DEVELOPMENT OF AN ONLINE QTL MAP OF DAIRY CATTLE TRAITS

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SUMMARY

Results from quantitative trait locus (QTL) studies in dairy cattle are accumulating rapidly. From an extensive survey of public domain information on QTL, we have prepared an online map for dairy production traits to enhance the utility of this resource and to make these data more easily available to the research community. The majority of reports on QTL concentrated on routine milk production traits (milk, fat and protein yield, and fat and protein percent). The combined QTL map shows some chromosomal segments consistently harbour QTL reported from various resource populations. Based on the requirement of the meta-analysis, we have proposed minimum guidelines for publishing QTL results, and for the establishment of a web-based QTL database.

Key words: quantitative trait loci; dairy cattle; online QTL map

INTRODUCTION

Many experiments have been conducted on livestock to detect quantitative trait loci (QTL) to find markers that can be implemented in breeding programs via marker-assisted selection or as an entry into a gene discovery programme. Development of a comprehensive microsatellite map of the bovine genome has facilitated whole genome scans for QTL with major effect on economically important traits in many elite dairy populations. Many partial and full genome scans have been published from a number of the populations. To date there have been no comprehensive attempts to assemble a consensus map of the QTL derived from different studies. In isolation most QTL studies are of limited power and usefulness, however in combination QTL results will have implications beyond the specified studies in which they were obtained. Therefore comparing the results across studies is of considerable interest. While it would be preferable to have access to source data, such an analysis will usually be restricted to working with summary published data. The purpose of this article is to survey the results of QTL mapping in dairy cattle with a view to construct an online QTL map, based on summary published data.

SURVEY OF LITERATURE

Dairy resource populations and experimental design. A number of dairy cattle populations have been studied using a granddaughter design (GDD). The first QTL detection experiment by Georges *et al.* (1995) consisted of 14 half-sib families with a total of 1518 sons from the US population. Another such population of the U.S. Holstein Friesians is the Dairy Bull DNA Repository, which has been extensively used for QTL detection. QTL detection studies using GDDs have also been published based on the New

Zealand / Dutch dairy population (1158 sons), German Holstein (1393 sons), Finish Ayrshire (453 sons), Canadian Holstein (434 sons), Swedish Holstein (515 sons) and Norwegian cattle (300 sons). The daughter design has been used for QTL detection only in a few studies. Mosig *et al.* (2001) used selective DNA pooling with a daughter design in an Israeli Holstein population. Daughter designs have also been used to support or validate the QTL detected from GDD (e.g. Grisart *et al.* 2002). There have also been limited attempts to apply the more flexible procedures using a complex pedigree analysis of dairy cattle. Fine mapping of QTL for economic traits has been undertaken to improve the location of QTL. Riquet *et al.* (1999) used a fine mapping approach for QTL affecting milk composition based on the utilization of historical records of recombination and identity-by-descent (IBD) mapping using linkage disequilibrium in the Holstein Frisian population.

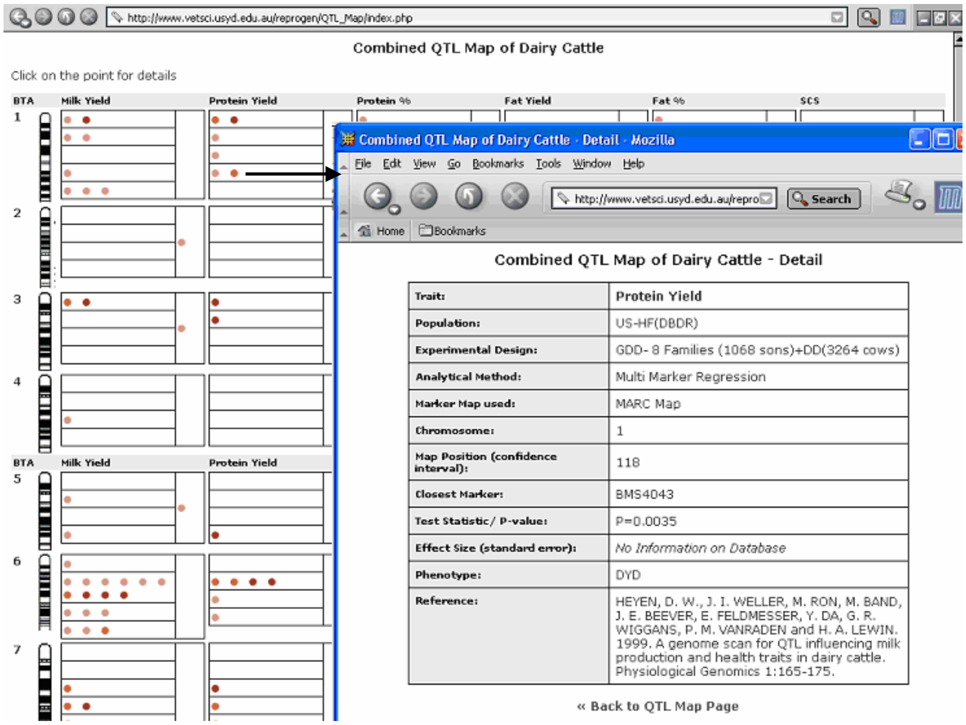
Map/marker used. The panels of the markers used in these primary QTL mapping studies were almost exclusively microsatellites (STRs) although single nucleotide polymorphisms (SNP) markers are being deployed in fine mapping studies. Some of the experiments used marker distances computed from the experimental data while other used the reference map (MARC) distances.

