GENETIC MARKERS FOR QUANTITATIVE TRAIT LOCI IN DAIRY CATTLE

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SUMMARY

Genetic marker-lactation trait investigations conducted in the Holstein and Guernsey breeds involved about 6000 cows in each breed. Associations of blood group, blood protein, and milk protein polymorphisms with yield and component content were examined using least squares techniques. Effects due to marker pleiotropy or tightly linked quantitative genes were examined at the population level, while effects of quantitative genes more distant from markers were evaluated within sire half-sib families. More associations were found with component content than with milk yield. The most conspicuous associations involved milk protein loci and component percentages. Transferrin, blood group F, and J x L interactions were significantly associated with several traits. The detected significant effects are considered in the context of the literature.

INTRODUCTION

When the first reports on cattle blood groups emanated from the laboratory of M. R. Irwin at the University of Wisconsin in the early 1940's (Ferguson, 1941; Ferguson et al., 1942; Stormont and Cumley, 1943), they were greeted with eager anticipation of their possible usefulness in verifying parentage and assisting in the selection of animals with superior production. The former potential was promptly realized, but the latter has proven much more elusive. Even now, almost 50 years and many studies later, the relationships of most blood group genotypes to quantitative trait differences are far from clear.

Early attempts to find associations between blood groups and milk production traits yielded mixed results (McClure, 1952; Nair, 1957), but as additional blood group systems and factors continued to be discovered throughout the 1950's and early '60's (Stormont, 1962), euphoric expectations persisted. The development of gel electrophoretic methods fueled these hopes by opening the door to the discovery of many additional polymorphic systems - primarily proteins of red cells, serum, and milk. With a few exceptions, studies of possible associations between markers and lactation traits have yielded inconsistent results, producing predictable disenchantment with this line of investigation. The pendulum has probably swung too far.

In retrospect, it is not surprising that so many of the results have lacked either statistical or biological significance. Most of the examined markers were not chosen because of any known connection with the target trait; they were chosen simply because they comprised the known repertoire of readily detectable polymorphic variants in the species. It is also not surprising that the consistently strongest results have involved those loci for which the lactation connection is obvious, namely the milk protein loci.

MATERIALS AND METHODS

Ohio genetic marker-quantitative trait investigations have included three projects which will be summarized here. The first involved 3000 Holstein cows in eight institutional herds in Ohio. The markers analyzed were blood groups A, B, C, F, J, L, S, and Z, transferrin (Tf), and β-lactoglobulin (β-Lg). Quantitative traits were milk and fat yield and fat percentage. A second Holstein study involved 3600 cows in herds from the northeastern part of the U.S., Minnesota and Utah. Markers examined were blood group systems A, B, C, F, J, L, M, S, and Z, serum Tf, and milk proteins β-Lg, α_{s1}-Cn, β-Cn, and k-Cn. The third study was conducted in the Guernsey breed in cooperation with the Delaware Agricultural Experiment Station.

It involved 6000 cows and included typing of all of the markers of the previous study plus hemoglobin (Hb) and serum alkaline phosphatase (Ap). Traits examined in the latter two investigations were milk yield and percentages of fat, protein, and solids-not-fat. Data from all studies were analyzed by least squares procedures. The latter two projects were also subjected to linkage analyses in which comparisons were made within sire between the two groups of daughters receiving alternative alleles from their heterozygous sire. Component of variance analyses were conducted at each of the marker loci for allele marker groups nested within sires.

RESULTS AND DISCUSSION

The results of these investigations, previously reported by Brum et al. (1968), Gonyon et al. (1987), and Haenlein et al. (1987), are summarized in Table 1. Potential marker-lactation trait "hot spots" suggested by the literature are also portrayed in this table. Only marker-lactation trait combinations represented by at least eight independent, statistically evaluated studies were summarized. All milk yield, fat yield, and fat percentage combinations met these criteria, but only those protein percentage combinations involving milk protein markers did. Combinations for which more than 40% of the publications report significant association are indicated by double-lined boxes; those for which 25 - 40% of the publications report significant association are indicated by single-lined boxes.

Several trends are evident. There is much more evidence of marker association with component content than with yield traits; significance values were fewer in number and generally of lesser magnitude for the yield traits than for the component traits. (Fat yield, however, was only analyzed in our first Holstein study, and this study did not include casein variant typing.)

