Current and future impact of DNA technologies on the New Zealand sheep industry

J.C. MCEWAN

AgResearch Invermay, Private Bag 50-034, Mosgiel 9053, New Zealand

ABSTRACT

DNA technologies are already widely used in the New Zealand sheep industry. Parentage determination in extensively managed flocks is currently the most widely used test. Increasingly, these tests are being supplemented by the use of performance markers, either by themselves or in conjunction with parentage. Commercial single marker tests currently available in New Zealand include: two for meat yield, two for prolificacy, parasite resistance and production, lamb survival, footrot, scrapie susceptibility, and several monogenic trait tests including: microphthalmia, horns, and spider lamb. However, the future is likely to be some form of 'genomic selection' where the test explains a major, perhaps majority, of the genetic variation in an animal. This technology depends on the creation and use of high density SNP (single nucleotide polymorphism) probe chips. In New Zealand dairy cattle it is expected to increase the rate of genetic gain by 50 to 70%. A similar chip has been created for sheep and New Zealand animals are currently being genotyped. If successful the expectation is that industry release will occur in late 2009. New Zealand sheep industry delivery will be as breeding values created using a blend of DNA and existing Sheep Improvement Ltd. information.

Keywords: genomic selection, SNP chip, ovine, genetic improvement.

INTRODUCTION

McEwan (2007) outlined the current New Zealand sheep breeding system and described how DNA technologies were being used for parentage, traceability, and marker assisted selection. The core message was that a single DNA sample could be used in multiple ways at different tiers of the sheep industry and subsequent processing chain. The long term objective was to DNA sample animals in the stud breeding tier, and where necessary also commercial and carcass samples, and that these samples plus genotypes derived from them were stored in a database that was fully linked and integrated with the genetic evaluation system. Samples would be bar-coded and animals tagged with an electronic identification to aid tracking and data collection.

In the same issue Dodds *et al.* (2007) and Hayes and Goddard (2007) described genomic selection and its prospects in the New Zealand sheep industry. Genomic selection is where tens of thousands of markers are genotyped in several thousand animals that have phenotypic information on the trait or traits of interest. From this 'training set' marker trait associations across the genome are derived and then used to predict breeding values, commonly called molecular breeding values or MBVs. Typically the accuracy of these MBVs is determined by comparing these predictions with actual breeding values in an independent or 'validation' population. Commonly this is progeny of the same training set population but whose phenotypic and genetic information was excluded during training. This technology was first comprehensively described by Meuwissen *et al.* (2001). Various derivatives have been proposed since. Usually these have been proposed to reduce genotyping costs. A common variant is identification and use of a reduced set of markers that can explain a significant proportion of the observed variation; often called a 'SNP key'.

MBVs can be calculated solely from marker information, but they can also be combined with traditional breeding values after each has been calculated separately (Goddard, 1999). The result is a more accurate breeding value than either. These are often called genomic breeding values, blended breeding values, or GBVs.

In the last year genomic selection has been implemented in the dairy industry of several countries including New Zealand and USA. In fact the New Zealand industry adopted the technology within a year of an appropriate tool, called a SNP chip, becoming available. For the New Zealand situation it is estimated that it will lift genetic progress by 50 to 70% for the dairy industry. Similarly, implementation is currently being actively researched in many other species including chicken, pig, sheep and salmon industries. The current rate of scientific progress and level of industry adoption of this technology is almost unprecedented for agricultural species. Salient factors affecting these changes appear to be dramatic reductions in genomic sequencing and genotyping costs, coupled with an increasing understanding of the molecular variation within mammalian species and strains that affects traits of economic importance. This review updates recent advances in genomics in sheep over the past two years,

progress towards implementation of genomic selection in sheep, and future challenges to its wider adoption.

WHAT IS A SNP AND A SNP CHIP?

A single nucleotide polymorphism or SNP is where a DNA variant consists of a single base change in the approximately 3 billion nucleotide bases that make up the ovine genome. Because of their properties they make very suitable genetic markers. Spurred by human research, ways of genotyping many thousands of these variants in parallel have been developed. One method is a SNP chip where probes to test many thousands of different variants are arrayed on a slide (Fig 1). The introduction of this technology has been accompanied by a dramatic reduction in price per DNA variant assayed.

REQUIREMENTS FOR GENOMIC SELECTION

In order to undertake genomic selection you need the following: a genome sequence for the species, identified SNPs, a SNP chip created from that resource, and several thousand well phenotyped animals that have high quality DNA samples derived from the population that you hope to implement the technology in.

