

BLOOD GROUP POLYMORPHISMS AND PRODUCTION AND TYPE TRAITS
IN DAIRY CATTLE: AFTER FORTY YEARS OF RESEARCH

J.L. Rocha, J.F. Taylor, J.O. Sanders, and D.M. Cherbonnier
Texas A&M Univ., Animal Science Dept., College Station, TX 77843

SUMMARY

A broad strategy was implemented to bring into perspective over forty years of research on associations between blood group polymorphisms and milk and type traits in dairy cattle, and to analyse the largest data set ever available for this type of study (2.5 million records since the 1940's), in an attempt to make a final assessment regarding the usefulness of blood groups as selection aids in current Holstein breeding schemes and in order to try to formulate general conclusions relative to the approach of resolving quantitative variation into individual locus effects. Inconsistency of results across different studies and across different analytical designs now pursued emphasize the importance of a problem which has been conveniently ignored in most of the theoretical studies published recently on QTL detection and marker-assisted selection: that posed by the intrinsic non-additivity of genetic and biological phenomena. To ignore this fact leads to inflated expectations and too easy promises regarding the usefulness of genetic markers for selection purposes. The L blood group has been found linked to gene(s) that impact milk component traits (fat and protein yields and percentages). Linear models establishing within-family contrasts, comparison of allele frequencies between extreme and opposite tails of individual families, chi-square tests assessing the occurrence of selection on a within-family basis, changes in allele frequencies across generations, and previous research results, all demonstrate beyond any reasonable doubt the biological validity of this finding.

INTRODUCTION

The number of recent publications on theoretical aspects of QTL detection and utilization is astounding (Rocha, 1994). However, the practical benefits of a research arena which has been evolving since the 1920's (Rocha, 1994) are scarce or null. In cattle, considering only associations between those blood groups and milk and type traits available for this study, 69 previous publications were found (Rocha, 1994), reporting on 3,664 statistical tests performed of which 301 were found to be significant at different levels of probability (.05, .01, or .001). This wealth of information available since 1951, the renewed interest in the utilization of genetic markers in animal breeding, the considerable progress made in recent years with regard to statistical tools and theoretical methods to support this type of genetic analysis, and the existence of an exceptionally informative data set (2.5 million observations) provided by the U.S. Holstein Association including records since the 1940's, were all reasons that coalesced to originate the present study.

MATERIALS AND METHODS

The data provided consisted of: Predicted Transmitting Abilities (PTAs) for milk production and type traits of 22,614 bulls; first lactation information on 98,685 cows registered since the late 1950's, and on 1,825,486 contemporaries (not blood typed) of these cows; and visual appraisal numeric scores for type and traits of 61,420 cows registered between 1979 and 1989, and of 386,380 contemporaries. Genotype determinations for the A, B, C, F, L, M, R', S, T', and Z systems, were performed routinely through the years by commercial laboratories contracted by the Holstein Association.

General linear models (Freund et al., 1986) including sire, maternal grandsire, and herd-year-season effects, were fitted under different types of experimental designs: half-sib family designs (Soller and Genizi, 1978) based on male progeny (PTA data; MFD); half-sib designs based on female progeny (FFD); granddaughter designs (GDD; Weller et al., 1990); and analyses based on the assumption of direct quantitative effects of the blood groups (DEA).

Within large half-sib families (> 500 sibs and out of heterozygous sires), and for each trait, animals were ranked based on their PTA or phenotypic value and comparisons of allele frequencies between opposite tails of the distribution were conducted based on a normal approximation to the binomial distribution (Lebowitz et al., 1987). Chi-square tests (Mackinnon and Georges, 1992) were also conducted within large families to assess whether the impact of selection on genotype frequencies could be detected.

RESULTS

When results from the two family designs and from the granddaughter design were integrated, only three associations emerged as consistently significant across the different approaches: a C blood group effect on rump angle; a L effect on milk composition traits; and a S effect on milk fat yield. Given the incoherent pattern of erratic and inconsistent results that has been observed in the early studies, given that inconsistencies among the results of different analytical approaches (that are based on partially overlapping sets of data) occur even when sophisticated statistical techniques are utilized, at this stage in this type of research the key element to be sought has to be "consistency" if the objective is to maximize the likelihood of meaningful achievements in the short-term. Therefore, those three associations were the only that were found deserving of further characterization. At this phase of the development of the project, strong statements cannot be made regarding the C and the S effects mentioned.

