Review

Genome Assembly Anchored QTL Map of Bovine Chromosome 14

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Bovine chromosome 14 (BTA14) has been widely explored for quantitative trait loci (QTL) and genes related to economically important traits in both dairy and beef cattle. We reviewed more than 40 investigations and anchored 126 QTL to the current genome assembly (Btau 4_0). Using this anchored QTL map, we observed that, in dairy cattle, the region spanning 0 – 10 Mb on BTA14 has the highest density QTL map with a total of 56 QTL, mainly for milk production traits. It is very likely that both somatic cell score (SCS) and clinical mastitis share some common QTL in two regions: 61.48 Mb - 73.84 Mb and 7.86 Mb – 39.55 Mb, respectively. As well, both ovulation rate and twinning rate might share a common QTL region from 34.16 Mb to 65.38 Mb. However, there are no common QTL locations in three pregnancy related phenotypes: non-return rate, pregnancy rate and daughter pregnancy rate. In beef cattle, the majority of QTL are located in a broad region of 15 Mb – 45 Mb on the chromosome. Functional genes, such as *CRH*, *CYP11B1*, *DGAT1*, *FABP4* and *TG*, as potential candidates for some of these QTL, were also reviewed. Therefore, our review provides a standardized QTL map anchored within the current genome assembly, which would enhance the process of selecting positional and physiological candidate genes for many important traits in cattle.

Key words: cattle, BTA14, QTL, review

1. Introduction

Livestock species, especially cattle, play an important role in economic development worldwide [1]. To increase profitability, cattle with superior, economically important traits such as growth, milk production and meat quality, have been selected and used as breeding stock. Traditionally, phenotypic and pedigree data have been used to select and pair the best sires and dams, which would in many cases result in offspring with improved phenotype values compared to the previous generation. This simple method of data collection and selection tripled U.S. milk production from 1940-1991 with fewer cows [2]. Therefore, any sophisticated techniques to choose sires and dams that are genetically superior will further enhance the process, leading to further improvement and economical gain.

Finding genes responsible for these economically important traits, however, is challenging because they are quantitative traits in nature [3, 4]. In other words, these traits are polygenic and are controlled by the accumulative action of many Mendelian genes. Moreover, the number of genes involved is unknown,

and environmental factors can also complicate the process because they can have a confounding effect on phenotypes [3, 4, 5, 6]. Nonetheless, recent developments in molecular biology and statistical methodologies allow the possibility to localize regions/genes in the genome or chromosome that are responsible for traits of interest [7, 8, 9].

To date, bovine chromosome 14 (BTA14) has been one of the most widely studied chromosomes for quantitative trait loci (QTL) related to many economically important traits in cattle [10]. There are more than 40 investigations dealing with QTL or genes for various traits, reporting a total of 126 QTL spanning this chromosome alone. In the present review, we surveyed QTL or genes on BTA14 discovered in both dairy and beef cattle. Since many of these studies used different sets of markers, mostly microsatellites, we integrated them into the current genome assembly (Btau 4_0) (http://www.ncbi.nlm.nih.gov/projects/genome/guide/cow/) in order to standardize QTL locations. Such a genome assembly anchored QTL map provides the best view on QTL density for each phenotype and the potential links between QTL and functional genes for future study.

2. QTL detected on BTA14 in dairy cattle

In dairy cattle, the majority of QTL mapping on BTA14 are related to milk production traits, such as milk yield (MY), fat percentage (FP) or fat content, fat yield (FY), protein percentage (PP) or protein content and protein yield (PY) [2, 4, 5, 6, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25]. Other traits, such as reproduction (REPRO) (calving ease, CE; daughter pregnancy rate, DPR; non return rate, NRR; ovulation rate, OVR; pregnancy rate, PR and twinning, TWIN)

[2, 18, 23, 26, 27], health (somatic cell score, SCS, and clinical mastitis, CLM) [18, 21, 25, 28, 29, 30] and udder related traits (URT) (fore udder attachment, FUA; front teat placement, FTP; rear udder width, RUW and udder somatic cell score, USCS) [2, 4, 23] were also investigated on BTA14. References, significance levels (p values or F values), peak or flanking marker(s), genome-anchored locations (in Mb), and linkage map locations (in cM) for each of these QTL are listed in Table 1.

