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How well is the sheep industry positioned to capture the benefits of genomic technologies?

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The cost of reading the DNA at a single point of the genome (all the DNA a person carries), has dropped by more than 100 times in the past five years. This dramatic reduction in cost has been driven by human disease applications of DNA technology. This is such a strong driver that we can expect even greater reductions in cost of obtaining DNA information in the next couple of years. Can sheep breeders and the meat and wool industries benefit from this rapidly advancing technology?

The answer is clearly yes. Three obvious applications of DNA technology are:

1. Parentage. Provided DNA is available from rams and ewes, lambs can be assigned using DNA markers to their parents.

2. Breeding for traits controlled by a single gene. An example here is polled. Polled rams can be carriers of the horned gene variant, and so can pass this onto their progeny, however, a genetic test can identify polled rams which only carry the polled gene variant.

3. Breeding for industry traits with Genomic breeding values. These traits are controlled by many genes so many DNA markers are needed. DNA taken can from a young ram or ewe can now be tested and used to accurately predict their genetic merit for a large range of traits, including carcass and meat quality traits.

This paper will focus on the technology of genomic breeding values. The value to the meat and wool sheep industries of genomic breeding values depends on four criteria: for what traits they can be predicted, how accurate they are, how much they cost the breeder, and what opportunities are there to take advantage of genomic breeding values in the breeding program. Let's go through each of these in turn.

For what traits can genomic breeding values be predicted? Some of the key traits in wool and meat breeding programs are either expensive to measure, cannot be measured in breeding animals, can only be measured late in life, or can only be measured in ewes. For example, lean meat yield is expensive to measure and can only be measured on slaughter animals, after which there is no opportunity to breed from them. Number of lambs weaned can only be measured in females, and can only be measured after the ewe has been selected to be retained in the flock. For these traits, genomic breeding values have great potential, because they can be obtained for young rams (and even ewes) from only a DNA sample, and can be used to make selection decisions before the breeder would usually have good information on these traits.

However, in order to be able to predict genomic breeding values for these traits, the correlation between the DNA information and the traits must be derived in a very large data set. That is, these traits must be recorded on a large number of animals, which have also been scored (genotyped) for a large number of DNA markers. The Sheep CRC Information Nucleus is an ideal and unique resource here, as a large number of traits relevant to meat and wool production have been measured on many progeny (see Rowe et al. in these proceedings for detail). Each of these progeny have also been scored for 50,000 DNA markers (this technology is called a 50K SNP chip, as the DNA markers are Single Nucleotide Polymorphisms or SNPs). This allows the DNA marker profiles associated with excellent performance for these traits to be identified. Then Genomic breeding values can be predicted for any young ram or ewe from their SNP chip genotype.

How accurate are genomic breeding values? The value of the Genomic breeding values for making selection decisions depends on their *accuracy*. Accuracy is how well the genomic breeding value predicts the real value of an animal's genetics, the true breeding value. When a selection decision is made, the accuracy of the genomic breeding value determines how many of the truly genetically elite animals are actually selected, Figure 1.

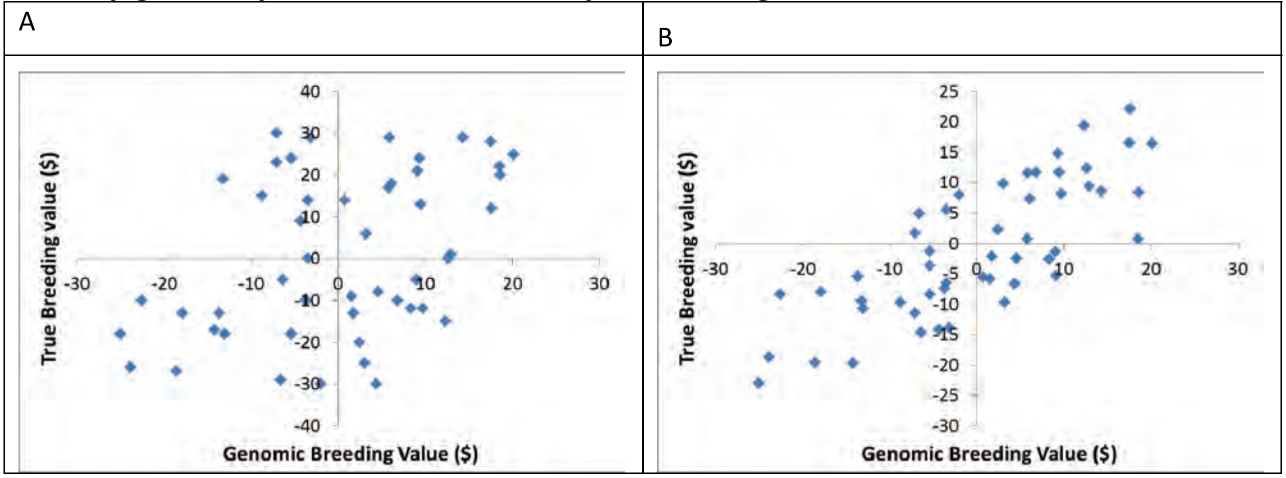

Figure 1. The relationship between genomic breeding values and true breeding values, for the example of Intra Muscular Fat, (but measured in $ of value), for 50 young rams. In A, the accuracy of the genomic breeding values is 0.35. With an accuracy of 0.35, the rams selected on high genomic breeding values mostly have high true breeding values, but a few rams have poor true breeding values. In B, the accuracy of the genomic breeding values is 0.7. Now, selection on genomic breeding values results in selection of very few rams with poor true breeding values.

