and 17.11 lb for YW. The difference between alternate homozygote for QTL detected by LOKI were 0.13 in for MH, 20.07 lb for MW, 1.86 lb for WW, 0.03 in for YH, and 3.70 lb for YW (Table 3.4).

A general linear model analysis (SAS, v9.1) revealed that the QTL detected in this study explain a substantial amount of the genetic variation in each trait within our population (Tables 3.5, 3.6, 3.7, 3.8, and 3.9). When all QTL for a trait were included in the model, 67.33 % of the genetic variance in WW was explained, 65.62 % for MH, 80.71 % for MW, 40.46 % for YH, and 89.46 % for YW. On average a single QTL explained 2.1% of the genetic variation within a trait.

Discussion

A recent survey of the Mouse Genome Database revealed that 34% of viable knockout mice had a body weight change when compared to control mice (Reed *et al.* 2008). Although the total number of naturally occurring alleles that affect murine body weight is unknown this survey suggests that a large number of genes affect variation in growth. The results reported here imply that a large number of loci also influence the growth potential of cattle. Even though there has been considerable selection pressure on the mature size of American Angus cattle over the past 60 years a wide range in the allele frequency of economically beneficial traits remains, with the estimated average allele frequency of growth enhancing QTL alleles estimated to be 0.441 for CW, 0.488 for MH, 0.501 for MW, 0.708 for YH, and 0.488 for YW (Table 3.4). Chamberlain *et al. (*2007) found similar frequencies for milk production enhancing QTL alleles in dairy cattle.

While the amount of genetic variation explained by the QTL ranged from 40% to almost 90% these estimates are biased as they were determined in the discovery population (Lou *et* al. 2003; Xu, 1998). The allele substitution effects estimated by QTL Express in the smaller half-sib

families are likely to be overestimated (Lou *et al.* 2003). A separate population is needed to better assess the true genetic variation explained by these QTL (Van Eenennaam *et al.* 2007)

Although 20 putatively pleiotropic QTL were identified (Table 3.3), we do not have sufficient resolution to determine whether a single or multiple QTNs underlie the QTL peaks influencing both traits. The phase relationship between potentially distinct QTN cannot be identified from our analysis and because LD extends for 500 kb in cattle (McKay *et al.* 2007), therefore it is possible that selection on these pleiotropic QTL could result in divergent economic responses in both traits.

The majority of QTL individually explain small amounts of a trait's genetic variation, consequently genetic improvement programs that implement information from one, or a few economically important QTL will have little value in beef cattle. Genetic improvement decisions based on a suite of genetic markers that explain significant amounts of genetic variance in several traits are required to maximize economic gain. Integrating QTL information with available phenotypic data for the estimation of EPDs will allow producers to accurately select genetically superior animals.

Table 3.1. Growth QTL data summary.

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	QTL Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
MH	1	36.78	*BMS574*	*BMS4017*	0.536	3.77**					HH (1), WH (6)
MW	1	44.78	*BMS4017*	*TGLA57*	32.612	3.305*					
WW	1	103.5	*BM864*	*BMS4040*			19.64	0.82	-0.079	2.088	
WW	1	123.5	*BM1824*	*BMS599*	13.774	2.892*	22.35	0.84	-0.002	1.5376	
YW	1	125.5	*BM1824*	*BMS599*			14.92	0.85	0.0134	3.1655	
WW	1	144.5	*BMS599*	*BMS4014*	13.11	3.537**					
YW	1	153.5	*BMS4014*	*URB014*	23.644	3.359***	22.62	0.81	-0.008	-2.85	
MH	2	18.78	*DIK1172*	*CSSM50*	0.304	2.552*					
MW	2	30.78	*TGLA377*	*SRC23*	20.76	3.263**					
MW	2	128.78	*IDVGA2*	*FCB11*	33.597	3.294**					
MW	3	20.5	*URB006*	*BMS2904*			58.25	0.67	0.0693	25.32	
MH	3	46	*BMS482*	*BM723*	0.884	2.466*					
YH	3	55.5	*BM723*	*INRA003*			11.7	0.84	-0.001	0.0031	
MH	3	59.5	*INRA003*	*HUJ246*			15.76	0.84	0.0004	0.0454	
YW	3	71.5	*HUJ246*	*BMS1266*			12.45	0.83	-0.019	2.4389	
MW	3	76.5	*HUJ246*	*BMS1266*			11.88	0.75	0.0422	-19.29	
YW	3	127.5	*BMC4214*	*RM309*			28.19	0.85	0.0738	-5.134	

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	QTL Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
YW	4	42.5	*DIK2956*	*BMS1840*			31.75	0.82	0.0428	3.9715	
WW	4	47.5	*BMS1840*	*BMS885*			14.71	0.8	-0.015	0.9595	
YH	4	48.5	*BMS1840*	*BMS885*			10.12	0.85	0.0005	0.0013	
YW	4	50.5	*BMS1840*	*BMS885*			38.16	0.84	-0.014	4.4641	
YW	4	86.5	*BMS2809*	*UASMS2*			39.6	0.84	-5E-04	-7.09	
MW	4	87.5	*Lep_Ex2*	*RM088*			199.8	0.58	-0.014	-33.5	
YW	4	105.5	*BR6303*	*AGLA227*			18.24	0.82	0.0487	-3.063	
YW	4	110.5	*AGLA227*	*DIK4542*			18.29	0.82	-0.047	-0.833	
YW	5	88.5	*RM029*	*BMS1248*			29.96	0.8	-0.102	-4.269	YW (3,4)
WW	5	92.5	*BMS1248*	*BM315*			10.33	0.82	0.0121	-2.412	
MW	5	94.5	*BMS1248*	*BM315*	38.105	4.182**	13.24	0.78	-0.015	26.081	
YW	5	100.5	*BMS1248*	*BM315*			32.5	0.8	-0.047	-4.403	YW (3)
MH	5	111	*RM029*	*BM2830*	0.515	2.822*					HH (1)
MW	5	116.5	*BMS1658*	*BM2830*			220.77	0.63	0.0599	33.039	
YH	6	57.5	*BM143*	*DIK082*	0.283	2.08*					HH (1)
WW	6	61	*DIK082*	*BMS360*	8.032	2.795*					
MW	6	62	*DIK082*	*BMS360*	36.041	3.631*					
MH	6	95	*CSN3*	*BM8124*	0.433	2.917*					

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	QTL Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
YW	7	9.5	*RM012*	*DIK4378*			38.7	0.85	0.0241	-7	
WW	7	11.5	*RM012*	*DIK4378*			11.46	0.8	0.002	1.3714	
YW	7	17.5	*DIK4378*	*RM006*			31.34	0.83	-0.021	-6.658	
WW	7	18.5	*DIK4378*	*RM006*			11.54	0.8	-0.017	-0.018	
MH	7	19.5	*DIK4378*	*RM006*			10.91	0.87	0.0085	-0.144	
WW	7	25.5	*RM006*	*IL4*			31.57	0.85	-0.019	1.9948	
MH	7	36.5	*IL4*	*BM6105*			29.88	0.89	0.0073	-0.2	
YW	7	54.5	*DIK2819*	*UWCA20*			48.34	0.86	0.0524	-9.504	
YW	7	73.5	*BMS2840*	*BMS2258*			12.72	0.81	0.0069	2.2861	
MW	7	77	*BMS2840*	*BMS2258*	40.968	3.314**					
YW	7	107.5	*BM9065*	*ILSTS006*			12.47	0.84	0.0855	-6.662	
MW	7	134	*BMS1247*	*BL1043*	42.117	2.968*					
MH	7	135	*BMS1247*	*BL1043*	0.372	3.724**					
YW	7	135.3	*BMS1247*	*BL1043*			10.81	0.83	0.0693	1.1046	
MH	8	7.5	Centromeric	*IDVGA11*			21.06	0.89	0.0026	-0.182	
WW	8	10.5	Centromeric	*IDVGA11*			27.89	0.85	0.0271	-5.38	
MW	8	39.5	*BP2*	*BMS678*			19.3	0.82	0.0568	22.974	
MW	8	49.5	*BMS678*	*BM4006*			55.8	0.7	-0.04	31.97	
YH	8	74.34	*MCM64*	*DIK2868*	0.349	3.812**					
WW	8	97.5	*BM711*	*CSSM047*			14.07	0.84	-0.011	-1.779	
WW	8	120.5	*CSSM047*	*BMS836*			15.33	0.83	0.046	1.8541	
YW	8	121.5	*CSSM047*	*BMS836*			14.98	0.8	-0.139	3.0526	

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	QTL Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
YW	9	9.5	*BM757*	*ETH225*			16.81	0.82	0.0775	2.7391	
WW	9	11.5	*BM757*	*ETH225*			15.1	0.81	0.0144	0.5289	
YW	9	25.5	*BM1227*	*BMS817*			12.51	0.82	-0.098	4.2753	
MW	9	58.5	*BMS434*	*BMC701*			45.89	0.79	0.0038	-28.05	LW (5)
MW	9	71.5	*BMS2377*	*BMS1724*			91.64	0.64	-0.006	-19.41	
MW	9	90.89	*BM4208*	*BMS2295*	28.591	2.857*					
MH	10	34.86	*BMS528*	*BRN*	0.515	3.72**					
MW	10	34.86	*BMS528*	*BRN*	30.721	3.592*					
YW	11	17.5	*INRA044*	*BMS2325*			12.13	0.79	0.0447	2.1125	YW (3)
WW	11	20.5	*INRA044*	*BMS2325*			17.43	0.81	0.0096	-2.984	YW (3)
WW	11	66.5	*ILSTS036*	*RM150*			11.76	0.81	-0.053	1.5359	
YW	11	67.5	*ILSTS036*	*RM150*			14.19	0.84	-0.022	2.2486	
YW	11	75.5	*RM150*	*IDVGA3*			29.17	0.84	0.0597	4.2935	
YW	11	94.5	*BMS989*	*BL1103*			60.2	0.79	0.007	-6.101	
MH	12	1	*BMS410*	*TGLA36*	0.37	3.519**					
YH	12	12	*TGLA36*	*BMS2252*	0.383	2.731*					
MH	12	54	*BM1827*	*BMS975*	0.542	3.234*					
YW	12	54.5	*BM1827*	*BMS975*			15.9	0.83	0.0245	2.0793	
MW	12	59.5	*BM1827*	*BMS975*			20.96	0.89	-0.17	-32.45	
YW	12	67.5	*BMS975*	*BM4028*			15.97	0.82	-0.095	-1.1	
MW	12	80.5	*BMS975*	*BM4028*	59.836	4.466***	53.54	0.94	-1E-04	10.688	LW (5)
MW	12	93.5	*INRA5*	*BMS1316*			46.87	0.96	0.0661	17.438	
MW	12	104.5	*BMS1316*	*BMS2724*	33.618	3.44**					
YW	12	107.5	*BMS1316*	*BMS2724*			24.33	0.81	-0.03	4.0058	

		QTL Peak[1]			QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	QTL Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
WW	13	27.5	*TGLA23*	*BMC1222*			13.66	0.79	-0.036	-2.223	
WW	14	4.5	*DGAT*	*CSSM66*			10.05	0.74	0.0096	1.1178	
MH	14	5	*DGAT*	*CSSM66*	0.438	2.469*					
MH	14	41	*RM180*	*RM011*	0.618	2.684*					
YW	14	70.5	*BMS947*	*NRKM020*			21.15	0.82	0.0488	-3.328	
MH	14	76	*NRKM020*	*DIK2742*	0.642	3.177**					
YW	14	96	*BM6425*	*BL1036*	17.497	2.438*					
MW	14	97.5	*BM6425*	*BL1036*			13.07	0.71	0.0186	5.6285	
MW	14	103.5	*BL1036*	Telomeric			22.53	0.65	0.0204	-8.714	
WW	15	5.5	*DIK2777*	*MGTG13B*			14.98	0.85	-0.044	2.4354	
WW	15	12.5	*BR3510*	*ADCY2*			18.49	0.85	0.0136	2.3655	
MH	15	46	*HEL1*	*MBO76*	1.155	3.17*					
MH	15	76	*INRA046*	*DIK2768*	0.67	3.589**					
MH	15	85	*BMS812*	*BL1095*	0.737	3.445**					
MW	15	85	*BMS812*	*BL1095*	30.387	2.586*					
MH	16	6.91	*TGLA245*	*BMS1348*	0.458	2.227**					
YH	16	16.91	*BMS1348*	*BY22*	0.25	2.559*					
MW	16	18.91	*BMS1348*	*BY22*	42.528	2.565*					LW (5)
YW	16	36.5	*BY22*	*TGLA53*			17.42	0.82	0.0171	-4.339	
YW	16	94.25	*DIK4437*	*BMS462*			13.25	0.8	0.0356	-3.751	
YW	17	8	*BMS1825*	*DIK5379*	10.792	2.671*					
MW	17	61.5	*DIK2668*	*BM8125*			16.64	0.97	-2E-04	19.811	LW (5)
MW	17	85	*BM1862*	*BM1233*	26.65	3.105*					
YW	17	92.5	*BM1233*	Telomeric			18.38	0.8	0.0219	-5.506	

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	QTL Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
MW	18	0.5	Centromeric	*BMS1355*			114.64	0.92	-0.127	-16.3	
MW	18	18.5	*BMS1322*	*BMS2213*	36.874	3.819**	13.47	0.91	-0.101	-7.594	
WW	18	40.5	*BR4406*	*BM7109*	11.258	2.937*					
YH	18	81.86	*BM2078*	*TGLA227*	0.223	3.402**					
MW	19	0	*BM9202*	*BM6000*	27.34	3.586*					
WW	19	5.5	*BM6000*	*BMS745*			17.96	0.83	0.0158	-2.79	
YW	19	15.5	*BM6000*	*BMS745*			17.56	0.81	-0.039	-2.197	
YW	19	26.5	*X82261*	*BMS2142*			11.59	0.82	-0.058	-0.854	
WW	19	56.5	*BMS2142*	*BMS650*			21.81	0.81	0.0437	1.7462	
MW	19	75.5	*CSSM065*	*IDVGA44*			16.47	0.65	-0.181	-32.04	
YH	19	80	*CSSM065*	*IDVGA44*	0.29	3.748**					
YW	19	95.5	*RM388*	*BMC1013*			10.76	0.84	-0.031	4.6752	
YW	20	10.5	*BM1225*	*BMS1282*			25.03	0.79	0.0097	-4.454	
WW	20	15.5	*BM1225*	*BMS1282*			24.91	0.79	-0.02	-2.721	
YW	20	25.5	*BMS1282*	*DIK2467*			16.88	0.8	0.0062	-2.42	
WW	20	26.5	*DIK2467*	*DIK5354*			24.94	0.81	0.0352	-2.964	
MW	20	47.5	*GHR*	*BMS703*	41.269	2.947**	24.9	0.55	-0.021	-6.687	

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	QTL Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
WW	21	26.5	*ILSTS095*	*BM103*			10.94	0.81	-0.045	2.09	
YW	21	35.5	*BM103*	*BMS2557*			10.08	0.79	0.1162	-4.374	
YH	21	36	*BMS2557*	*RM222*	0.224	2.65*					
MW	21	36.5	*BMS2557*	*RM222*			15.77	0.89	-0.085	6.2397	
MH	21	40	*BMS2557*	*RM222*	0.548	3.104*					
YW	21	61.5	*BM846*	*ILSTS054*			43.54	0.87	0.008	3.7013	
MH	21	74.5	*ILSTS054*	*BMS743*			12.99	0.9	-0.001	0.1388	
YH	21	74.5	*ILSTS054*	*BMS743*			16.73	0.86	-0.002	0.0514	
YW	22	19.5	*BM1558*	*DIK2694*			11.21	0.81	0.1324	-3.501	
YH	22	27	*BM1558*	*DIK2694*	0.307	2.453*					
MH	22	48	*BM3628*	*BM2613*	0.316	3.116*					
YW	22	68	*BMS875*	*OARFCB304*	22.153	3.59***					
YH	22	76	*OARFCB304*	*BM4102*	0.216	2.685*					
MW	22	78	*OARFCB304*	*BM4102*	26.213	4.289***					
YH	22	85	*BM4102*	*DIK115*	0.213	2.58*					
MH	23	5.7	*INRA132*	*SRC119*	0.382	4.056**					
MW	23	16.7	*BM47*	*UWCA1*	23.098	4.062**					LW (2), SW (3)
YW	23	26.7	*UWCA1*	*BOLADRB1*	17.793	2.992*					
MW	23	73.7	*BM1905*	*BM1443*	33.989	3.731**					
YW	24	7.5	Centromeric	*BMS2526*			10.59	0.81	0.0167	-0.439	
YH	24	49.15	*BMS466*	*BMS1926*	0.186	2.516*					
YW	24	51.5	*BMS466*	*BMS1926*			20.93	0.85	0.0087	4.9852	
MW	24	61.5	*BMS1926*	*BMS3024*	46.99	2.572*	54.34	0.93	0.1729	-11.89	

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	QTL Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
YW	25	9.5	*RM074*	*BMS130*			19.35	0.84	0.0311	4.7212	YW (3)
WW	25	14.5	*BMS130*	*BMS2843*			19.7	0.83	0.0329	-1.744	
YW	25	28.5	*BMS2843*	*BM737*			20.11	0.87	-0.006	3.6484	
WW	25	37.5	*BM737*	*BMS1353*			10.42	0.82	0.0236	-0.01	
YW	25	41.5	*BM737*	*BMS1353*			14.35	0.86	0.0085	3.0863	
WW	25	52.59	*BMS1353*	*AF5*	9.369	1.94*					
YW	25	62.59	*AF5*	*BM1864*	16.57	3.131*					
MH	25	66.59	*AF5*	*BM1864*	0.471	3.744**					
MH	26	15.5	*BMS651*	*FASMC2*			19.76	0.87	0.0009	-0.138	
YH	26	15.5	*BMS651*	*FASMC2*			13.28	0.84	0.0004	-0.06	
YH	26	25	*FASMC2*	*INRA081*	0.565	2.784*					
MH	26	28	*FASMC2*	*INRA081*	0.889	7.486***					
MW	26	29	*BM1314*	*INRA081*	50.981	4.168***					
YW	26	42.5	*INRA081*	*BMS2567*	11.328	2.6*	14.98	0.81	-0.046	-4.818	
MW	26	60	*BMS2567*	*BM804*	35.243	3.427*					
MW	27	5.5	*BMS2168*	*BM6526*			35.1	0.71	0.0372	16.114	
MW	27	22.5	*BMS2137*	*CSSM043*			47.67	0.78	-0.125	15.626	
MH	27	34	*BMS2137*	*CSSM043*	0.347	2.557*					
YH	27	39	*CSSM043*	*CSSM36*	0.351	4.779***					
MH	28	24.5	*IDVGA29*	*BMS510*	0.832	3.047*	11.5	0.82	-0.003	0.0918	
MW	28	24.5	*IDVGA29*	*BMS510*	39.207	2.567*					
YH	28	29.5	*BL25*	*BMS2608*	0.616	2.96*					

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	QTL Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
MW	29	18.92	*BMS764*	*BMS1787*	38.496	2.435*					
MH	29	25.92	*BMS1787*	*BMS1600*	1.068	3.343**					
MW	29	32.92	*BMS1600*	*RM040*	56.116	3.366**					LW (5)
YH	29	33.92	*BMS1600*	*RM040*	0.681	3.827***					
YW	29	34.5	*BMS1600*	*RM040*			12.25	0.84	-0.025	4.2452	
YW	29	53.5	*BL1100*	*BMS1948*			14.82	0.84	-0.001	4.391	

[1] Listed iare each QTL's most likely location in cM, flanking markers, associated information from QTL Express and LOKI, and whether the QTL has previously been identified.

[2] Significance levels for QTL Express: *=P ≤ chromosome-wide 0.01, **=P ≤ genome-wide 0.05, ***=P ≤ genome-wide 0.01. Freq_1 is the frequency of the 1 allele; effect values estimated in LOKI assume that the 11 genotype has an effect of 0.

[3] Abbreviations: weaning weight (WW); mature height (MH); mature weight (MW); yearling height (YH), yearling weight (YW); hip height (HH); withers height (WH); live weight (LW); slaughter weight (SW).

[4] References: 1= (Boichard *et al.* 2003) 2=(Elo *et al.* 1999); 3=(Kim *et al.* 2003); 4=(Machado *et al.* 2003); 5=(MacNeil & Grosz 2002); 6=(Malau-Aduli *et al.* 2005).

Table 3.2. Count of growth QTL by chromosome.

Trait	*Bos taurus autosome*																												
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
Mature Height	1	1	2		1	1	3	1		1		2		3	3	1					2	1	1		1	2	1	1	1
Mature Weight	1	2	2	1	2	1	2	2	3	1				2	1	1	2	2	2	1	1	1	2	1		2	2	1	2
Weaning Weight	3			1	1	1	3	3	1		2		1	1	2			1	2	2	1				3				
Yearling Height			1	1		1		1				1				1		1	1		2	3		1		2	1	1	1
Yearling Weight	2		2	5	2		6	1	2		4	3		2		2	2		3	2	2	2	1	2	4	1			2
Pleiotropic	1		1	2	2		2	1	1	1	1	0			1	1				1	1	1		0	1	2		1	1
Total	6	3	6	6	4	4	12	7	5	1	5	6	1	8	5	4	4	4	8	4	7	6	4	4	7	5	4	2	5

Table 3.3. Summary of growth QTL identified as pleiotropic.

BTA	Position	Trait 1	Trait 2	Trait 3	Express 1	LOKI 1	Express 2	LOKI 2	Express 3	LOKI 3
1	124.00	WW	YW		13.774	1.538		3.166		
3	57.50	YH	MH			0.003		0.045		
4	48.00	WW	YW	YH		0.960		4.464		0.001
4	87.00	YW	MW			-7.090		-33.497		
6	61.50	WW	MW		8.032		36.041			
7	18.50	WW	YW	MH		-0.018		-6.658		-0.144
7	135.00	YW	MW	MH		1.105		42.117		0.372
8	121.00	WW	YW			1.854		3.053		
9	10.00	WW	YW			0.529		2.739		
10	34.86	MW	MH		30.721		0.515			
11	67.00	WW	YW			1.536		2.249		
15	85.00	MW	MH		30.387		0.737			
16	17.50	YH	MW		0.250		42.528			
20	26.00	WW	YW			-2.963		-2.420		
21	74.50	YH	MH			0.051		0.139		
22	77.00	YH	MW		0.216		26.213			
25	64.50	YW	MH		16.570		0.471			
26	15.50	YH	MH			-0.060		-0.138		
26	28.00	YH	MW	MH	0.565		50.981		0.889	
28	25.00	YH	MH	MW	0.616		0.832	0.092	39.207	
29	34.00	YH	MW		0.681		56.116			

Express 1, 2, 3 and LOKI 1, 2, 3 are the allele substitution effect from QTL Express and the difference between alternate homozygotes for traits 1, 2, and 3 respectively.

Table 3.4. Statistical summary of growth QTL.

Trait	QTL Count	Reference Count	LOKI		QTL Express	EPD					Acc >0.05
			Freq [1]	Effect [2]	Effect [3]	StDev	Var	Kurt	Skew	Count [4]	Count [5]
Mature Height	30	2	0.488	0.130	0.577	0.650	0.4	0.6	0.1	1830	1325
Mature Weight	44	6	0.501	20.069	36.629	37.52	1407.7	0.6	-0.2	1830	1325
Weaning Weight	28	1	0.558	1.861	11.109	14.41	207.7	0.0	-0.4	1998	1992
Yearling Height	19	1	0.708	0.033	0.342	0.420	0.2	0.9	0.3	1956	1630
Yearling Weight	52	4	0.488	3.694	17.111	26.48	701.3	0.0	-0.5	1998	1991

[1] The average frequency of the economically desirable allele as determined by LOKI.
[2] The average effect of the economically desirable homozygote as determined by LOKI.
[3] The allele substitution effect economically desirable allele as determined by QTL Express.
[4] Count of animals with an EPD value recorded.
[5] Count of animals with an EPD accuracy value >0.05.
Statistical information is based the EPDs from the mapping population.

Table 3.5. Analysis of variance results for weaning weight QTL.

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	792	277245	350.056	3.01	<.0001
Error	1158	134509	116.156		
Corrected Total	1950	411753			

R-Square	0.6733
Coeff Var	32.3912
Root MSE	10.7776
Mean	33.2732

Table 3.6. Analysis of variance results for mature height QTL.

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1118	991891	887.20	1.42	<.0001
Error	832	519617	624.54		
Corrected Total	1950	1511508			

R-Square	0.6562
Coeff Var	-310.4931
Root MSE	24.9908
Mean	-8.0487

Table 3.7. Analysis of variance results for mature weight QTL.

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1311	4055926	3093.77	2.04	<.0001
Error	639	969389	1517.04		
Corrected Total	1950	5025315			

R-Square	0.8071
Coeff Var	213.1793
Root MSE	38.9492
Mean	18.2706

Table 3.8. Analysis of variance results for yearling height QT.

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	636	160300	252.044	1.4	<.0001
Error	1314	235883	179.515		
Corrected Total	1950	396183			

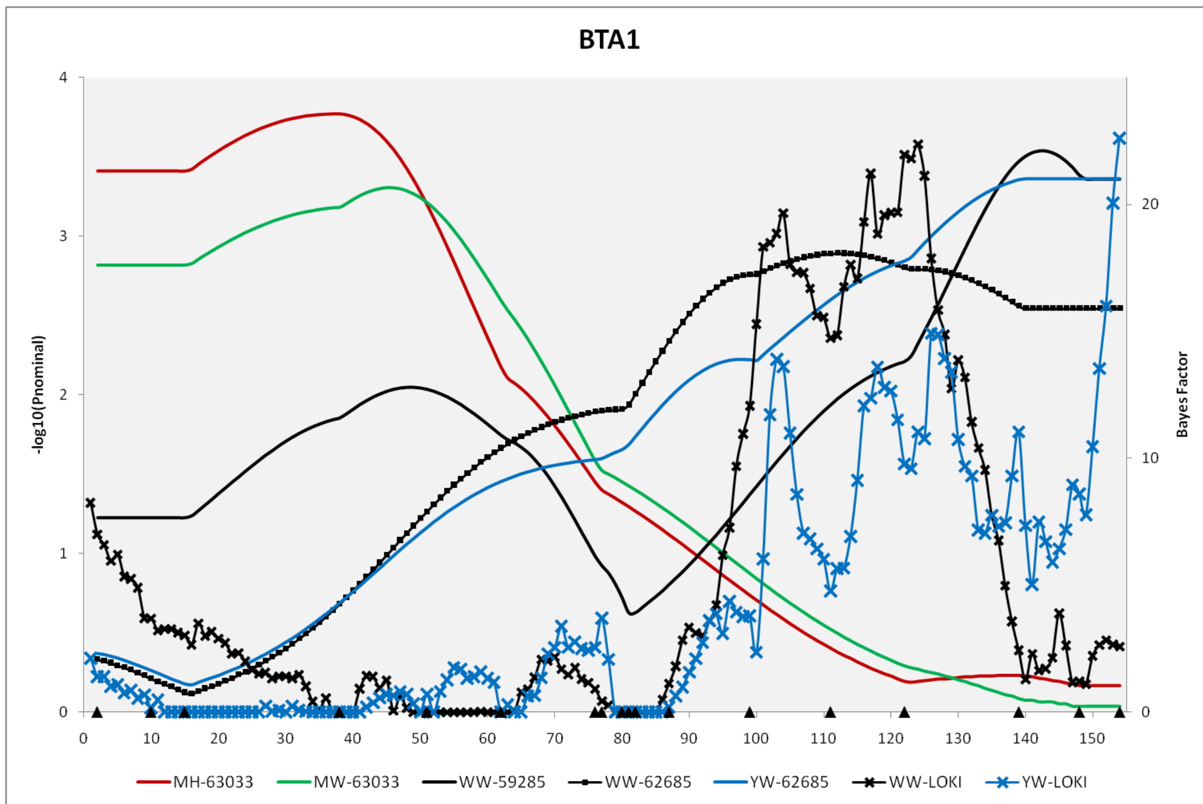
R-Square	0.4046
Coeff Var	-752.4813
Root MSE	13.3983
Mean	-1.7806

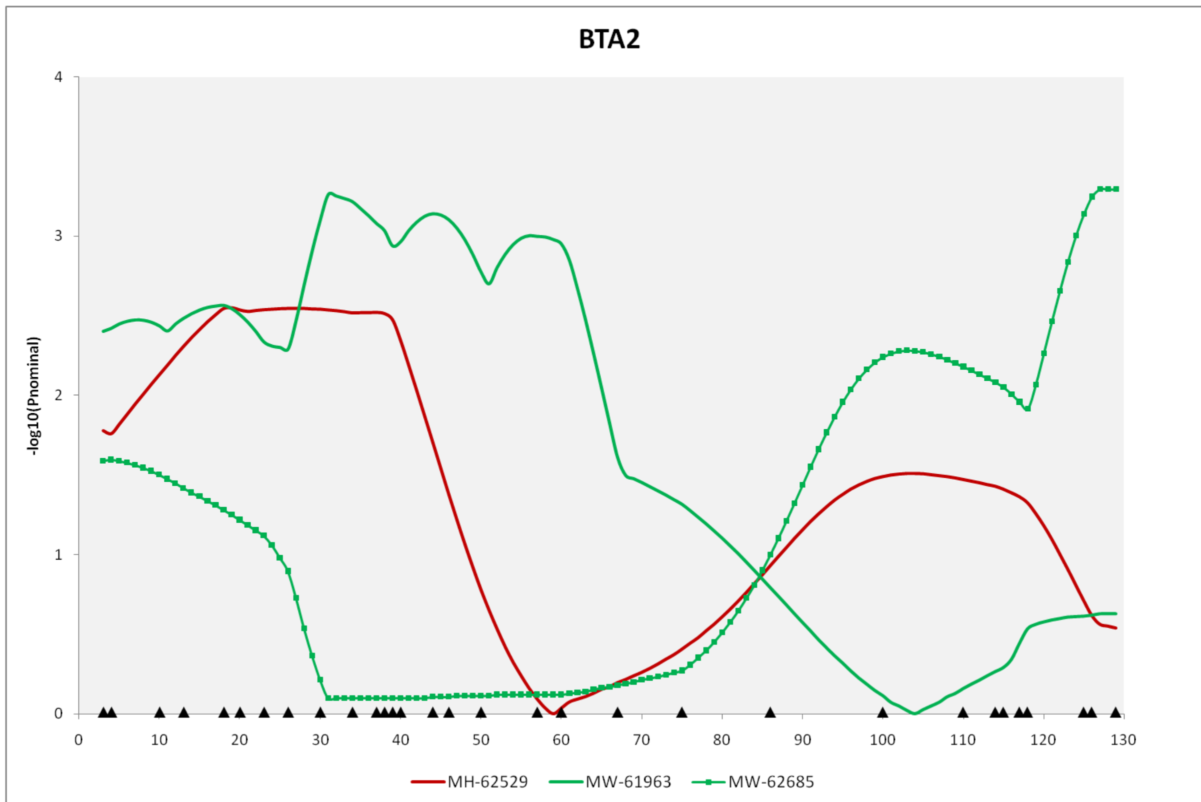
Table 3.9. Analysis of variance results for yearling weight QTL.