Table 1. QTL reported on BTA14 for milk production traits in dairy cattle.

Reference	P or F* value	Markers	Mb	cM
FAT PERCENTAGE (FP) (or FAT CONTENT)				
Ashwell et al. 1997	0.0181	BM302	33.62	52.37
Ashwell et al. 2002	0.001	BMS1678	9.19	14.01
Ashwell et al. 2002	0.073	BMS1678	9.19	14.01
Ashwell et al. 2002	<0.0001	BMS1678	9.19	14.01
Ashwell et al. 2004	23.1*	ILSTS039-BMS1678	1.20-9.19	0-14.01
Bennewitz et al. 2003	<0.01	KIEL_E8	0.26	0
Bennewitz et al. 2003	<0.01	KIEL_E8-RM180	0.26-17.16	0-33.31
Bennewitz et al. 2004	<0.001	DGAT1	0.44	18.70
Boichard et al. 2003	<0.001	CSSM066	3.81	5.13
Boichard et al. 2003	0.0004	CSSM066	3.81	5.13
Boichard et al. 2003	0.11	CSSM066	3.81	5.13
Heyen et al. 1999	0.0023	BM1508	8.27	17.85
Heyen et al. 1999	<0.00001	ILSTS039	1.2	0
Kaupe et al. 2007	<0.001	CYP11B1	1.29	29.80
Kaupe et al. 2007	<0.001	DGAT1	0.44	18.70
Kuhn et al. 2004	<0.0001	CSSM066-ILSTS039	1.20-3.81	0-5.13
Rodriguez-Zas et al. 2002		ILSTS039	1.2	0
Ron et al. 1999	0.0003	CSSM066	3.81	5.13
Thaller et al. 2003	<0.001	CSSM066-ILSTS039	1.20-3.81	0-5.13
Viitala et al. 2003	<0.0029	ILSTS039-BMS1747	1.20-7.87	0-10.50
Zhang et al. 1998		ILSTS011-BM302	11.78-33.62	25.71-52.37
FAT YIELD (FY)				
Ashwell et al. 2002	<0.0001	BMS1678	9.19	14.01
Ashwell et al. 2004	12.1*	ILSTS039-BMS1678	1.20-9.19	0-14.01
Ashwell et al. 2004	10.5*	BMS1941-BM8215	24.67-27.34	41.71-48.23
Bennewitz et al. 2003	<0.01	KIEL_E8-CSSM066	0.26-3.81	5.13
Bennewitz et al. 2003	<0.01	KIEL_E8-CSSM066	0.26-3.81	5.13
Bennewitz et al. 2003	<0.01	KIEL_E8	0.26	0
Bennewitz et al. 2004	<0.01	DGAT1	0.44	18.70
Boichard et al. 2003	0.0011	CSSM066	3.81	5.13
Harder et al. 2006	0.01	BM4513-BL1036	61.48-76.75	79.79-100.16
Heyen et al. 1999	0.0005	CSSM066	3.81	5.13
Heyen et al. 1999	0.00002	ILSTS039	1.2	0
Kaupe et al. 2007	<0.001	CYP11B1	1.29	29.80
Looft et al. 2001	<0.01	ILSTS039-CSSM066	1.20-3.81	0-5.13
Thaller et al. 2003	<0.001	ILSTS039-CSSM066	1.20-3.81	0-5.13
Viitala et al. 2003	0.0398	ILSTS039-BMS1747	1.20-7.87	0-10.50
Winter et al. 1998	<0.0001	ILSTS039-BM1508	1.20-8.27	0-17.85
Zhang et al. 1998	2.25*	ILSTS011-BM302	11.78-33.62	25.71-52.37

