MOLECULAR MAPPING OF QTL IN BEEF CATTLE

Harris A. Lewin, Jonathan E. Beever, and Rohan L. Fernando
Department of Animal Sciences, University of Illinois at Urbana-Champaign,
1207 West Gregory Drive, Urbana, Illinois 61801, USA

SUMMARY

A paternal half-sib family of purebred Angus cattle was used to examine the associated effects of six marker loci on growth and carcass traits. Among 146 half-siblings, offspring that inherited the paternal $BGKO_xY_2A'O'$ B blood group system phenogroup had 9.1 kg heavier 205-day (weaning) and 17.3 kg heavier 365-day (yearling) weights than half-sibs that inherited the alternative paternal B system phenogroup $I_2Y_2E'_1Y'$ ($P<.05$). Steers that inherited the $BGKO_xY_2A'O'$ phenogroup also had significantly leaner carcasses (-2.6 mm fat thickness at the 12th rib) than sibs that inherited $I_2Y_2E'_1Y'$. A highly significant association between BoLA-A and rib-eye area in steers was found ($P<.001$). The four other genetic systems, RBC-C, F-V, Tf and Gc, had no significant effect on growth or carcass traits ($P>.05$). These results indicate that the B blood group and BoLA systems are linked to genes that affect preweaning growth and lean muscle content, respectively.

INTRODUCTION

Gene mapping research encompasses a broad array of technologies and goals. In man, the rationale behind the ambitious plan to map and sequence the entire human genome is to develop methods of detection and treatment of genetic and neoplastic diseases. The mapping efforts being developed in parallel for model organisms, such as *Drosophila* and *Caenorhabditis*, are directed at improving our understanding of developmental biology and how simple organisms function. In contrast, the emphasis of gene mapping in agriculturally important species of plants and animals is quite different. For animal geneticists the most important objective is the identification of loci which govern quantitative traits (QTL), such as growth, reproduction and lactation. It is well known that these traits are under polygenic control and may be heavily influenced by environmental factors. However, QTL with large effects have been identified in animals and plants (Geldermann, *et al.*, 1985; Paterson *et al.*, 1988; Beever *et al.*, 1990). The need to identify QTL presents many theoretical and experimental challenges, and this topic has received much attention in the current literature (Beckmann and Soller, 1987). The identification and chromosomal localization of polymorphic QTL has been proposed as a means to improve breeding programs (Beckmann and Soller, 1987) and for the production of transgenic animals (McLaren *et al.*, 1990). In this study, we employed a large family of paternal half-siblings for detecting polymorphic QTL affecting growth and carcass traits in beef cattle.

MATERIALS AND METHODS

Animals. The Angus sire selected for study was determined to be heterozygous at six polymorphic loci; BoLA-A (class I major histocompatibility complex), the B, C and F blood group systems, serum transferrin (Tf) and vitamin D binding protein (Gc). Paternal half-sibs were produced in a commercial herd of purebred Angus cattle located in western Kansas. Calves were born between August 18 and October 22, 1986 and raised in two contemporary groups. Steers were implanted at 2, 7, and 10 months of age with Ralgro and one month previous to slaughter with Synovex-S. Steers were fed in a commercial feedlot in western Kansas and slaughtered in two contemporary groups.

Typing for lymphocyte, red blood cell, protein and enzyme polymorphisms. Typing for BoLA-A antigens was performed using the lymphocyte microcytotoxicity test and BoLA specificities were standardized to the results of the Third International BoLA Workshop (Bull *et al.*, 1989). The panel of typing reagents included sera for nineteen internationally recognized (w) BoLA-A specificities and three local BoLA specificities. Blood group phenotypes were determined for the blood group systems A, B, C, F-V, J, L, M, S, Z, and R'-S' using a standard hemolytic test. Biochemical polymorphisms tested were hemoglobin (Hb), carbonic anhydrase (CA), albumin (Alb), transferrin (Tf) and vitamin D binding protein (Gc). Typing for red blood cell and biochemical polymorphisms was performed by Stormont Laboratories, Woodland CA, USA.