SHEEP DNA SEQUENCING AND SNP CHIP CREATION

In order for genomic selection to be undertaken, a major fraction of the genome has to be sequenced and assembled, then SNP variants and their likely location identified. The assembly is required for selecting variants which are evenly paced across the genome. The sequence surrounding the variant is also required so a high quality testing probe can be designed.
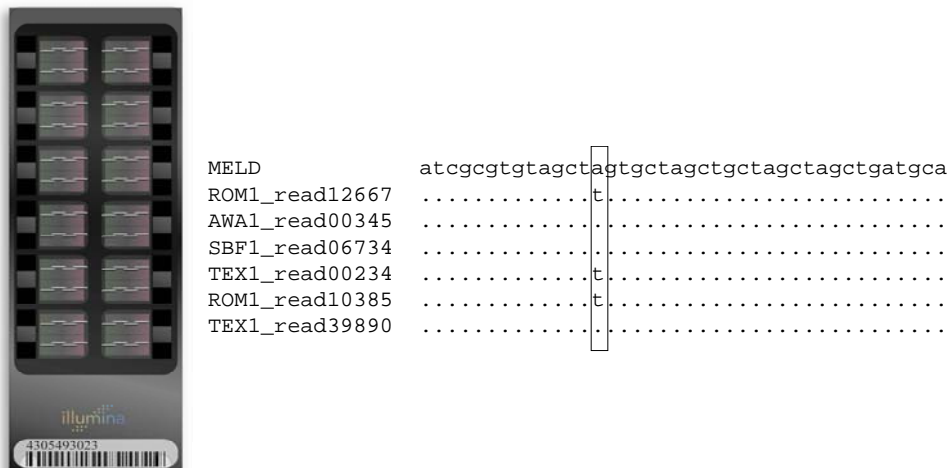
To do this six sheep were partially sequenced by the International Sheep Genomics Consortium or ISGC (www.sheephapmap.org). The animals included Romney, Texel, Merino, Poll Dorset, Scottish Blackface and Awassi ewes. The sequencing commenced in late July 2007 and was completed early in January 2008. This sequence was then positioned and assembled using the bovine genome as a framework and subsequently reordered into sheep chromosomes (McEwan *et al.*, 2009). Over 594 thousand SNPs were identified and this was supplemented by further 76 thousand SNPs detected using an alternative method. From these SNPs 59,454 were selected based on their characteristics and used to create a SNP chip in conjunction with illumina (Dalrymple *et al.,* 2009). This chip was commercially released in January 2009 and called the Ovine SNP50 BeadChip (www.illumina.com). Upon validation of this chip, in excess of 50 thousand SNPs provided reliable information across a wide variety of breeds.

OVINE HAPMAP PROJECT

While not explicitly required, understanding the genetic variability within and across the global repertoire of sheep breeds provides many benefits when implementing genomic selection. Two results are extremely useful: the ability to characterize any animal's breed composition and the ability to infer what populations may be suitable for genomic selection when using a training set developed in a different population(s). The latter result is derived by understanding the level of nearby marker associations that are shared between various populations. The ISGC has therefore undertaken a

FIGURE 1: Picture of an Illumina SNP (single nucleotide polymorphism) chip 2.5 x 8 cm (left), each square equals a sample measurement area with 12 samples per chip. To the right is an example of an ovine SNP identified from comparing individual sequencing reads from various breeds against a reference sequence at the top. Dots represent identity with the reference sequence.


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MELD              atcgcgtgtagctagtgctagctgctagctagctgatgca
ROM1_read12667    .............t..........................
AWA1_read00345    .......................................
SBF1_read06734    .......................................
TEX1_read00234    .............t..........................
ROM1_read10385    .............t..........................
TEX1_read39890    .......................................
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large study involving 2,890 sheep from 64 breeds, 120 wild sheep and a further 50 samples from outgroup species (www.sheephapmap.org/hapmap.php). An earlier pilot study has already been published for sheep (Kijas *et al*., 2009) as has a more comprehensive study in cattle (Bovine HapMap Consortium, 2009).