		MILK YIELD (MY)		
Ashwell et al. 1997	0.0302	BM302	33.62	52.37
Bagnato et al. 2008	0.0501	CSSM066	3.81	5.13
Bagnato et al. 2008	0.0485	BMS1747	7.87	10.5
Bagnato et al. 2008	0.00148	BMS947	51.274	69.8
Bagnato et al. 2008	0.000311	BL1036	76.75	100
Bennewitz et al. 2003	<0.01	KIEL_E8	0.26	0
Bennewitz et al. 2003	<0.01	KIEL_E8-CSSM066	0.26-3.81	5.13
Boichard et al. 2003	0.02	CSSM066	3.81	5.13
Boichard et al. 2003	0.0002	CSSM066	3.81	5.13
Herder et al. 2006	<0.01	KIEL_EB-CSSM066	0.26-3.81	5.13
Heyen et al. 1999	0.0052	BM4305	65.03	83.31
Kaupe et al. 2007	<0.01	CYP11B1	1.29	29.80
Kaupe et al. 2007	<0.001	DGAT1	0.44	18.70
Looft et al. 2001	<0.01	ILSTS039-CSSM066	1.20-3.81	0-5.13
Rodriguez-Zas et al. 2002		CSSM066	3.81	5.13
Schnabel et al. 2005	16.32*	BMC1207-BMS1899	34.16-51.17	51.94-69.01
Thaller et al. 2003	<0.001	CSSM066-ILSTS039	1.20-3.81	0-5.13
		PROTEIN PERCENTAGE (PP) (or PROTEIN CONTENT)		
Ashewell et al. 2004	9.5*	BMS1678-ILSTS011	9.19-11.78	14.01-25.71
Bagnato et al. 2008	0.014	ILSTS039	1.20	0
Bagnato et al. 2008	0.0045	CSSM066	3.81	5.13
Bagnato et al. 2008	0.015	DIK2201	6.378	8.1
Bagnato et al. 2008	0.012	BMS2055	74.473	93.7
Bennewitz et al. 2004	<0.001	DGAT1	0.44	18.70
Boichard et al. 2003	<0.001	CSSM066	3.81	5.13
Boichard et al. 2003	<0.00001	CSSM066	3.81	5.13
Heyen et al. 1999	0.0048	ILSTS039	1.2	0
Kaupe et al. 2007	<0.001	CYP11B1	1.29	29.80
Mosiq et al. 2001	<0.01	BM6425	73.84	95.14
Rodriguez-Zas et al. 2002		BM6425	73.84	95.14
Schnabel et al. 2005		BMC1207-BMS1899	34.16-51.17	51.94-69.01
Thaller et al. 2003	<0.001	ILSTS039-CSSM066	1.20-3.81	0-5.13
Viitala et al. 2003	<0.0029	BMS1747-BMS740	7.87-39.55	10.50-60.69
Bennewitz et al. 2003	<0.01	RM180-CSSM066	3.81	5.13-35.31
Bennewitz et al. 2003	<0.01	KIEL_E8	0.26	0
Kaupe et al. 2007	<0.001	DGAT1	0.44	18.70
Kaupe et al. 2007	<0.001	CYP11B1	1.29	29.80
		PROTEIN YIELD (PY)		
Ashwell et al. 2002	0.0005	BM6425	73.84	95.14
Ashwell et al. 2004	14.7	BM4305-INRA100	65.03-75.88	83.31
Bennewitz et al. 2003	<0.01	KIEL_E8	0.26	0
Kaupe et al. 2007	<0.001	DGAT1	0.44	18.70
Looft et al. 2001	<0.01	ILSTS039-CSSM066	1.20-3.81	0-5.13
Thaller et al. 2003	<0.01	ILSTS039-CSSM066	1.20-3.81	0-5.13