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1495	1255183	839.587	2.58	<.0001
Error	455	147929	325.118		
Corrected Total	1950	1403112			

R-Square	0.8946
Coeff Var	29.3531
Root MSE	18.0310
Mean	61.4280

Figure 3.1. Growth QTL graphs for each *B. taurus* autosome. Plots are for half-sib data analyzed from American Angus sire linage by QTL Express, unless indicated from LOKI. QTL Express data are expressed in $-\log_{10}P_{nominal}$ values units while LOKI data are express as Bayes Factors. Colored lines represent different traits as follows: red = MH; green = MW; black = WW; gold = YH; and blue = YW. Significance levels for QTL Express are as follows: chromosome-wide $P\leq0.01$ = 2.8, genome-wide $P\leq0.05$ = 3.3, genome-wide $P\leq0.01$ =4.1. Significance levels for LOKI are $\geq$10. All X-axis values are in cM, ▲ represent genomic markers.

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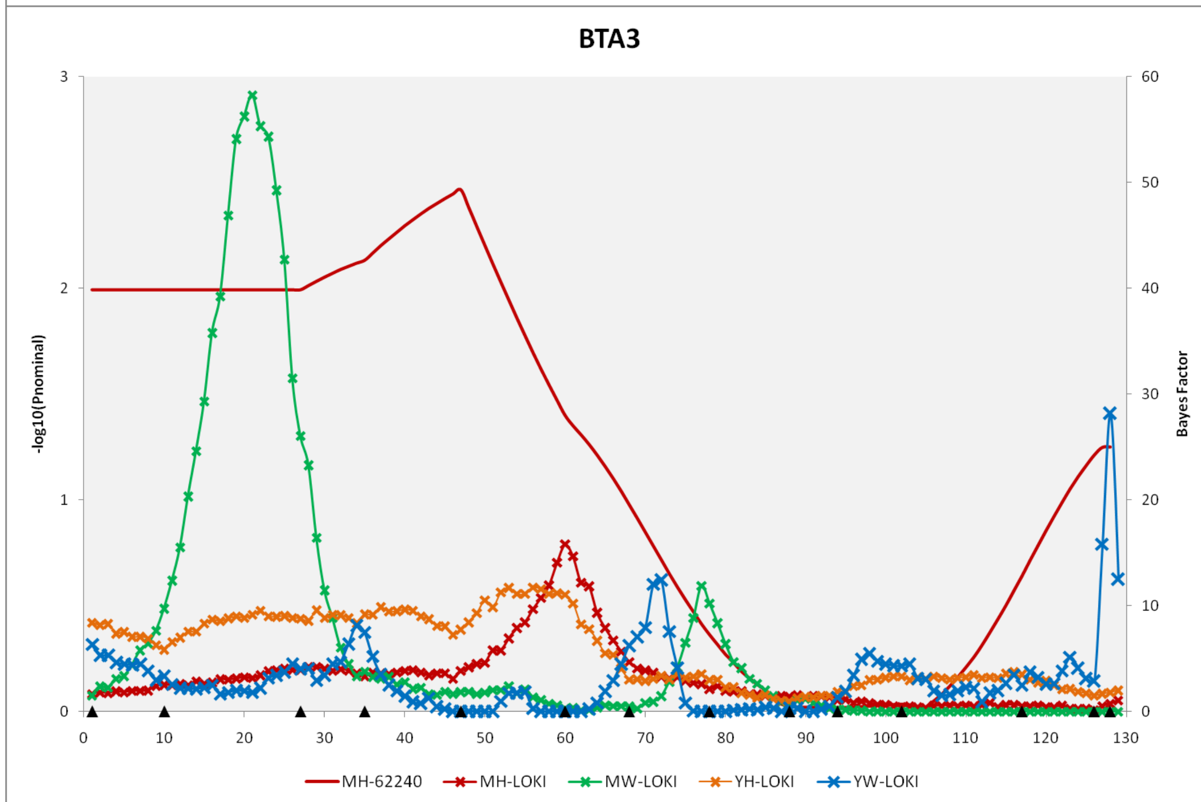
MW-62685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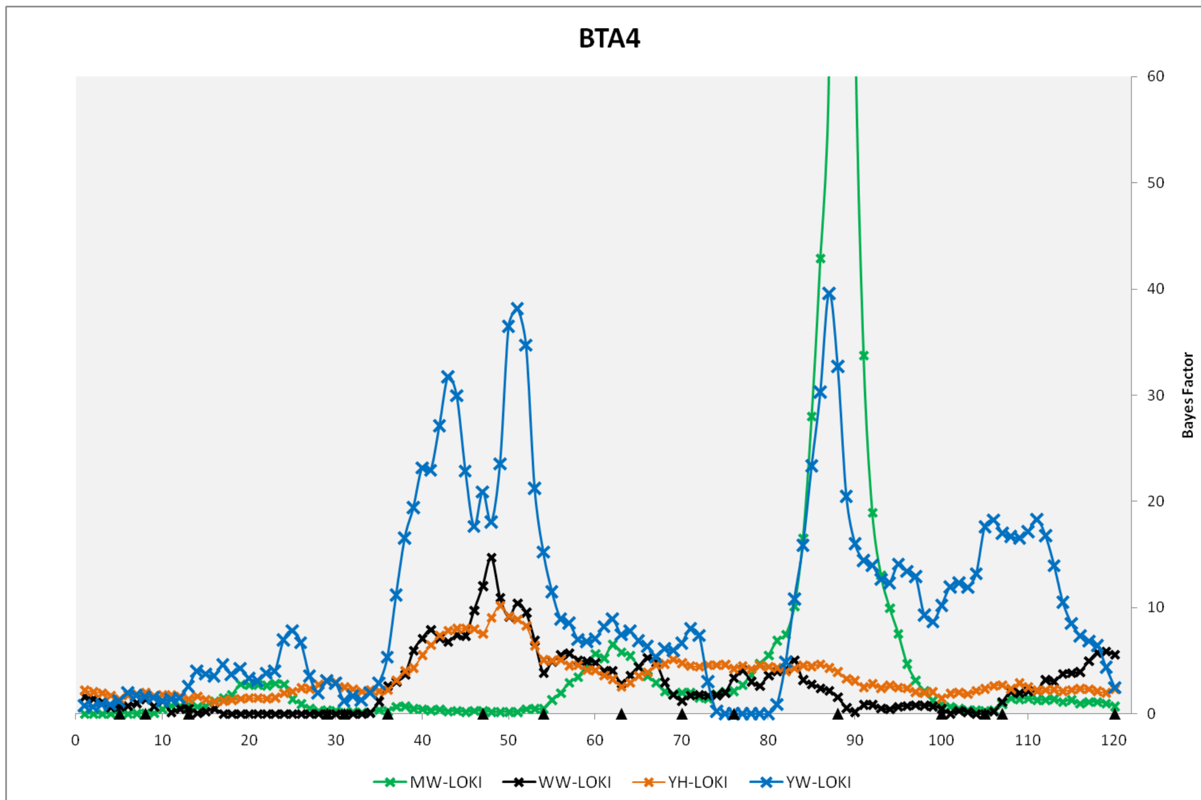
YW-LOKI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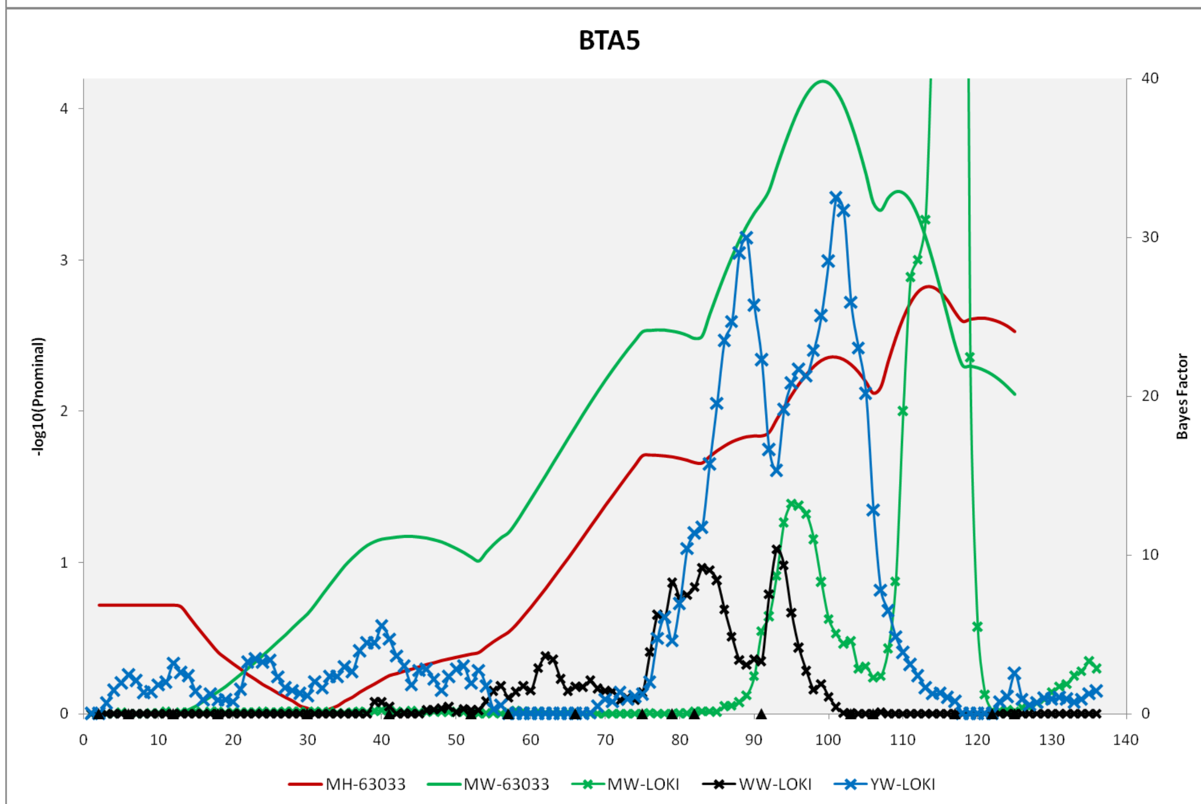
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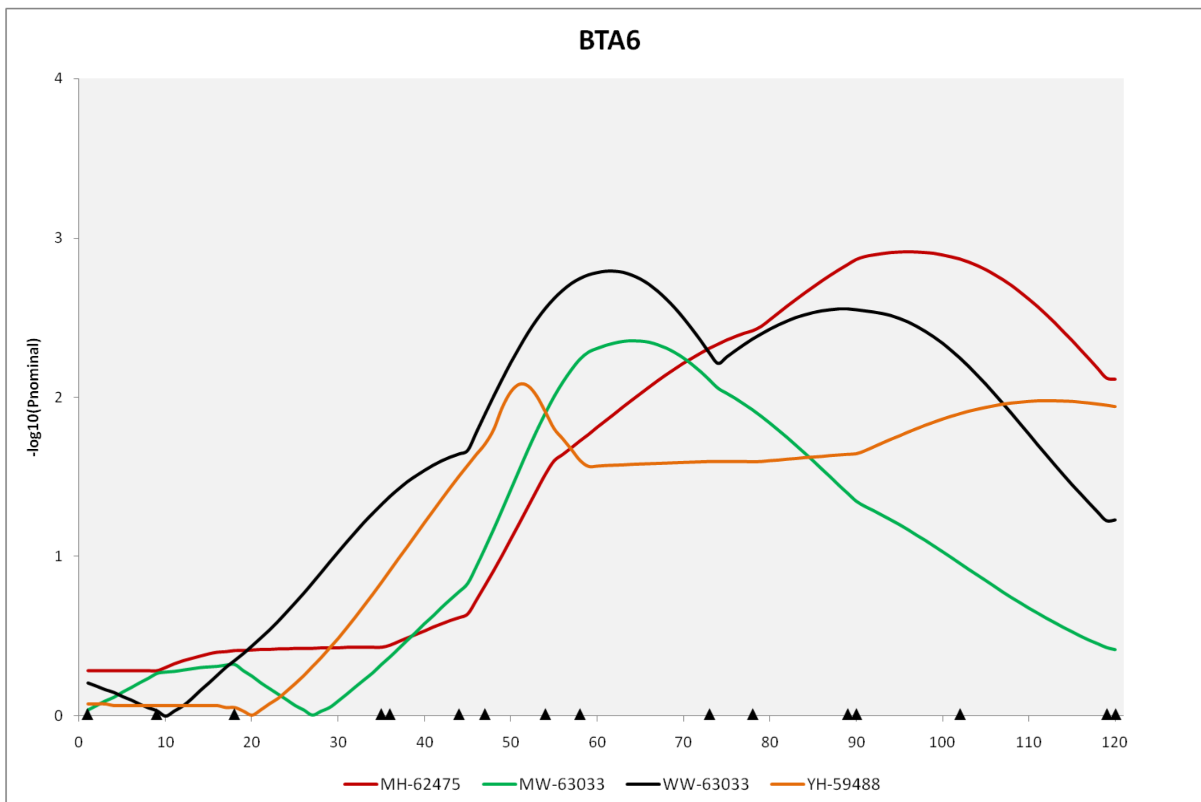

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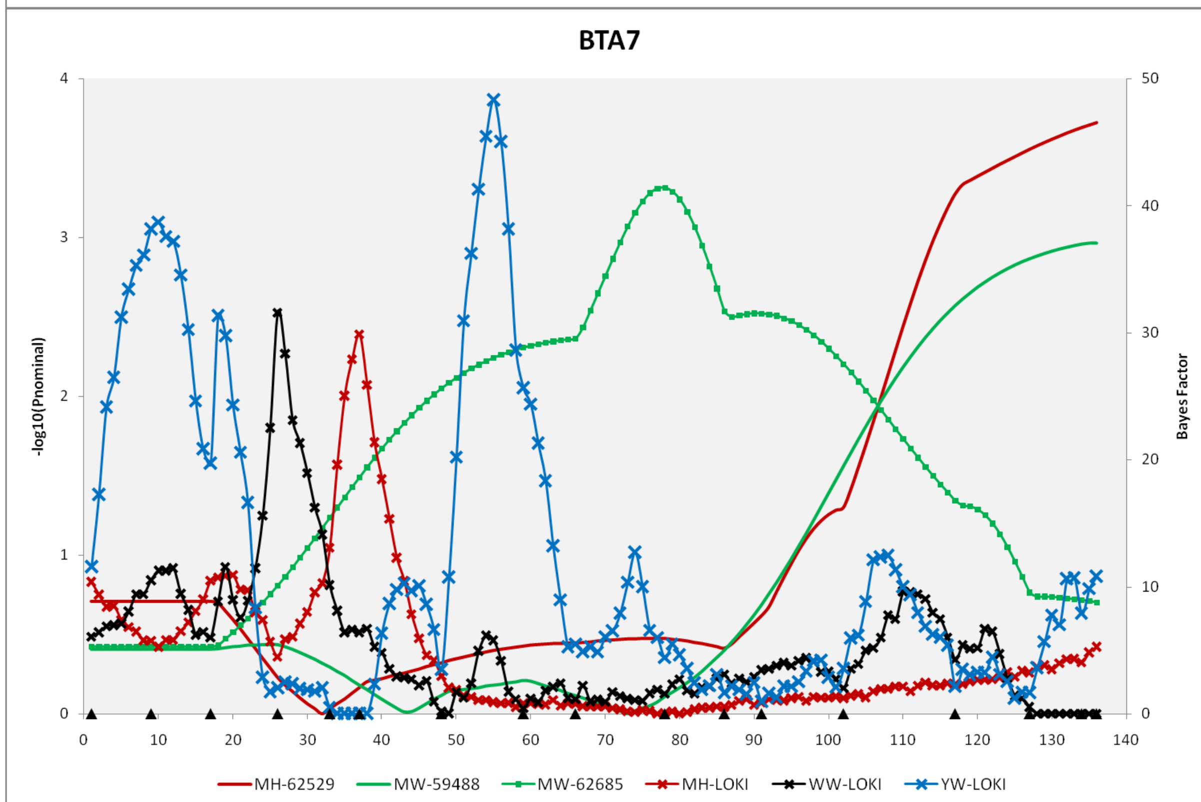

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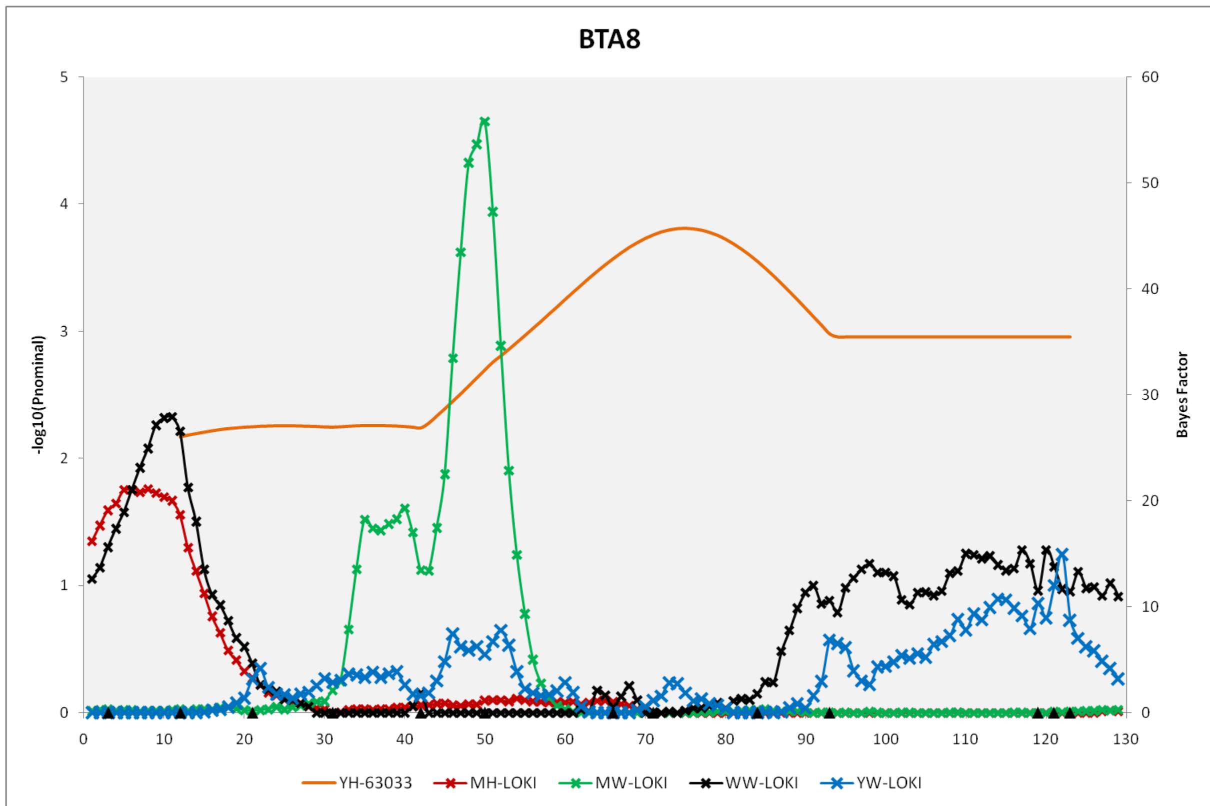

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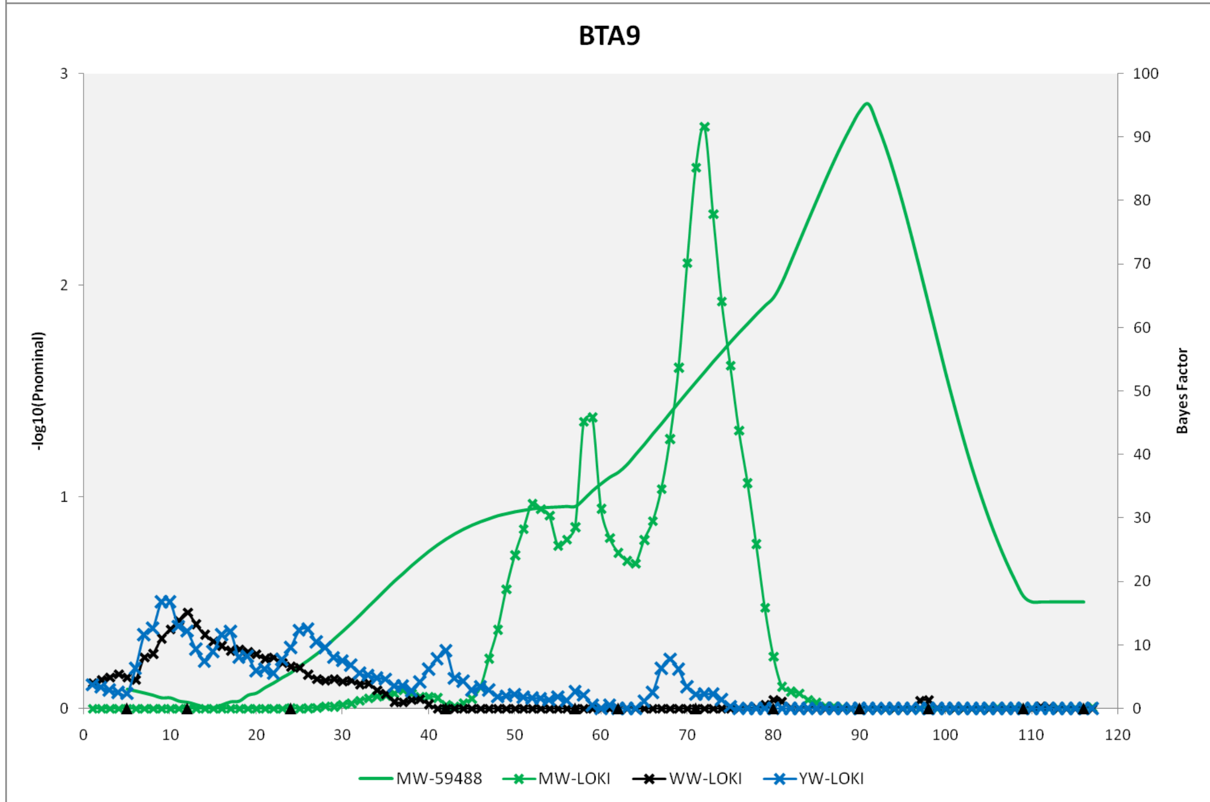

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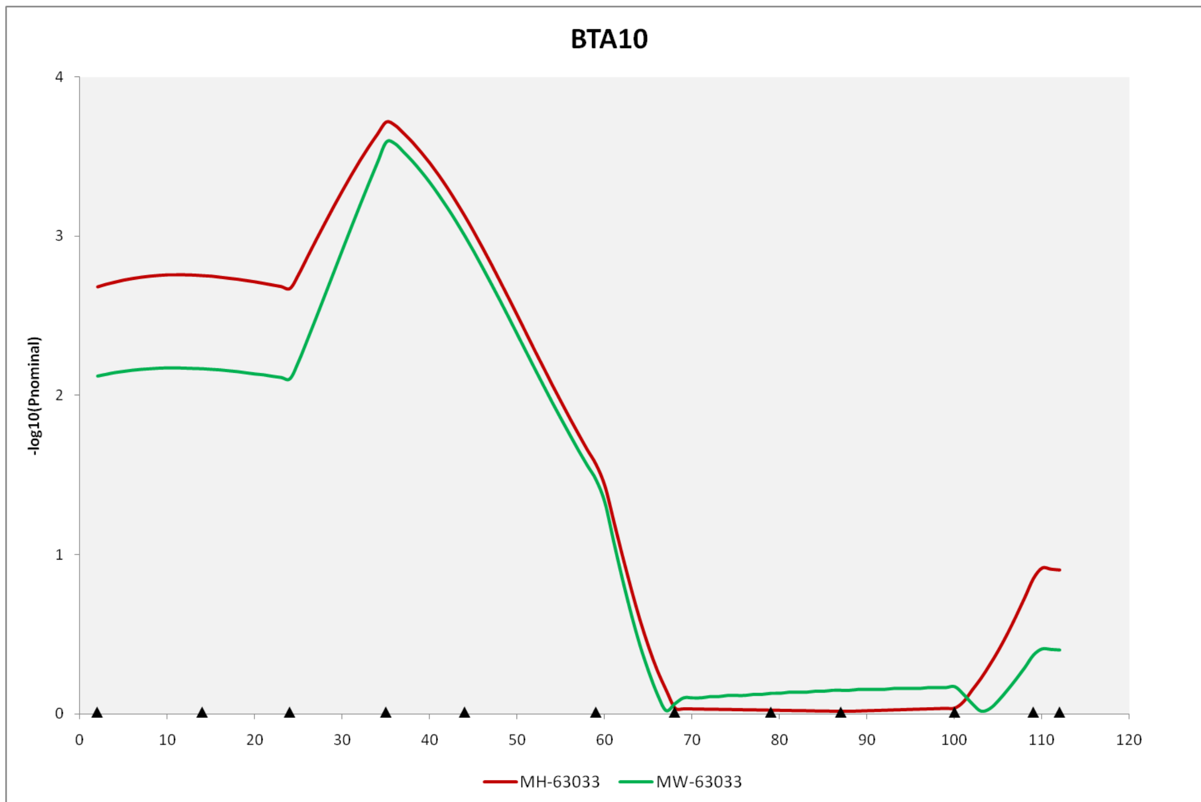
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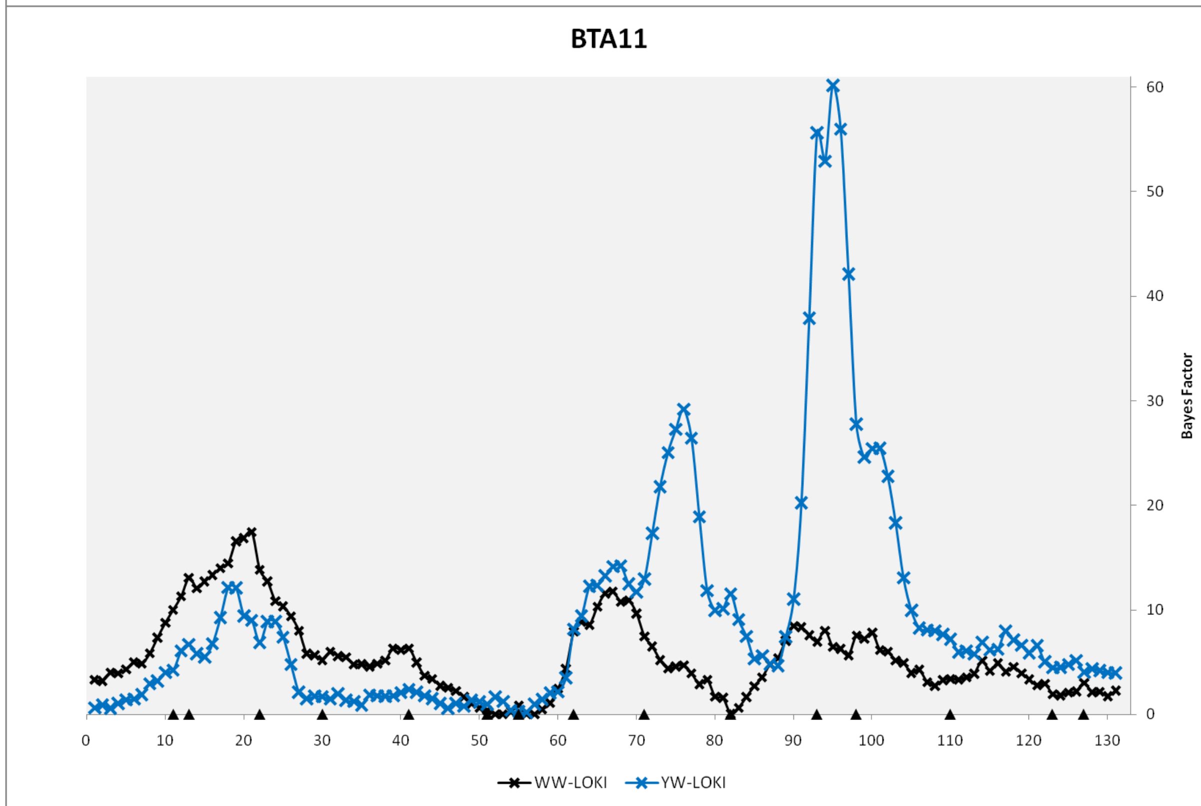
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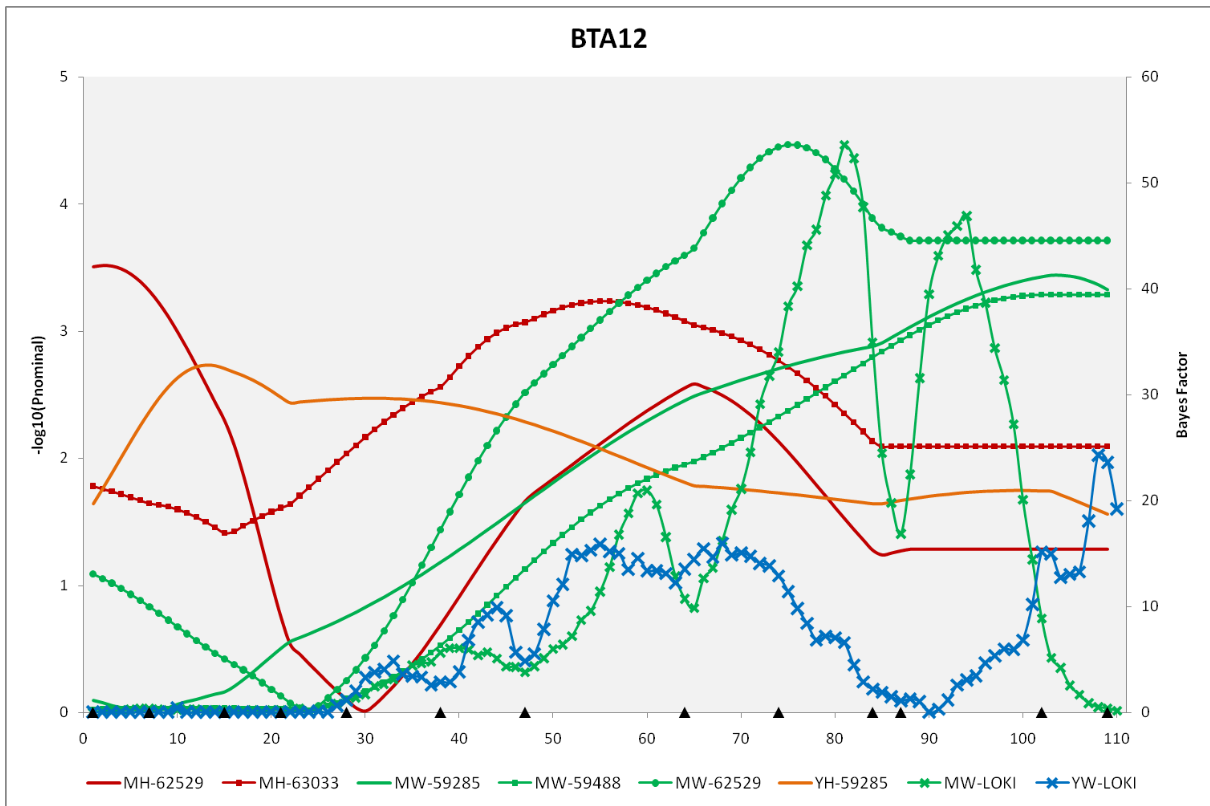

