

# Genomic Selection Abounds on New Zealand Pastures

Genotyping is improving sheep breeding selection and the quality of the flocks.

## **Breeding Better Sheep**

A flock of sheep speckling the vibrant green New Zealand landscape may not immediately evoke thoughts of genomic analysis technology, but on many pastures here and across the world, an agrigenomic revolution is occurring. Scientists like John McEwan at AgResearch in New Zealand are using the power of DNA sequencing and microarray technologies to vastly improve breeding selection strategies for a number of agriculturally important animals.

For the last 30 years, John has worked with sheep in agrigenomics research, a field that, as he describes it, aims to "improve the pastoral industry, from the soils to the grass and the animals that grow on them, and the products that come off of them." While his group primarily focuses on breeding sheep that can better resist diseases, particularly parasites, they are also interested in a number of other economically important traits like reproduction, meat quality, and feed intake.

Scientists have been successfully improving sheep lineage for some time using breeding selection based on genetic analysis. According to John, "since 1990 the actual production per year has increased by over 70%, and it continues to grow." Traditionally they relied on phenotypic measurements and parentage to calculate breeding values for animals. "For many years we used a CT scanner to measure fat content and things like that, but the best opportunities now are in DNA technologies," he explains.

Many agriculture industries are starting to realize the value of using genotypic information, rather than phenotypic measurements, to evaluate the genetic merit of animals. The most successful approach has been to use single-nucleotide polymorphisms (SNPs) to predict the performance of animals in the breeding stock. In order to bring this technology to the sheep industry, John's team along with colleagues from the Ovita<sup>1</sup> consortium, set out to identify the markers in the ovine (sheep) genome that could be used to predict specific traits.



New Zealand sheep grazing with Mt. Cook in the distance



John McEwan, Senior Scientist, AgResearch

# Sequencing The Ovine Genome

Starting in the mid 1990s, John began doing quantitative trait loci (QTL) studies and expressed sequence tag (EST) sequencing with ovine genes. At the time, an ovine genome was not available, so identifying markers was quite slow and extremely expensive. He recalls, "we would develop single-gene markers for say increased muscling in animals or decreased fat, or some monogenetic diseases, and then later we said we need to do this more appropriately—we need to sequence the genome."

John and colleagues turned to next-generation sequencing to assemble the ovine genome and to identify useful variants, a project that was carried out through the International Sheep Genomics Consortium (ISGC)<sup>2</sup>. Initially using long-read sequencing, they were able to align the reads against the bovine (cattle) sequence for the assembly. The hefty cost of whole-genome sequencing at the time meant that there weren't many reference genomes available. Bovine was selected simply because the ISGC happened to have access to the recently assembled cattle genome.

Once the genome was assembled, they turned to short-read and reduced representational sequencing to identify the SNPs. John says of these efforts, "Illumina technology provided the depth to find the

SNPs. We actually found quite a lot in just the ordinary sequencing that we did as well. That allowed us to get all the SNPs at quite a reasonable cost."

These sequencing efforts at AgResearch, along with contributions from Baylor University and Australia's Commonwealth Scientific and Industrial Research Organization, eventually led to the Illumina OvineSNP50 BeadChip, a whole-genome microarray containing 50,000 sheep markers that was introduced in 2009. Where in the early days identifying these SNPs and evaluating animals was a monumental task, "now people are able to use the Illumina chip and pretty much go directly from that to the markers that are useful in the industry immediately," John explains.

## Implementation and Industry Adoption

In many pastoral industries, new technologies have to be implemented in a strategic manner to make fiscal sense. In some industries, like with cattle, the animals are so valuable that each can be cost-effectively genotyped. However, for animals like sheep that are less monetarily valuable, the introduction of a new technology must be applied more selectively.

According to John, sheep are only worth probably \$50–70 USD in most places around the world. That is roughly ten times less than a cow, so breeders need to be very selective about what animals are tested. The key animals in any industry are called the "sires to breed sires"; these are the animals that produce the males that are used across the whole industry. One sire can likely influence around 30,000 ewes, so breeders can spend quite a bit of money on them because, for the number of ewes they affect, it doesn't cost much per ewe. By genotyping thousands of sires, scientist can now evaluate a vast number of variants for economically important traits.

In addition, the falling cost of whole-genome sequencing offers researchers the opportunity to identify new, more powerful markers. These efforts can bring the technology to even more animals by eventually leading to more economical tests that work across multiple breeds.

Using a cascading approach, where each year researchers sequence the most influential animals from the lamb crop, they should be able to quickly develop an extensive catalog of variation within each population. John expects that they be able to sequence hundreds or thousands of animals in the coming years. As he explains, there are about 3,000 animals used each year as sires to breed sires in New Zealand. These animals are in the top nucleus tier to breed sires for selling to commercial farmers, who mate them to the ewes to produce lambs for consumption. At the next tier, there's about 300,000 lambs born each year. In the long term they would like to sequence the top-tier 3,000 animals, but in the short term, they will simply genotype them using the Illumina OvineSNP50 BeadChip. They will then sequence a number of the ancestral sires that follow that top-tier 3,000. John elaborates, "Within a couple of years we will have basically sequenced all the ancestral chromosomes in that population. There might be 25 million sheep, but there are only really about 3,000 unique chromosomal segments at any location. And that will allow us to impute down to any animal from the 50K SNP array, basically the full genomic variation."

As the technology adoption rate continues to increase, John and colleagues would like to eventually develop content for an even lower density array, which would help bring these tools to more animals. SNPs on the low-density array can be used to impute up to most of the 50K SNPs on the OvineSNP50 BeadChip. John explains, "for the animals genotyped with a low-density SNP array, in theory, you could take them right through to actually predict 95–99% of the variants without sequencing."

This concept is already being implemented in the cattle industry. Illumina recently introduced the low-density Bovine 3K genotyping panel to complement the higher density bovine arrays it offers. While most agrigenomic industries are still largely in the research phase of implementing genomic analysis technologies, the cattle industry has started to move beyond that. According to John, "it's basically moving to full-scale adoption right across the general industry, and as a consequence, there has almost been an explosion—almost a 10-fold increase in the adoption rates."

He believes that for such a paradigm shift to occur with sheep, the return on investment for breeders will have to reach a certain point. As he explains it, traditional genetic selection methods in sheep lead to around a 1% financial return per annum in a compounding manner. However, breeding selection based on whole-genome analysis provides the opportunity to double that per annum. As the cost of whole-genome arrays and sequencing continues to decrease, and breeders see higher and higher returns, the amount of investment should reach a point where the technology rapidly undergoes full-scale adoption across the industry. With the dedicated work of John and his colleagues, the future for sheep and other pastoral industries promises greater breeding efficiency, healthier livestock, and better quality products.

### Acknowledgements

- 1. Ovita: a partnership between Beef + Lamb New Zealand, AgResearch, and the New Zealand government. www.ovita.co.nz
- 2. The International Sheep Genomics Consortium. www.sheephapmap.org

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