As shown in Figure 1, the region around 0 – 10 Mb has many QTL on the chromosome. Specifically, there are 56 QTL for five milk production traits, and seven QTL for other traits. In particular, 52 of these 56 milk production related QTL were clustered in a region of ~3.6 Mb (0.26-3.81 Mbp), including 15 QTL for fat % or fat content [11, 13, 5, 6, 14, 17, 18, 21, 22, 24], 13 QTL for fat yield [5, 6, 11, 13, 14, 18, 19, 24, 25, 31], 10 QTL for milk yield [4, 5, 14, 16, 18, 19, 21, 24], 10 QTL for protein % or protein content [5, 6, 14, 18, 24], and four QTL for protein yield [13, 18, 19, 24], respectively. Interestingly, this region of ~3.6 Mb on the assembly was expanded to a region of ~30 cM reported by different groups in the linkage map (Table 1). Therefore, our genome anchored QTL map significantly narrows the physical distance of QTL regions and perhaps provides the precise locations for identification of candidate genes.
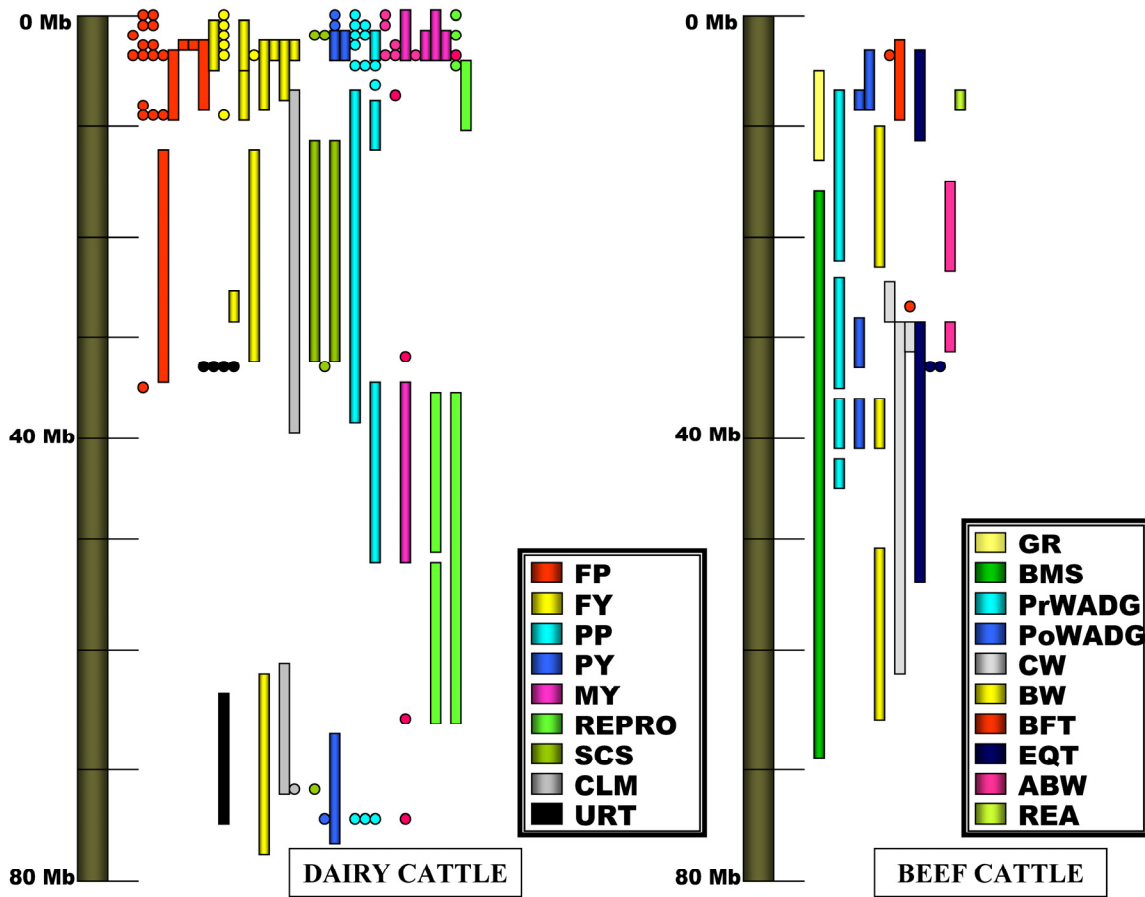
Figure 1. Genome assembly anchored QTL map of BTA14 (see Tables 1-3). The gray bar on the left represents the visualization of BTA14 from 0 Mb to 80 Mb. Studies on dairy cattle are graphed on the left side with phenotypes represented by different colors, whereas studies in beef cattle are summarized on right side of the graph with phenotypes represented by different colors.