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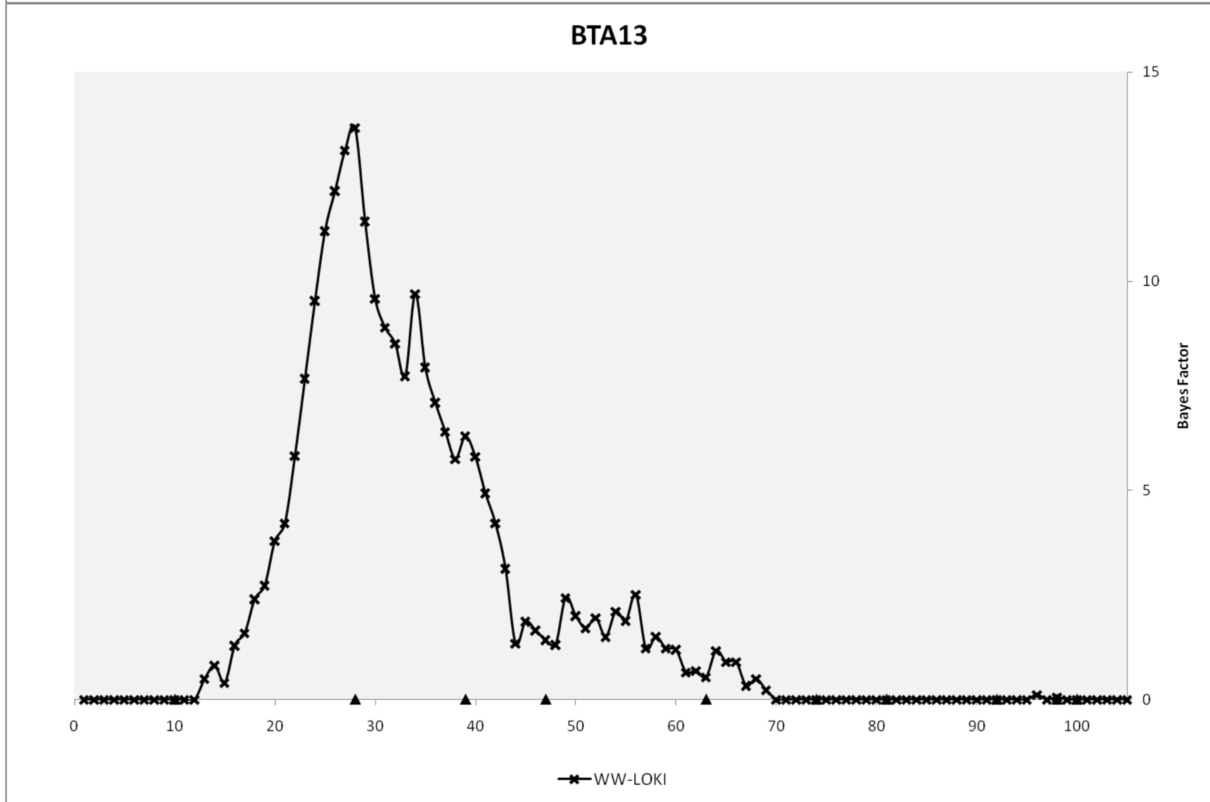

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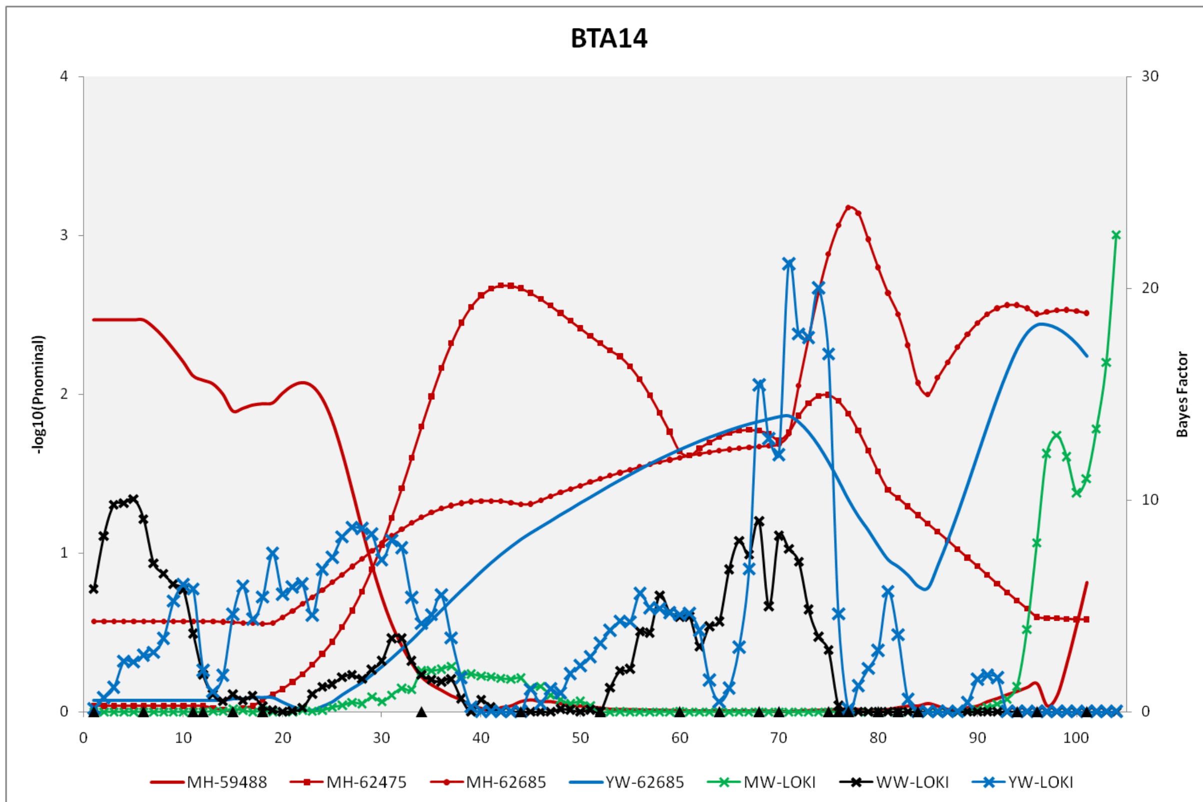
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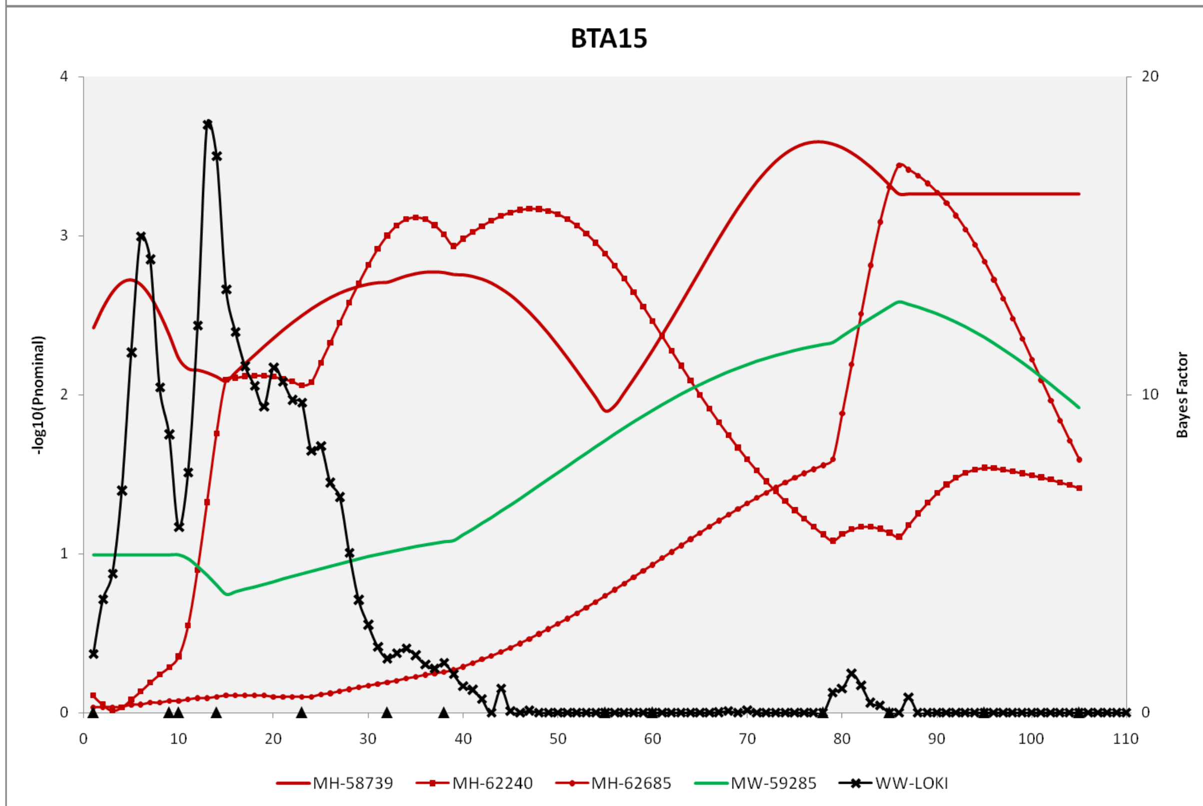
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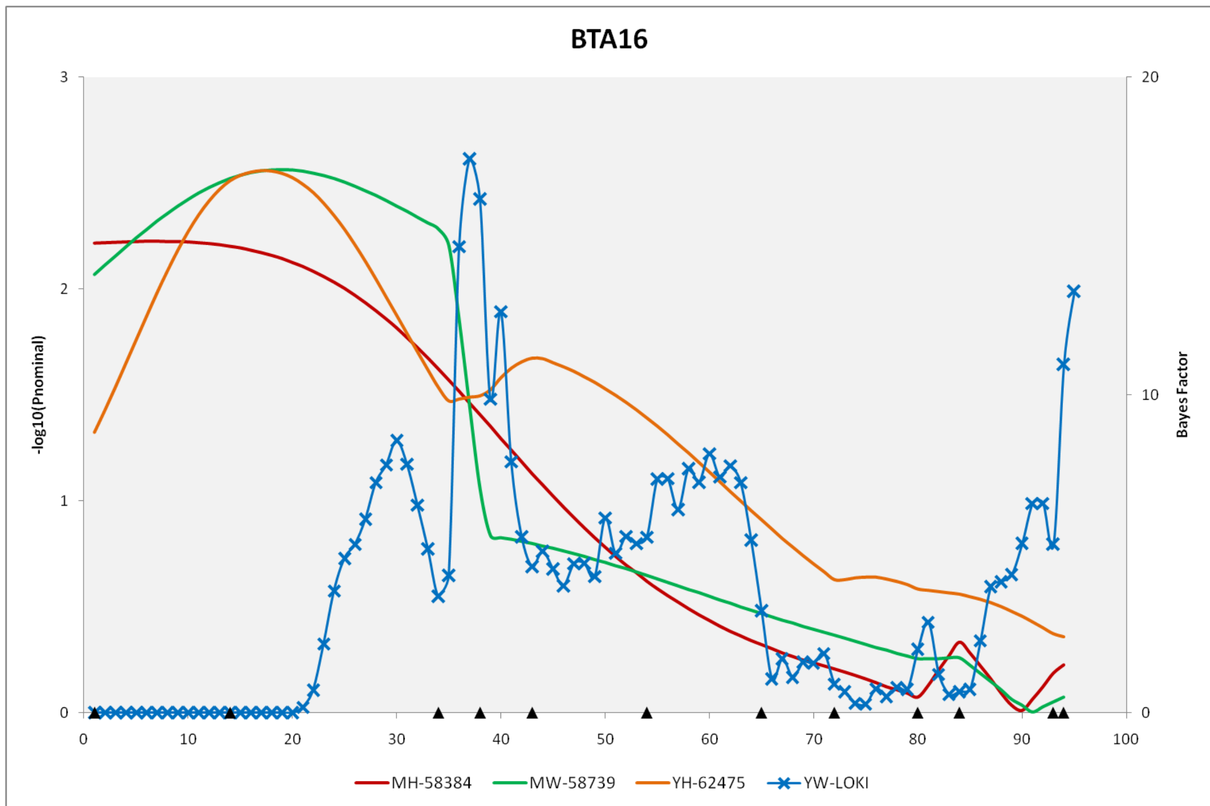
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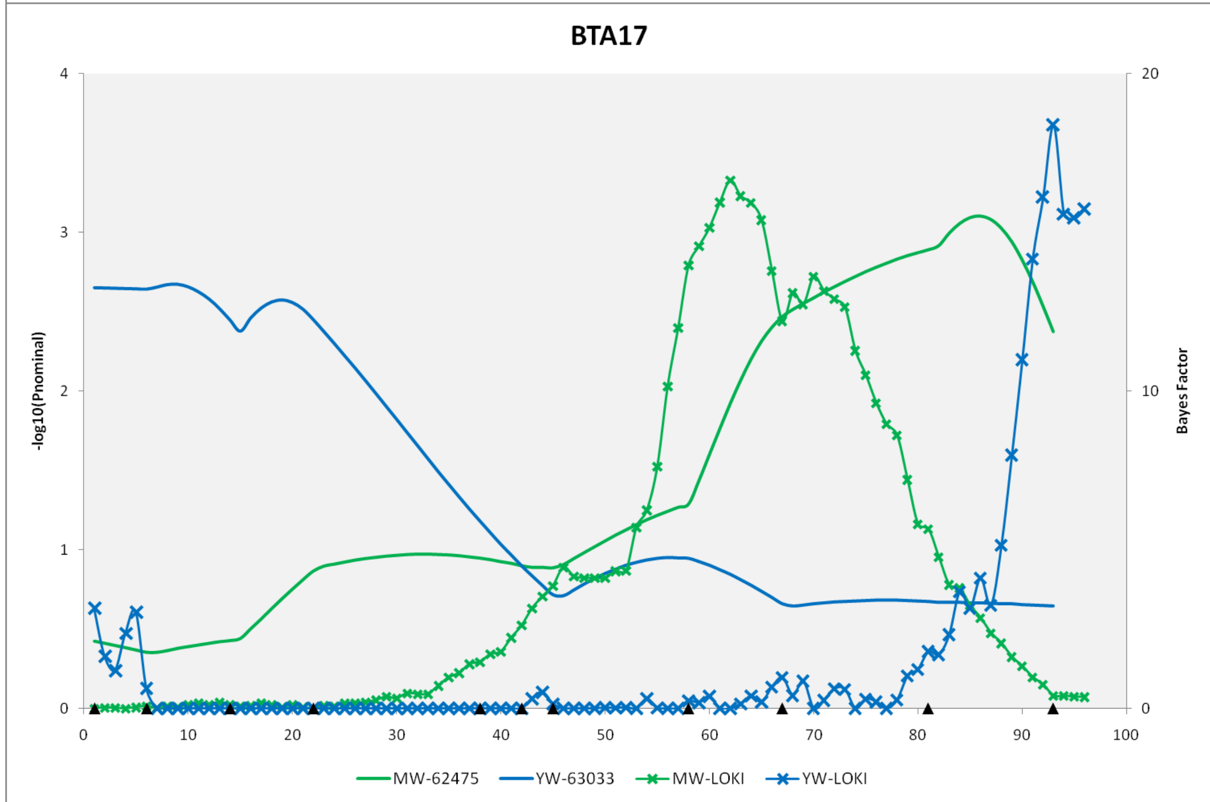
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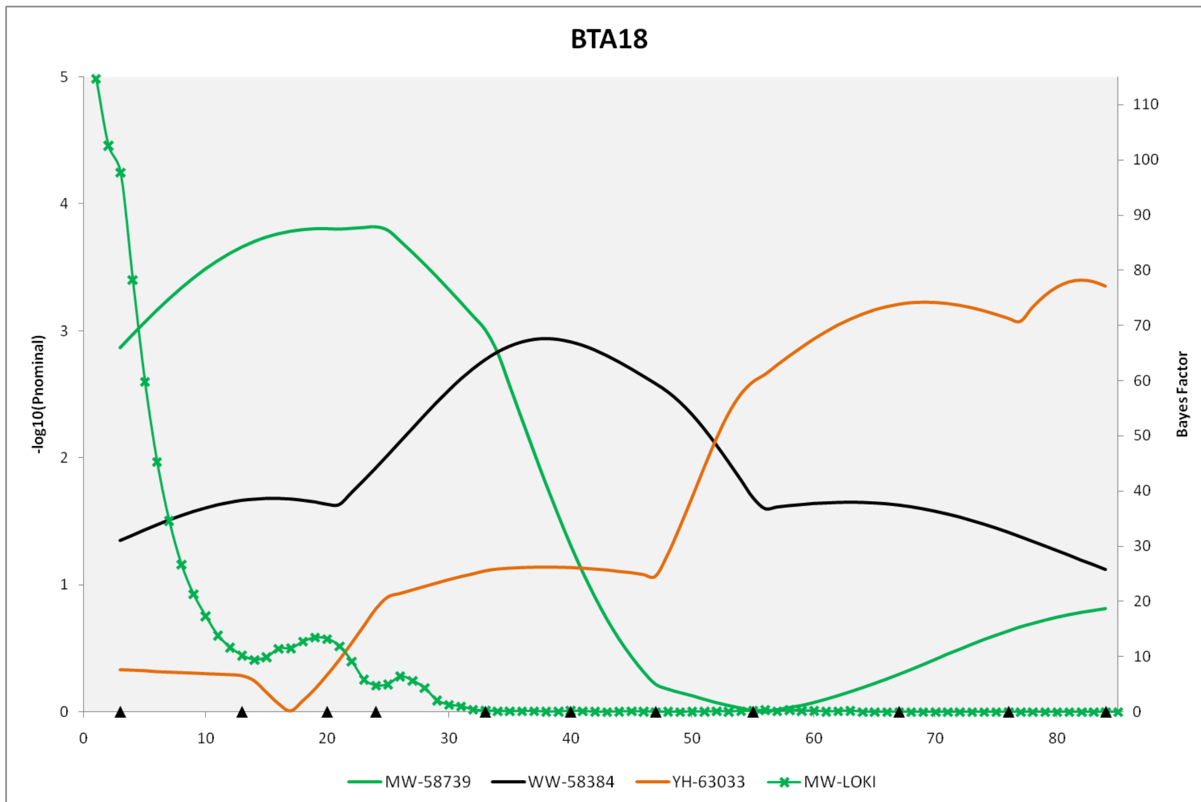
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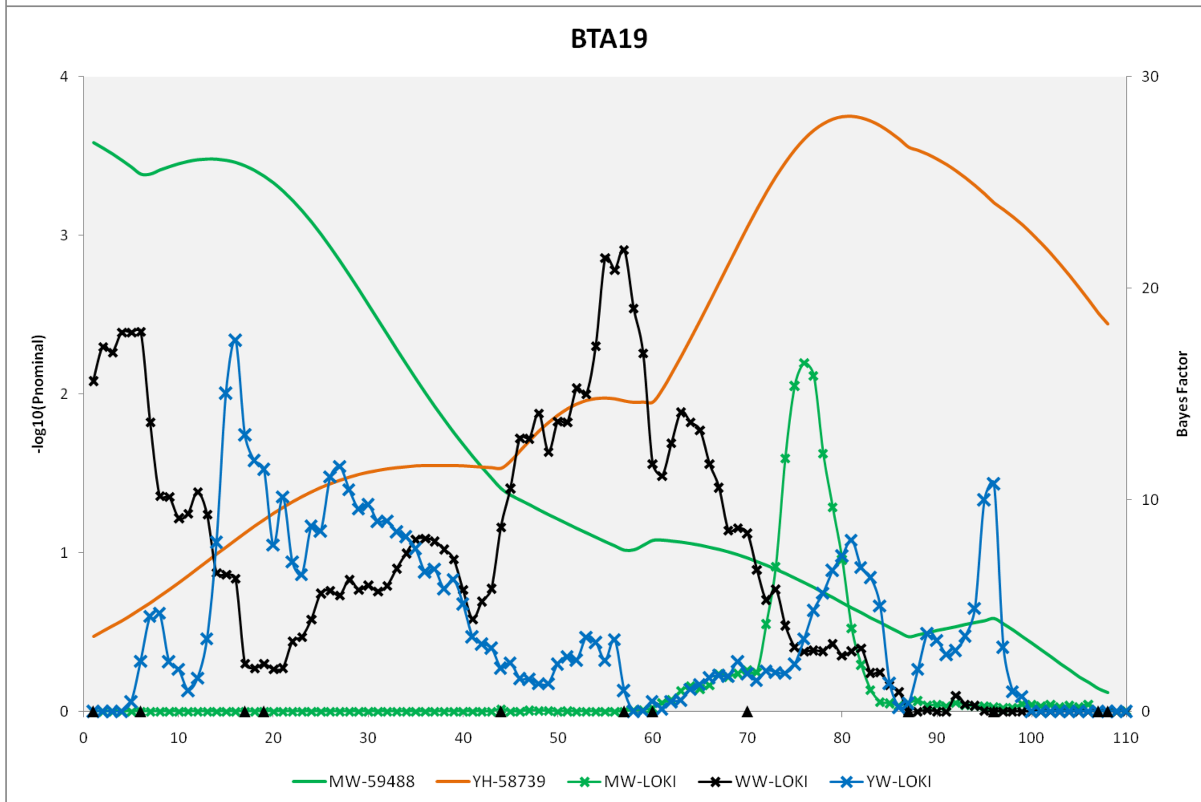
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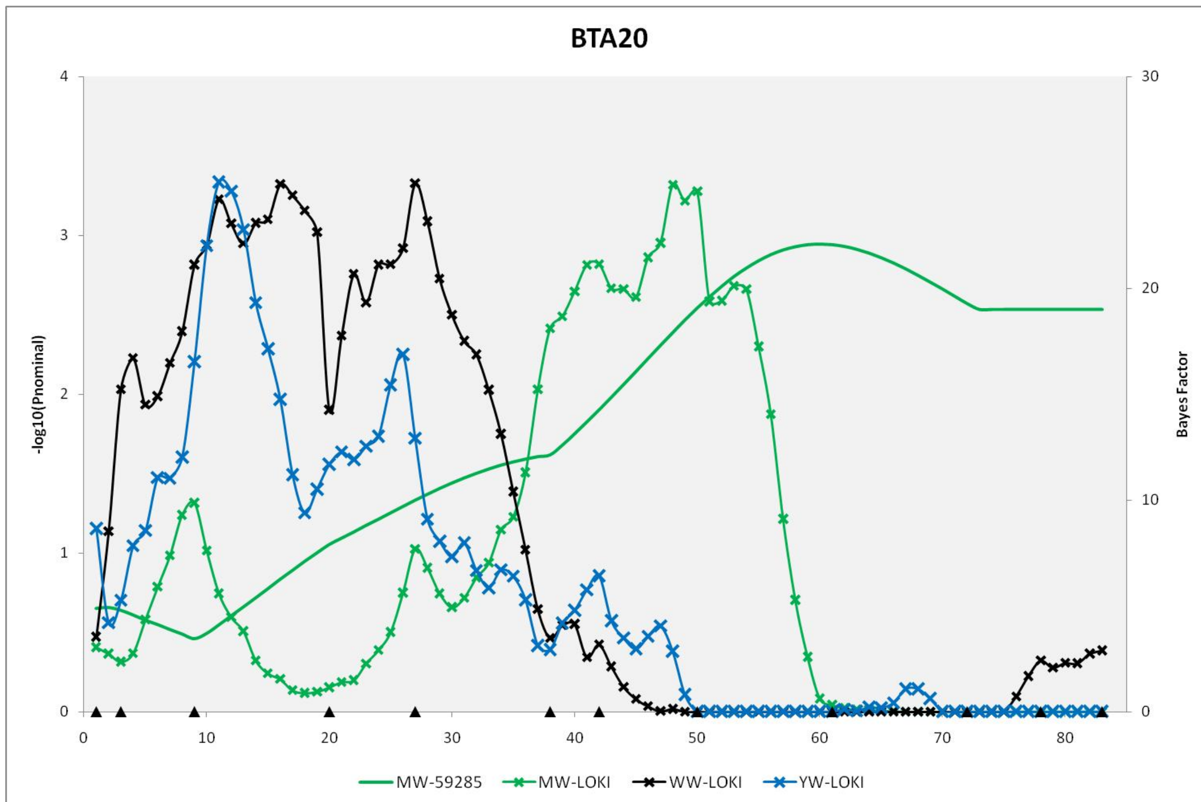
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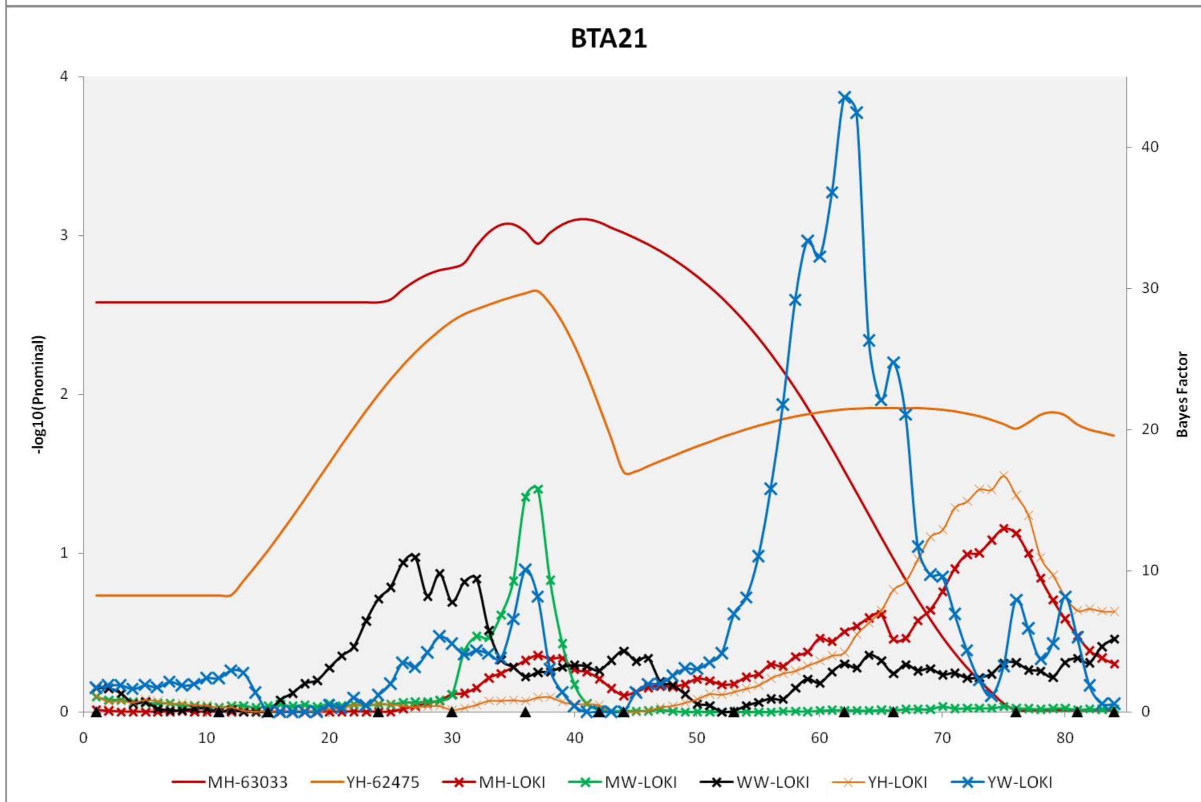
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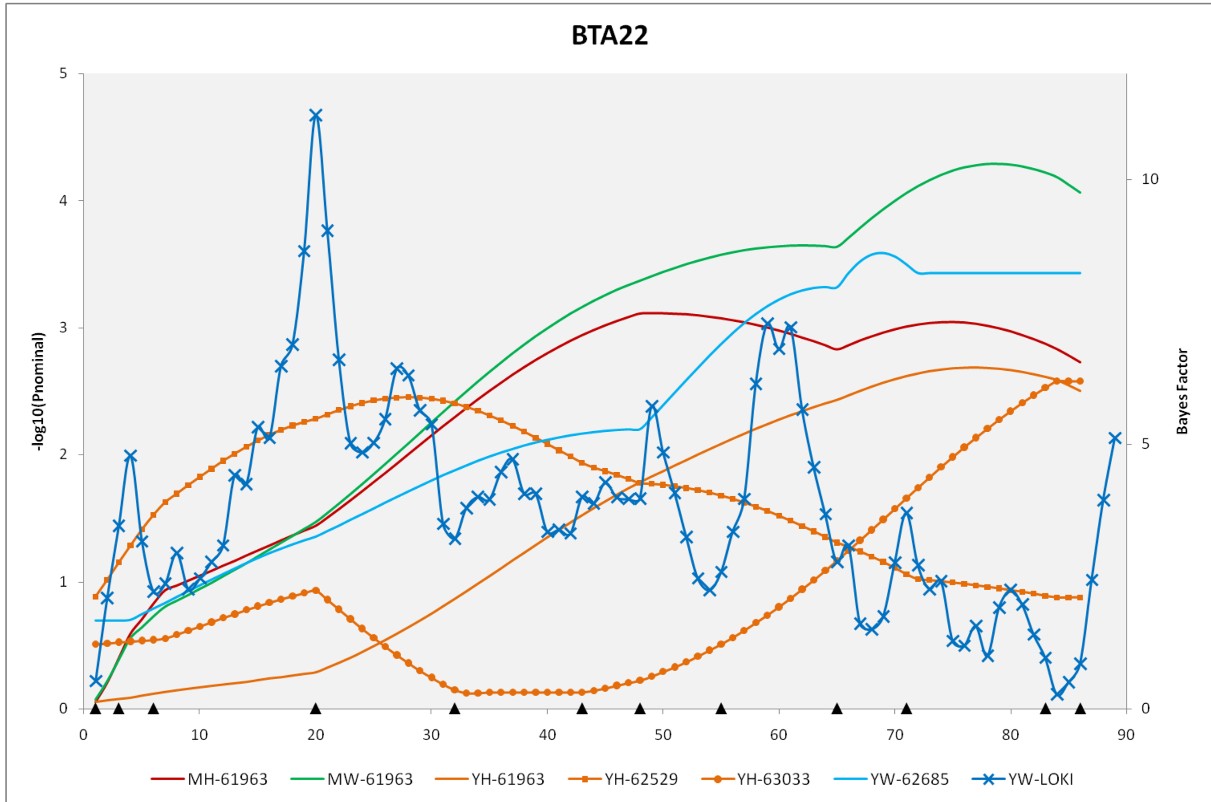
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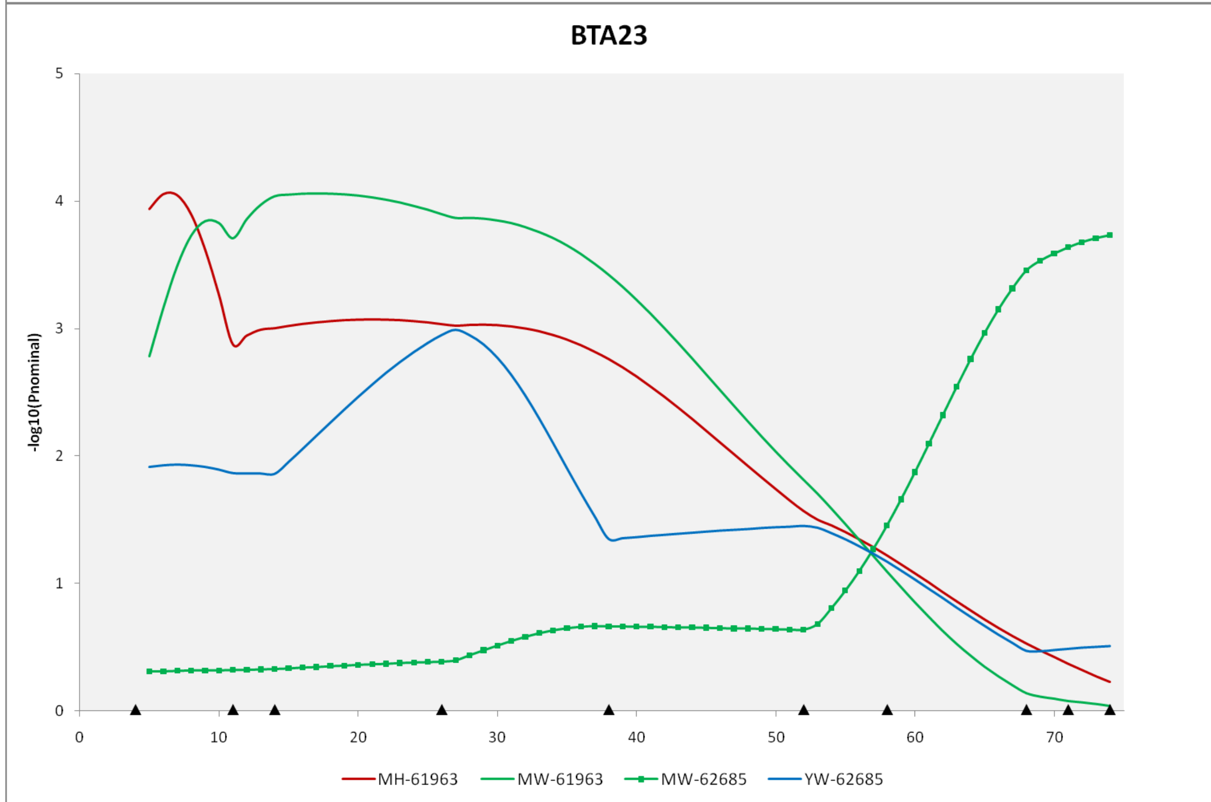
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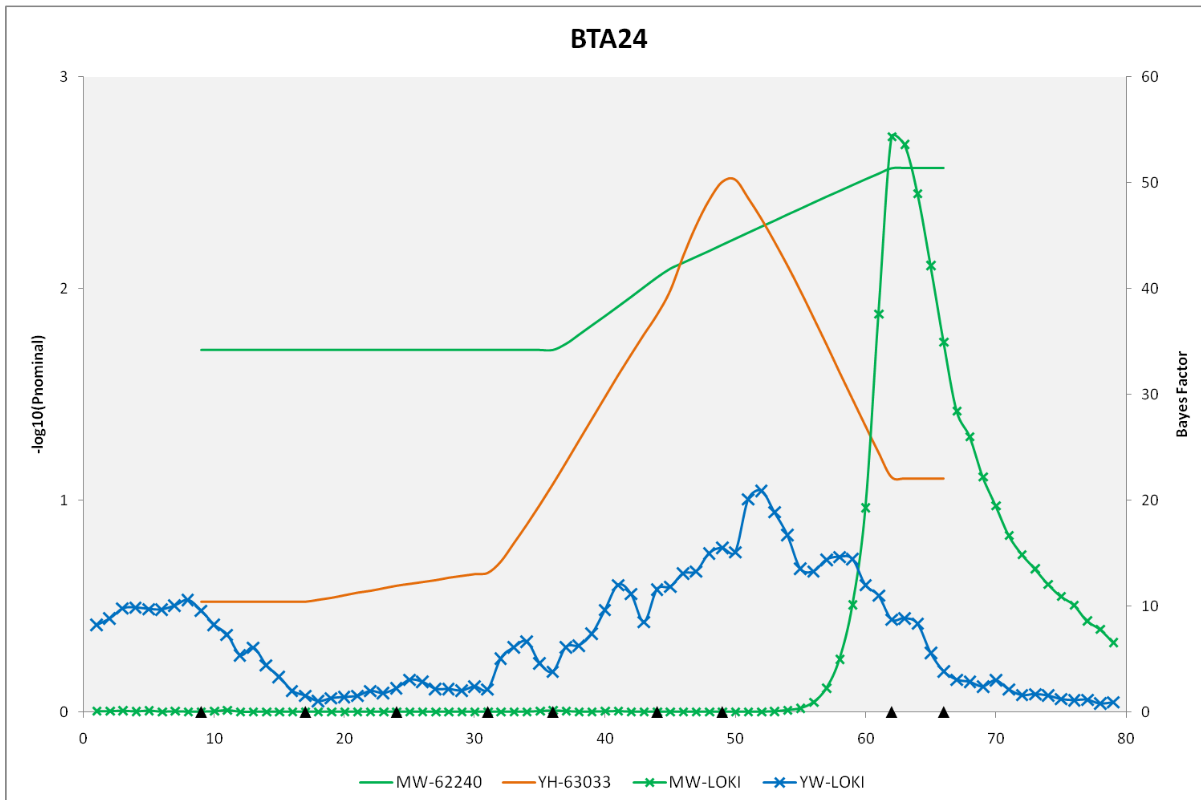
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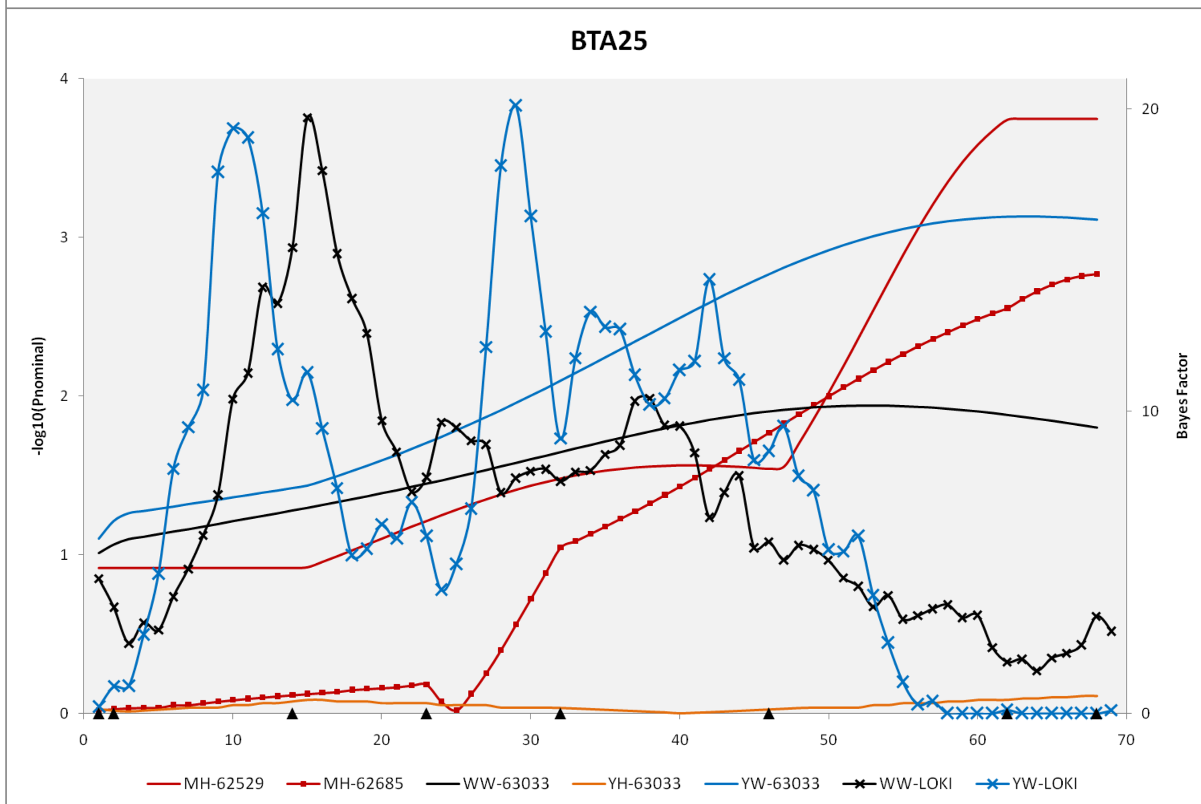
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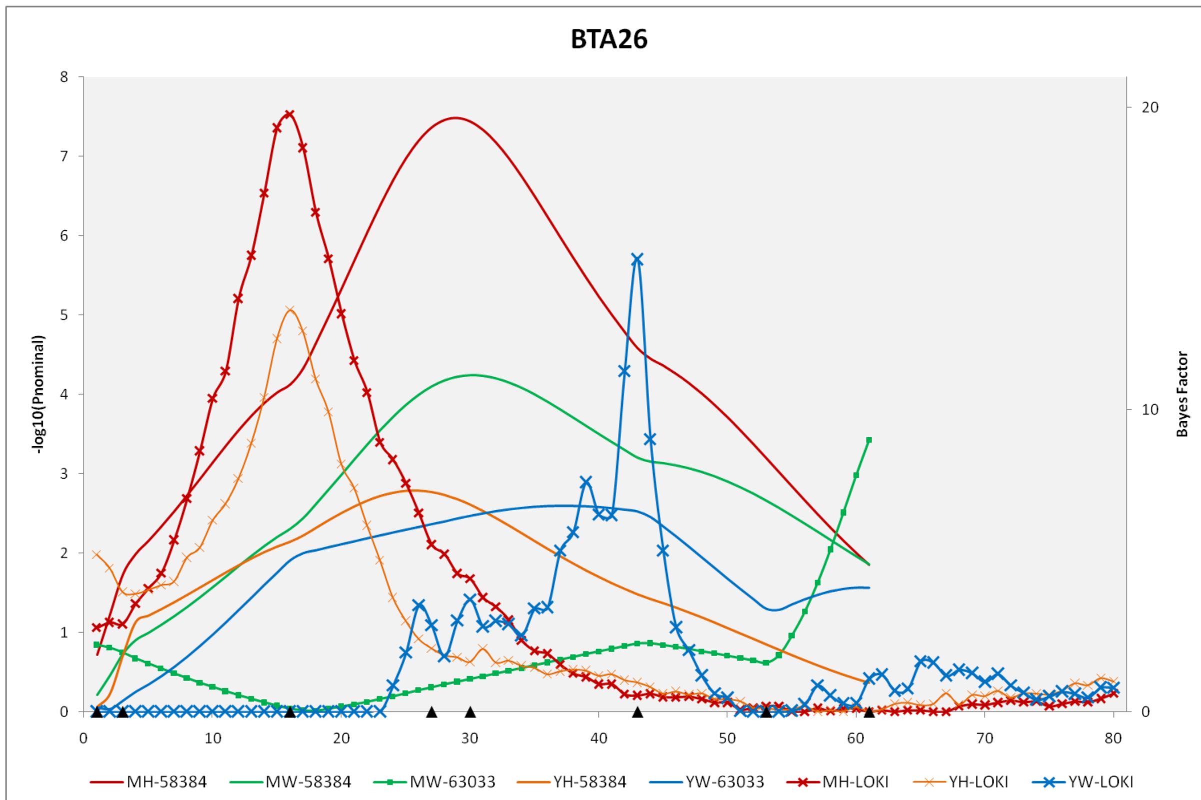
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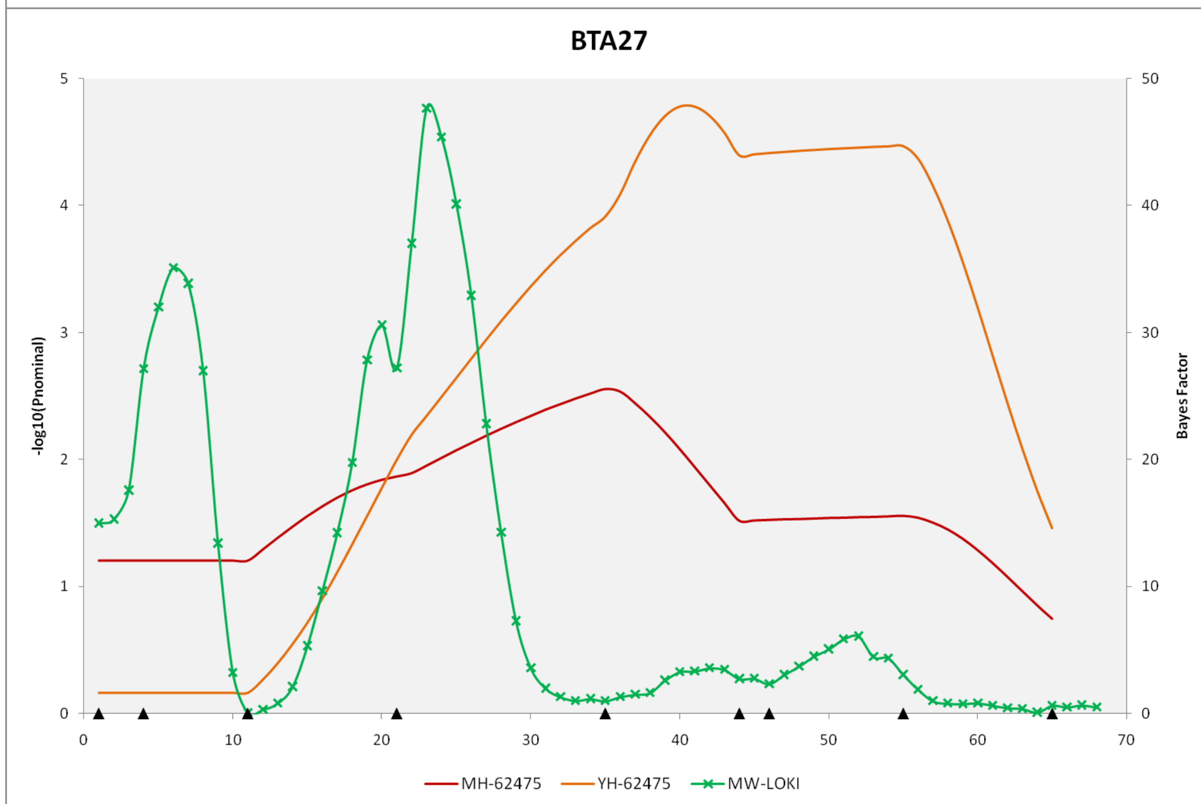
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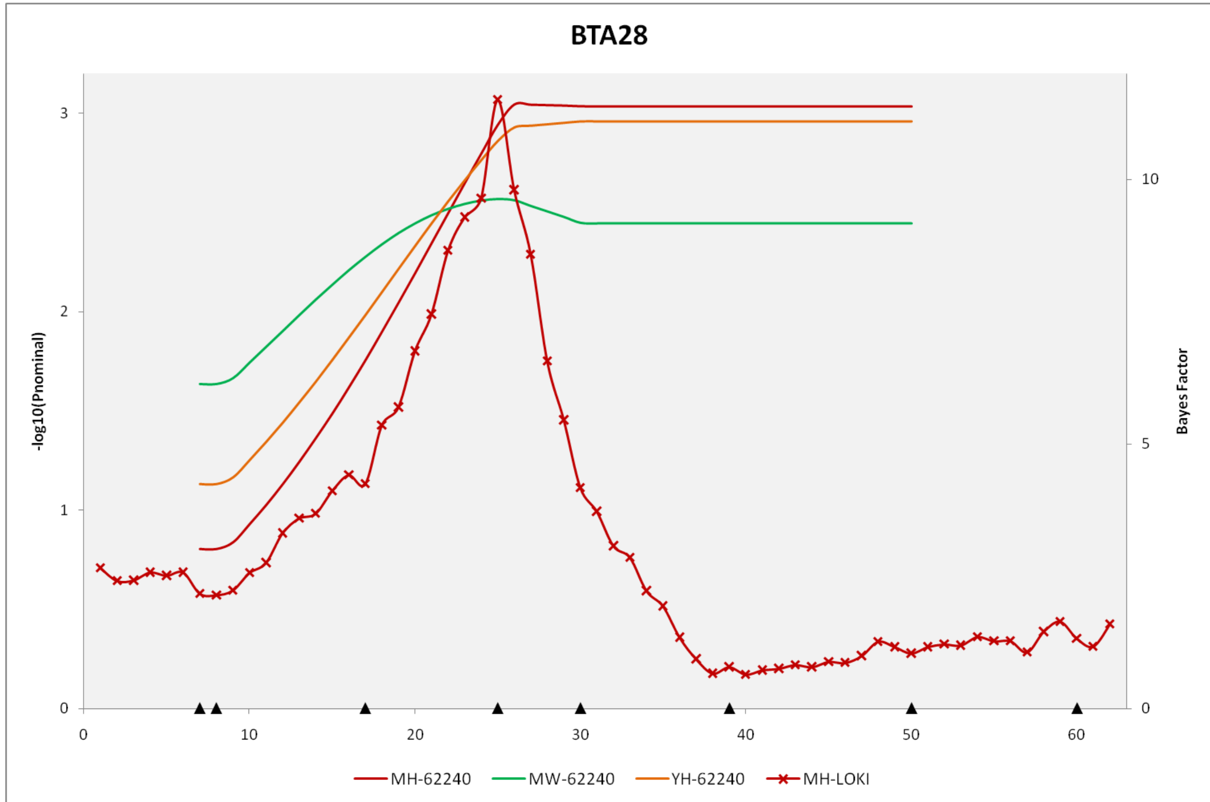
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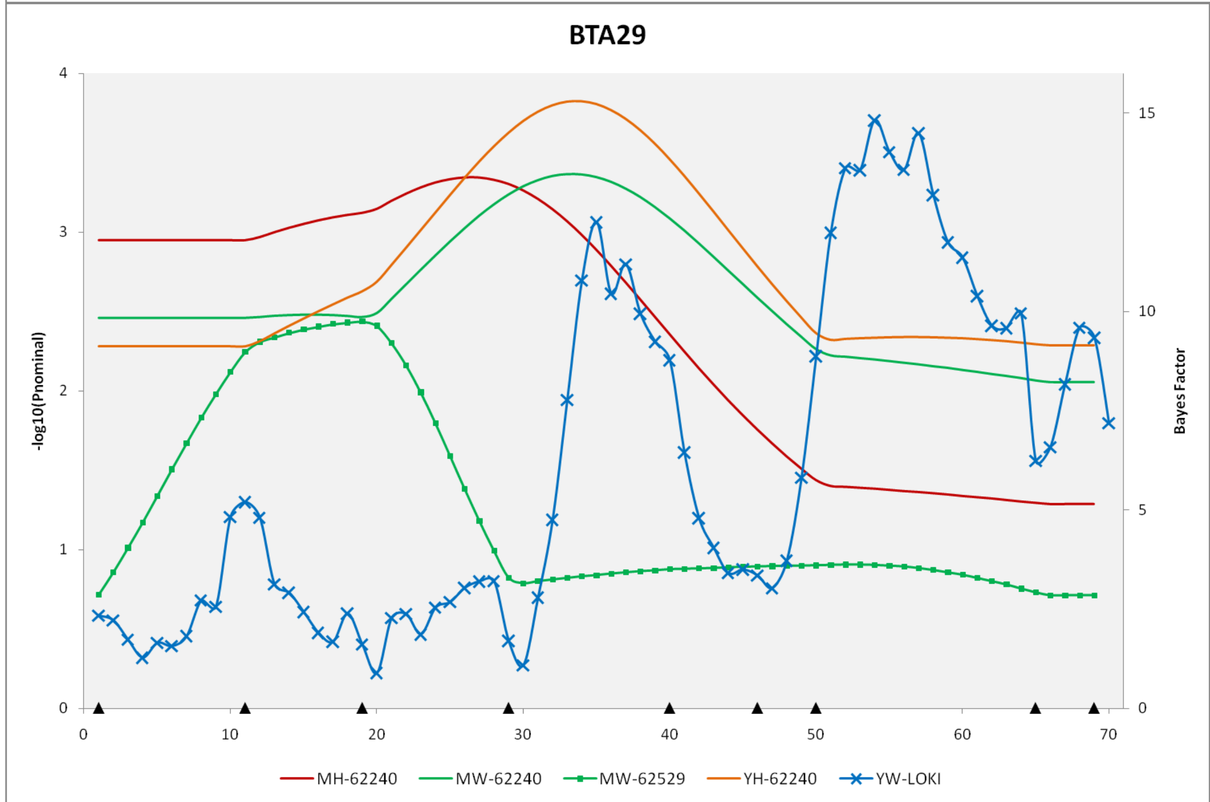
YH-62240
MH-LOKI