There is a reasonably good agreement between our results and those summarized from the literature. Two marker-trait combinations with striking numbers of significant results in the literature are B blood group with fat percentage, and transferrin with milk yield. Our findings are in agreement.

Our results also corroborate those prevalent in the literature implicating the involvement of the milk protein loci in fat and protein percentage differences. This is presently the premier example of genetic marker-lactation trait relationship in dairy cattle. The amount of the effect that is due to pleiotropy of the milk protein genes themselves and the amount attributable to other linked genes remains to be elucidated. The effects noted for J, particularly the linkage effect (indicated by underlining), suggests that there may be some QTL bracketed by the J and β-Lg loci. The highly significant J x L interaction effects on milk yield and component content in Holsteins are worthy of note, but not readily explainable.

The casein results illustrate another general observation - namely that the results from the Guernsey and Holstein breeds do not corroborate each other very well. Some of the casein difference arises from inter-breed gene frequency differences (Hines et al., 1977; Haenlein et al., 1980) which render the casein loci differentially useful for marker purposes. Some of the difference may result from the pleiotropic effects of different marker alleles in the two breeds, and some may be attributable to a different complement of linked genes. Finally, there is some indication that a portion of the difference is attributable to "noise" not completely eliminated by the analytical methodology. This is most strongly suggested by the rather profound outcome changes which sometimes result from seemingly minor modifications in the statistical model. The noise hypothesis is bolstered by the published record, which reveals that almost every marker locus investigated has been found in one or more studies to be associated with lactation trait differences. With so many markers and traits typically being examined, the contribution of chance to variable results must be recognized.

Table 1. Association Between Genetic Markers and Lactation Traits

genetic markers	Lactation Traits: milk yield	fat yield	fat %	protein %
A	G*		H*	
B			H**	
C				G*
F	G*H*	H**	H**H**	
J			G*	H**
L				G**
JxL	H**		H**	H***
M			G*	H*
S				
Z	H*		G*	H*
Tf	H*	H*		H**
β-Lg			G***	
α-Cn			G*	G*
β-Cn				H***
k-Cn			H**	H***

- significant results in 25-40% of publications.
- significant results in >40% of publications.

* - p <.05
** - p <.01
*** - p <.001
G - Guernsey breed; H - Holstein breed
Underlined letters indicate linkage results.

Among all loci examined in numerous investigations, the notable absentee from the positive result column is the C blood group locus or complex. This is probably a result, in part, of the often ambiguous relationship of C phenotypes to genotypes; because large numbers of genotypes frequently yield the same phenotype it often impossible to deduce the genotype for this system. It is impressive that the only C system associations reported have been found by linkage analysis (Geldermann et al., 1985; Gonyon et al., 1987). The effect identified by this marker is probably due to linked QTL rather than pleiotropy. Linkage effects were also observed for both milk protein linkage groups studied - the caseins and the J, β-Lg chromosomal segment. Geldermann et al. (1985) also found positive results for these linkage groups. Another marker with impressive statistics was the F blood group, which had significant values in both linkage and direct effect analyses, in both the Guernsey and Holstein breeds, and for both yield and component content traits. There is little published support for this finding; of thirteen other reports on milk and fat traits, only Hogreve and Koch (1966) found significant F system effects. Interestingly, in both Guernsey and Holsteins the F locus was also significantly associated with differences in the protein-fat yield ratio. In Guernseys, β-Lg likewise had a significant effect on this ratio.

Linkage studies offer the potential of identifying many more QTL than population studies which are limited to detecting pleiotropic marker effects and the effects of very tightly linked genes. However, efficiencies are lost when combining data from different families and when dealing with 2 allele systems which, even at optimum gene frequencies have many homozygous sires and many uninformative progeny. As has been pointed out by Fries et al. (1989), it will be advantageous to study highly variable marker loci ideally spaced about 20 centimorgans apart throughout the genome. Linkage groups with some indication of QTL inclusion constitute candidates for expansion and further QTL linkage study. These include the caseins; J and β-Lg; BoLA, blood group M, prolactin, and TCP1; transferrin and ceruloplasmin; and blood group A, hemoglobin, and PTH. RFLPs offer the best hope for expanding these linkage groups, but informative conventional markers should not be abandoned. Unfortunately, the most polymorphic blood group systems, i.e. B and C, have not yet been placed in linkage groups. Our work indicates not only that QTL are part of marked linkage groups, but that there is the potential through marker assisted selection of dissecting the fat-protein genetic correlation so as to increase the yield of protein while decreasing that of fat.

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