The high density of QTL for milk production traits in this small region of BTA14 has led to exploration of candidate genes in the region. In 2002, Grisart and colleagues [53] proposed that bovine *diacylglycerol acyltransferase 1* (*DGAT1*) (at 0.44 Mb) is a promising candidate gene because a missense mutation (Lysine232Alanine) in the gene could explain the phenotypic variance in milk fat content and other milk characteristics. DGAT1 is a microsomal enzyme that utilizes diacylglycerol and fatty acyl CoA as substrates in order to catalyze the final stage of triacylglycerol synthesis [32]. Therefore, this gene should affect fat metabolism, including fat yield and percentage in the milk [33]. A knock-out study showed that both male and female Dgat$^{-/-}$ mice, even those fed a high fat diet, stabilized their weights and resisted fat storage [34], indicating the importance of *DGAT1* in fat metabolism. Winter et al. [31] further found that the lysine variant was associated with higher milk fat content compared to its counterpart alanine variant in several cattle breeds.

Interestingly, Bennewitz and colleagues [14] observed a genome-wide significant conditional QTL effect on fat percentage at the proximal end of the chromosome and for protein percentage at a more distal chromosomal region in addition to the diallelic *DGAT1* effects on milk, fat, and protein yield and fat and protein percentage. The authors argued that this conditional QTL effect might be caused by one or more additional alleles segregating at *DGAT1* that were not previously detected, or by a second quantitative trait locus affecting these traits. Indeed, Kuhn et al. [17] reported strong evidence for segregation of at least three alleles in the promoter region of the *DGAT1* gene that affects milk fat percentage. In the centromeric region of BTA14, cytochrome P450, family 11, subfamily B (*CYP11B1*) was also suggested to be the causative gene for the QTL related to fat metabolism [35]. The *CYP11B1* gene was negatively associated with milk yield and protein yield, but positively associated with fat content [18].

Thirteen additional QTL for milk production traits were also identified outside this first 10Mb region on BTA14, including two at 33.62 Mb and 11.78 Mb – 33.62 Mb for fat percentage or fat content [4, 6], two at 24.67 Mb – 27.34Mb and 61.48 Mb – 76.75 Mb for fat yield [11, 16], three at 33.62 Mb, 34.158 Mb – 51.17 Mb and 65.03 Mb for milk yield [4, 6, 23], five (one at 7.87 Mb – 39.55 Mb, one at 34.16 Mb – 51.17 Mb and three at 73.84 Mb) for protein % [2, 20, 21, 23, 25] and one at 65.03 Mb – 75.88 Mb for protein yield [11] (Figure 1 and Table 1). However, no candidate genes have been explored for these QTL on BTA14.

During the past several decades, the high intensity of selection for milk yield has led to a significant improvement in milk production, but it has also led to a decline in reproductive efficiency in dairy cattle. In the United States, Washburn and colleagues [36] reported that from 1976 to 1999 the average number of days open increased from 122 to 152 days for Jerseys and from 124 to 168 days for Holsteins. Services per conception also increased, from 1.91 to 2.94 services for both breeds during the same period. There are at least 6 QTL for reproductive traits detected on BTA14 (Figure 1 and Table 2). Calving ease QTL is located at 1.294 Mb [18], while both ovulation rate and twinning rate might share a common QTL region from 34.16 Mb to 65.38 Mb [26, 27]. However, it seems that three pregnancy related phenotypes have no common QTL locations: non-return rate is placed at 0.44 Mb [18], pregnancy rate at 3.81 Mb – 11.78 Mb [11], and daughter pregnancy rate (DPR) at 34.16 Mb – 51.17 Mb [23] (Figure 1). Defining QTL ontology should be considered by the community in the future to search for common QTL for a given phenotype.

Table 2. QTL reported on BTA14 for health, reproduction and udder related traits in dairy cattle.