BTA29
-log10(Pnominal)
Bayes Factor
0
1
2
3
4
0
5
10
15
0
10
20
30
40
50
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70
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CHAPTER 4

Genome Scan in Commercial Angus Cattle for Quantitative Trait Loci Influencing Reproductive Traits

Abstract

A genome scan performed in a commercial Angus mapping population resulted in the identification of 135 quantitative trait loci (QTL) associated with reproductive traits. Expected progeny differences for birth weight (BW), calving ease direct (CED), calving ease maternal (CEM), maternal milk (MILK), and scrotal circumference (SC) were analyzed in a 29 generation pedigree comprised of 1,769 registered sires. Two separate analytical methods were used; half-sib least squares regression and Bayesian Monte Carlo Markov Chain modeling linkage analysis. Multiple QTL for each trait were found across the genome: 24 BW QTL, 18 CED QTL, 18 CEM QTL, 44 MILK QTL, and 31 SC QTL. Thirty-nine to 82 % of a trait's total genetic variance in this population was explained by these QTL. This is the first report of QTL for maternal milk and the second report of QTL for scrotal circumference in beef cattle.

Introduction

Since their inception and promotion in the beef industry, EPDs have been used by producers to increase the rate of genetic progress and propagate livestock that meet industry expectations. In an effort to identify the alleles responsible for the wide range of genetic variation in a trait, researchers have performed numerous QTL mapping studies. The ultimate goal of this research is to enable producers to be able to identify breeding stock with the best

genes for utilization in marker assisted selection (MAS). MAS is expected to be especially beneficial for improving traits that are determined postmortem, occur late in life, or are difficult and (or) expensive to accurately measure. Unfortunately many of the experimental designs used for QTL mapping in cattle have captured a limited number of parental chromosomes and therefore have only detected the few QTL that were heterozygous within these parents (Casas *et al.* 2003; Mizoshita *et al.* 2004; Alexander *et al.* 2007). Therefore, most genome scans performed in beef cattle have identified a small number of QTL influencing any one trait (Allan & Smith 2008). While 326 reproductive-related QTL have been reported in cattle, only 82 of these are for fertility based traits and a few affect male reproductive traits (http://www.animalgenome.org/QTLdb/cattle.html, last accessed June 13, 2009).

Using sires from the major American Angus bloodlines and assembling the largest commercial beef cattle mapping population to date (N=1,769), we were able to analyze the majority of the chromosomes found in the US Angus population for economically important QTL. The analytical flexibility permitted by this experimental design allows the detection of variations segregating within a family and within the complete pedigree using alternative analytical approaches.

Material and Methods

Material and methods for this study are described in Chapter 2: Genome Scan in Commercial Angus Cattle for Quantitative Trait Loci Influencing Carcass Traits.

Results

Analysis to detect QTL influencing birth weight (BW), calving ease direct (CED), calving ease maternal (CEM), maternal milk (MILK), and scrotal circumference (SC), resulted in the detection of QTL on every autosome (Table 4.1). At a chromosome-wide $P \leq 0.01$ significance level or ≥ 10 Bayes Factor (Jefferys 1961), 135 reproductive related QTL were identified: 24 BW, 18 CED, 18 CEM, 44 MILK, 31 SC QTL. Of these only 9 BW, 5 CED, and 5 CEM QTL had previously been identified (Table 4.2). While this is the first report of MILK QTL in beef cattle, milk yield QTL have previously been reported in dairy cattle within the confidence intervals for 16 of those detected here (Table 4.2). Of the 135 possible QTL, 3 appear to be pleiotropic (Table S2), leaving 132 independent reproductive trait QTL identified in this study.

On average each chromosome contains 4 reproductive QTL, and approximately 0.93 QTL per trait (range of 0 to 5). While significant numbers of QTL for reproductive traits were found on every chromosome, on average 11 chromosomes did not contain a QTL for a given trait. Twenty chromosomes contained multiple QTL for at least one trait (Figure 4.1 and Table 4.1). The average allele substitution effect from QTL Express for BW was 2.722 lb, 7.344 units for CED, 4.866 units for CEM, 9.419 lbs of calf weaning weight for MILK, and 0.732 cm for SC. Alternate homozygote effects from LOKI for the economically beneficial alleles were 0.285 lb for BW, 0.864 units for CED, 0.585 units for CEM, 2.368 lbs of calf weaning weight for MILK, and 0.078 cm for SC (Table 4.3).

A general linear model analysis (SAS, v9.1) indicates that the detected QTL explain a substantial amount of the genetic variation in each trait within our population. With all QTL

included in the model 51.61% of the genetic variance was explained for BW, 39.31% for CED, 50.27% for CEM, 82.45% for MILK, and 59.94% for SC (Tables 4.4, 4.5, 4.6, 4.7, 4.8, and 4.9). The mean genetic variation explained by an individual QTL was 2.2%.

Discussion

One hundred and twenty five QTL distributed across the genome were detected to influence reproductive traits in American Angus cattle. With an average QTL allele frequency of 0.770 for BW, 0.824 for CED, 0.827 for CEM, 0.421 for MILK, and 0.510 for SC (Table 4.3), the chance that any one sire or dam will have all of the beneficial alleles at all QTL for even one trait is extremely low. This allele frequency for highly selected, economically important traits is similar to the frequency of milk production QTL in dairy cattle (Chamberlain *et al.* 2007). While the amount of genetic variation explained by the QTL ranged from almost 40% to 82% these genetic variance estimates are biased as they were determined in the discovery population (Lou *et* al. 2003; Xu, 1998). The allele substitution effects estimated by QTL Express in the smaller half-sib families are likely to be overestimated (Lou *et al.* 2003). A separate population is needed to better assess the true genetic variation explained by these QTL (Van Eenennaam *et al.* 2007). While many of these are newly identified reproductive QTL, it is likely that the majority segregate within all *B. taurus* breeds.

For the 3 pleiotropic QTL (Table 4.9) identified in this analysis, the low marker resolution means that we cannot statistically determine if a single quantitative trait nucleotide (QTN) influences both traits or if a separate QTN for each trait lies within the QTL. As the phase relation between potentially separate QTN could not be identified from our analysis and LD in

cattle extends for 500 kb (McKay *et al.* 2007) it is possible that use of these potentially pleiotropic QTL in a MAS program could result in divergent selection in each trait.

As the majority of QTL explain only a small amount of a trait's genetic variation, genetic improvement programs that implement information from one, or a few economically important QTL will have little value in beef cattle. Genetic improvement decisions based on a multitude of genetic markers will maximize ones economic gain. Integrating QTL information with available phenotypic data for the estimation of EPDs will allow producers to select for genetically superior animals.

Table 4.1. Count of reproductive QTLs by chromosome.

Trait	*Bos taurus autosome*																												
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
Birth Weight	1	2	1		1	2		1		1	1	1			1	1			1	2	1	1	1			2		3	
Calving Ease Direct	2					2		1		1				1		1			1		1		1		2	3		2	
Calving Ease Maternal	1	2		2	1		1	1	1	1				1		2			1			1	1	1	1				
Maternal Milk	2		1	2		1	5			2	3	3	2	1	5	4	1	2					1	1	2	1	1	3	1
Scrotal Circumference				1	2	1	1	1	2	2	2	1	1	1		1	1	1	2	1	1	2	1		1	1	1	2	1
Pleiotropic	1							1																					
Total	5	4	2	5	4	6	7	3	3	7	6	5	3	4	6	9	2	3	5	3	3	4	5	2	6	7	2	10	2

Table 4.2. Reproductive QTL data summary.

