Proc. Assoc. Advmt. Anim. Breed. Genet. Vol 14

MAPPING QUANTITATIVE TRAIT LOCI FOR FEED EFFICIENCY IN MICE – A PRELIMINARY ANALYSIS

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SUMMARY

Mice from high and low feed efficiency selection lines were used in an F_2 mapping design. The mouse lines differed in feed intake by approximately 25% with only small differences in growth and body composition. One hundred and twenty progeny from 2 F_1 sires were selectively genotyped. A genome scan was done using 80 microsatellite markers evenly spaced every 20cM throughout the genome. A preliminary analysis using an analysis of variance resulted in the following 16 putative quantitative trait loci (QTL) (F Prob<0.01): three for net feed intake, one for daily feed intake, four for body fat %, three for average daily gain and five for metabolic mid-weight. A QTL affecting fat and weight mapped to the same region (chromosome 13) as other mouse studies.

Keywords: Feed efficiency, mice, QTL.

INTRODUCTION

Feed is a major cost in all livestock industries with over 50% of feed consumed in a typical beef enterprise being used to maintain the breeding herd (Ferrell and Jenkins 1984). Evidence in beef cattle suggests that there is genetic variation in feed efficiency (Ferrell and Jenkins 1984) making it possible to improve feed efficiency by selection which would hopefully lead to improved profitability of the overall production system (Barwick *et al.* 1999).

Net feed intake may be a useful selection criterion to improve feed efficiency. Net feed intake is defined as the variation in intake independent of differences in weight gain and weight maintained, i.e. feed intake net of size and growth rate differences. Thus, it is hoped that selection for net feed intake will have a greater effect on improving the efficiency (low intake) of the whole production system rather than simply resulting in animals that eat less but are also smaller and slower growing. Net feed intake has been shown to be moderately heritable in cattle, poultry, pigs and mice (Korver *et al.* 1991; Luiting 1991; Mrode and Kennedy 1993; Hughes *et al.* 1997).

Currently, the major limitation of including net feed intake as part of the selection criteria in cattle is the cost of measurement, approximately $500 per animal. This is prohibitively expensive for phenotypic selection. However, a DNA test for markers of genes affecting intake has the potential to significantly reduce both costs and generation interval.

The objective of this study was to map the gene(s) associated with feed intake and efficiency in mice. This information will be utilised in cross-species comparative genome mapping, physiological studies and development of tests for genes or quantitative trait loci affecting feed efficiency in cattle.

MATERIALS AND METHODS

Mice from the eighth generation of selection for net feed intake (NFI) (Hughes *et al.* 1997) were mated in an F_2 intercross. The selection for the original lines was based on a 3 week feed intake test where weekly weights and intakes were recorded as described in Hughes *et al.* (1997). Net feed intake was then calculated using a linear model (PROC GLM, SAS 1989) fitted to daily feed intake (DFI), including terms for class variates of sex and management group, average daily gain (ADG) and metabolic mid-weight (MMWT = average weight$^{0.75}$) as covariates, and interactions of each class variate with the covariates. NFI was calculated as the residual error term in the model.

Fifteen high NFI animals were mated to 15 low NFI animals to produce the F_1 progeny. Four F_1 sires were chosen at random and were mated to 32 F_1 females (8 per sire) to produce approximately 440 F_2 progeny. The F_2 animals were placed on a five week feed intake test immediately after weaning, and weaning weight, metabolic mid-weight (weight$^{0.75}$) (MMWT), average daily gain (ADG), and daily feed intake (DFI) were measured. NFI was calculated as above. Following the post-weaning feed intake test, the animals were measured for body fat percentage (Fat) with an EM scanning machine. The two sire families that contained the most variation in NFI were then used for mapping. Selective genotyping for NFI was done using 60 (76%) progeny per sire (30 progeny per tail of the NFI distribution) (Table 1).

Table 1. The least squares means and standard errors within the high and low NFI distribution tails for the traits measured and the number of males and females within each tail

Trait	High NFI Tail	*Low NFI Tail*	Significance level
NFI	0.36 ± 0.04	-0.23 ± 0.03	***
DFI	3.81 ± 0.05	3.22 ± 0.05	***
Fat	14.03 ± 0.23	14.31 ± 0.23	ns
ADG	0.23 ± 0.01	0.23 ± 0.01	ns
MMWT	8.35 ± 0.11	8.40 ± 0.11	ns
No. males	29	30	
No. females	30	29	

*** F Prob<0.0001, ns not significant

Eighty microsatellite markers covering the genome (19 autosomes and the X-chromosome) were genotyped for the two sires, 16 dams and 60 progeny. CRIMAP (Green *et al.* 1990) was used to check for non-Mendelian inheritance and to confirm the marker positions and order. The average spacing of markers was 21 cM, ranging from 6.6 cM to 40 cM. As a preliminary analysis, a simple linear model containing the fixed effects of sire, dam nested within sire, and marker genotype was fitted to the data to determine differences in phenotypes that were associated with differences in genotypes. The marker genotypes were not necessarily fixed in the parental lines and allele source was not fitted in this preliminary analysis of variance. Significance was defined simply as $P<0.01$ with more stringent significance levels proposed for subsequent analyses.