Reference	P value	Markers	Mb	cM
CLINICAL MASTITIS (CLM)				
Klungland et al. 2001		BM4513-BM6425	61.48-73.84	79.79-95.14
Rupp et al. 2003	<0.01	BM6425	73.84	95.14
Viitala et al. 2003	0.01	BMS1747-BMS740	7.86-39.55	10.50-60.69
REPRODUCTIVE TRAITS				
Kaupe et al. 2007 for CE	<0.05	CYP11B1	1.29	29.80
Schnabel et al. 2005 for DPR		BMC1207-BMS1899	34.16-51.17	51.94-69.01
Kaupe et al. 2007 for NRR	<0.05	DGAT1	0.44	18.70
Gonda et al. 2004 for OVR	0.014	BMS947-BM4305	51.27-65.03	83.31
Ashwell et al. 2004 for PR	0.01	ILSTS011-CSSM066	3.81-11.78	5.13-25.71
Cobanoglu et al. 2005 for TWIN	0.001	BMC1207-BM2934	34.16-65.38	51.94
SOMATIC CELL SCORE (SCS)				
Ashwell et al. 1998	0.0096	BM302	33.62	52.37
Kaupe et al. 2007	<0.001	CYP11B1	1.29	29.80
Kaupe et al. 2007	<0.05	CYP11B1	1.29	29.80
Rodriguez-Zas et al. 2002		BM6425	73.84	95.14
Rupp et al. 2003	<0.10	ILSTS011-BM302	11.78-33.62	25.71-52.37
Zhang et al. 1998		ILSTS011-BM302	11.78-33.62	25.71-52.37
UDDER RELATED TRAITS (URT)				
Ashwell et al. 1997 for udder	0.0052	BM302	33.62	52.37
Ashwell et al. 1997 for USCS	0.006	BM302	33.62	52.37
Ashwell et al. 2002 for FUA	0.0703	BM302	33.62	52.37
Ashwell et al. 2002 for FTP	0.04	BM302	33.62	52.37
Schnabel et al. 2005 for RUW	0.01	BM4305-BL1036	65.03-76.75	83.31-100.16

Mastitis affects every dairy farm and up to 50% of all dairy cattle in the United States [37]. Economic losses are an estimated $180 per cow per year or $2 billion annually in the United States of America [38]. A total of 10 QTL for the disease were reported on BTA14, including three for clinical mastitis [25, 29, 30] and seven for somatic cell score (SCS) [4, 18, 21, 28, 30]. A region around 1.29 Mb with CYP11B1 harbors a significant QTL for SCS, but two other regions, one at 7.86 Mb – 39.55 Mb and the other at 61.48 Mb - 73.84 Mb might share QTL for both clinical mastitis and SCS. These data indicate that QTL information on SCS would help reduce incidence of clinical mastitis in dairy cattle. In addition, SCS has been widely used to indirectly measure udder traits in dairy cattle [39]. As shown in Figure 1 and Table 2, QTL for udder traits are also found in the same region as QTL for SCS, indi-

cating that these traits are either controlled by the same gene or by genes in a linkage.

3. QTL detected on BTA14 in beef cattle

In beef cattle, QTL mapping has been mainly focused on growth traits, carcass and meat quality. The targeted phenotypes include hot carcass weight [7, 40], rib eye area (REA) [8, 41], average daily gain (ADG) [40, 42], intramuscular fat deposition (marbling) [9] and subcutaneous fat depth (backfat-EBV or fat thick-

ness) [9, 8, 43, 44] (Table 3). *Bos indicus* (Brahman) and *Bos taurus* (Angus or Hereford) breeds have been heavily used in QTL mapping by Casas et al. [9], Kneeland et al. [42], Stone et al. [41] and Kim et al. [7]. Other commonly used breeds include: Wagyu [40], Belgian Blue [9] or composite breeds (½ Red Angus, ¼ Tarentaise and ¼ Charolais) [8], or mixed breeds, such as ¼ Angus, ¼ Hereford, ¼ Red Poll and ¼ Pinzgauer cows with Piedmontese X Angus sire [44].