QTL mapping results. We constructed an online QTL map based on 47 published reports of QTL for milk yield, milk composition traits and somatic cell score (SCS) (http://www.vetsci.usyd.edu.au/reprogen/QTL_Map/, see Figure 1). This includes 17 full genome scans, 10 partial genome scans, 13 analysis of single chromosomes and 8 reports on fine mapping of a chromosomal segment. In a number of instances the results from the same resource population were reported more than once using different marker density or different statistical approaches but all the reports were included in this map. The map shows the distribution of reported QTL over the entire cattle genome at 30 cM intervals. Each dot on the figure represents a different QTL with the colour intensity increasing as statistical significance increases. Clicking on a particular QTL displays the table of detailed information about that QTL.

QTL for milk production traits have been identified on all the autosomal chromosomes of the bovine genome. Perusal of the QTL map would suggest that there is strong evidence of the presence of QTL affecting milk production traits segregating on chromosomes 1, 3, 6, 9, 14, and 20. A notable number of studies detected the presence of QTL related to milk yield on BTA6. There is also strong support for the presence of QTL for milk yield on chromosomes 1, 3, 9 and 20. There is strong evidence of QTL on chromosomes 3, 6 and 20 for protein percentage and on chromosomes 1, 3, 6, 9 and 20 for protein yield. Recently Blott *et al*. (2003) identified a phenylalanine-to-tyrosine substitution in bovine growth hormone receptor gene on BTA20 associated with a major effect on milk yield and composition. Grisart *et al.* (2002) identified a SNP in the DGAT1 gene on BTA14, which explained 51 percent of the phenotypic variance for fat percent. BTA3 is also a strong candidate for fat yield and percent QTL. Several chromosomes particularly BTA3, 6, 9, 14, 20 and 23 have been reported to harbour QTL with pleiotrophic effects. There are quite a few studies on QTL for somatic cell score (SCS). QTL for SCS on

BTA18 have been reported from the US, Dutch and Finnish cattle populations. BTA23 and BTA8 are also strong candidates for SCS QTL.

Figure 1. Online QTL map for milk production traits in dairy cattle.



Combined QTL Map of Dairy Cattle - Detail

Trait:	Protein Yield
Population:	US-HF(DBDR)
Experimental Design:	GDD- 8 Families (1068 sons)+DD(3264 cows)
Analytical Method:	Multi Marker Regression
Marker Map used:	MARC Map
Chromosome:	1
Map Position (confidence interval):	118
Closest Marker:	BMS4043
Test Statistic/ P-value:	P=0.0035
Effect Size (standard error):	*No Information on Database*
Phenotype:	DYD
Reference:	HEYEN, D. W., J. I. WELLER, M. RON, M. BAND, J. E. BEEVER, E. FELDMESSER, Y. DA, G. R. WIGGANS, P. M. VANRADEN and H. A. LEWIN. 1999. A genome scan for QTL influencing milk production and health traits in dairy cattle. Physiological Genomics 1:165-175.

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The online QTL map indicates that there is a large number of reports of QTL for milk production traits. The reports on QTL detection also indicate a marked difference in the location and magnitude of the effects of individual QTL. There are differences between families, even in the same study, in the level of significance, estimated effect size and predicted location of a particular QTL. Reports vary considerably in the completeness in describing analysis methods, QTL locations, support interval, effect sizes and phenotypic and genetic parameters. There are also differences among studies in the criteria defining the significance thresholds, design methodologies, etc, which make the results of different studies difficult to compare. However, there is a need to determine consensus location(s) of the QTL, as well as consensus estimates of the effects of these QTL. The use of meta-analysis across studies can provide a more precise and consensus estimate of the location of a QTL and its effect sizes as compared with any single study (Goffinet and Gerber 2000). Such a meta-analysis is underway for dairy cattle (Khatkar *et al.* 2003).

A thorough meta-analysis is hampered by the publishing of partial information on QTL mapping, and also by publication bias with the current focus on only on the most significant results. Thomson *et al.* (2003) detail the parameter estimates required for an effective meta-analysis. From these requirements we recommend that authors publish essential input data. At a minimum, this would include (1) study population; (2) analytical method for QTL mapping; (3) marker map used; (4) interval map / profile test-statistic (or estimated map position and confidence interval); and (5) estimated effect size of QTL(s) and standard error(s). Clearly, a web-based repository, with appropriate quality control, would be a major step forward, allowing for easy incorporation of additional information, and providing rapid dissemination of QTL regions of interest.

The online QTL map presented here is a step in the direction of combing the results and setting up the QTL database. We have displayed the above mentioned minimum set of information for each QTL on this map. The map indicates the incompleteness for the many studies that have been reported and reinforces the importance of reporting the minimum set of information for a typical QTL study in dairy cattle.

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