Persistent, clear, linear trends in allele frequencies across decades could be perceived for some of the alleles of the A, B, C, L, M, and Z blood group systems in both males and females (Rocha, 1994). Judgement is reserved with regard to the C blood group changes in allele frequency at this stage. As for the remainder, only the L blood group allele frequency changes clearly match results from the linear models fitted and from the other analytical approaches implemented. Probability levels associated with the significant L blood group effects were: $P=.015$ for PTA-milk protein yield in MDEA

(PTA-milk yield was a covariate in the model - see Rocha, 1994); $P=.0001$ for milk yield, $P=.007$ for milk fat percentage, and $P=.0009$ for milk protein yield in FDEA; $P=.0001$ for PTA-milk protein yield and $P=.0003$ for PTA-milk fat yield in MFD (PTA-milk yield was a covariate in both these models - see Rocha, 1994); $P=.01$ for milk yield and $P=.0001$ for milk protein percentage in FFD; $P<.01$ for milk fat percentage in GDD. Averages of the within-family differences that were significantly associated with the transmission of alternative sire alleles were: 4.5 kg for PTA-milk fat yield (after adjustments for PTA-milk yield); 2.6 kg for PTA-milk protein yield (after adjustments for PTA-milk yield); 1122 kg for milk yield; .19 for milk protein percentage; and .61 for milk fat percentage. Transmission of the null allele was predominantly associated with significant decreases in yield traits and increases in percentage traits, result that matches previous research findings. However, there were some families in which the reverse was true. The magnitude of the direct effects detected was smaller than that of linked effects, and both these facts indicate that the QTL is (are) not closely linked to the L locus, but some linkage disequilibrium between the two loci occurs.

Significant ($P<.01$) differences in allele frequencies between opposite tails were detected within some families: the frequency of the null allele in the lower tails was usually higher than in the upper tails for the yield traits. The reverse was usually true for percentage traits. Chi-square tests (Mackinnon and Georges, 1992) revealed that the null allele is clearly at a selective disadvantage within some families and results in Table 1 show that changes in allele frequencies for the L group are occurring in the overall population. These changes are not very pronounced (Table 1) but they emphasize that some linkage disequilibrium between the two loci exists.

DISCUSSION

The existence of one or more QTL impacting milk composition (fat and protein yields and percentages) traits in the chromosomal segment marked by the L blood group is a biological fact that this research project validates beyond any doubt. The effect(s) are fairly consistent across environments and genetic backgrounds, as the constancy of significant results across different analytical approaches emphasizes, and allele frequency changes are occurring in result of the selection schemes practiced in the Holstein breed. At this stage of the development of the research project, clear and simple recommendations with regard to L blood group-assisted selection cannot yet be made, but they will be formulated. An element of imprecision that remains to be clarified relates to the exact nature of the effect: is it mediated through effects on milk yield? Or are there at least two QTL, one impacting milk protein, the other milk fat yield?

Lack of consistency in results of marker-QTL association studies is an observation whose relevance and practical implications should not be underestimated. Well in advance of any theoretical or experimental work in this area, Sewall Wright in 1939 was already

Table 1. L blood group allele frequency changes with time

Allele	1950's	1960's	1970's	1980's	Early80s	Late80s
Males ^a						
null-	.78	.77	.79	.73	-	-
L-	.22	.23	.21	.27	-	-
Females ^a						
null-	-	.80	.80	.76	.79	.75
L-	-	.20	.20	.24	.21	.25

^e Unbiased (M.L.) estimates of frequencies obtained by the square root method (simple dominant system).

providing us with the explanation: "Separate genes cannot be classified as good or bad. Only the genotype as a whole can be so classified (and even this is relative to environmental conditions)." To ignore this simple principle so lucidly stated in 1939 represents an illusion with an additivity that is not present in production/biological/genetic phenomena. Rocha et al. (1994) analyse in detail the problems this illusion poses for the utilization of genetic markers in breeding schemes, and frame the biochemical and mathematical nature of a QTL effect in light of the Kacser and Burns (1979) model.

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