Table 3. QTL reported on BTA14 for growth, carcass, meat quality and eating quality traits in beef cattle.

Reference	P value	Markers	Mb	cM
PRE-WEANNING AVERAGE DAILY GAIN (PrWADG)				
Kneeland et al. 2004	0.046	BMS1941-BMC1207	24.67-34.16	41.71-51.94
Kneeland et al. 2004	0.041	BM1577-BMS108	41.23-46.69	63.16-67.67
Kneeland et al. 2004	0.023	BMC1207-BM1577	34.16-41.23	51.94-63.16
Mizoshita et al. 2004		BM1508-BMS1941	8.27-24.67	17.85-41.71
POST-WEANNING AVERAGE DAILY GAIN (PoWADG)				
Kneeland et al. 2004	0.026	BMS1747-TG	7.66-7.87	10.50-11.95
Kneeland et al. 2004	0.025	CSSM66-BMS1747	3.81-7.87	5.13-10.50
Kneeland et al. 2004	0.039	BMC1207-BM1577	34.16-41.23	51.94-63.16
Mizoshita et al. 2004		BM8125-ILSTS008	27.34-32.08	50.92-66.48
BIRTH WEIGHT (BW)				
Kneeland et al. 2004	0.031	BMS1899-RM137	51.17-67.66	69.01-85.18
Kneeland et al. 2004	0.006	BMS1678-BMS1941	9.19-24.67	14.01-41.71
Kneeland et al. 2004	0.049	BMC1207-BM1577	34.16-41.23	51.94-63.16
CARCASS WEIGHT (CW)				
Kim et al. 2003	0.611	RM011-BM4513	27.20-61.48	43.63-79.79
Mizoshita et al. 2004	0.016	BMS1941-INRA094	24.67-28.80	41.71-49.83
Mizoshita et al. 2004		BM8125-ILSTS008	27.34-32.08	50.92-66.48
BACKFAT THICKNESS (BFT)				
Casas et al. 2000	0.47	RM180-RM011	17.16-27.2	35.31-43.63
Casas et al. 2003	0.24	ILSTS039-DIK5082	1.20-9.86	0-21.30
Moore et al. 2004	0.0058	CSSM066	3.81	5.13
BEEF MARBLING SCORE (BMS)				
Casas et al. 2003	0.45	DIK2008-DIK4087	16.43-68.33	31.26-86.63
AVERAGE BODY WEIGHT (ABW)				
Mizoshita et al. 2004		BM8125-ILSTS008	27.34-32.08	50.92-66.48
Mizoshita et al. 2004		MNB-14-BMS1941	16.97-24.67	32.12-41.71
EATING QUALITY TRAITS (EQT)				
Casas et al. 2003 for CHOICE	0.26	ILSTS039-DIK4681	1.20-12.58	0-25.71
Guiterez-Zas et al. 2007 for pH	0.0013	RM011-PZ271	27.20-54.15	43.63
Guiterez-Zas et al. 2007 for GBFI	0.0084	BM302	33.62	52.37
Guiterez-Zas et al. 2007 for GAFI	0.0166	BM302	33.62	52.37
GROWTH RATE (GR)				
Miyata et al. 2004	0.05	CSSM066-ILSTS011	3.81-11.78	5.13-25.71
RIB EYE AREA (REA)				
Stone et al. 1999		DIK5377-DIK5082	8.54-9.86	17.85-21.23

In contrast to the high number of QTL discovered in dairy cattle, the region between 0 Mb – 10 Mb on BTA14 harbors only a few QTL for beef cattle traits, including two for post-weaning average daily gain

(PoWADG) [42], one for backfat thickness (BFT) [9, 43], one for % USDA choice (CHOICE) [9] and one for average body weight (ABW) [40] (Figure 1 and Table 3). *DGAT1*, which is responsible for lipid metabolism

traits in dairy cattle, was also tested in beef cattle. Unfortunately, Moore and colleagues [43] failed to observe any significant association of the *DGAT1* polymorphism with backfat EBV. On the other hand, Barendse et al. [45] found that the *TG* gene, which is located at 7.658 Mb on the chromosome, is significantly associated with marbling score in beef cattle. The association was further confirmed by the same group using another population of feedlot cattle [46]. In contrast, Moore and colleagues [43] failed to confirm the association of polymorphisms in the *TG* gene with any lipid metabolism traits (backfat EBV). Even so, Moore et al [43] did not exclude the possibility of other polymorphisms in *DGAT1* or *TG* that might have a significant effect on backfat reported in other studies.