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
MILK	1	0.5	Centromeric	*BM6438_29*			40.64	0.845	-0.0061	-2.564	MY (15)
CED	1	15.5	*BMS574*	*BMS4017*			30.7	0.84	0.0093	-1.0949	
CEM	1	15.5	*BMS574*	*BMS4017*			20.76	0.83	0.0164	-0.5983	
BW	1	17.5	*BMS574*	*BMS4017*			31.07	0.791	0.0001	0.0868	
MILK	1	50.5	*BMS4017*	*BMS527*	6.9616	3.172*	38.26	0.838	-0.0017	-2.1089	MY (15)
CED	1	106.78	*BM864*	*BMS4040*	8.2877	2.334*					
BW	2	19.5	*DIK1172*	*CSSM50*			27.08	0.792	-0.0014	0.179	BW (13)
BW	2	41.5	*BMC9002*	*BMS803*			33.91	0.81	-0.0017	0.215	BW (6)
CEM	2	60.5	*BM4440*	*BY32*			13.75	0.827	0.0194	-0.587	CE (19)
CEM	2	95.78	*TGLA226*	*BM1223*	5.1114	3.272*					
BW	3	20.5	*URB006*	*BMS2904*			15.63	0.788	-0.0016	0.2083	BW (6)
MILK	3	66.5	*INRA003*	*HUJ246*			20.22	0.788	-0.0398	-2.6769	MY (22)
CEM	4	3.5	Centromeric	*BMC1410*	7.8209	2.884*	12.93	0.828	0.0626	-0.649	
MILK	4	52.5	*BMS1840*	*BMS885*			76.86	0.785	-0.0043	-2.414	
CEM	4	69.5	*INRA072*	*BMS2571*			15.6	0.834	0.045	-0.6874	
MILK	4	72.5	*BMS2571*	*BMS2809*			19.39	0.767	-0.0133	-2.1525	
SC	4	88.5	*Lep Ex2*	*RM088*	0.7743	3.175*					
SC	5	1.17	*BMS695*	*BM6026*	0.7653	3.085*					
CEM	5	73.5	*BR2936*	*CSSM22*			11.39	0.818	0.0141	-0.4178	
BW	5	105.5	*BM315*	*BMS1658*			39.63	0.775	-0.0041	0.4628	
SC	5	126.5	*BMS597*	Telomeric			14.73	0.807	-0.0017	0.0351	

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
CED	6	32.5	*BMS5006*	*URB016*			14.1	0.796	0.0005	-0.6977	CE (9)
MILK	6	33	*BMS5006*	*URB016*	12.4132	2.492*					MY (18)
BW	6	33.5	*BMS5006*	*URB016*			11.76	0.783	-0.001	0.2888	BW (13)
CED	6	47.5	*OPN3907*	*BM143*			14.31	0.804	-0.0103	-0.8372	CE (9)
BW	6	57.5	*OPN3907*	*DIK082*			34.13	0.804	0.0036	0.4313	BW (4,13)
SC	6	90	*CSN3*	*BM8124*	0.7889	3.151*					
MILK	7	0.5	*BM7160*	*RM012*			71.1	0.795	0.0205	-2.6079	
SC	7	27.5	*RM006*	*IL4*			12.38	0.803	-0.0011	0.0604	
MILK	7	37.5	*BM6105*	*DIK2819*			13.04	0.732	0.0121	0.0346	MY (1)
MILK	7	59.5	*UWCA20*	*BMS2840*	8.889	4.519***	10.71	0.821	-0.0089	1.122	MY (17)
MILK	7	74.5	*BMS2840*	*BMS2258*			31.89	0.833	-0.0184	2.7192	MY (3)
MILK	7	91.5	*BMS1331*	*BM9065*			15.6	0.779	-0.0153	-2.4636	
CEM	7	125.5	*ILSTS006*	*BMS1979*	4.8655	3.451**					
SC	8	11.5	*IDVGA11*	*RM372*			17.7	0.798	-0.0002	-0.0654	
CEM	8	113.5	*BM711*	*CSSM047*			18.46	0.833	0.0276	-0.6525	CE (2)
CED	8	118.5	*BM711*	*CSSM047*			12.44	0.807	-0.0023	-0.8398	CE (2)
BW	8	126.5	*BMS836*	Telomeric			10.45	0.805	-0.0002	-0.0593	
CEM	9	12.5	*BMS836*	*ETH225*	4.1567	2.728*	10.5	0.832	0.0204	-0.5728	
SC	9	42.5	*BMS817*	*BMS434*			12.22	0.814	0.0042	-0.0844	
SC	9	109.5	*BMS1967*	*BMS2094*			31.24	0.815	-0.0011	0.0596	

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
BW	10	32.86	*BMS528*	*BRN*	2.8637	2.91*					
CED	10	40.86	*SPS113*	*BMS2742*	5.634	3.114*					
CEM	10	43.5	*SPS113*	*BMS2742*			10.14	0.829	0.0355	-0.5892	
MILK	10	87.5	*INRA037*	*BMS614*	10.5487	4.416***					
SC	10	98.5	*BMS2641*	*BMS614*			11.71	0.795	0.0001	-0.0172	
MILK	10	99.5	*BMS2641*	*BMS2614*			42.13	0.857	-0.0133	2.1501	MY (1)
SC	10	118.45	*BL1134*	Telomeric			36.68	0.832	-0.0017	0.1255	
MILK	11	23.5	*BMS2325*	*BM2818*			13.18	0.744	-0.0377	1.6429	
SC	11	28.5	*INRA044*	*BM2818*	0.6664	2.775*	20.67	0.812	0.0014	-0.0683	
MILK	11	45.5	*RM096*	*BM7169*			11.8	0.697	-0.0214	-0.7057	
BW	11	56.5	*BMS1716*	*ILSTS036*			17.13	0.803	0.0017	0.4355	
MILK	11	68.5	*ILSTS036*	*RM150*			10.12	0.631	0.0265	4.2987	MY (14)
SC	11	93.08	*BMS989*	*BL1103*	0.4821	2.657*					
SC	12	1	*BMS410*	*TGLA36*	0.8914	2.75*					
BW	12	16.5	*BMS2252*	*BMS2057*			26.99	0.792	-0.0026	0.0348	
MILK	12	65.5	*BMS975*	*BM4028*			34.98	0.875	-0.035	-2.1666	
MILK	12	92.5	*INRA5*	*BMS1316*			21.88	0.871	-0.0265	-1.9175	
MILK	12	109.5	*BMS2724*	Telomeric			47.76	0.803	-0.012	-2.8054	
MILK	13	29.5	*BMC1222*	*BMS1352*			10.27	0.791	0.0166	-1.7596	
SC	13	37.99	*BMC1222*	*BMS1352*	0.9648	2.701*					
MILK	13	71.5	*BM9248*	*RM327*			11.93	0.772	0.0389	2.5519	MY (1)

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
CED	14	12.5	*TG*	*DIK4438*			38.31	0.851	0.0063	-1.2814	
CEM	14	33.5	*RM180*	*RM011*			23	0.841	0.0535	-0.7892	CE (10)
MILK	14	40	*RM180*	*RM011*	7.3373	3.441**					MY (11)
SC	14	95.5	*BM6425*	*BL1036*	0.5999	2.988*	18.47	0.822	-0.0039	0.1048	
MILK	15	6.5	*DIK2777*	*MGTG13B*			25.62	0.827	-0.0635	3.0593	
BW	15	20.5	*BMS2533*	*ADCY2*			17.18	0.788	-0.0016	0.2083	
MILK	15	20.5	*BMS2533*	*ADCY2*			31.12	0.781	0.0069	3.3809	
MILK	15	29.5	*ADCY2*	*JAB8*			42.99	0.784	0.0002	2.9	
MILK	15	94.5	*BMS812*	*BL1095*			29.48	0.754	-0.0058	-2.6981	
MILK	15	102.5	*BL1095*	*BMS927*			21.44	0.748	0.0166	-2.8803	
MILK	16	11.5	*TGLA245*	*BMS1348*			11.28	0.836	0.0109	1.2539	
CED	16	20.5	*BMS1348*	*BY22*	5.7414	3.523**					
MILK	16	42.5	*TGLA53*	*BMS1907*			20.88	0.84	0.0066	-3.1361	
MILK	16	53.5	*BMS1907*	*IDVGA49*			10.29	0.83	-0.0493	-2.1711	
CEM	16	54.5	*IDVGA49*	*IDVGA69*			11.04	0.824	0.0274	-0.5453	CE (19)
BW	16	56.5	*IDVGA49*	*IDVGA69*			10.57	0.803	0.0017	0.4355	
SC	16	61.91	*IDVGA49*	*IDVGA69*	0.7809	2.487*					
MILK	16	68.5	*IDVGA69*	*INRA048*			15.2	0.85	0.0138	-2.627	
CEM	16	71.5	*IDVGA69*	*INRA048*			15.4	0.832	0.0026	-0.6307	
MILK	17	26.5	*DIK4665*	*BMS941*	10.8008	3.059*	33.14	0.857	0.0081	-2.5299	
SC	17	82	*BM1862*	*BM1233*	0.6359	3.253**					

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
MILK	18	9.86	*BMS1355*	*BMS1322*	8.4841	2.636*					
MILK	18	76.5	*IDVGA55*	*BM2078*			58.44	0.868	0.0425	-3.2645	MY (8)
SC	18	76.5	*IDVGA55*	*BM2078*			22.65	0.788	0.0022	-0.0386	
SC	19	19	*BM9202*	*BM6000*	0.7463	3.059*					
CED	19	69.5	*BM17132*	*CSSM065*			28.12	0.829	0.0115	-0.9903	
BW	19	70.5	*CSSM065*	*IDVGA44*			25.54	0.81	0.0005	0.4543	BW (21)
SC	19	86	*CSSM065*	*IDVGA44*	0.7115	2.349*					
CEM	19	103.5	*RM388*	*BMC1013*			27.5	0.826	0.0176	-0.5696	
SC	20	0.5	*BM3517*	*RM106*			11.66	0.806	0.001	-0.0775	
BW	20	20.5	*BMS1282*	*DIK2467*			38.55	0.788	-0.0016	0.2083	BW (5,7)
BW	20	50.5	*BMS2361*	*BMS703*	2.3351	3.206*					
SC	21	29.5	*ILSTS095*	*BM103*			84.57	0.854	-0.0037	0.1627	
BW	21	70.5	*ILSTS054*	*BMS743*			20.26	0.81	0.0005	0.4543	BW (12)
CED	21	73.5	*ILSTS054*	*BMS743*			14.42	0.841	-0.0064	-0.9958	
SC	22	15	*BMS672*	*BM1558*	0.8718	2.763*					
BW	22	19	*BMS672*	*BM1558*	3.2798	2.601*					
SC	22	53	*BM3628*	*BM2613*	0.783	3.012**					
CEM	22	58	*BM2613*	*BMS875*	3.8175	2.729*					
CED	23	0.5	Centromeric	*INRA132*			11.04	0.829	-0.0246	-0.8384	
MILK	23	22.5	*INRA132*	*UWCA1*	9.7899	5.447***	52.22	0.848	-0.012	-2.6769	MY (16)
CEM	23	24.5	*BM47*	*BOLADRB1*	4.2915	3.214*					
BW	23	37.5	*UWCA1*	*BOLADRB1*			28.27	0.797	-0.0039	0.0665	BW (13)
SC	23	38.7	*BOLADRB1*	*RM185*	0.5702	3.232*					

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
CEM	24	30.5	*BMS2270*	*AGLA269*			19.64	0.829	0.0135	-0.6686	CE (2)
MILK	24	36.5	*BMS1862*	*BMS1743*	5.4578	2.544*	104.09	0.782	0.0056	2.9702	
CEM	25	14.5	*BMS130*	*BMS2843*	3.996	3.008*	16.95	0.818	0.0276	-0.5024	
CED	25	20.5	*BMS130*	*BMS2843*			16.89	0.823	-0.0211	-0.9841	
CED	25	31.5	*BMS2843*	*BM737*			37.52	0.827	-0.0003	-1.0424	
MILK	25	35.59	*BM737*	*BMS1353*	11.6938	2.759*					
SC	25	48.59	*BMS1353*	*MBO63*	0.8465	3.148**					
MILK	25	60.5	*BMS1353*	*AF5*			15.72	0.798	0.0215	-1.8203	MY (22)
CED	26	0.5	*RM169*	*BMS651*			10.71	0.837	-0.0076	-0.9123	CE (19)
SC	26	3	*BMS651*	*FASMC2*	0.6062	2.938*					
CED	26	27.5	*BM1314*	*BM188*	9.7138	4.074**	44.17	0.824	0.0211	-0.5415	CE (19)
BW	26	30.5	*INRA081*	*BM188*	3.5671	2.766*	11.08	0.777	-0.0014	0.3935	
MILK	26	45.5	*BM188*	*BMS2567*			16.11	0.709	0.0033	0.3089	MY (16)
CED	26	68.5	*BM804*	Telomeric			13.14	0.821	-0.0122	-0.8925	
BW	26	79.2	*BM804*	Telomeric			12.96	0.803	-0.001	0.2869	
SC	27	49	*INRA134*	*BMS2116*	0.6785	2.465*					
MILK	27	67.2	*BM203*	Telomeric			11.42	0.746	-0.0279	2.4811	

QTL Peak[1]					QTL Express[2]		LOKI				Reference[4]
Trait[3]	BTA	Position	Flanking Markers		$-\log_{10}$ ($P_{nominal}$)	Effect	Bayes Factor	Freq 1	Effect 12	Effect 22	
MILK	28	18.04	*IDVGA29*	*BL25*	11.2346	3.507**					
BW	28	29.5	*BL25*	*BMS2608*	1.5621	2.128*	17.43	0.774	0.0002	0.4163	
CED	28	29.5	*BL25*	*BMS2608*			43.52	0.849	0.0127	-1.0826	
SC	28	29.5	*BMS510*	*BMS2608*	0.9593	3.785***					
MILK	28	31.5	*BMS510*	*BMS2608*			12.23	0.808	-0.0282	-2.8895	MY(1)
SC	28	43.04	*BMS2608*	*BMS1714*	0.525	2.493*					
BW	28	44.5	*BMS2608*	*BMS1714*			18.8	0.808	-0.0015	0.1378	
BW	28	54.5	*BMS1714*	Telomeric			16.5	0.805	-0.0013	0.3932	
CED	28	57.5	*BMS1714*	Telomeric			12.55	0.83	0.0144	-0.8383	
MILK	28	61.35	*BMS1714*	Telomeric			22.47	0.775	-0.0036	-2.7136	
SC	29	12.5	*BMS764*	*BMS1787*			25.65	0.824	-0.0004	0.1135	
MILK	29	32.5	*BMS1600*	*RM040*			42.03	0.875	0.0197	2.6661	

[1] Listed is each QTL's most likely location in cM, flanking markers, associated information from QTL Express and LOKI, and whether the QTL has previously been identified.

[2] Significance levels for QTL Express: *=P $\leq$ chromosome-wide 0.01, **=P $\leq$ genome-wide 0.05, ***=P $\leq$ genome-wide 0.01. Freq_1 is the frequency of the 1 allele; effect values estimated in LOKI assume that the 11 genotype has an effect of 0.

[3] Abbreviations: birth weight (BW), calving ease (CE), calving ease direct (CED), calving ease maternal (CEM), maternal milk (MILK), milk yield (MY), scrotal circumference (SC).

[4] References: 1=(Ashwell *et al.* 2004), 2=(Ashwell *et al.* 2005), 3=(Boichard *et al.* 2003), 4=(Casas *et al.* 2000), 5=(Casas *et al.* 2003), 6=(Casas *et al.* 2004a), 7=(Casas *et al.* 2004b), 8=(Harder *et al.* 2006), 9=(Holmberg & Andersson-Eklund 2006), 10=(Kaupe *et al.* 2007), 11=(Kim *et al.* 2003), 12=(Kneeland *et al.* 2004), 13=(Kucerova *et al.* 2006), 14=(Nadesalingam *et al.* 2001), 15=(Plante *et al.* 2001), 16=(Ron *et al.* 2001), 17=(Ron *et al.* 2004), 18=(Schnabel *et al.* 2005), 19=(Taylor *et al.* 1998), 20=(Viitala *et al.* 2003)

Table 4.3. Statistical summary of reproductive QTL.

	Count		LOKI		QTL Express	EPD					Acc >0.05
Trait	QTL	Reference	Freq [1]	Effect [2]	Effect [3]	StDev	Var	Kurt	Skew	Count [4]	Count [5]
Birth Weight	24	9	0.77	0.29	2.722	2.4	5.7	0	0	1998	1989
Calving Ease Direct	18	5	0.82	0.86	7.344	5.6	31	1	-1	1998	1997
Calving Ease Maternal	18	5	0.83	0.59	4.866	4.9	24	2	-1	1998	1997
Maternal Milk	44	16	0.42	2.37	9.419	9.4	88	0	0	1998	1990
Scrotal Circumference	31	0	0.51	0.08	0.732	0.6	0.3	0	0.1	1967	1704

[1] The average frequency of the economically desirable allele as determined by LOKI.
[2] The average effect of the economically desirable homozygote as determined by LOKI.
[3] The allele substitution effect economically desirable allele as determined by QTL Express.
[4] Count of animals with an EPD value recorded.
[5] Count of animals with an EPD accuracy value >0.05.
Statistical information is based the EPDs from the mapping population.

Table 4.4. Analysis of variance results for birth weight QTL.

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	652	6045.1496	9.2717	2.12	<.0001
Error	1298	5666.9868	4.3659		
Corrected Total	1950	11712.1365			

R-Square	0.5161
Coeff Var	92.8439
Root MSE	2.0895
Mean	2.2505

Table 4.5. Analysis of variance results for calving ease direct QTL.

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	458	23265.1545	50.79728	2.11	<.0001
Error	1492	35908.826	24.06758		
Corrected Total	1950	59173.9805			

R-Square	0.393165
Coeff Var	148.7621
Root MSE	4.905872
Mean	3.297796

Table 4.6 Analysis of variance results for calving ease maternal QTL.

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	644	22203.5368	34.47754	2.05	<.0001
Error	1306	21966.6139	16.81977		
Corrected Total	1950	44170.1507			

R-Square	0.502682
Coeff Var	85.32121
Root MSE	4.101191
Mean	4.806766

Table 4.7 Analysis of variance results for maternal milk QTL.

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1365	147572.966	108.1121	2.01	<.0001
Error	585	31405.6758	53.6849		
Corrected Total	1950	178978.642			

R-Square	0.824528
Coeff Var	47.19839
Root MSE	7.326999
Mean	15.52383

Table 4.8 Analysis of variance results for scrotal circumference QTL.

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1022	174366.66	170.61	1.36	<.0001
Error	928	116531.84	125.57		
Corrected Total	1950	290898.50			

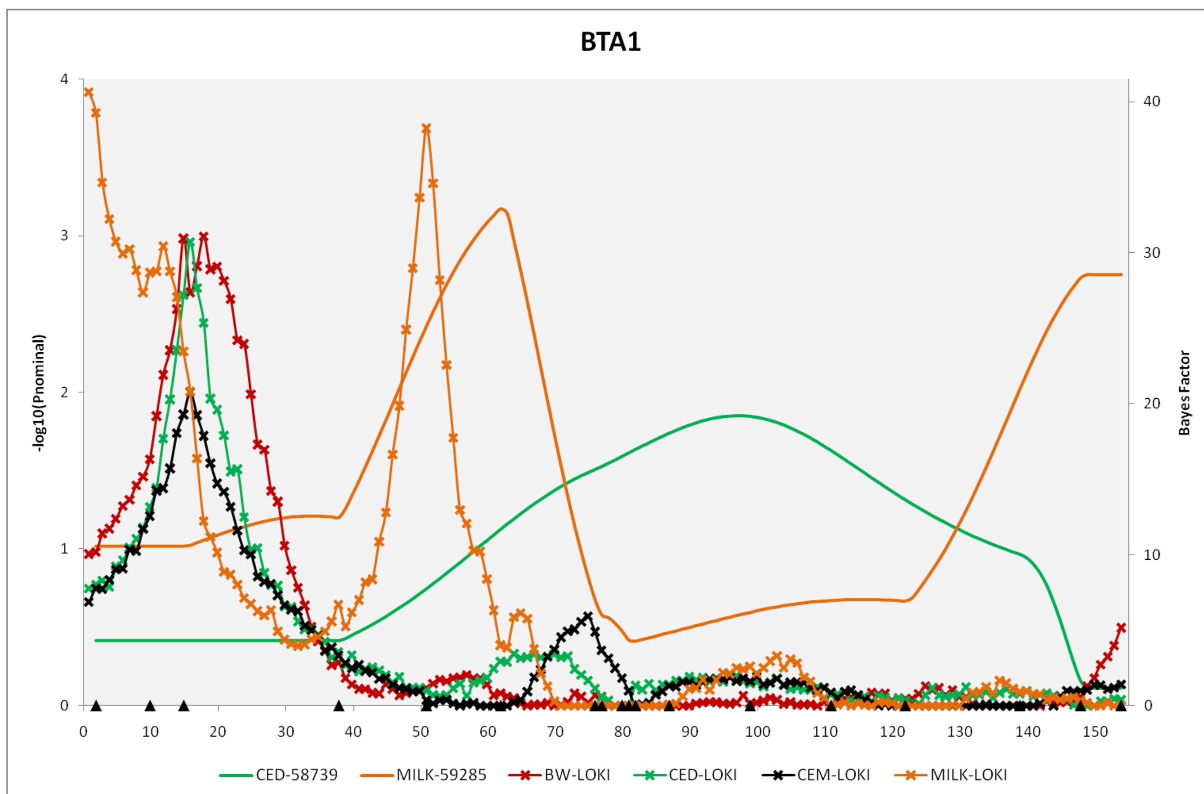
R-Square	0.5994
Coeff Var	-805.7852
Root MSE	11.2059
Mean	-1.3907

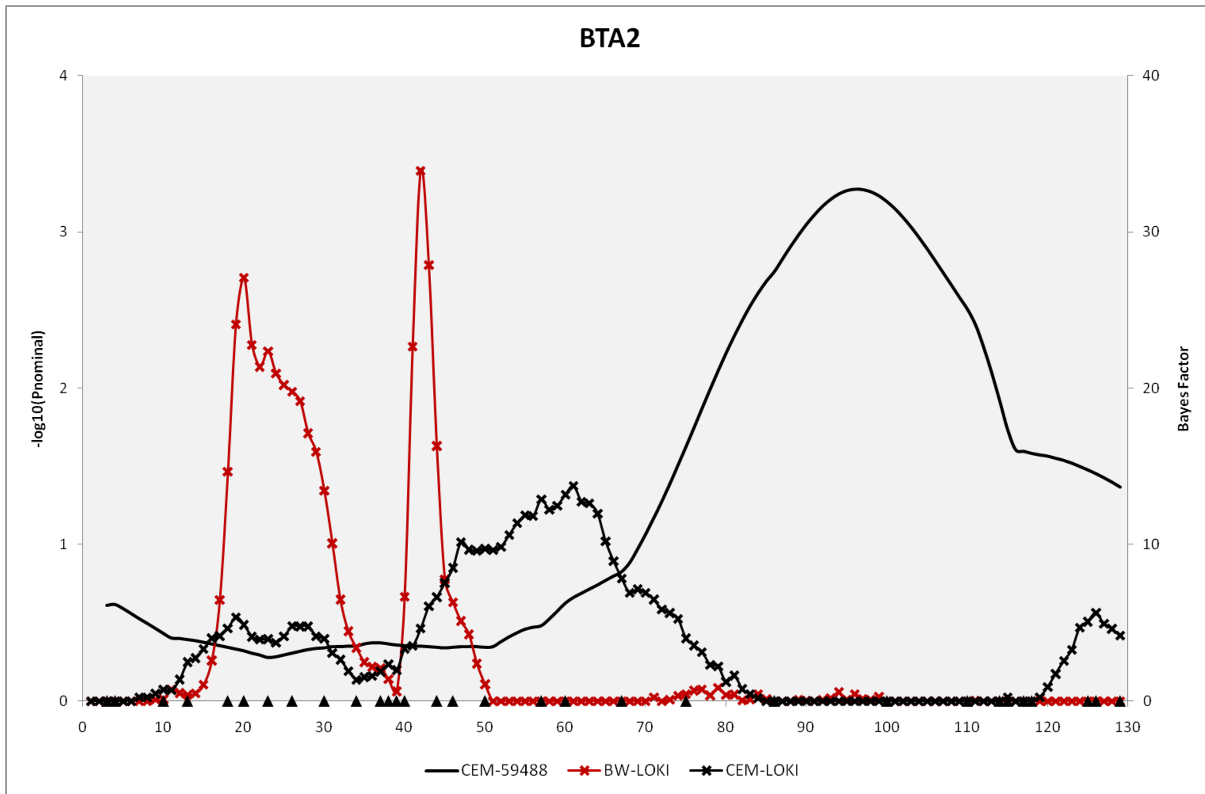
Table 4.9. Summary of reproductive QTL identified as pleiotropic.

BTA	Position	Trait 1	Trait 2	Express 1	LOKI 1	Express 2	LOKI 2
1	16.0	CED	CEM		-1.095		-0.598
8	115.5	CED	CEM		-0.840		-0.652
25	17.0	CED	CEM		-0.984	3.996	-0.502

Express 1, 2 and LOKI 1, 2 are the allele substitution effects from QTL Express and the difference between alternative homozygotes effect for traits 1 and 2 respectively.

Figure 4.1. Statistical support profiles for reproductive QTL for each *Bos taurus* autosome. Plots are for half-sib data analyzed for an American Angus sire lineage by QTL Express, unless otherwise indicated as being from LOKI. QTL Express data are expressed in $-\log_{10}P_{nominal}$ values units while for LOKI are expressed as Bayes Factors. Colored lines represent different traits as follows: red = BW; green = CED; black = CEM; gold = MILK, and blue = SC. Significance levels for QTL Express are as follows: chromosome-wide $P \leq 0.01 = 2.8$, genome-wide $P \leq 0.05 = 3.3$, genome-wide $P \leq 0.01 = 4.1$. Significance levels for LOKI are ≥ 10 Bayes Factor. All X-axis values are in cM, ▲ represent genetic markers

