APPLICATION OF GENOMIC INFORMATION IN A DAIRY CATTLE BREEDING SCHEME

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SUMMARY

Marker assisted selection has been applied in dairy cattle breeding schemes with minor to moderate improvements in genetic gain. The cost effectiveness of it has been neutral at best in most cases. The completion of the sequencing of the bovine genome in 2006 has generated a large number of single nucleotide polymorphisms that are now commercially available. In addition, the cost of genotyping single nucleotide polymorphisms is markedly reduced compared to microsatellite genotyping. LIC has undertaken extensive genotyping of the sires that have been progeny tested in the last 20-30 years. Analysis of this data has allowed LIC to identify combinations of markers that allow the genetic evaluation of bulls from their DNA. By utilising this genomic information, two-year-old sires are now being sold to New Zealand dairy farmers. It is expected that selection based on genomic information (genomic selection) will increase the rate of genetic gain in New Zealand by 50-70%.

INTRODUCTION

DNA information has been used in dairy cattle breeding schemes since the early 1990's when parentage testing was transferred from blood protein polymorphisms to microsatellite markers. At the same time, the detection of quantitative trait loci (QTL) for dairy cattle had just commenced (Georges et al. 1995). Since this date there has been a flood of QTL being reported for dairy cattle traits. In at least three instances, the QTL have been positionally cloned; chromosome 14 – DGAT1 (Grisart et al., 2002), chromosome 20 – GHR (Blott et al. 2003) and chromosome 6 (Ron et al 2006, Schnabel et al 2005). In the instance of chromosome 6 there is some debate over which gene and polymorphism underlies the QTL. With the small number of QTL that have been positionally cloned, there has been a reliance of using linked markers rather than the functional polymorphism itself in dairy cattle breeding schemes.

Utilisation of QTL in dairy cattle breeding schemes via marker-assisted selection (MAS) has been thoroughly researched in a theoretical setting through simulation studies (eg. Meuwissen and Goddard 1996, Spelman and Garrick 1997). The increases in rates of genetic gain through MAS varied from 2-3% to an increase of 50%. The variation in response was mainly due to the underlying genetic model that was simulated and the proportion of genetic variance that was explained by the QTL.

The implementation of marker assisted selection has occurred in a number of dairy cattle breeding schemes (Spelman 2002, Boichard et al. 2006). Boichard et al. 2006 reported that the French dairy industries use of 43 markers had resulted in a improvement in genetic response by approximately 5-19%. They concluded that MAS was economically beneficial to the French breeding companies.

The sequencing of the bovine genome by the international consortium (Kappes et al. 2006) has generated a large number of single nucleotide polymorphisms that have been deposited in the public domain. In conjunction with companies such as Affymetrix and Illumina, large scale SNP (single nucleotide polymorphism) genotyping at low cost can now be undertaken in bovine. Whereas the genotyping cost for a microsatellite was approximately NZ$2.50 per genotype two years ago, now a SNP genotype costs less than one NZ cent when tens of thousands of SNP are typed in parallel. The technology shift to large scale SNP genotyping has and will have a major effect on the utilisation of markers in dairy cattle breeding schemes.

This paper will outline the current use of markers in the LIC breeding scheme and describe the biological resources that have been generated to develop the next wave of markers and genomic tools that will be used in LIC's breeding business.

MARKER ASSISTED SELECTION

As reported by Spelman (2002), LIC started MAS in 1998 using 6 QTL that had been identified from a grand-daughter design. The QTL, which affected milk production traits, were used in a within-family MAS setting where the phase of the QTL alleles were re-estimated for each of the sire families. The sires that were identified to be heterozygous for the QTL of interest were used to generate multiple full-sib sons. This was undertaken through a combination of MOET and IVP reproductive programmes. Full-sibs were deemed to be required as generating half sibs through artificial insemination would result in the selection advantage of the QTL information being negated through the loss of selection differential on the cow to dam pathway. The resulting male offspring were genotyped, with the sons that received the desired alleles selected to enter progeny testing.

The reproductive performance of the donor cows was poor and very few of the families had enough sons to allow within-family marker-assisted selection. After two years of poor reproductive performance the within-family MAS was abandoned. The results from these two years indicated that methods that used markers in a BLUP setting or markers that were in linkage disequilibrium would be required for more effective utilization of MAS.