Broadly speaking, most QTL on BTA14 discovered in beef cattle fall into a region of 30 Mb, from 15 Mb to 45 Mb, including two QTL for PoWADG, four for pre-weaning average daily gain (PrWADG) [42], three for birth weight (BW) [42], three for carcass weight (CW) [7, 40], one for BFT [9], one for beef marbling score (BMS) [9] and two for ABW [40] (Figure 1 and Table 3). In addition, there is evidence that somewhere along these two regions on BTA14, there are also QTL for some eating quality traits (EQT) (24.67-46.69 Mbp): pH at 24h post-mortem and grilled beef flavor intensity (GBFI) bracketed by RM11-PZ271, and grilled abnormal flavor intensity (GAFI) bracketed by CSSM066-RM11 markers [3].

Since both *DGAT1* and *TG* are located in the region of 0 Mb – 10 Mb on BTA14, it is obvious that they cannot serve as candidate genes for QTL located in the region of 15 Mb – 45 Mb. Therefore, we targeted two candidate genes in the 15 Mb – 45 Mb region: corticotrophin releasing hormone (*CRH*) and fatty acid binding protein 4 (*FABP4*). The former is located at position 31.49 Mb, while the latter is positioned at 41.95 Mb on the newly assembled bovine genome map. CRH, which is a stress hormone, is released to the anterior pituitary to stimulate the secretion of adrenocorticotrophic hormone (ACTH), which upregulates cortisol. Cortisol has many significant metabolic effects that include stimulating gluconeogenesis in the liver, inhibiting glucose uptake in muscle and adipose tissue, and stimulating fat breakdown in adipose tissue [47]. In addition, transgenic mice with overexpression of *CRH* exhibit muscle wasting, decreased linear growth and obesity [48], whereas porcine CRH was reported to be significantly associated with backfat thickness, carcass length, average daily mass gain and REA [49]. Thus, *CRH* is a good positional candidate gene for fat-related traits. Buchanan et al. 2005 [52] showed three SNPs that were associated with REA (P < 0.034) and hot carcass mass (P < 0.0015) in a Charolais-cross

steer population. In 2007, Wibowo et al. [47] discovered a new SNP in the bovine *CRH* gene that is highly associated with backfat thickness (P < 0.001) in a Wagyu X Limousin F_2 population.

FABP4, on the other hand, is a member of the fatty acid binding protein family that is thought to play a major role in the regulation of lipid and glucose homeostasis through its interaction with perioxisome proliferator-activated receptors (PPARs) [50]. In addition, *FABP4* is also shown to interact with lipase, a primary enzyme involved in lipid catabolism, which regulates lipid hydrolysis and intracellular fatty acid trafficking [51]. Hence, *FABP4* is a strong candidate gene for obesity as it is also located in the region of quantitative trait loci (QTL) for serum leptin levels in mice [54]. In 2006, Michal et al. [51] reported a significant association of *FABP4* gene with marbling score and fat thickness in a Wagyu X Limousin F_2 cross with P-values of 0.0246 and 0.0398, respectively.

4. Conclusion

We reviewed more than 40 investigations related to identification of QTL for economically important traits on BTA14 in both dairy and beef cattle and anchored 126 QTL into the current bovine genome assembly. Such a process standardized the QTL locations by avoiding many conflicts reported on different linkage maps and linked the QTL to the functional gene regions. We believe that such an anchored QTL map further improves our ability to understand the genetic complexity of economically important traits located on BTA14 in both dairy and beef cattle.

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Conflict of interests

The authors have declared that no conflict of interest exists.

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