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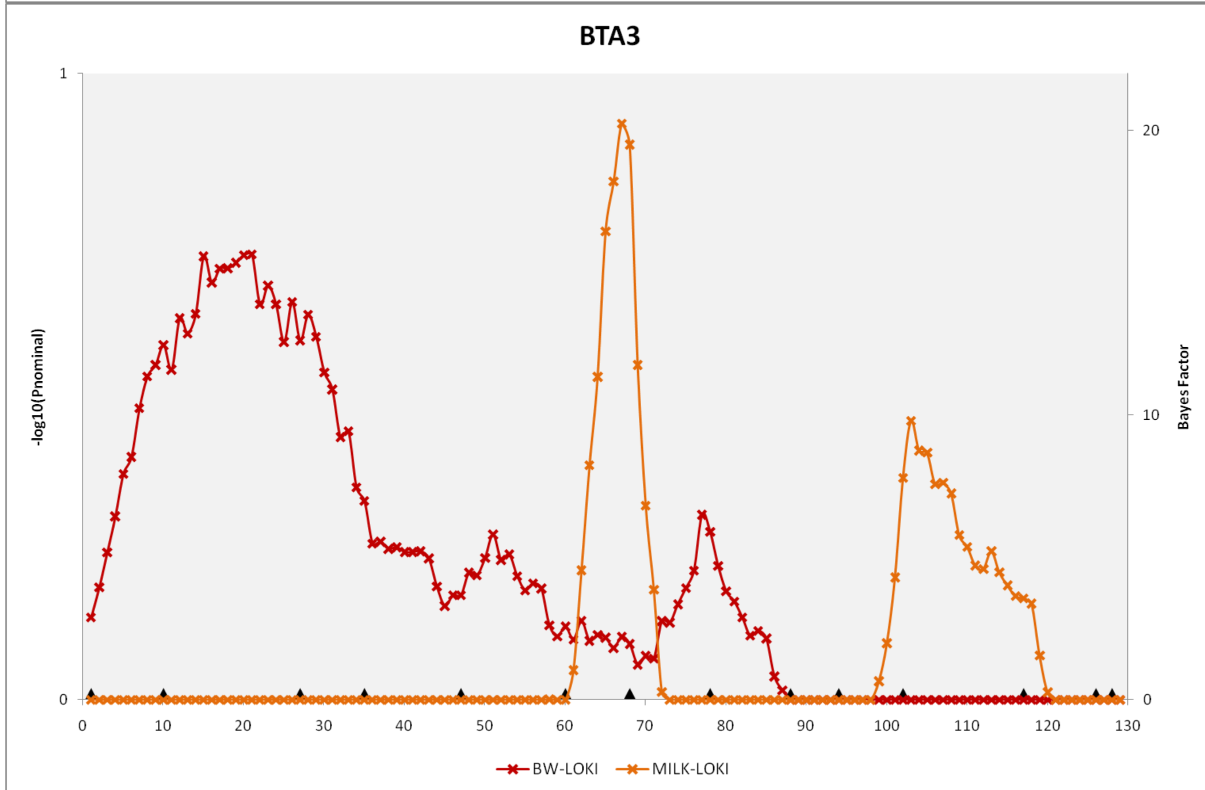
BW-LOKI
CEM-LOKI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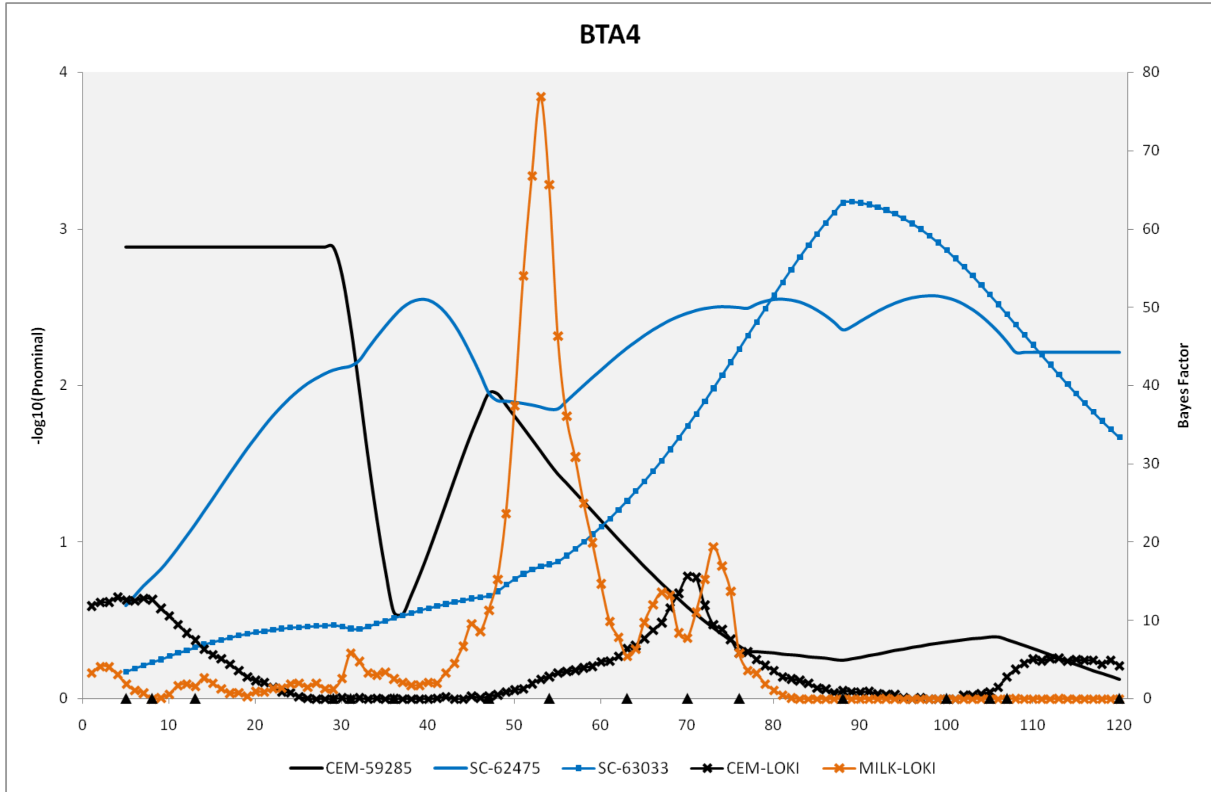
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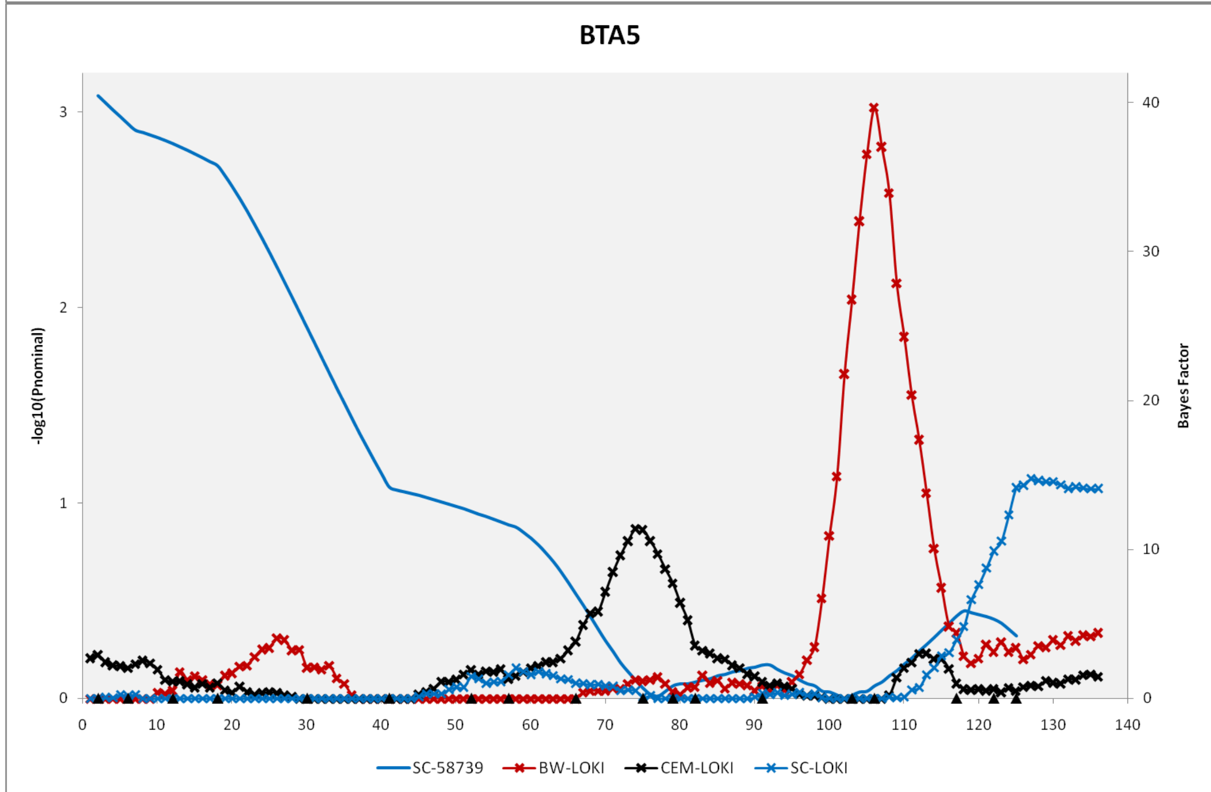
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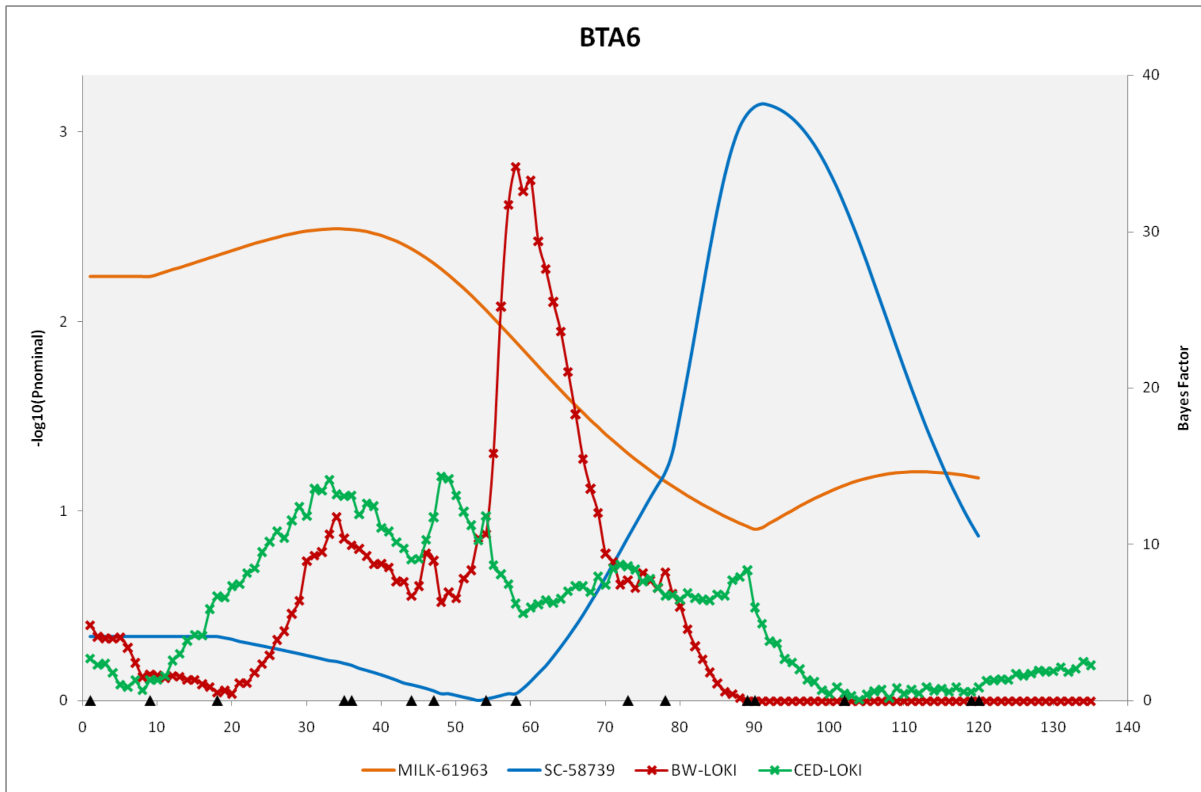
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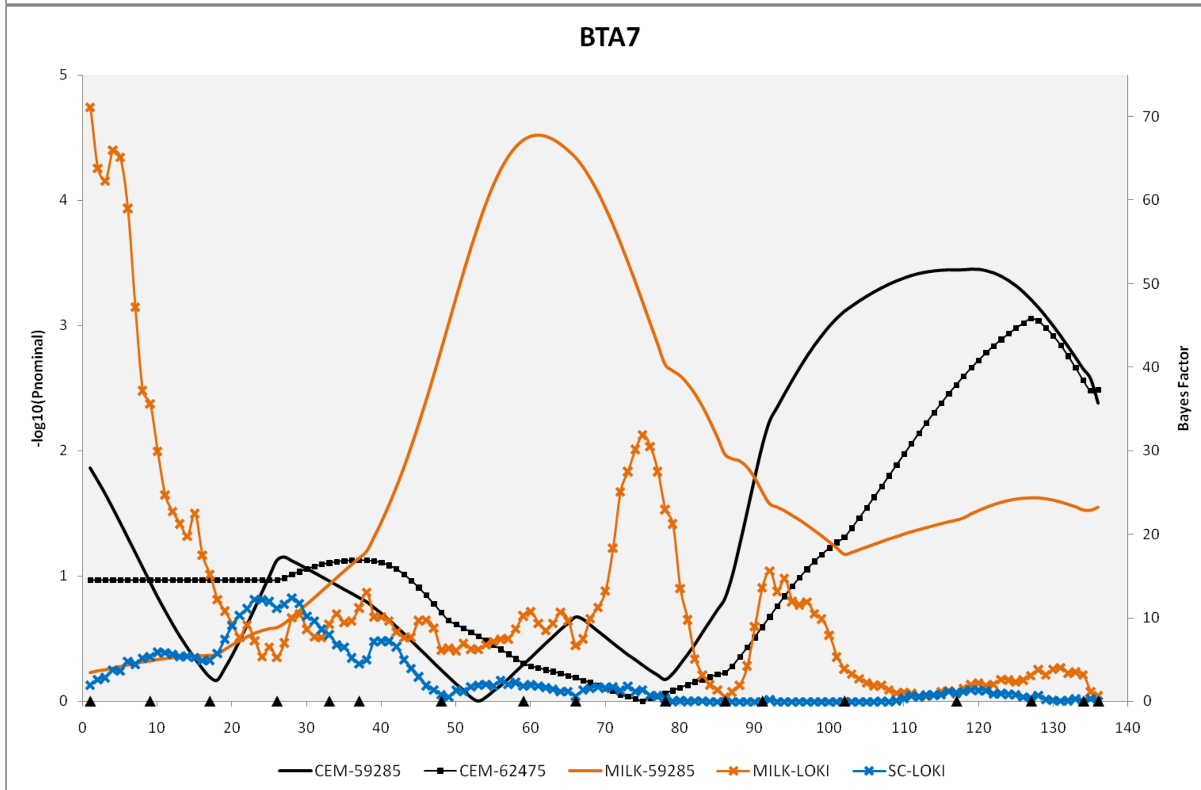
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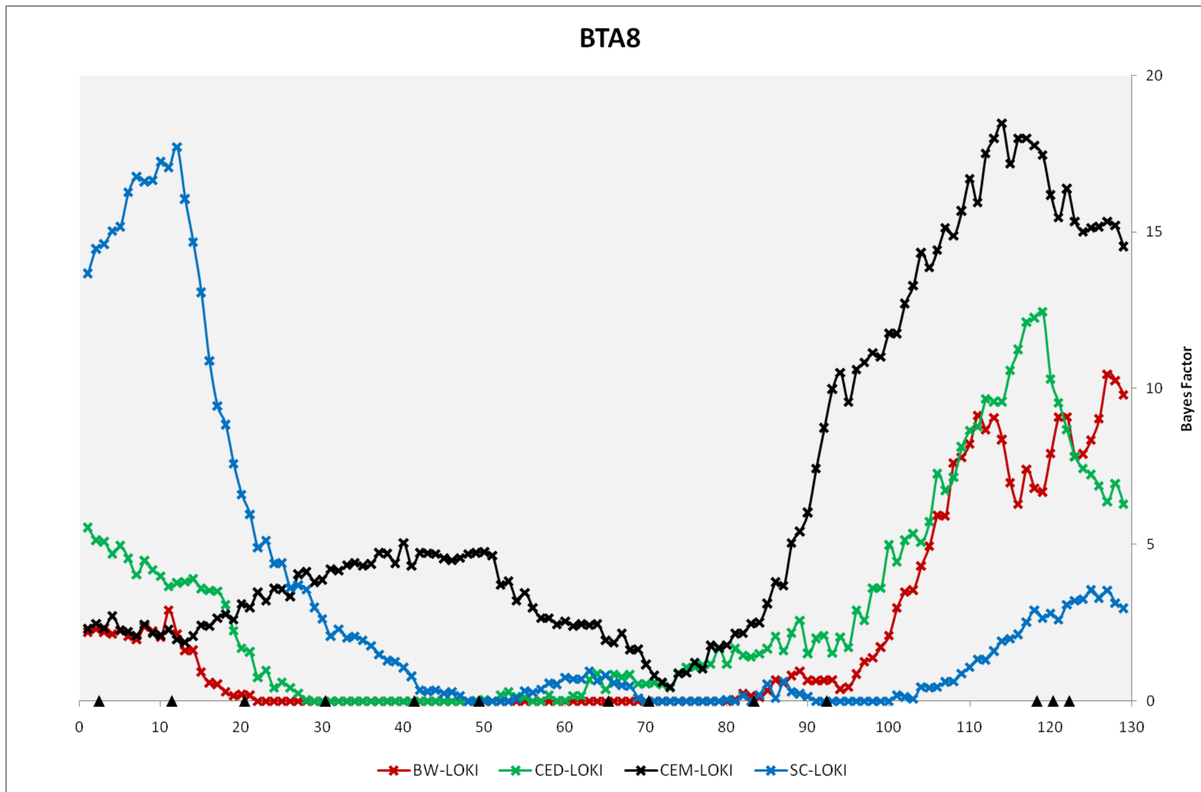
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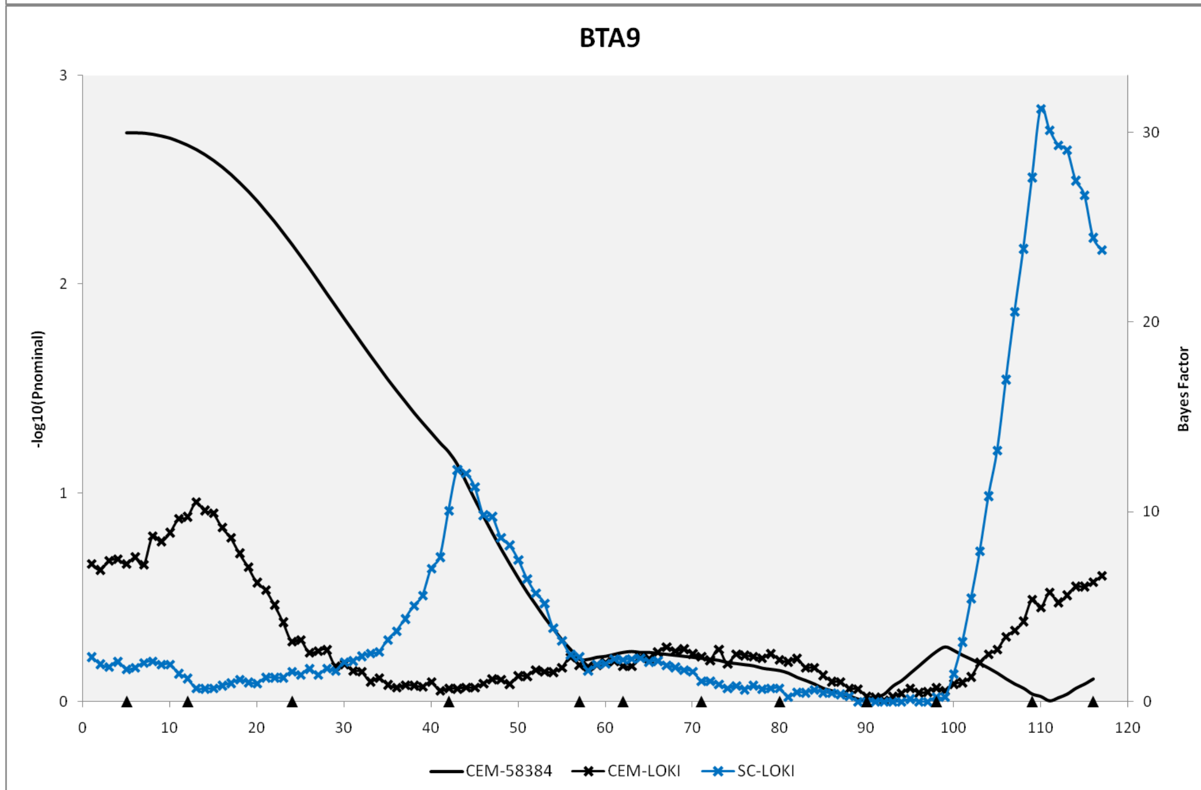
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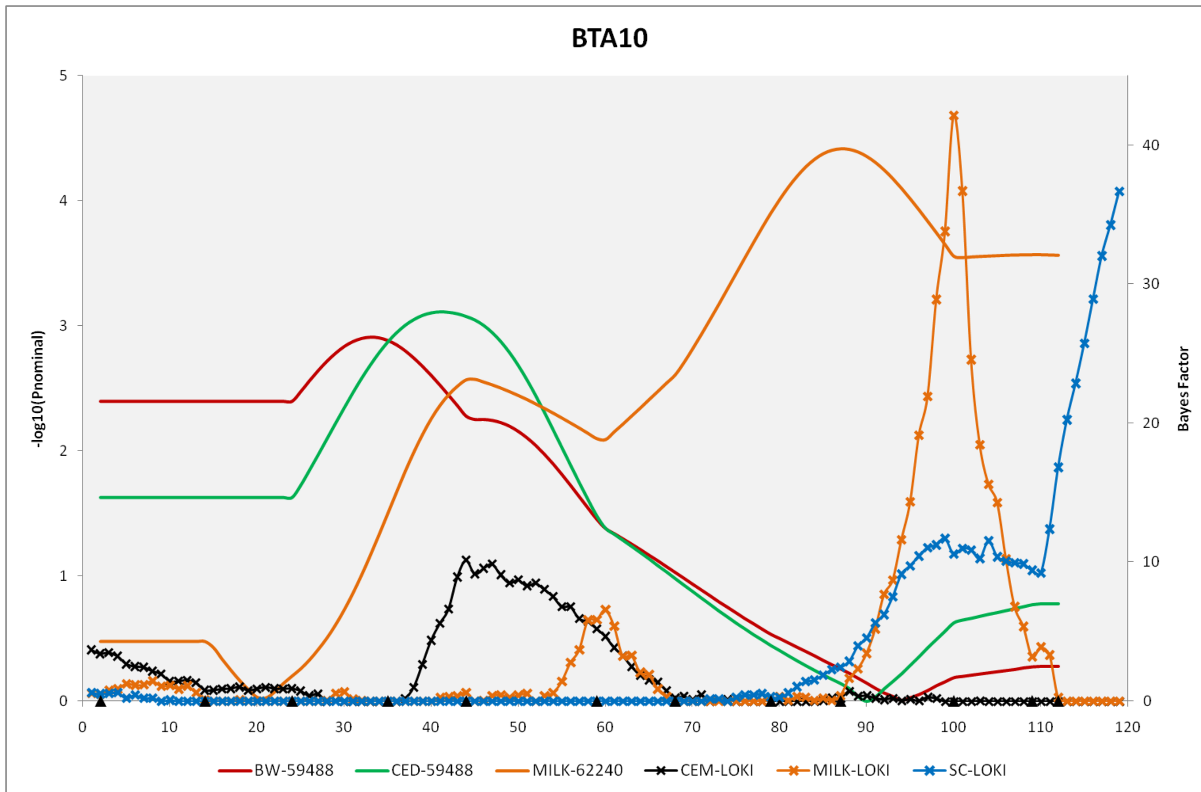
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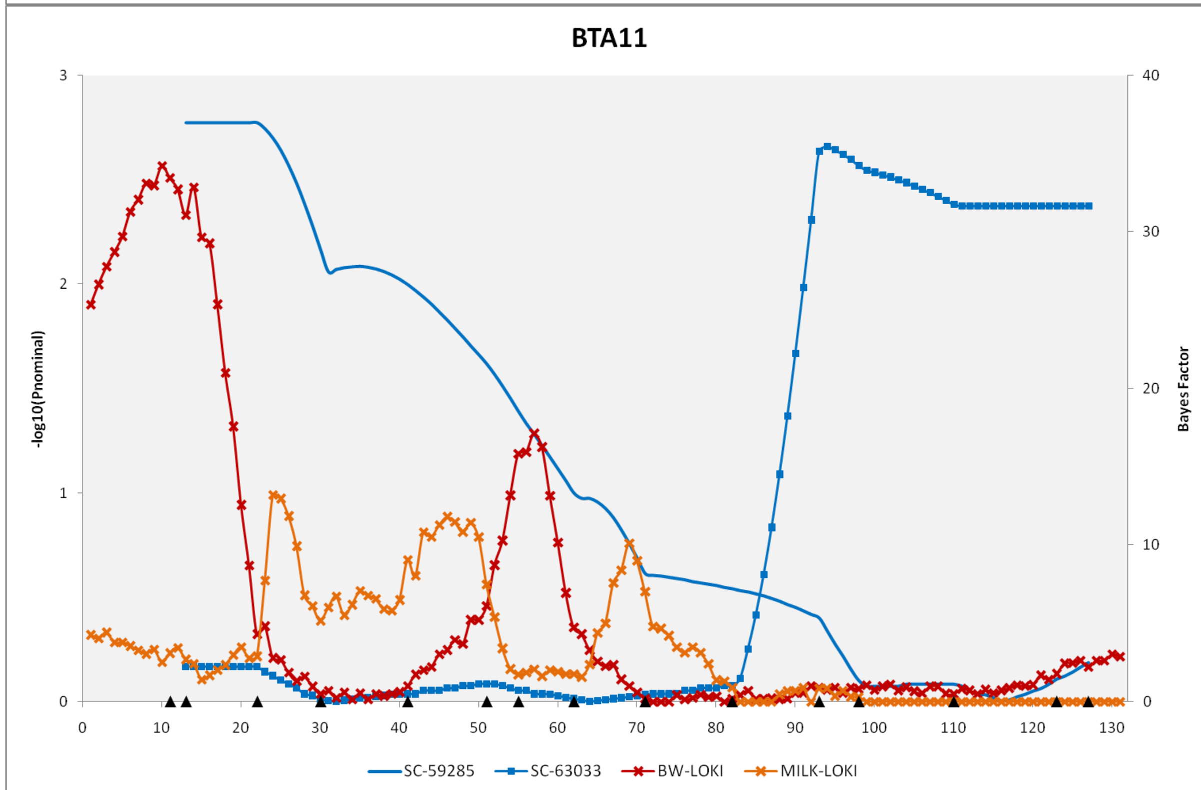
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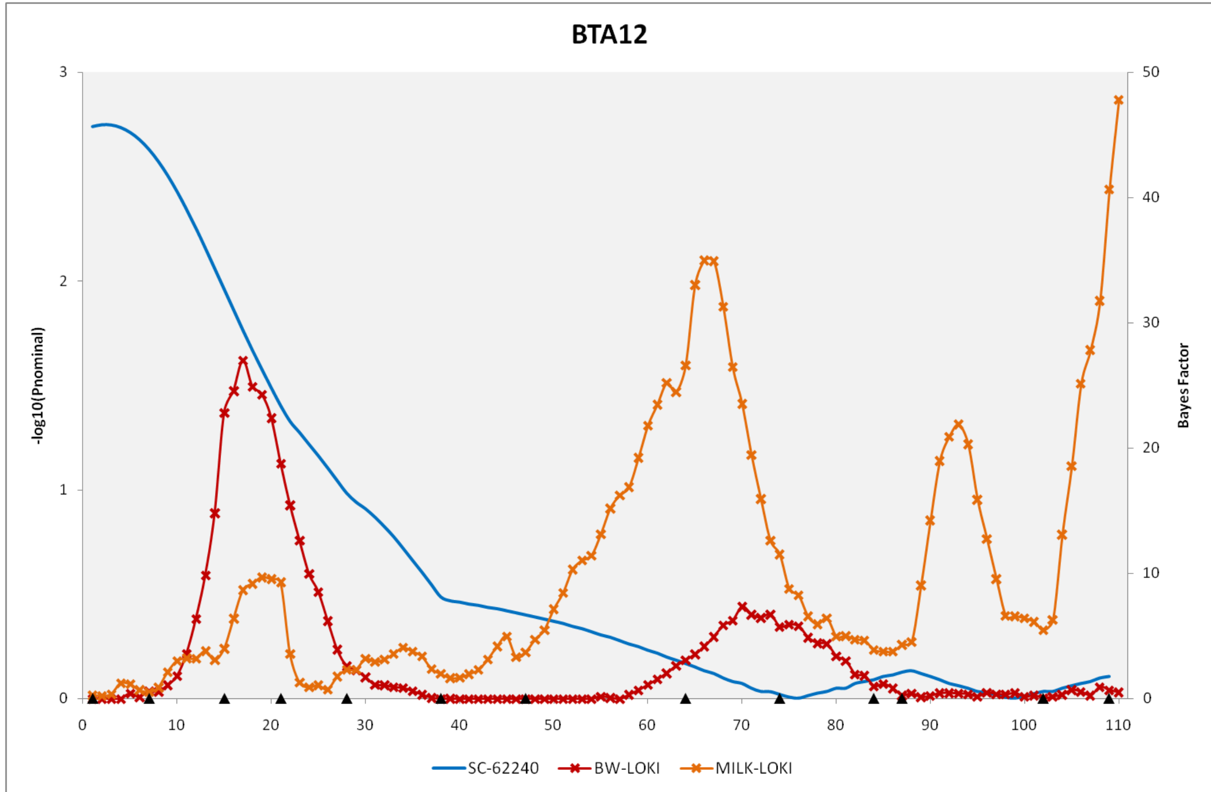
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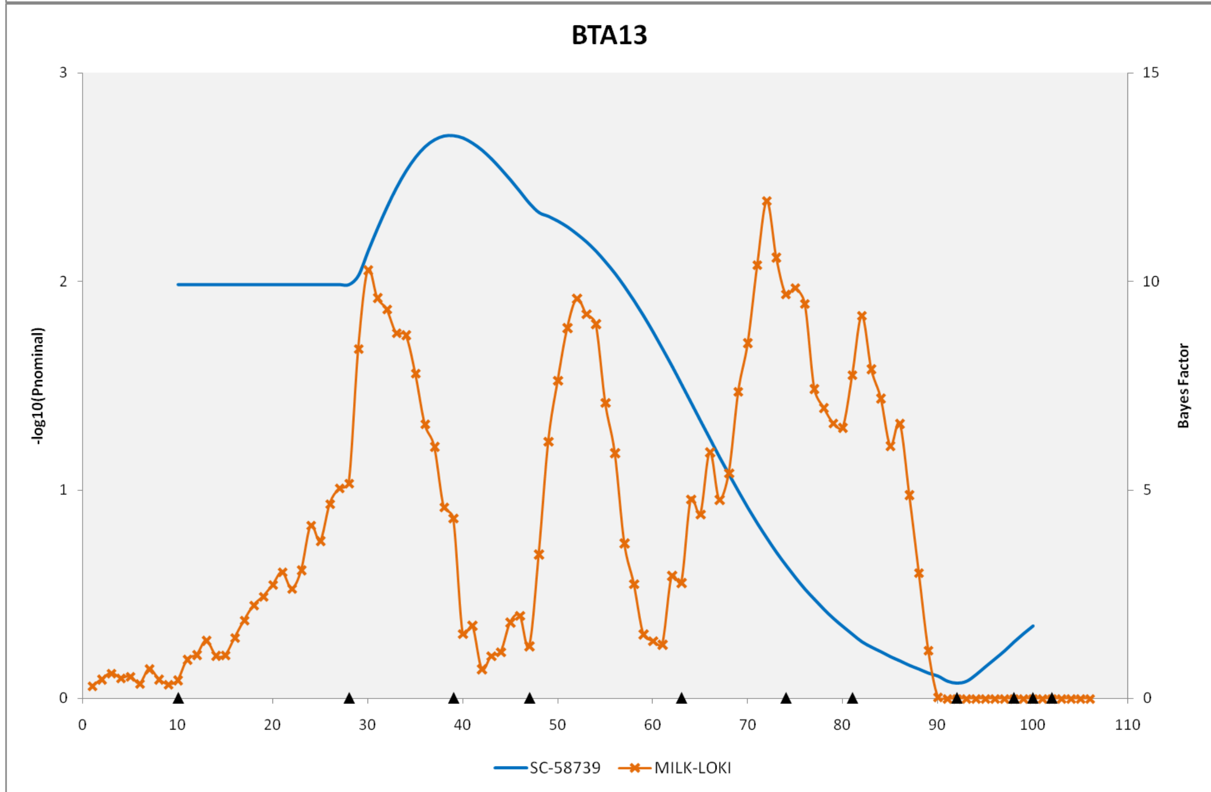
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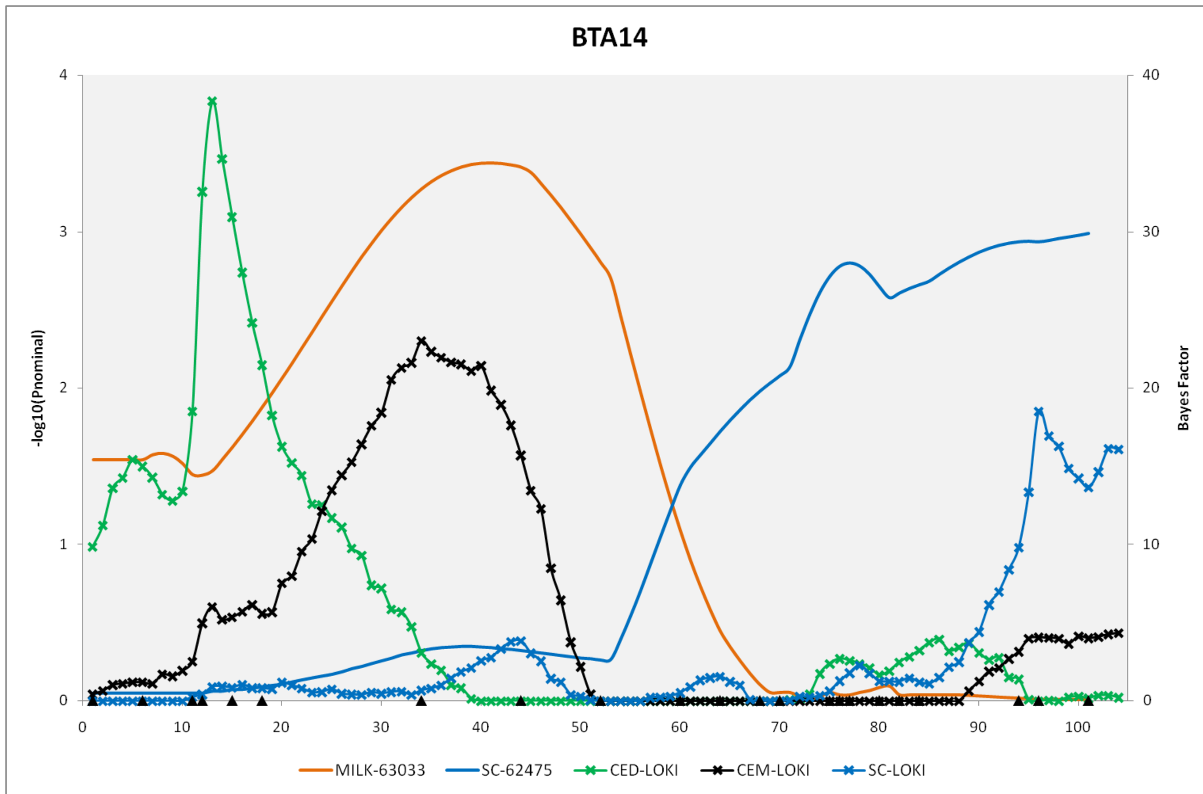
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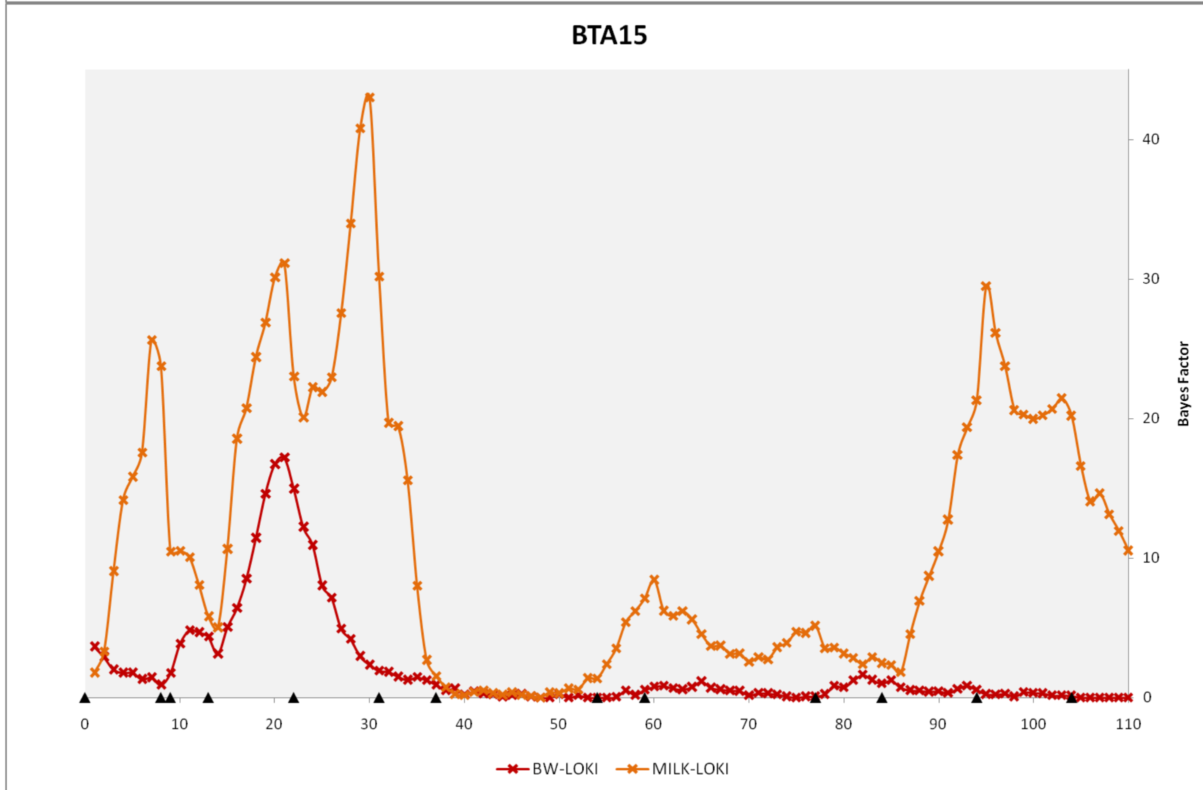
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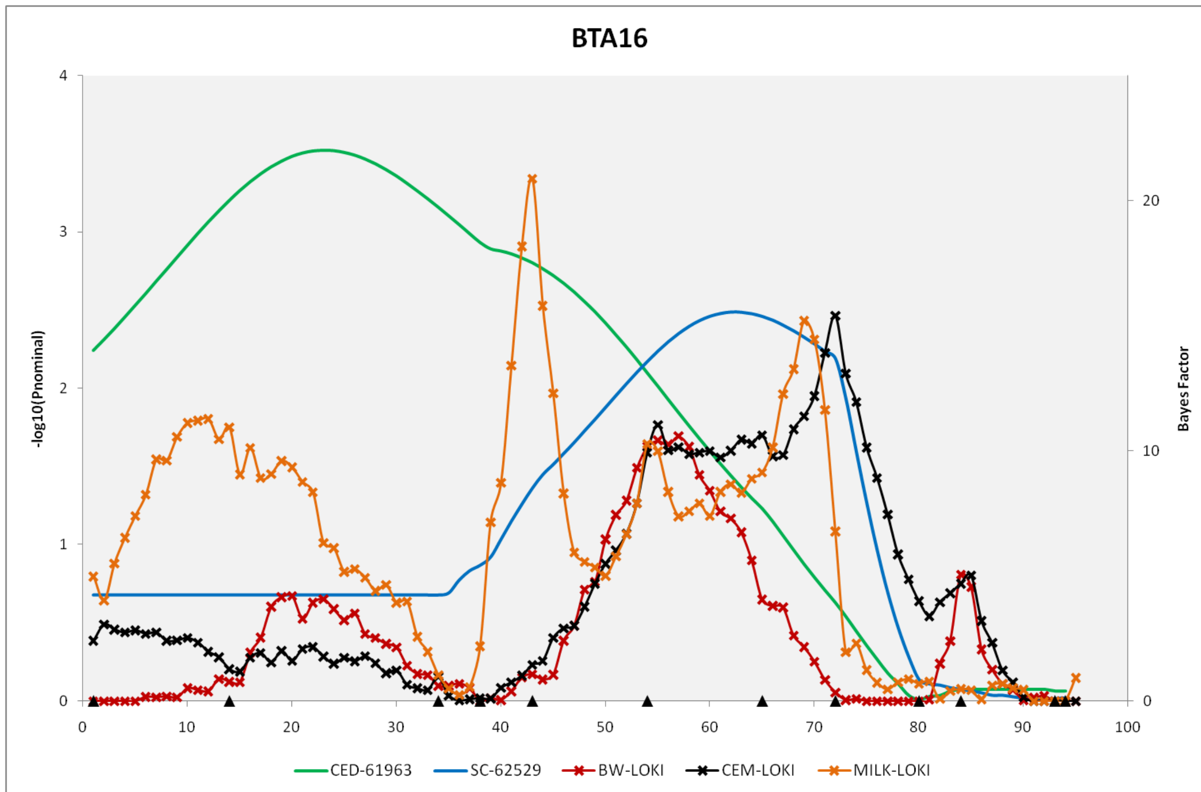