Data. Performance data were collected on all half-sibs (n=146); carcass data were collected on steers only (n=61). Performance data included birth, weaning and yearling weights. The recommendations of the Beef Improvement Federation (Hubbard, 1981) were used to adjust these weights for age of dam and age at weighing and to calculate pre- and postweaning average daily gains. Carcass data included carcass weight, rib-eye area, 12th rib fat thickness and percent kidney, heart and pelvic fat. Yield grade was derived according to Hubbard (1981).

Statistical analyses. A general linear model procedure (SAS) was used for the analyses of performance and carcass data. Dependent variables included adjusted birth weight (ABW), 205-day adjusted weaning weight (WW205), 365-day adjusted yearling weight (YW365), pre- and post-weaning average daily gain (ADG and ADG2, respectively), carcass weight (CARW), rib-eye area (REA), 12th rib fat thickness (BKFAT), percent kidney, heart and pelvic fat (KHP) and yield grade (YG). The model used for the analysis of effects of marker alleles on performance traits was: $y_{ijk} = \mu + s_i + m_j + e_{ijk}$, where y_{ijk} = the ijkth observation; μ = a constant common to all observations; s_i = the fixed effect of the ith sex (i = male, female); m_j = the fixed effect of jth paternal chromosomal segment marked by paternal alleles within each system; e_{ijk} = the random residual term. For carcass traits the model used was: $y_{ijk} = \mu + g_i + m_j + e_{ijk}$, where μ, m_j and e_{ijk} were as defined in the previous model and g_i = the fixed effect of the ith contemporary feeding and slaughter group (j = 1, 2). Interactions between sex and marker for performance traits and group and marker for carcass traits were tested and found not to be significant ($P>.05$) for all dependent variables; therefore, interactions were not included in the models. Least squares means were compared between groups of sibs that inherited homologous chromosomal segments identified by the genetic markers within each system.

RESULTS

Associated Effects of Alternative Paternal Alleles. Half-sibs that inherited the chromosomal segment (CS) marked by the paternal RBC-B system $BGKO_xY_2A'O'$ phenogroup had significantly heavier WW205 (9.1 kg) and YW365 (17.3 kg) and greater ADG1 (0.4 kg) than sibs that inherited the CS marked by $I_2Y_2E'_1Y'$ (Fig. 1). The effects associated with the B system were more exaggerated in females from birth to weaning (data not shown). Steers that inherited the paternal CS marked by the $BGKO_xY_2A'O'$ phenogroup also had less BKFAT (-2.6 mm) than steers that inherited the CS marked by $I_2Y_2E'_1Y'$ (Fig. 2). Consequently, steers that inherited the paternal $BGKO_xY_2A'O'$ phenogroup tended to have more desirable yield grades than their counterparts (data not shown). The B system was associated with 2.9%, 3.1%, .7% and 7.8% of the phenotypic variation in ADG1, WW205, YW365 and BKFAT, respectively (data not shown). The BoLA system accounted for 9.3% of the phenotypic variation in REA (data not shown). Steers that inherited the CS marked by the BoLA-w2 allele had larger REA (4.1 cm^2) than sibs that inherited BoLA-w28 (Fig. 2). The RBC-C, F-V, Tf and Gc marker systems had no effects on performance or carcass traits ($P>.05$).

DISCUSSION

Results of this study indicate the likely presence of QTL linked to or within the RBC-B system that affects preweaning growth and fat content, and QTL linked to or within the BoLA system that affects rib eye area, a measure of lean muscle content. Our data demonstrate the power of paternal half-sib families as a means of detecting associations between marker loci and QTL. Furthermore, quantitative traits were measured within the same environment; therefore, environmental variance was minimized, allowing for a clearer evaluation of the genetic variance attributed to the marker locus or closely linked QTL.