In 2002 Grisart et al. reported the identification of a functional mutation in DGAT1, which was closely followed by Blott (2003) for the identification of a polymorphism in the GHR gene. Both of these genes have been used in the LIC breeding scheme for the last 4-5 years. For each of the two genes allelic effects have been estimated from over 3000 sires for the New Zealand dairy population (Spelman et al. 2002, 2003). All bull dams and bulls entering the progeny testing scheme are genotyped for the two genes.

GENOMIC SELECTION

Meuwissen et al. (2001) first proposed the use of dense marker maps in a genomic selection (GS) setting. Through simulation they found that by estimating breeding values from genomic information (one microsatellite per cM), the accuracies of selection were 0.75-0.85. At the time of the paper being published,

cost estimates to undertake the work on 2000 sires with 4000 microsatellites was approximately NZ$20 million. With the sequencing of the bovine genome and the commercial SNP panels being developed, the cost of this experiment is a now a factor of 10-20 less.

LIC has completed the genotyping of approximately 4500 sires that have been progeny tested over the preceding 30 years. LIC had the foresight to store DNA from every sire that was progeny tested since 1980. This has enabled LIC to genotype sires that were the best and the worst of their progeny test cohort and thus evaluate markers across the genetic range. Genotyping has been undertaken on the Illumina 50K SNP panel.

The dataset was split into two parts: i) Research dataset and ii) Validation dataset. The research dataset was all bulls that were progeny tested prior to 2002. For the HF breed there were 1410 sires in the research dataset. The genotypes for the 1410 sires were analysed to identify which SNPs affected the estimated breeding values for the sires for 25 different traits. The objective of the research dataset was to find a subset of SNPs that predict (or explained) the genetic merit of the sires. Once the effects for the SNPs had been estimated they were then tested on the validation dataset. For the HF breed there were 420 sires in the validation dataset and they were the bulls that had been progeny tested between 2002 to 2004. The validation dataset was used to "test or validate" the SNP effects that had been estimated from the research dataset. The validation was undertaken by comparing the progeny test BVs with the genomic BVs estimated for the relevant sires. The degree of accuracy of the DNA-based BVs was measured by their correlation with the progeny test BVs. The correlations varied from 0.45 to 0.60 for the production and non-production traits for the Holstein-Friesian breed (Table 1).

Table 1. Correlations between DNA-based and progeny test BVs in the validation population for the Holstein-Friesian breed.

Trait	Correlation
Protein yield	0.57
Milk fat yield	0.47
Milk volume	0.60
Live weight	0.51
Fertility	0.59
Somatic cell score	0.54
Total longevity	0.60
Shed temperament	0.47
Farmer opinion	0.45
Udder overall	0.45
Dairy conformation	0.51

Currently there are 3 sources of information that can be used in the estimation of breeding values; parental information, own performance and progeny performance. DNA is now the fourth source of information. A dairy bull of one year of age has only information from his parents for dairy related traits. The parental information is combined with the DNA information to estimate a genomic breeding value for the bull.

This has been undertaken in New Zealand in 2008 for the first time. The reliabilities for the genomic breeding values for the Holstein-Friesian breed are approximately 50-55%. This is in contrast to a reliability of 75%-85% for a progeny tested bull and 30-35% for a bull entering progeny test. LIC has selected a team of Holstein-Friesian bulls based on their genomic BVs and these are being sold commercially. It is expected that over the 3 breeds sold by LIC that the genomically selected sires will undertake 10-20% of inseminations.

The LIC breeding scheme, which has been based on progeny testing 300 bulls per annum, is being altered to incorporate the DNA information. For the first time in 2009, LIC will screen over 1000 bulls based on their DNA profile and then select the best 100-150. These bulls will enter progeny test as one year olds and then their semen will be sold commercially as two-year-old bulls. The bulls will be retained until they receive their progeny test BV and semen will be sold to farmers that prefer to purchase genetics based on progeny test information.

With the shorter generation interval due to bulls being used as two year olds instead of five year olds, it is estimated that the rate of genetic gain in the New Zealand population could increase by 50-70%.

The utility of DNA in dairy cattle breeding schemes has now reached the level of accuracy that dramatic changes and improvements to breeding schemes can occur. With denser marker maps becoming available in the coming years and more sophisticated statistical tools it is expected that the level of accuracy from DNA will continue to improve.

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