

High Resolution QTL Maps Of 31 Traits in Contemporary U.S. Holstein Cows

J.B. Cole^{*}, G.R. Wiggans^{*}, L. Ma[†], T.S. Sonstegard[‡], B.A. Crooker[†],
C.P. Van Tassell^{*,‡}, J. Yang[†], L.K. Matukumalli[‡] and Y. Da[†]

Introduction

The availability of a large number of single nucleotide polymorphism (SNP) markers allows the construction of QTL maps with unprecedentedly high resolutions. Combined with bovine whole-genome sequence information, many SNP effects could be readily localized to specific genes or gene regions. Such high resolution QTL maps will provide valuable information for applying SNP markers in dairy breeding and selection practice and for understanding the genetic mechanism underlying traits of economic importance in dairy cattle. We have constructed high resolution QTL maps of the twenty nine bovine autosomes and the X chromosome in contemporary U.S. Holstein cows using a high density SNP panel for 31 dairy traits: net merit, its eight component traits, four calving traits, and eighteen body conformation traits (Cole et al. 2010; Wiggans et al., 2010). Here, we present an overview of these QTL maps.

Material and methods

The study population included 1654 contemporary U.S. Holstein cows from Holstein Association USA, Genetic Visions, Genex Cooperative Inc., Pennsylvania State University, Iowa State University, University of Florida, Virginia Polytechnic Institute and State University, and University of Minnesota. A total of 45,878 SNP markers from the Illumina BovineSNP50TM chip were selected based on two conditions: the minor allele frequency (MAF) was greater than zero in the contemporary population or the allele frequency difference was 2% or greater between the 1654 Holstein cows and a group of Holstein cattle that remained unselected since 1964. Of the 45,878 SNP markers, 45,461 had known chromosome positions with an average marker spacing of 58.45Kb. Predicted transmitting ability (PTA) values were used as the phenotypic values of the 31 traits (trait names and abbreviations are listed in the footnote of table 1). QTL effects were tested using the epiSNP computer package (Ma *et al.*, 2008). SNP and gene locations were based on University of Maryland bovine genome assembly version 3.0 (UMD 3.0) and the Baylor College of Medicine bovine genome assembly Build 4.0 (Btau_4.0). The contribution of the top 100 SNP effects of each trait was measured by the determination coefficient (R^2).

^{*} Animal Improvement Programs Laboratory, 10300 Baltimore Avenue, Beltsville, MD 20705-2350, USA

[†] Department of Animal Science, University of Minnesota, Saint Paul, MN 55108, USA

[‡] Bovine Functional Genomics Laboratory, 10300 Baltimore Avenue, Beltsville, MD 20705-1350, USA

Results and discussion

A large number of significant additive SNP effects reached genome-wide significance with the Bonferroni correction ($P < 3.6 \times 10^{-7}$), and only top 100 effects of each trait were summarized for a total of 3100 SNP effects involving 1586 SNPs. All the 3100 SNP effects were additive effects. As expected, only a few dominance effects reached genome-wide significance and were far less significant, because PTA values used as the phenotypic values are additive genetic effects. The 100 SNPs of each trait accounted for 0.38-0.56 of the phenotypic variation ($R^2 = 0.38-0.56$). Some of the most significant QTL effects are summarized in table 1.

Table 1: Summary of most significant QTL effects on 31 dairy traits

Chr	SNP position (UMD 3.0)	Gene or nearest gene	^a Trait and effect ranking
1	28362687	<i>LOC521010</i>	#1 for RLS
2	35004695	<i>TBR1</i>	#1 for RUH
5	43736571	<i>MGC139000</i>	#1 for RA
6	109719477	<i>LETM1</i>	#1 for FTP; #6 for RTP
7	17403976	<i>INSR</i>	#1 for DPR,SCS; #3 for PL
7	91946384	<i>CETN3</i>	#1 for UC,RTP
11	23741433	<i>LOC615674</i>	#1 for TL
11	85153576	<i>OSR1-TRIB2-LPIN1</i>	#2-5 for STA
13	58070117	<i>GNAS-ZBP1</i>	#1 for MY, #4 for FY, #5 for PY
14	1.4-4.8Mb	<i>DGAT1-NIBP</i>	#1 and #2 for FPC
15	75749702	<i>CD82</i>	#1 for DSB
16	1756016	<i>REN</i>	#1 for RW, FUA; #2 for STR, FS; #4 for BD; #9 for RUH
18	53948569	<i>PGLYRP1-IGFL1</i>	#1 for FY,PY,NM,SCE,DCE; #8 for SSB; #9 for MY; #16 for PL; #25 for FPC,PPC
18	58696066	<i>LOC787057</i>	#1 for SSB
23	3320932	<i>DST</i>	#2 for DSB
23	14.6-15Mb	<i>MOCSI-LRFN2</i>	9 effects for DSB, #3-#47
25	5836611	<i>A2BP1</i>	#1 for UD
26	49137602	<i>MGMT</i>	#1 for FA,FL; #2 for PPC,TL; #10 for PY, RLR
X	106241123	<i>LOC520057</i>	#1 for DF
X	12754120	<i>LOC100139353</i>	#1 for RLR
X	131766182	<i>LOC515732</i>	#1 for STA,STR,BD,FS; #2 for RW,FUA