The RBC-B system has been found to be associated with traits such as milk fat percentage in dairy cattle (Rendel, 1961) and preweaning growth and 12th rib fat thickness shown here for beef cattle. Thus, it is plausible that the associated effects are the result of closely linked locus that affects lipid metabolism. Also, the fact that the preweaning growth rate tended to be greater in prepuberal females than in hormone implanted steers (data not shown) implies that the gene may be influenced by sex hormones. Because all steers received hormone implants, we cannot determine whether the effects on performance and carcass traits would be observed if implants were not used.

Performance and carcass traits were selected for study because they are among the most heritable of all traits of economic importance in beef cattle (Kennedy and Henderson, 1975; Bourdon and Brinks, 1982).

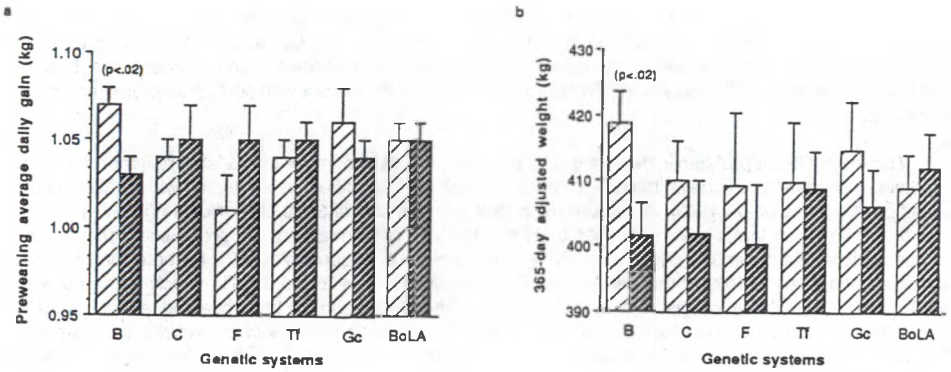

Figure 1. Effects of alternative paternal alleles on the growth traits preweaning average daily gain (a) and yearling weight (b). Paternal genetic systems and alleles were: RBC-B, $BGKO_xY_2A'O'$and I_2Y_2E',Y'; RBC-C, C,EW and W; RBC-F-V, FN* and F; Tf, D_2 and E; Gc, A and B; BoLA-A, w2 and w28, respectively as shown.

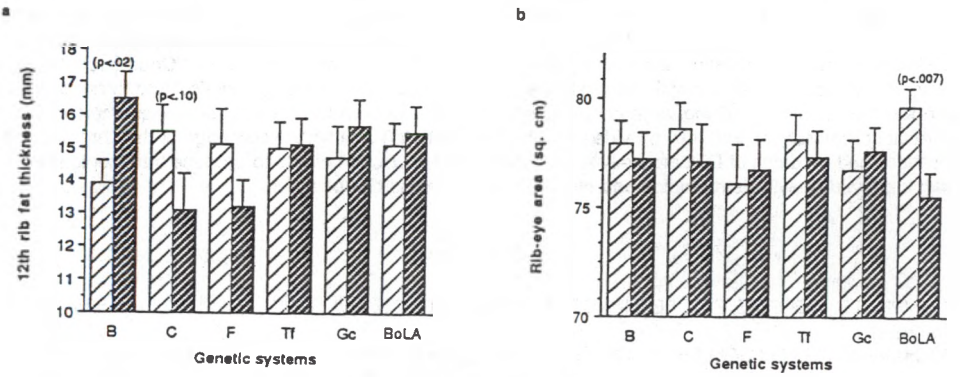

Figure 2. Effects of alternative paternal alleles on the carcass traits rib eye area (a) and 12th rib fat thickness (b). Paternal alleles are as described in the legend to Figure 1.