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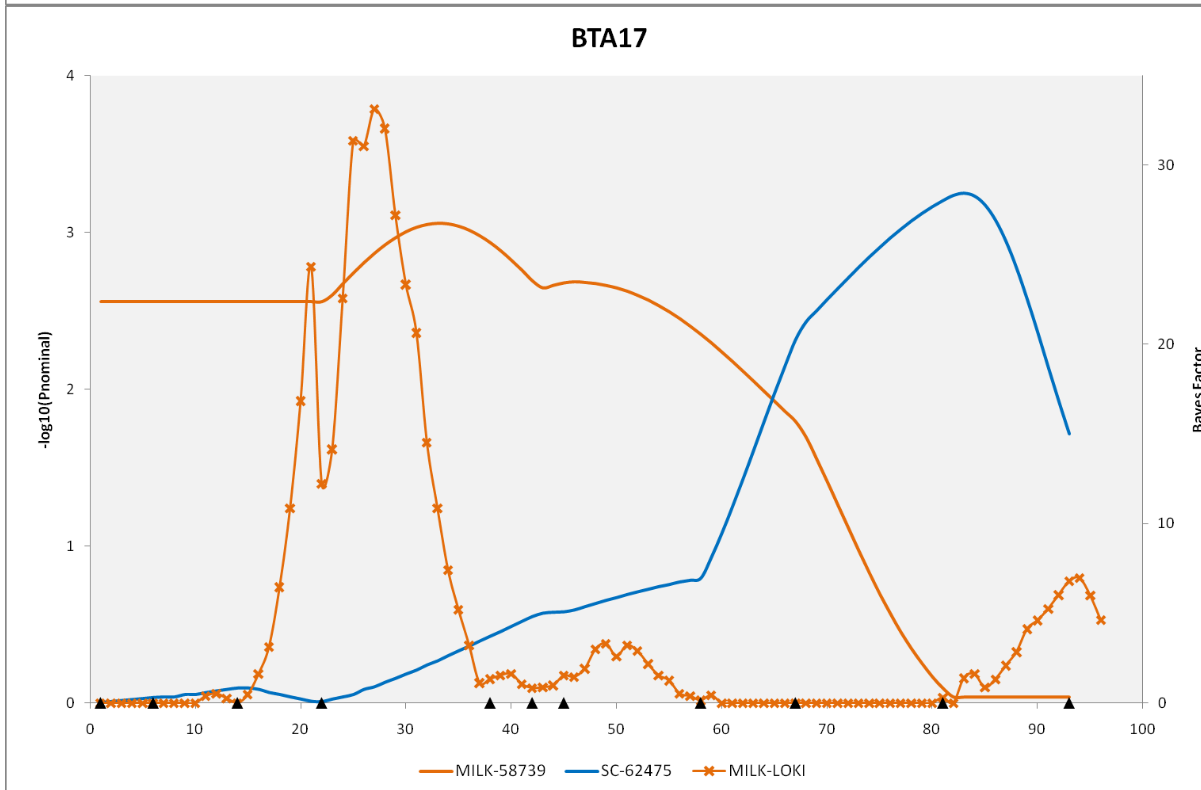
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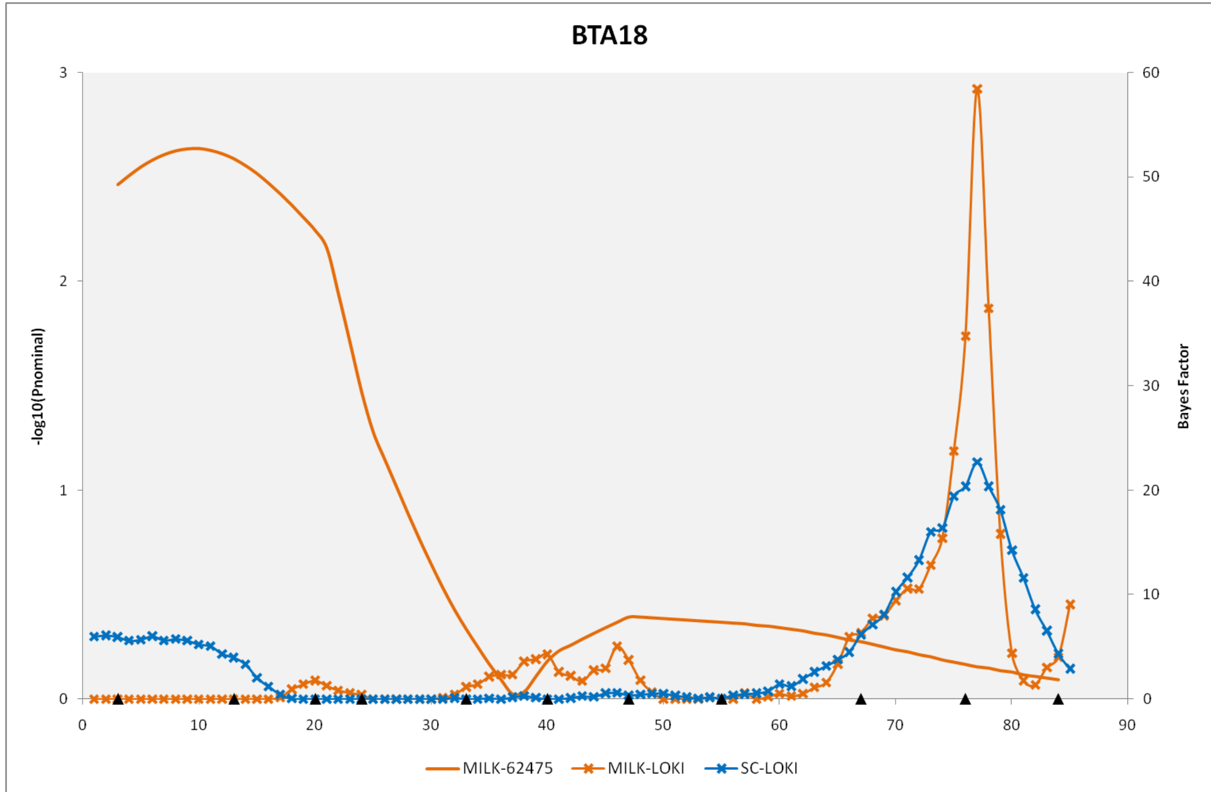
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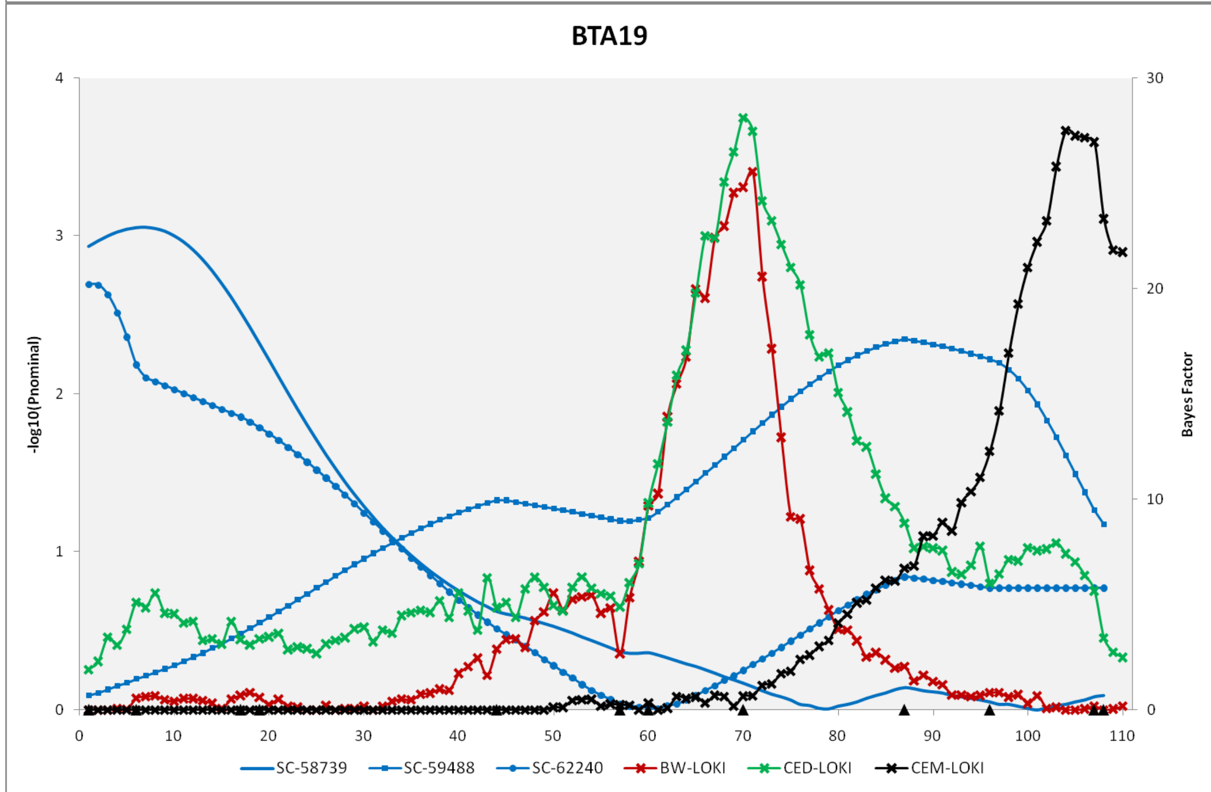
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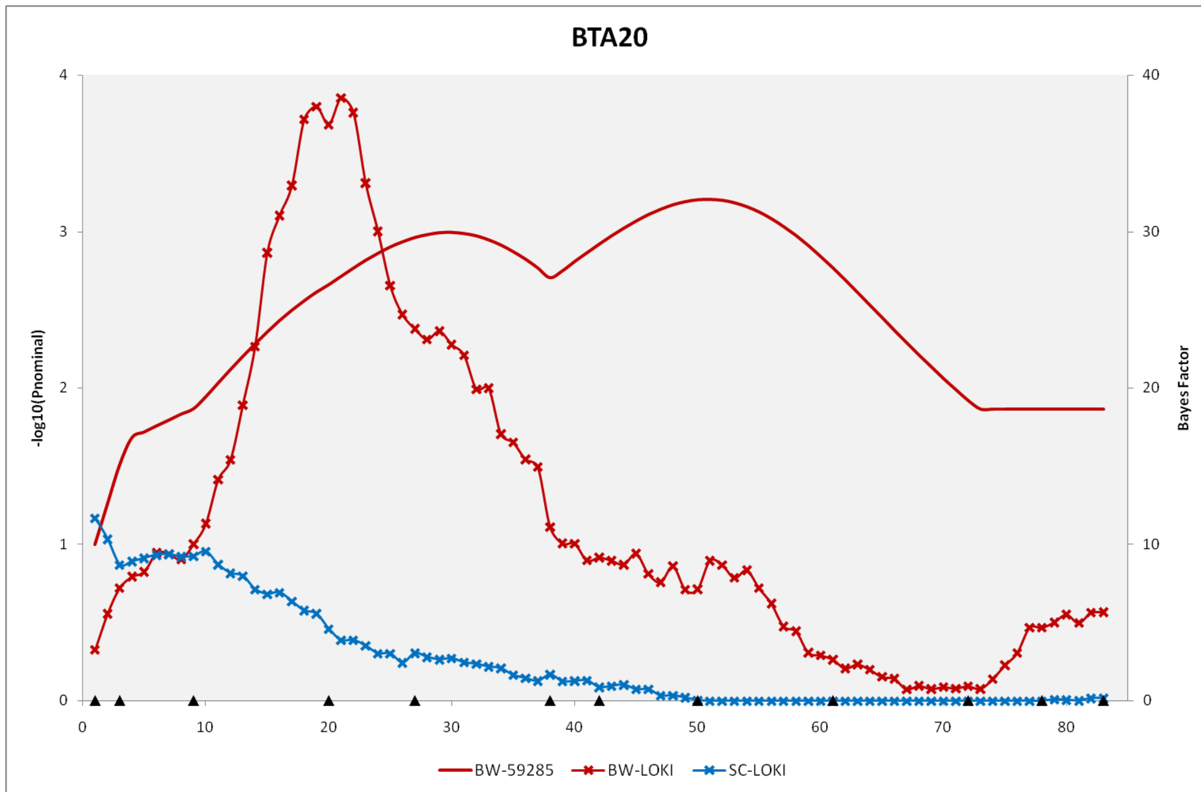
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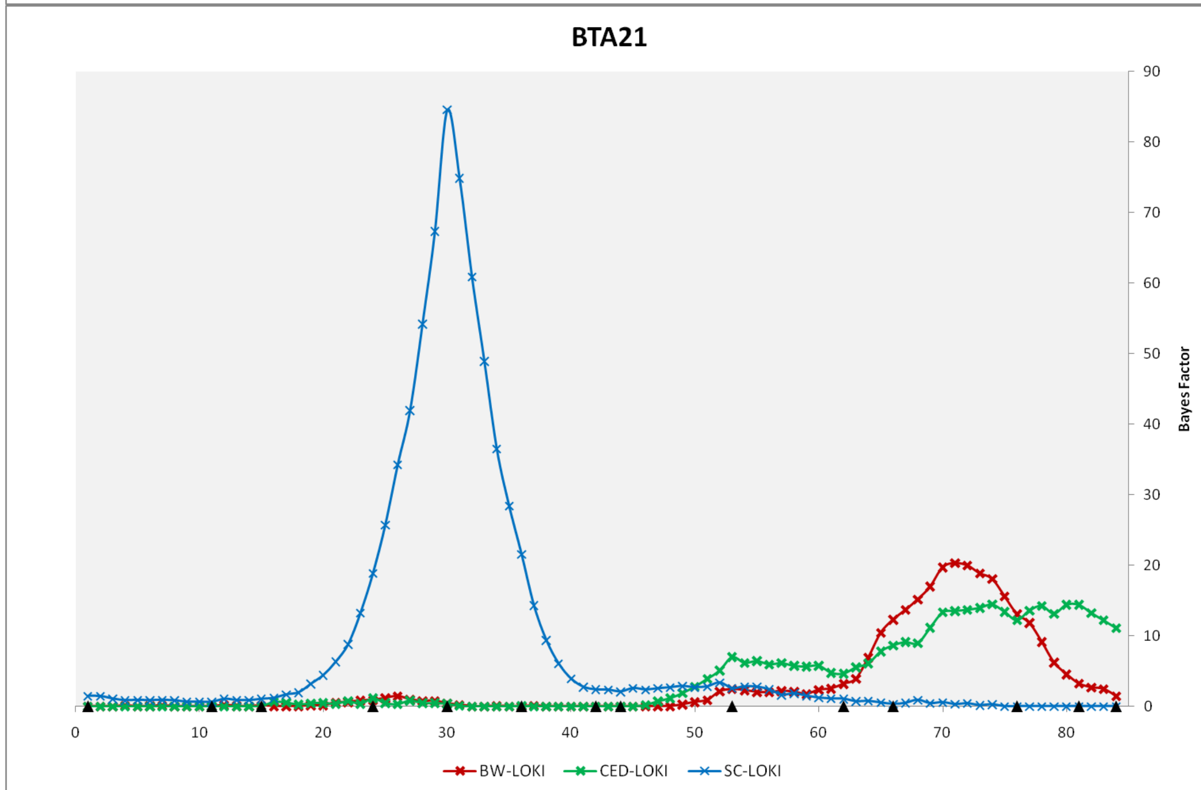
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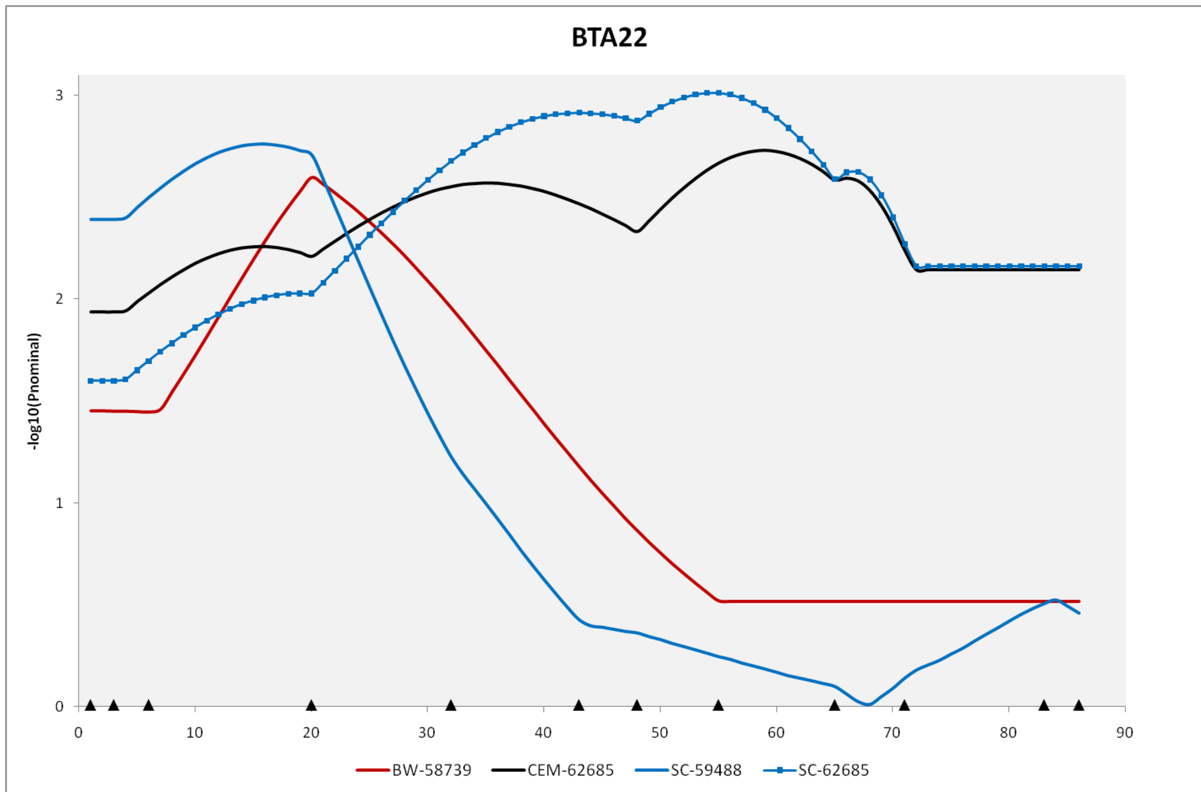
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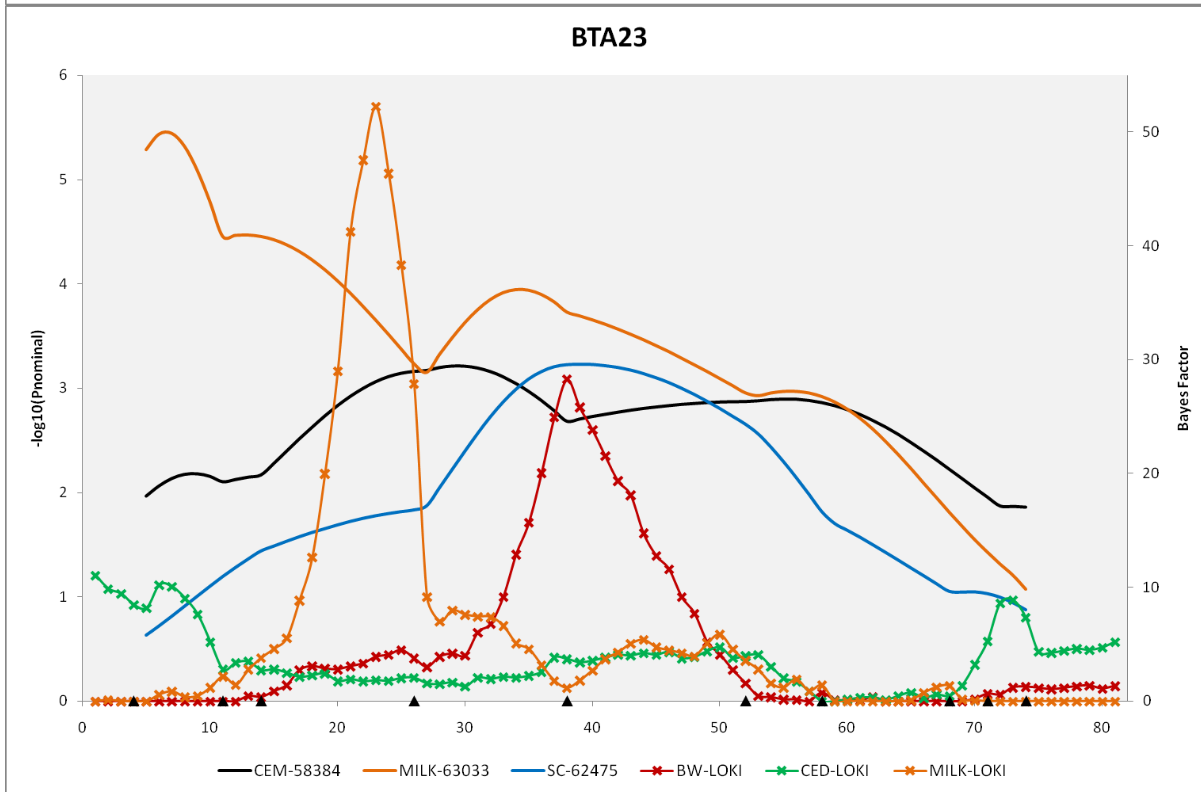
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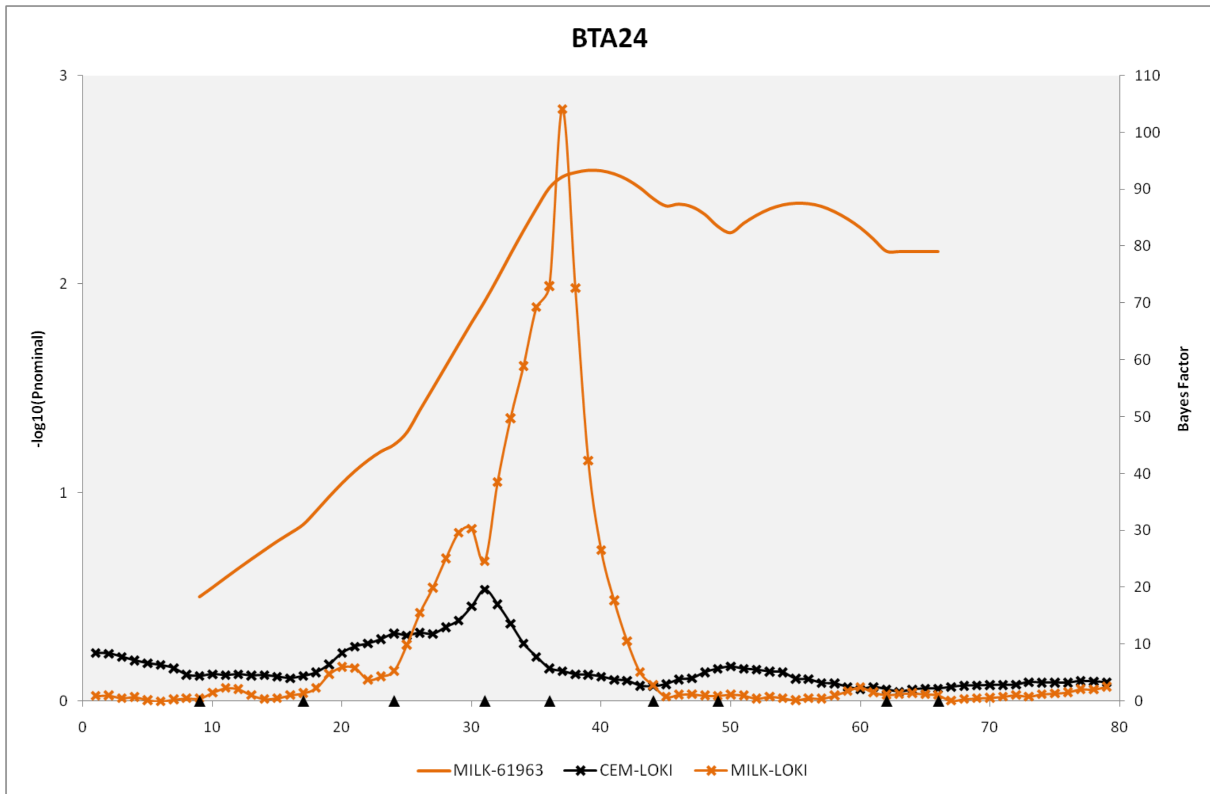
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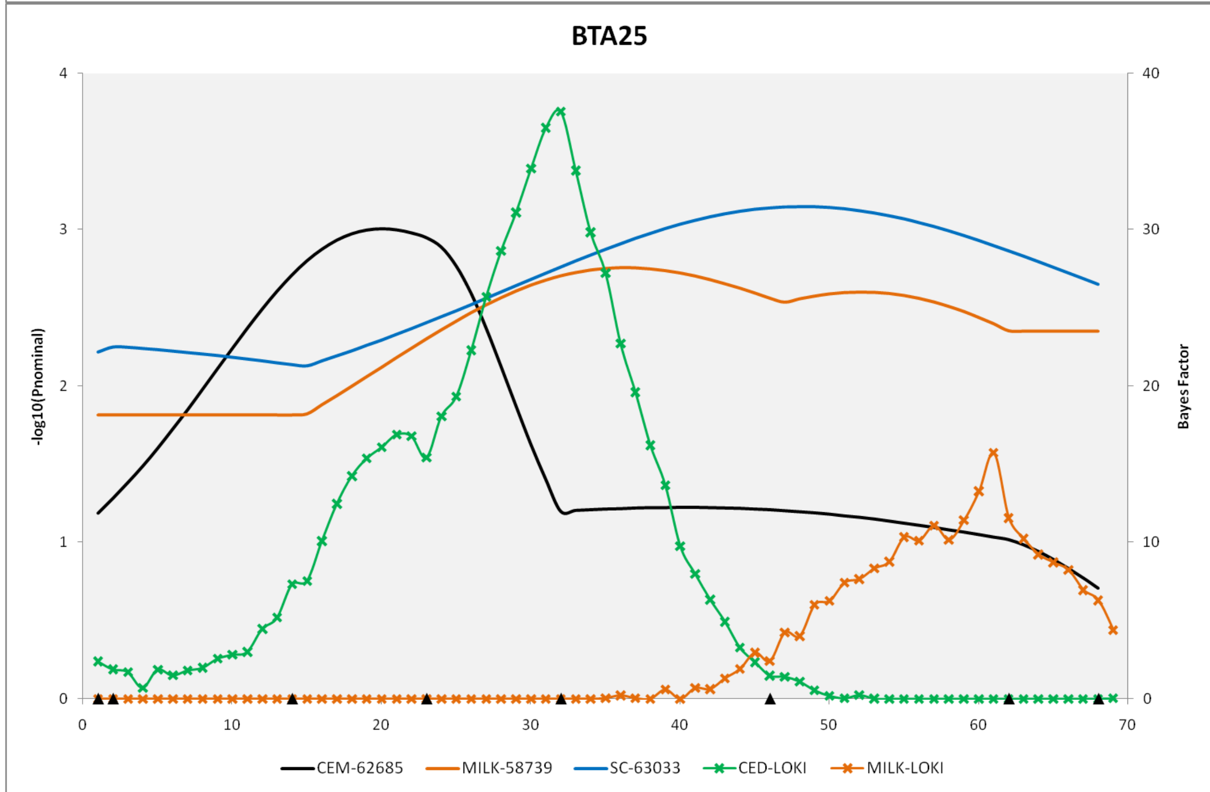
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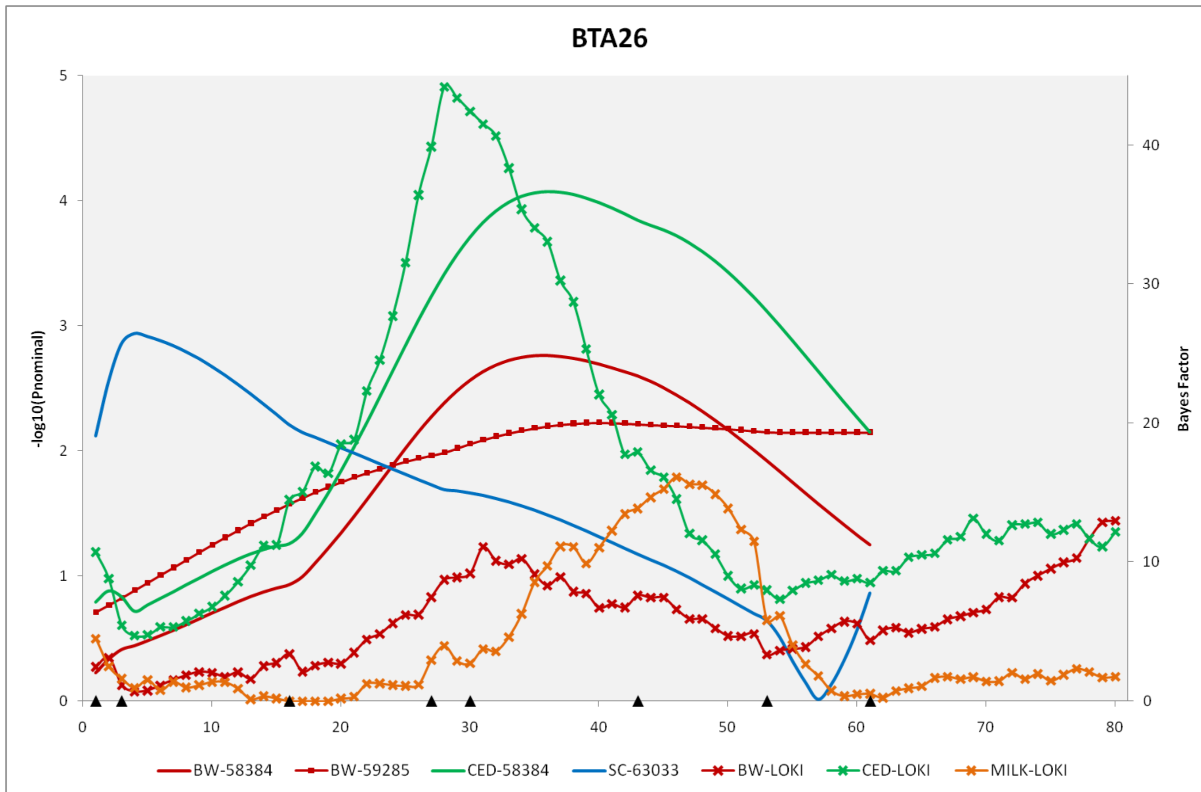
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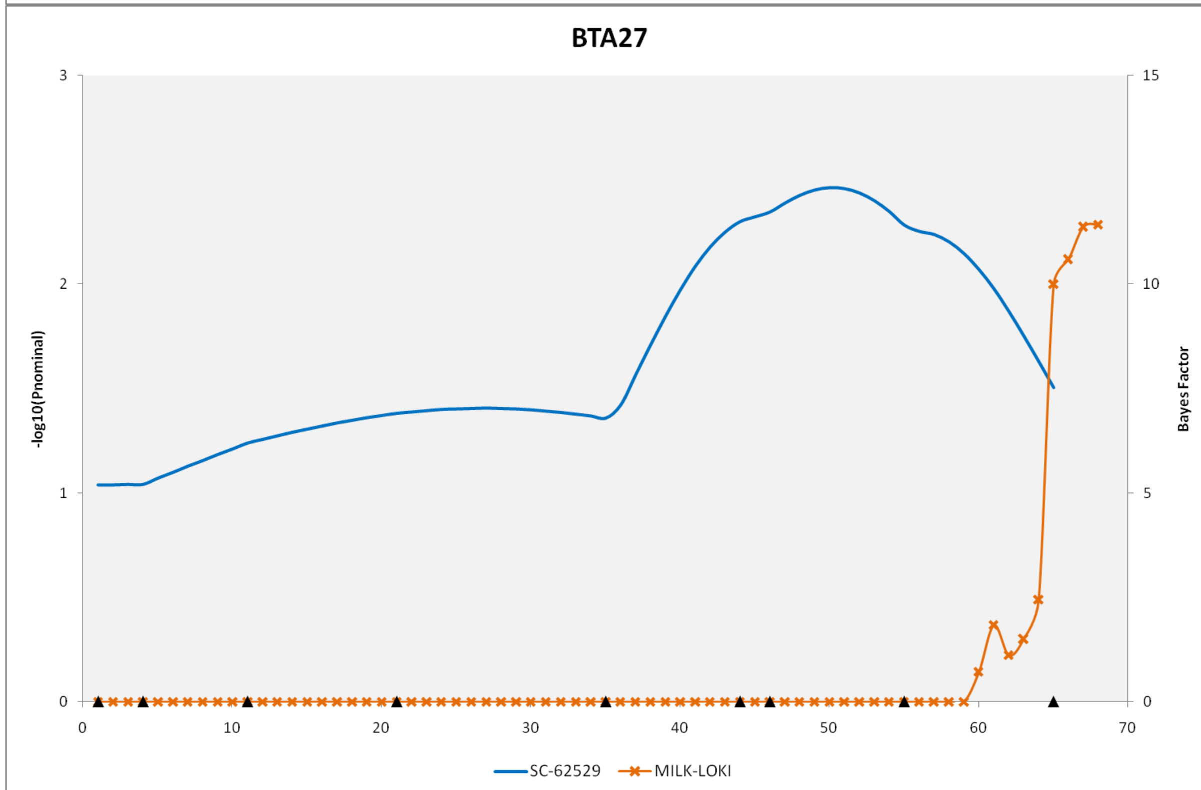
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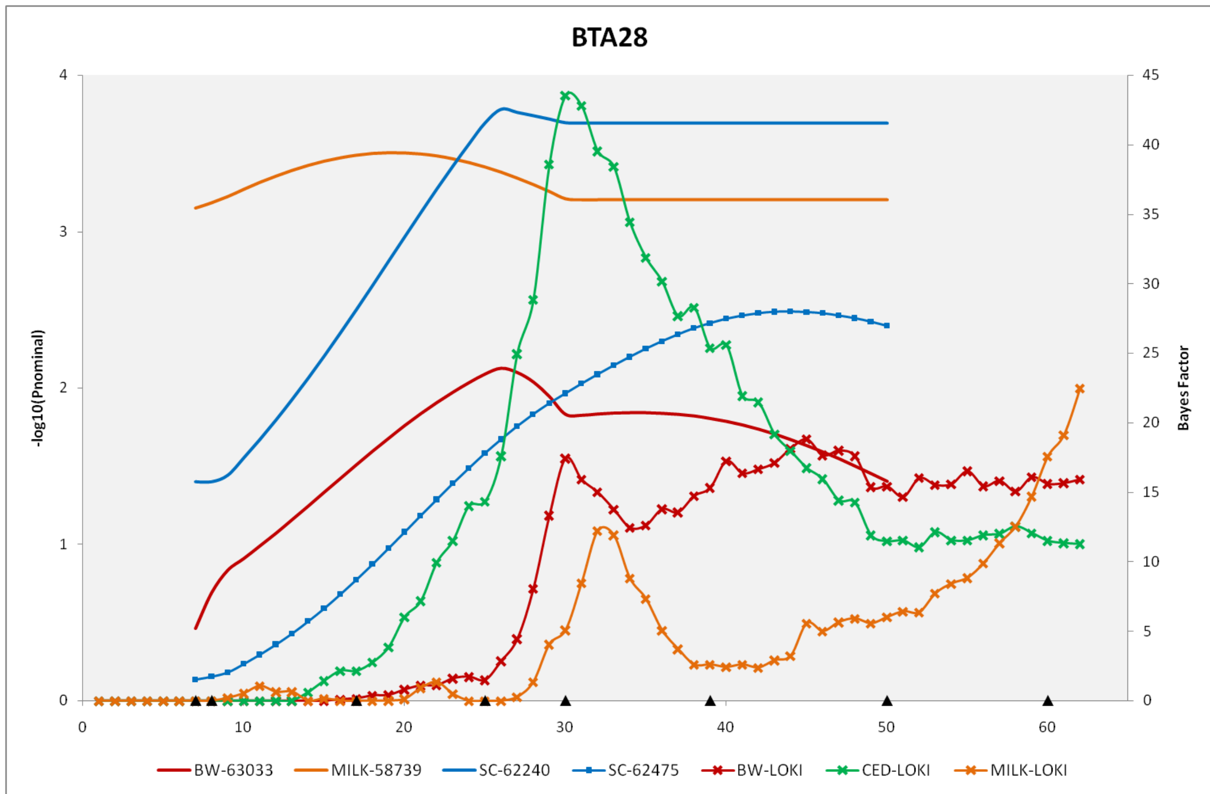
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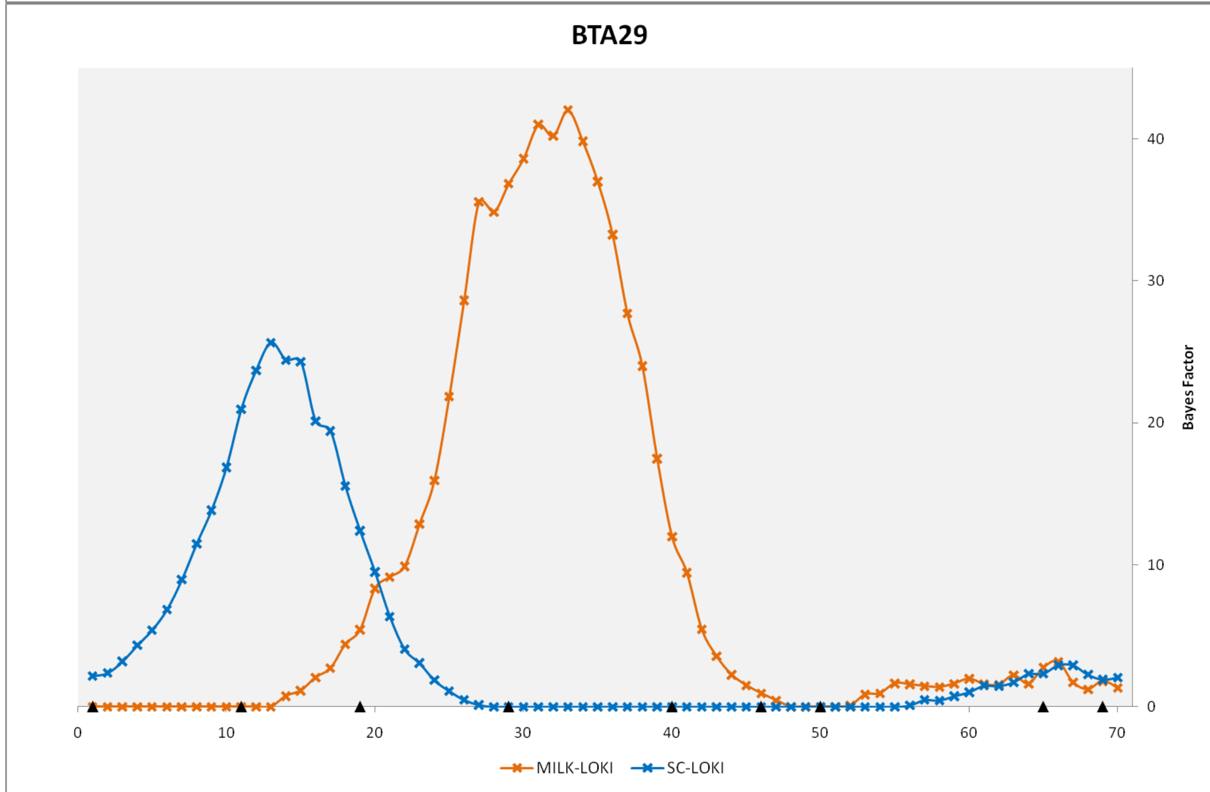
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CHAPTER 5