^a MY = milk yield, FY = fat yield, PY = protein yield, FPC = fat percent, PPC = protein percent, SCS = somatic cell score, DPR = daughter pregnancy rate, PL = productive life, NM = net merit, SCE = sire calving ease, DCE = daughter calving ease, SSB = sire stillbirth, DSB = daughter stillbirth, STA = stature, STR = strength, BD = body depth, RW = rump width, DF = dairy form, RA = rump angle, FUA = fore udder attachment, RUH = rear udder height, UD = udder depth, UC = udder cleft, FTP = front teat placement, RTP = rear teat placement, FA = foot angle, RLS = rear legs side-view, RLR = rear legs rear-view, FL = feet-legs, FS = final score.

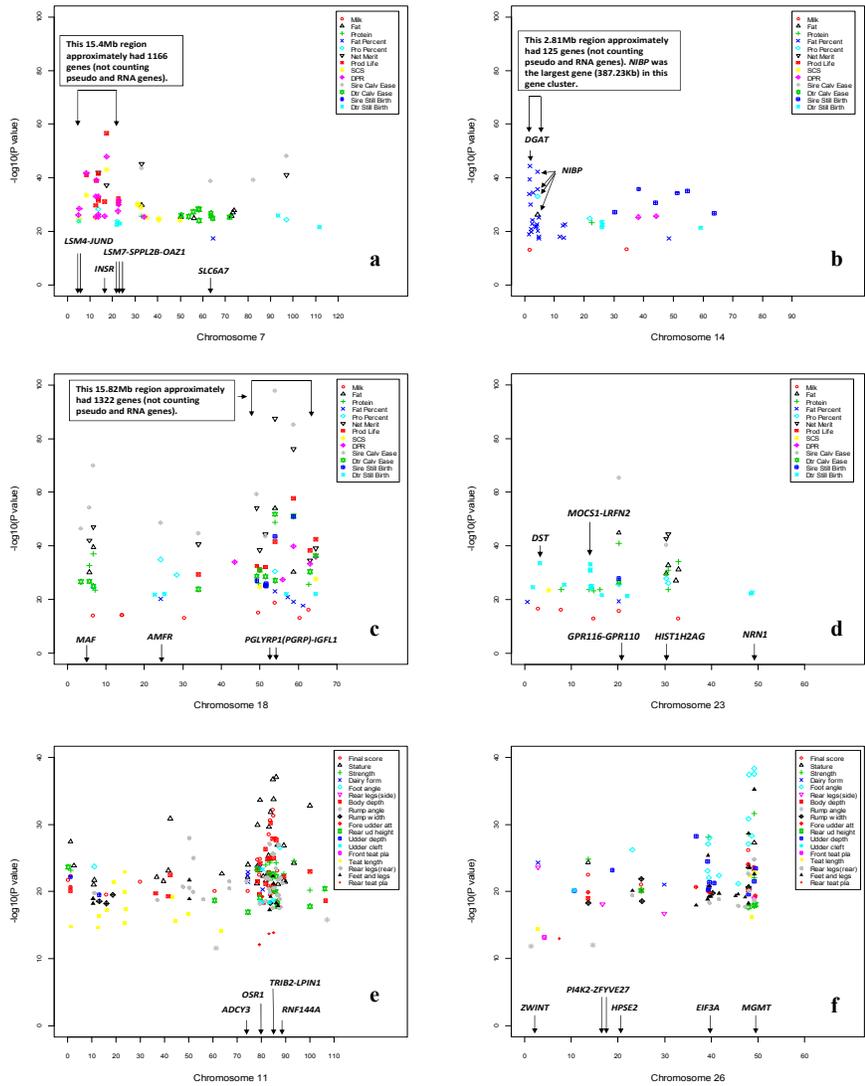


Figure 1: QTL maps of BTA7, BTA14, BTA18, and BTA23 for net merit and calving traits (a-d), and BTA11 and BTA26 for type traits (e-f)