Furthermore, because growth traits such as preweaning average daily gain, weaning weight and yearling weight are positively correlated, both phenotypically and genetically, we can assume that genes controlling one of these traits will also affect the others. The positive associations found between the B system phenogroup $BGKO_xY_2A'O'$ and ADG1, WW205 and YW365 are consistent with such phenotypic and genetic correlations.

The most difficult problem in detecting QTL in cattle is the small number of available polymorphic genetic markers. To date there have been approximately 125 loci identified in cattle, of which about 50 are polymorphic (Fries *et al.*, 1989). If we assume a total genome size of 3000 cM for cattle (Fries *et al.*, 1989) and that the marker locus covers 50 cM (25 cM to each side of the marker), the six unlinked markers used in our study would cover 300 cM or 10% of the bovine genome. Assuming 10 QTL for both the growth and carcass traits, then in 10% of the genome we might expect to have found 2 QTL, which is the number of markers with significant effects found in this study. The magnitude of the observed effects were also consistent with expectations (Beever *et al.*, 1990). Another interesting aspect of our results is the amount of the genome covered by the marker systems showing effects. For example, the RBC-B locus has not yet been mapped but it has been demonstrated that the locus covers a genetic distance of approximately .7 centimorgans (Grosclaude, 1982), allowing extended coverage of the chromosome on which it is located.

To the authors' knowledge, these are the first results with beef cattle demonstrating significant associations between genetic markers and quantitative traits in a paternal half-sib family. Since growth traits are highly heritable, and can be measured at a relatively early age in both sexes, the application of marker assisted selection for growth-rate in beef cattle would appear to have limited economic advantage. In contrast, marker assisted selection for carcass traits appears to have some potential because of the difficulty in selecting for such traits on live animals.

With the advent of powerful gene mapping technologies, most notably the use of restriction fragment length polymorphisms, the genetic map of the bovine genome is rapidly expanding. One of our goals is to identify a DNA marker for the unmapped B blood group system. Such a marker will provide us with a landmark for eventual isolation and cloning of the B system-linked gene(s) of interest. Once such QTL are mapped to a recombinant clone(s), the product(s) can be elucidated by "reverse genetics" and their regulation and function studied. Cloning large chromosomal segments of DNA is now feasible, for example in yeast artificial chromosomes, and may provide us in the future with "QTL banks". Knowledge of the chromosomal locations and products of QTL are likely to have long-range impact on efforts to produce transgenic animals with improved growth performance and more desirable carcass composition.

REFERENCES

BEEVER, J.E., GEORGE, P.D., FERNANDO, R., STORMONT, C.J. and LEWIN, H.A. 1990. J. Anim. Sci. 68: (in press).

BECKMANN, J.S. and SOLLER, M. 1987. BioTechnology 5:573-576.

BOURDON, R.M. and BRINKS, J.S. 1982. J. Anim. Sci. 55:543-548.

BULL, R.W., LEWIN, H.A., WU, M.C., PETERBAUGH, K., *et al.* 1989. Anim. Genet. 20:109-132.

FRIES, R., BECKMANN, J.S., GEORGES, M., SOLLER, M. and WOMACK, J. 1989. Anim. Genet. 20:3-29.

GELDERMANN, H., PIEPER U. and ROTH, B.. 1985. Theor. Appl. Genet. 70:138-146.

GROSCLAUDE, F. 1982. Proc. Second World Congr. Genet. Appl. Livestock Prod. VI:350-358.

HUBBARD, D.D. 1981. United States Department of Agriculture. pp 6-12.

KENNEDY, B.W. and HENDERSON, C.R. 1975. Can. J. Anim. Sci. 55:493-502.

MCLAREN, D.G., FERNANDO, R.L, LEWIN, H.A. and SCHOOK, L.B. 1990. J. Dairy Sci. (in press).

RENDEL, J. 1961. Nature 189:408-409.

PATERSON, A.H., LANDER, E.S., HEWITT, J.S., PETERSON, S., *et al.*, 1988. Nature 335:721-726.