EXPLORING THE BOVINE X CHROMOSOME FOR QTL’S IN A GRANDDAUGHTER DESIGN SETTING

W. Coppieters¹, P. Berzi¹, J.J. Kim¹, D. Johnson², F. Farnir¹ and M. Georges¹

¹ Department of Genetics, Faculty of Veterinary Medicine, University of Liège, 20 Boulevard de Colonster, 4000 Liège, Belgium
² Livestock Improvement Corporation, Cnr. Ruakura and Morrinsville Roads, Private Bag 3016, Hamilton, New Zealand

INTRODUCTION
A classic design commonly used in QTL mapping experiments in dairy cattle is the grand daughter design (GDD) Weller et al. (1990). In this design only male animals are genotyped and consequently, a drawback of this design is the lack of recombinants within the X chromosome, with the exception of the pseudo autosomal region. As a consequence it is not possible to map QTL’s on the X chromosome using the classical analysis methods. Here we nevertheless propose to exploit the GDD to map QTL’s for production traits on the X chromosome by using a linkage disequilibrium (LD) approach exploiting the sons’ X-chromosomes. Farnir et al. (2000) already showed clearly that the level of LD in the dairy cattle population is considerable for all the autosomes. The X chromosome was not considered in this former study.

MATERIAL AND METHODS
Design and genotyping. Twenty-two microsatellites (XBM411, BM6017, BMS903, URB010, BMS811, BMS1616, HUMM2.21, HUJ121, BL1098, XBM7, BMS417, ILSTS017, BM4604, BMC6021, TGLA68, BMS2798, HAUT37, XBM16, XBM25, INRA120, MCM74 and BMS911) on the non-pseudo autosomal part of the X chromosome were genotyped on a grand daughter design comprising 22 half sib sire families with a total of 947 sons of Dutch Holstein Friesian population (Coppieters et al., 1998). Three microsatellites mapping to the pseudo autosomal region were also genotyped (TGLA325, MAF45, XBM451). Distances between pseudo autosomal markers were estimated using the genotypes generated on the GDD. Distances between the other markers were obtained from public available maps (Kappes et al., 1997).

Measures of linkage disequilibrium. The level of linkage disequilibrium was evaluated in a similar manner as described in Farnir et al. (2000). Linkage disequilibrium between markers was quantified using Lewontin's normalized D' value and the statistical significance was determined using a Monte Carlo approximation of Fischers exact test.

Traits. Analyses were performed for five production traits: milk yield, protein yield, fat yield, protein percentage and fat percentage. The phenotypic observations used were daughter yield deviations (DYD) (Van Raden and Wiggans, 1991) obtained from CR-Delta (Arnhem-The Netherlands)
QTL mapping on the non pseudoautosomal part of the X chromosome. The method used to analyze these data has been described in detail by Kim and Georges (2002). In short, the method consists of three main parts: in a first step, all pairwise identity-by-descent (IBD) probabilities are calculated between all the sons X-chromosome haplotypes, at regularly spaced distances along the chromosomes. The IBD probabilities were calculated based on a method described by Meuwissen and Goddard (2001). As only males are genotyped, phasing of the genotypic data is unnecessary and the genotypic data directly generates the maternally transmitted haplotypes.

Based on these IBD probabilities, the X-chromosome haplotypes are clustered using the UPGMA clustering algorithm (Mount, 2001) producing a dendogram reflecting their relationships for each position considered along the chromosome. Haplotypes with IBD probabilities above a certain threshold were effectively clustered in the subsequent analysis.

In a last step, the sons phenotypes were analyzed using a linear model, including the haplotype cluster as a random effect. $Z_{bh}$ was the incidence matrix indicating the cluster to which a sons' X chromosome belongs.

$$y = Xb + Z_{bh}h + Z_{nu}u + e$$

Variance components were estimated using AIREML (Johnson and Thompson, 1995).

The threshold used to consider haplotypes as IBD, was varied and for each threshold the analyses was repeated. The threshold generating the highest likelihood for the data was retained as being the optimal one, generating haplotype clusters reflecting the different hypothetical QTL alleles at that position of the chromosome.

RESULTS AND DISCUSSION

Extensive chromosome wide LD. The observed D' values (figure 1) are very similar compared to the ones observed for the autosomal chromosomes in Farnir et al. (2000). For all D' values nominal significance levels were estimated. For distance d between marker couple below 25 cM all nominal significance values were below 0.0001. (figure 2).

The level of linkage disequilibrium even with the relatively low density of the marker map clearly justifies a QTL mapping approach based on linkage disequilibrium information.

LD based QTL mapping. Figure 2 represents the lod score curves for the milk production traits analyzed. The highest lod score of 1.7 was observed for fat yield at position 48. Kim and Georges (2002) determined significance levels by simulation. Based on these results the significance of a lod score of 1.7 corresponds to 11 %. In conclusion no significant indication was found for a major effect on the milk production traits examined on the X chromosome.
Figure 1. D' values as a function of the distance between markers

Figure 2. Lod score curves along the X chromosome for the 5 traits analysed
REFERENCES