ASSOCIATION STUDIES IN SHEEP

Various studies are currently underway around the world in sheep with the Ovine SNP50 Beadchip with a view to introducing genomic selection, or at least identifying regions or genes of interest. In fact enough SNP chips to do several tens of thousands of animals were purchased upon their initial availability. In New Zealand, Ovita are currently genotyping close to 5,000 samples and the expectation is a somewhat smaller number will continue to be used annually. The initial samples consist primarily of dual purpose animals with Romney, Coopworth and Perendale breeds making up the majority supplemented by a small number of Texels and composite breed animals. These samples span the great majority of the New Zealand dam genetics. A large proportion of these animals are leading sires whose progeny have been measured for a wide variety of traits including live weight, wool weight, number of lambs born and lamb survival with smaller numbers measured for parasite and facial eczema resistance, dagginess and ultrasonic fat and muscle depth.

EXISTING INFRASTRUCTURE

The adoption of this technology does not exist in a vacuum, but instead builds on existing industry resources. DNA technologies are already widely used in the New Zealand sheep industry. Parentage determination in extensively managed flocks is currently the most widely used test. This enables animal model BLUP evaluations to estimate breeding values within the Sheep Improvement Ltd. (SIL) genetic evaluation system via a modified genetic engine. Increasingly, these tests are being supplemented by the use of performance markers, either by themselves or in conjunction with parentage. Commercial single marker tests currently available in New Zealand include: two for meat yield, two for prolificacy, parasite resistance and production, lamb survival, footrot, scrapie susceptibility, and several monogenic trait tests including microphthalmia, horns, and spider lamb. The number is increasing by one to two additional tests per year. The impact of these tests is significant. DNA parentage has allowed the low cost creation of scalable vertically integrated breeding schemes and these have captured an increasing market share of ram sales. Single marker tests have a

differing utility depending on their end use, but the test for the GDF8 mutation (MyoMax™) has led to widespread introgression breeding strategies in many New Zealand terminal and dual purpose breeds.

LIKELY SCENARIO FOR INDUSTRY ADOPTION

The exact method of industry implementation will depend on the results of scientific work currently being undertaken, including how transferable predictions will be across New Zealand dual purpose breeds and composites. However, it is expected that initially only a small proportion of the stud breeding tier will be genotyped, therefore some form of 'blending' to combine molecular and traditional breeding values will be used to generate genomic breeding values (Goddard, 1999). The key point is that the format of both molecular and genomic breeding values will be on the same scale as existing breeding values and can be used just like existing breeding values for selection indices. As both breeders and commercial farmers are already familiar with these concepts this greatly eases industry adoption. Based on results from the dairy industry there is likely to be a place for commercial use of both high density chips and lower density and slightly less accurate 'SNP keys'.

Industry interest is likely to be focused on sex limited and difficult to measure traits, and traits that can only be measured later in life. These include: disease resistance for parasites and facial eczema, reproductive performance, lamb survival, adult ewe live weight, feed efficiency, methane production and carcass and meat quality traits. However, the technology offers benefits for all traits and the key to its successful use will be its seamless adoption within existing recording systems.

FUTURE CHALLENGES

In the longer term sequencing and genotyping costs will continue to reduce in price, computing technology of genetic evaluation will advance, and all industry animals both commercial and stud will be electronically tagged, tracked and measured throughout their life including when processed at the meat plants. It is as yet unclear how these changes will affect the system described above.

One already proposed option is that DNA segments will be tracked through generations by sequencing key stud sires or alternatively genotyping them at a very high density followed by tracking these segments using a lower density chip with, say, 3,000 SNPs on their progeny. Even at current prices a number of dairy bulls are already planned to be sequenced. Such a system has the advantage that a single near constant set of markers can be used on the progeny for all situations and the

genotypes can also be used for breed and parentage assignment. It achieves this at the expense of an increase in computing complexity (Habier *et al.*, 2009).

Perhaps more immediately, as both data and industry experience increases, phenotypic and genomic data will be jointly analyzed to estimate breeding values in a one step process. A step towards that continuum would be to use MBVs as a correlated trait in existing BLUP which has the advantage that molecular information is transferred to all relatives as well (B. Tier, Personal communication). Such methods only truly become compelling when a large number of animals have been genotyped.

However, in my opinion the largest ongoing challenge will be collecting phenotypes in a cost effective manner, especially for difficult to measure phenotypes such as feed efficiency, meat quality and disease traits. There is a strong economic case for these traits to be measured only on a relatively small number of well phenotyped animals that are representative of the top tiers of the New Zealand breeding schemes, perhaps as part of a national progeny testing scheme such as the SIL-ACE central progeny test (Young & Newman, 2009).

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