Assessment of DNA extracted from FTA® cards for use on the Illumina iSelect BeadChip

Abstract

Background

FTA® cards provide an ideal medium for the field collection of DNA, therefore we sought to assess the quality of genomic DNA extracted from this source for use on the Illumina BovineSNP50 iSelect BeadChip which requires unbound, relatively intact (fragment sizes $\geq$2 kb), and high-quality DNA. Bovine blood and nasal swab samples collected on FTA cards were extracted using the commercially available GenSolve kit from GenVault Corp or the FTA Elute protocol from Whatman Inc, both with minor modification. The call rate and concordance of genotypes from each sample were compared to those obtained from whole blood samples extracted by standard PCI extraction.

Findings

An ANOVA on the BovineSNP50 genotype call rate indicated a significant difference ($P<0.0003$) between DNA extracted by FTA Elute, GenSolve, and PCI extraction methods. Two sample t-tests demonstrated that the DNA extracted from the FTA cards produced genotype call and concordance rates that were not different to those produced by assaying DNA samples

extracted by proteinase K treatment, Phenol:Chloroform:Isoamyl alcohol extraction, and ethanol precipitation from whole blood, while FTA Elute samples were statistically different ($P \leq 0.05$).

Conclusions

We conclude that DNA extracted from FTA cards by the GenSolve kit is of sufficiently high quality to produce results comparable to those obtained from DNA extracted from whole blood when assayed by the Illumina iSelect technology. Additionally, we validate the use of nasal swabs as an alternative to venous blood or buccal samples from animal subjects for reliably producing high quality genotypes on this platform.

Background

The advent of high-throughput SNP genotyping has revolutionized our ability to obtain high density genotypes, however, a key issue remains; the need to access, store, and extract DNA from each individual. While DNA collected for SNP analysis needs to be of sufficient quality to ensure high genotype call rates, the method of collection used in the field needs to be straightforward. FTA filter paper cards (Whatman Inc, Part of GE Healthcare, Florham Park, NJ, USA) simplify the harvesting and storing of samples, and once properly dried they can be stored at room temperature for years without DNA deterioration (Ledray & Netzel 1997). While the chemically infused paper kills microorganisms and prevents degradation of the matrix-bound DNA (Smith & Burgoyne 2004), the bound DNA must be extracted and

resuspended in an aqueous solution before it can be genotyped by high-throughput SNP genotyping platforms, such as the Illumina iSelect BeadChip (San Diego, CA, USA).

Previous research has shown that multiple genomic sources, including lymphocytes, buccal cells, whole genome amplified samples, and fingernails can be used to generate high-density SNP data provided the DNA sample is of adequate quality and quantity (Montgomery *et al.* 2005; Feigelson *et al.* 2007; Woo *et al.* 2007; Nakashima *et al.* 2008). While venous blood is often considered an optimal source for DNA, the invasiveness and cost of obtaining venous blood samples can be prohibitive (Saab *et al.* 2007; Woo *et al.* 2007), especially for large-scale studies or those that deal with livestock and wild animals. Additionally, fresh samples collected in the field may experience degradation before they can be processed (Smith & Burgoyne 2004). The ease of collection, transportation, storage, and protection from degradation of samples stored on FTA cards alleviates many of these issues (Vidal-Taboada *et al.* 2006).

While previous studies have shown that DNA harvested from FTA cards is suitable for genotyping 1,536 SNP on the Illumina GoldenGate platform and 10,000 SNP on the Affymetrix 10K GeneChip Human Mapping 10K Array XBA 142 2.0 (Whatman Inc), it is not known if these samples are appropriate for high-throughput genotyping on the Illumina iSelect platform, which currently assays up to 200,000 SNP (Illumina 2009). To determine the utility of FTA cards as a collection and storage media for DNA analyzed by iSelect BeadChips which requires unbound, relatively intact (fragment sizes $\geq$2 kb), and high-quality DNA (Steemers *et al.* 2006), we analyzed the call rate and concordance of 54,122 SNP genotypes produced by the BovineSNP50 BeadChip (Illumina). Whole blood and nasal swabs were collected on FTA and FTA Elute cards and DNA was harvested from the cards using either a minimally modified GenSolve protocol

(GenVault Corp, Carlsbad, CA, USA), or a minimally modified FTA Elute protocol from Whatman. Genotypes produced from these samples were benchmarked against genotypes produced from DNA extracted directly from buffy coats by proteinase K treatment, PCI extraction, and ethanol precipitation (Sambrook *et al.* 1989).

Materials and Methods

The following samples were collected from two Angus (*B. taurus*) bulls: 10 ml of whole blood (WB) collected and stored in vacuum tubes with 15 mg of EDTA (Covidien, Mansfield, MA, USA), WB was also collected from ear veins and applied to FTA and FTA Elute cards(McClure *et al.*2005 ; Whatman Inc), and nasal swab samples were collected using a sterile foam tipped applicator (Whatman Inc) which was rubbed for 10 seconds against the inside of the bull's nose and then pressed against an FTA Elute card to transfer cells to the card.

Buffy coats were isolated from each of the 10 ml WB samples and DNA was extracted by proteinase K treatment followed by PCI extraction and ethanol precipitation (Sambrook *et al.* 1989). Genotypes produced from these DNA samples were used as the standards against which genotypes produced from samples harvested from the FTA cards were compared. DNA was extracted from 3 mm punches obtained from each FTA and FTA Elute card using a GenSolve kit (GenVault Corp). We minimally modified the manufacturer's protocol by using a PCI extraction and ethanol precipitation instead of a Qiagen kit for DNA cleanup. A modified Whatman FTA Elute protocol was also used to extract DNA from 3 mm punches obtained from each FTA Elute card. The FTA Elute protocol was modified via the addition of a PCI extraction and ethanol precipitation for DNA cleanup. Three hundred nanograms of DNA from each extraction was

used as template for the BovineSNP50 BeadChip, which was processed and analyzed according to Illumina's protocol for the iSelect single base extension reaction (Steemers *et al.* 2006).

A one-way ANOVA was performed on BovineSNP50 BeadChip call rates from FTA extracted samples and those achieved from assaying 7,737 *B. taurus* samples extracted from WB or cryopreserved semen by PCI extraction in our laboratory (Tables 5.1, 5.2, 5.3). Thirty-five of these samples had two aliquots individually genotyped on the BovineSNP50 BeadChip which generated technical replicates that we used to calculate baseline concordance values. Genotypes produced from each FTA extracted DNA sample were compared for concordance to those obtained from WB for each animal. Call and concordance rates were analyzed with a two sample t-test assuming equal within-treatment variances (Table 5.4).

Results

The ANOVA indicated a statistical difference in call rate ($P<0.0003$) due to method of DNA extraction (Table 5.1). ANOVA on call rate between PCI extracted and GenSolve extracted indicated no statistical difference ($P>0.72$) due to use of the GenSolve kit, FTA card type or sample type (Table 5.2). While an ANOVA on call rate between PCI extracted and FTA Elute extracted samples indicated a significant difference ($P<0.00003$) (Table 5.3). We were concerned whether genotypes obtained from DNA harvested from FTA cards would yield reproducible genotypes that were highly concordant with those produced from DNA extracted from WB. Table 5.4 shows that >99% of called genotypes were concordant for every sample type and that discordances were primarily between the homozygous vs. heterozygous

genotype classes. In every concordance comparison, genotypes from DNA samples harvested from FTA cards were not different from those produced from the standard samples ($P \geq 0.39$).

Conclusion

This report shows that blood and nasal swab samples stored on FTA cards can be processed in a manner that results in high-quality DNA capable of producing robust results on Illumina's iSelect BeadChips. Samples extracted by the modified FTA Elute protocol produced lower call rates that those extracted by PCI, but for the called SNPs their concordance rate was similar. While the DNA extracted by the FTA Elute protocol will provide a high-quality data when analyzed using the Illumina BeadChip, we recommend using the modified GenSolve kit due to its higher call rate when analyzed by this platform. While only the BovineSNP50 BeadChip was tested, similar results should be obtainable on other iSelect BeadChips such as the CanineSNP20, EquineSNP50, OvineSNP50, and PorcineSNP60. DNA yields from individual FTA card punches vary between samples (Harty *et al.* 2000; Vidal-Taboada *et al.* 2006), and our FTA samples ranged in yield from 101 to 405 nanograms of DNA per punch, therefore we recommend that at least six 3 mm punches be extracted per sample to ensure sufficient DNA for genotyping. Assuming sufficient quantities are obtained, we speculate that DNA extracted from FTA cards by the GenSolve kit will also produce quality genotypes on other high-density SNP platforms such as Affymetrix Genome-Wide Human SNP Array 6.0 genechip and the Illumina Human1M-Duo BeadChip which both assay over 1 million SNP, although further studies are needed for confirmation due to the different chemistries used on each platform (Affymetrix Inc; Illumina Inc).

We conclude that FTA cards provide an excellent medium for harvesting DNA from multiple tissue types, and that when assayed using the Illumina iSelect technology, yield high genotype call rates and reproducibility, particularly when the DNA is extracted using the GenSolve kit. By demonstrating that high quality and repeatable genotypes can be obtained from DNA stored on FTA cards, we alert the community to the utility of this sample storage medium for DNA intended for high-throughput SNP genotyping.

Table 5.1. One-way ANOVA comparing call rates for BovineSNP50 genotypes produced from DNA extracted by the FTA Elute protocol and the GenSolve kit from blood and nasal swabs harvested on FTA cards to 7,737 samples extracted from whole blood or cryopreserved semen extracted by proteinase K treatment, Phenol:Chloroform:Isoamyl alcohol extraction, and ethanol precipitation.

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
PCI	7737	7648.816	0.988602	0.001462
FTA Elute	4	3.647186	0.911797	0.00322
GenSolve	6	5.865101	0.977517	0.000652

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	0.024316	2	0.012158	8.314988	0.000247	2.996891
Within Groups	11.32301	7744	0.001462			
Total	11.34732	7746				

Table 5.2. One-way ANOVA comparing call rates for BovineSNP50 genotypes produced from DNA on FTA cards extracted by the GenSolve kit to 7,737 samples extracted by proteinase K treatment, Phenol:Chloroform:Isoamyl alcohol extraction, and ethanol precipitation.

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
PCI	7737	7648.8155	0.9886	0.0015
Blood FTA	2	1.9807	0.9904	5.17E-06
Blood FTA Elute	2	1.9687	0.9844	6.97E-06
Nasal FTA Elute	2	1.9157	0.9578	0.0020

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	0.0019	3	0.0006	0.4414	0.7234	2.6061
Within Groups	11.3121	7739	0.0015			
Total	11.3141	7742				

Table 5.3. One-way ANOVA comparing call rates for BovineSNP50 genotypes produced from DNA on FTA elute extracted by the FTA Elute protocol to 7,737 samples extracted proteinase K treatment, Phenol:Chloroform:Isoamyl alcohol extraction, and ethanol precipitation.

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
7737-STD	7737	7648.816	0.988602	0.001462
Blood Elute	2	1.739053	0.869526	0.000153
Nasal Swab Elute	2	1.908134	0.954067	0.00236

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	0.030731	2	0.015366	10.51038	0.0000276	2.996892
Within Groups	11.3126	7738	0.001462			
Total	11.34333	7740				

Table 5.4. Genotype call and concordance percentage rates for DNA samples extracted from FTA cards, by sample type.

Extraction Method	PCI	GenSolve			FTA Elute	
Sample Type	Standard	Blood FTA	Blood FTA Elute	Nasal Swab FTA Elute	Blood FTA Elute	Nasal Swab FTA Elute
Call Rate %	98.860	99.036 (0.07)	98.437 (0.44)	95.780 (0.25)	86.953 (<0.001)	95.407 (0.10)
Concordance Rate %	99.006	99.817 (0.40)	99.786 (0.40)	99.573 (0.43)	99.124 (0.48)	99.883 (0.39)
Alternative Homozygous Rate %	0.006	0.000 (0.40)	0.000 (0.40)	0.002 (0.43)	0.001 (0.42)	0.000 (0.40)
Homozygous vs. Heterozygous Rate %	0.988	0.183 (0.40)	0.214 (0.40)	0.425 (0.43)	0.875 (0.49)	0.117 (0.39)

Two sample t-tests assuming equal within-treatment variances, the numbers in parentheses are the P-value corresponding to the comparison of that sample to the standard. Two samples from each FTA type were compared to 7,737 samples extracted by PCI for call rate and to 35 samples extracted for which dual aliquots were genotyped on the Bovine SNP50 BeadChip for concordance, alternative homozygous, and homozygous vs. heterozygous rate.

CHAPTER 6

CONCLUSIONS

The identification of QTL is the first step towards the identification of the genes involved in the regulation of a quantitative trait. This study's primary objective was to identify genomic intervals that harbor genes affecting carcass, growth, and reproductive traits in the American Angus population. Use of a large, multigenerational pedigree increased our power to detect QTLs segregating within sire families and within the full pedigree by linkage analysis. Since LOKI and QTL Express analysis methods both have their own strengths and weakness for detecting QTL their combined use allows the identification of QTL that may have been missed by one or the other (de Koning *et al*. 2003). QTL identified by both forms of analysis may be screened to identify suitable candidates for fine mapping and targeted sequencing to identify the causal polymorphisms.

Several economically important QTL (N=439) spread throughout the genome (Table 6.1), were discovered in this study. On average each chromosome contained 0.7 to 1.8 QTL per trait, with a range of 0 to 6 QTL. For every analyzed trait, except CEM, over 50% of the chromosomes contained at least one QTL. While the majority of these QTL are novel, with only 73 QTL having been previously reported, this list clearly is not definitive, even within the American Angus genome. When these QTL were simultaneously incorporated into a linear model in SAS to estimate the amount of genetic variation explained by the QTL, the R^2 values ranged from 39.3% with 18 QTL for CED to 89.5% with 52 QTL for YW (Table 6.2). There are two conclusions to be drawn for this. The first is simply that as more QTL are discovered, a greater amount of a

Table 6.1. QTL count by trait and chromosome

	Bos taurus autosome																												
Trait	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
BW	1	2	1	0	1	2	0	1	0	1	1	1	0	0	1	1	0	0	1	2	1	1	1	0	0	2	0	3	0
CED	2	0	0	0	0	2	0	1	0	1	0	0	0	1	0	1	0	0	1	0	1	0	1	0	2	3	0	2	0
CEM	1	2	0	2	1	0	1	1	1	1	0	0	0	1	0	2	0	0	1	0	0	1	1	1	1	0	0	0	0
CW	2	4	4	0	1	2	2	3	1	2	1	0	0	1	2	1	2	0	0	0	2	1	1	0	0	1	1	1	1
FAT	1	0	1	1	1	2	1	1	0	0	2	1	2	1	1	3	0	1	0	0	1	1	2	2	0	0	1	2	2
MARB	1	1	0	0	1	4	0	1	1	2	2	0	2	1	0	1	1	0	2	1	1	0	0	1	1	0	2	1	2
MH	1	1	2	0	1	1	3	1	0	1	0	2	0	3	3	1	0	0	0	0	2	1	1	0	1	2	1	1	1
MILK	2	0	1	2	0	1	5	0	0	2	3	3	2	1	5	4	1	2	0	0	0	0	1	1	2	1	1	3	1
MW	1	2	2	1	2	1	2	2	3	1	0	0	0	2	1	1	2	2	2	1	1	1	2	1	0	2	2	1	2
RIB	2	0	2	0	0	1	2	2	4	1	4	2	2	1	2	3	1	1	1	2	1	1	1	1	0	1	1	1	0
SC	0	0	0	1	2	1	1	1	2	2	2	1	1	1	0	1	1	1	2	1	1	2	1	0	1	1	1	2	1
WW	3	0	0	1	1	1	3	3	1	0	2	0	1	1	2	0	0	1	2	2	1	0	0	0	3	0	0	0	0
YH	0	0	1	1	0	1	0	1	0	0	0	1	0	0	0	1	0	1	1	0	2	3	0	1	0	2	1	1	1
YW	2	0	2	5	2	0	6	1	2	0	4	3	0	2	0	2	2	0	3	2	2	2	1	2	4	1	0	0	2
Total	19	12	16	14	13	19	26	19	15	14	21	14	10	16	17	22	10	9	16	11	16	14	13	10	15	16	11	18	13

trait's genetic variation can be explained, the other is that even with 52 QTL discovered less than 90% of the genetic variation in YW was explained. In reality the amount of genetic variation explained in commercial herds by these QTL will be less due to the inherent bias in QTL analyses when the same data are used to detect QTL and to estimate their effect size (Xu, 1998; Otto & Jones 2000; Allison *et al.* 2002). Additionally an individual QTL's effect within a herd may depend on the herd's overall genetic variation (architecture) and management conditions.

Table 6.2. Total QTL count for each trait, total R^2 explained by QTL for each trait and the marker with the largest R^2 value.

Trait	QTL count	Reference count	Total R^2	Largest single marker R^2	Marker	% of total R^2
BW	24	9	0.516	0.077	BMS574	14.89%
CED	18	5	0.393	0.071	BMS2742	18.08%
CEM	18	5	0.503	0.078	BMS574	15.54%
CW	36	6	0.687	0.081	BMS2533	11.74%
FAT	30	7	0.602	0.061	BMS1743	10.12%
MARB	29	8	0.552	0.056	AGLA232	10.12%
MH	30	2	0.656	0.047	BMS410	7.21%
MILK	44	16	0.825	0.121	BM6438_29	14.67%
MW	40	6	0.807	0.056	FCB11	6.97%
RIB	40	3	0.757	0.064	BM3509	8.43%
SC	31		0.599	0.078	BM103	13.05%
WW	28	1	0.673	0.159	BM864	23.67%
YH	19	1	0.405	0.031	BMS2252	7.70%
YW	52	4	0.895	0.184	BM1824	20.55%

A search performed at the Entrez Gene website (http://www.ncbi.nlm.nih.gov/sites/entrez) for human genes known to be responsible for variation in quantitative traits revealed 188, 301, and 270 that influence height, weight, and obesity, respectively. It has been estimated that up to 6,000 genes have an effect on the size of

a mouse (Reed *et al.* 2008) and it appears reasonable to predict that a similar number of genes will eventually be found in cattle for growth and developmental traits. While many allelic variations have a small effect on a trait's phenotypic variance their combined effects could explain significant proportions of the variation in genetic potential among animals.

Phenotypic selection of cattle has been practiced since domestication, and in recent decades focused selection on many economically important traits has been achieved through the use of EPDs. Even with this strong selection on phenotypes and EPDs there remains large variation in the frequency of trait-enhancing alleles in American Angus (Table 6.3). Even among traits that have been strongly selected a large number of moderate-to large-effect QTL remain segregating in American Angus (Tables 2.7, 3.4, 4.3)

Table 6.3. Average frequency of economically desirable QTL by trait in the mapping population based upon LOKI analysis.

	QTL Allelic Frequency			
Trait	Average	Minimum	Maximum	Count[1]
Birth Weight	0.770	0.195	0.810	23
Calving Ease Direct	0.824	0.796	0.851	17
Calving Ease Maternal	0.827	0.812	0.841	16
Carcass Weight	0.441	0.128	0.877	14
Marbling	0.856	0.810	0.895	8
Maternal Milk	0.421	0.125	0.875	29
Mature Height	0.488	0.109	0.903	8
Mature Weight	0.501	0.067	0.966	26
Ribeye Area	0.542	0.140	0.880	7
Scrotal Circumference	0.510	0.186	0.854	14
Weaning Weight	0.558	0.150	0.846	32
Yearling Height	0.708	0.160	0.855	5
Yearling Weight	0.488	0.138	0.867	51

[1] Number of QTL included in frequency calculation

For MAS to have the greatest effect genetic tests will need to be developed that can evaluate a large number of genetic markers while remaining cost-effective. While this study did not attempt to estimate the expected return on using genetic tests that explain varying amounts of genetic variation, it is clear that effective tests cannot be based upon microsatellite loci even though phase relationships may be established within the Angus breed. Strategies must quickly be devised to simultaneously test for multiple QTL and for multiple traits for MAS to be economically viable. It is clear that these strategies will be based upon the high-throughput SNP genotyping platforms which can genotype large numbers of SNP a relatively low cost per locus.

As FTA cards can be stored at room temperature for years without the need for specialized equipment (Ledray & Netzel 1997; Vidal-Taboada *et al.* 2006) DNA can be collected long before a producer decides which animals are to be tested. Furthermore, as testing technologies evolve, this method of sample capture allows testing organizations to return to a sample in the future as testing technologies are improved. The DNA extracted from tissues harvested onto these cards will provide genotypes with similar call and concordance rates as for DNA extracted from whole blood, but with the added benefit of decreased storage and shipping costs.

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VITA

Matthew McClure was born in Russellville Arkansas in 1977. In 1980 his family moved back to the family farm in Sedalia, Missouri where they implemented a diversified production system of corn, wheat, soybean, swine, and beef. He attended Green Ridge High School before obtaining a Bachelor of Science degree in Biochemistry at the University of Missouri-Columbia in 2001. In August, 2005 he was married to Jennifer Fessler. After working both in industry and in academic labs he joined Dr. Taylor's lab in January, 2004 to begin a Master's in Animal Science before switching in 2006 to the Genetics Area Program for his PhD.