Based on the statistical significance and number of the QTL effects on each chromosome, the following chromosomes had the most prominent QTL effects: BTA13 for MY, FY; BTA7 for SCS, DPR, PL, UC, RTP; BTA14 for FPC; BTAX for DPR, PL, PPC; BTA18 for SCE,

SSB, DCE; BTA23 for DSB; BTAX and BTA11 for STA, STAR, BD, RW; BTA26 for FA and FL; BTA1 for RLS; BTAX for RLR; BTA6 and BTA7 for FTP and RTP; and BTA5 for RA. Local concentrations of QTL effects were observed and some of these local concentrations overlapped with large gene clusters. The 15.4Mb region of BTA7 (figure 1a) had a local concentration of DPR, SCS and PL effects. A SNP marker 1.5Kb downstream of *INSR* was highly significant for DPR, SCS and PL (table 1). This region had 1166 genes, averaging 75 genes/Mb. This overlap between effect concentration and gene concentration should increase the likelihood that the observed QTL effects had underlying gene effects. The 2.81Mb region of BTA14 (figure. 1b) contained the well published *DGATI*. This region had 19 effects for FPC (with *DGATI* having the most significant and *NIBP* having the second most significant effect), one effect for MY in *VPS28*, and one effect for FY and one effect for PPC in *NIBP*. This region had 125 genes, averaging 44 genes/Mb. *NIBP* was the largest gene (387.23Kb) in this gene cluster. The 15.82Mb region of BTA18 had QTL effects involving many traits (figure. 1c) but was most pronounced for effects on SCE, SSB and DCE. This 15.82Mb region had approximately 1322 genes, averaging 83 genes/Mb. The *PGLYRP1(PGRP)-IGFL1* region had the most significant QTL effects in this gene cluster. BTA23 (figure 1d) is another example of local QTL effect concentration for one phenotype. This chromosome had the second most significant effect for DSB and 9 other DSB effects in the *MOCSI-LRFN2* region. BTA11 had the largest concentration of QTL effects affecting type traits (figure 1e). BTA26 was most prominent for effects on FA in or around *MGMT* (figure 1f). Interestingly, the *MGMT* region was also highly significant for PPC and PY.

Conclusion

High-resolution QTL maps of 1586 SNPs affecting 31 dairy traits (top 100 effects per trait) were constructed based on a genome-wide association analysis of 1,654 contemporary U.S. Holstein cows genotyped with 45,878 SNPs. The 31 traits include net merit and its 8 component traits, 4 calving traits, and 18 body conformation traits. Most significant and influential gene regions include: *INSR* of BTA7; *DGATI-NIBP* of BTA14, *PGLYRP1-IGFL1* of BTA18, *MGMT* of BTA26, *CD82* of BTA15, *DST* and *MOCSI-LRFN2* of BTA23, *REN* of BTA16, and a 10Mb region of BTA11 with type trait effects. *INSR*, *DGATI-NIBP*, and *PGLYRP1-IGFL1* each was located in a large gene cluster with multiple QTL effects.

Acknowledgements

This research was supported by National Research Initiative Grant no. 2008-35205-18846 from the USDA Cooperative State Research, Education, and Extension Service and by a financial contribution from Holstein Association USA. We thank the following collaborators for contributing DNA samples: T. Lawlor, M. Cowan, R. Wilson, C. Dechow, D. Spurlock, A. de Vries and B. Cassell. Supercomputer computing time was provided by the Minnesota Supercomputer Institute.

References

- Cole, J.B., Songstegard, T.S., Ma, L. *et al.* (2010). Abstract and Poster for PAG-XVIII.
Ma, L., Runesha, H.B., Dvorkin, D. *et al.* (2008). *BMC Bioinformatics* 9:315.
Wiggans, G.R., Ma, L., Sonstegard, T.S. *et al.* (2010). Abstract and Poster for PAG-XVIII.