RESULTS AND DISCUSSION

Sixteen putative QTL (F Prob<0.01) were detected on six different chromosomes in the preliminary analysis (Table 2). No NFI or DFI QTL were detected with an F probability of 0.001. However, at an F probability of 0.01, three QTL for NFI were detected and one for DFI. The QTL for DFI overlapped with one of the NFI QTL. This QTL had a large effect on feed intake: there was a 13% difference between the two homozygous genotypes (Homozygote 1 and 2) for DFI and a 12% difference in NFI (Figure 1). The high intake allele was from the high intake line and there was also some evidence for dominance. The fact that the DFI and NFI results were similar indicates that in mice with high *ad libitum* relative to maintenance intake, the traits are very similar.

Table 2. Putative QTL detected using ANOVA for each trait

Trait	F Prob < 0.01	F Prob < 0.001
NFI	3	-
DFI	1	-
Fat %	3	1
ADG	2	1
MWT	2	3

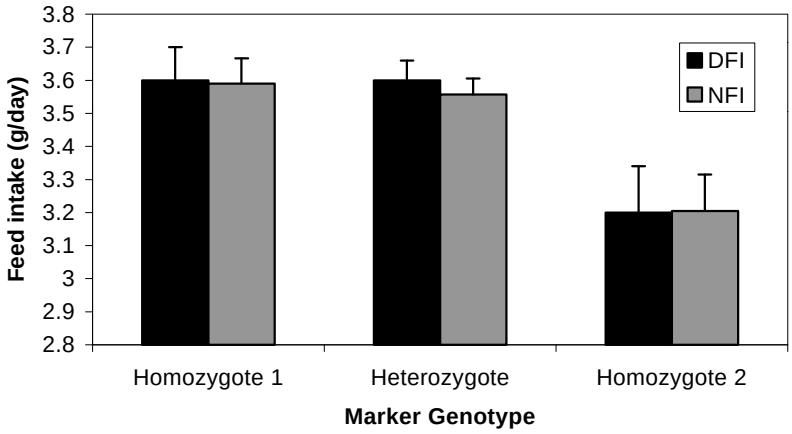

Figure 1. Least Squares Means for Daily Feed Intake and Net Feed Intake (+ mean intake) for the marker at a specific QTL.

There was stronger evidence for body fat, ADG and MMWT QTL than the intake QTL (P<0.001, Table 2). This was surprising since there was no significant difference between the distribution tails for these two traits (Table 1). Interestingly, the body fat QTL and one of the MMWT QTL occurred approximately half way along chromosome 13 (Figure 2) where a body weight QTL (Bw10) has previously been mapped (Brockmann *et al.* 1998). An abdominal fat percentage QTL and an abdominal fat weight QTL are also located on chromosome 13 (Brockmann *et al.* 1998).

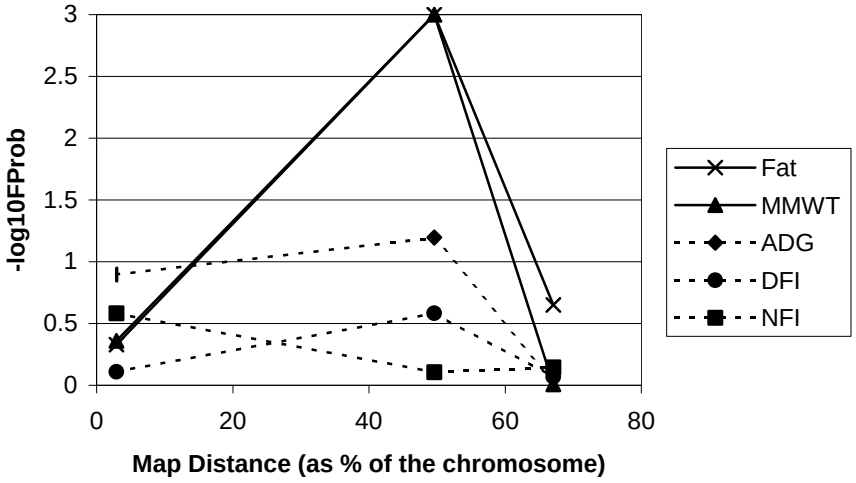

Figure 2. Evidence for QTL on Chromosome 13.

To confirm the 16 QTL identified in this preliminary analysis, the data will be re-analysed using maximum likelihood methods. It is widely accepted that selective genotyping individuals with extreme phenotypes for the quantitative trait increases the power per individual genotyped (Lander and Botstein 1989; Darvasi and Soller 1992; Muranty *et al.* 1997). However, it does limit the type of analysis that can be utilised. With regression analysis, only genotyped individuals are utilised which results upwards biasing of the estimated allele effects (Lander and Botstein 1989). In this study, this is not severe because 76% of the individuals were genotyped. However, it is still intended to utilise maximum-likelihood interval mapping techniques and some additional genotyping to verify the QTL reported herein.

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