In dairy cattle, the accuracy of genomic breeding values for milk production, in young bulls and heifers is very high, Table 1. This has resulted in very rapid adoption of genomic breeding values in the dairy industry. There are also high levels of accuracy for yearling fleece production that will help to make selection decisions in young rams and ewes. Many of the prediction accuracies for meat characteristics are similar in sheep and cattle. Although not as high as for milk and wool the use of these genomic breeding values is expected to have a significant impact on selection for meat eating quality in both sheep and cattle.

Table 1. Comparison of accuracies of genomic breeding value between species. For the latest meat sheep results see Banks et al. in this proceedings.

			Sheep	
Trait	**Dairy**	**Beef**	**Merino**	**Terminal**
Feed conversion, growth & fertility				
Net feed intake	0.42	0.43		
Fertility	0.60	0.20-0.35		
Milk production	0.78			
Birth Weight			0.37	
Yearling Weight			0.64	
Post weaning worm egg count			0.27	
Longevity	0.64			
Carcass and meat quality				
Tenderness (shear force)		0.33	0.10	0.14
Carcass IMF		0.30	0.23	0.31
Carcass WT		0.30	0.17	0.20
Scan fat depth		0.27	0.45	
Carcass fat depth			0.23	0.17
Scan eye muscle area		0.16	0.44	
Carcass eye muscle area			0.22	0.24
Iron			0.24	0.26
Omega-3			0.23	0.17
Wool traits				
Greasy fleece weight (Yearling)			0.70	
Fibre Diameter			0.77	
Staple Strength			0.35	

So how do we continue to make our genomic breeding values more accurate for meat sheep, and make them even more useful? The answer is more data. In dairy cattle the accuracy of genomic breeding values has improved substantially over time as more data has been added. So in sheep, more individuals with traits recorded and DNA markers scored will improve the accuracies. In fact we have already observed this: as the number of progeny the Sheep CRC Information Nucleus has trait recorded and genotyped has increased over time, we have observed a clear increase in the accuracy of genomic breeding values (eg. Daetwyler et al. 2010).

Another key driver of accuracy of genomic breeding values is how closely related the young rams, for which the genomic breeding values are being calculated, are to the resource population that was measured for the traits and have genotypes. Animals that are less related to the resource can be predicted less accurately (eg. Habier et al. 2010, Daetwyler et al. 2012). This is one reason why the Sheep CRC Information Nucleus has been designed to capture as much of the industry genetic diversity as possible.

How much do and will genomic breeding values cost? The other side of the equation is the cost of obtaining genomic breeding values on young rams. The total cost of genotyping for a breeder must obviously be less than the additional returns as a result of selecting on the genomic breeding values. Any innovation to drive down the cost of obtaining genomic breeding values increases the profit from the technology. One such innovation which is now widely used in the dairy industry is the use of low cost DNA markers panels with relatively low numbers of markers, which can be *imputed* to much higher density markers from which genomic breeding values can be predicted. The concept behind imputation is that when sires pass on their chromosomes to their offspring, the chromosomes are passed on in large complete chunks. This means that provided the sire is genotyped with high density DNA markers, his offspring can be genotyped with just enough markers to track these large chromosome chunks, and the rest of the

DNA markers can be filled in with a high degree of accuracy. The genomic breeding values can be predicted for the offspring. In the dairy industry, this innovation has allowed even heifers and cows to be screened cost effectively, as well as bulls (Boichard et al. 2012). In the dairy case, the low density panel has 7000 DNA markers, while the high density panel has 50,000 DNA markers. The cost of a low density panel can be a half or even a third of the cost of the high density panel. For imputation to be successful, a large number of animals must already be genotyped for the high density panel. Imputation also works best if the animals genotyped for the high density panel represent the genetic diversity of the industry (Boichard et al. 2012). Again, the Information Nucleus is an excellent resource here which will enable low density panels to be used in our meat and wool sheep. Sheep CRC researchers are currently devoting considerable effort to developing a low density marker panel for Australian sheep. To improve cost effectiveness the low density panel will also be used for parentage assignment, and include the marker for horned/polled (Dominik et al. 2012).

In the future, the rapid developments in genome sequencing technology, driven by human disease applications, will result in even lower cost of obtaining genomic breeding values for breeders. These developments are happening so rapidly, in sheep it may be possible to go straight to a “genotyping by sequencing” approach rather than developing a low density DNA marker panel (that is sequence rams and ewes rather than use SNP chips).

The final criteria for assessing value of genomic breeding values is *what opportunities are there to take advantage of genomic breeding values in the breeding program*? The opportunity to improve genetic gain is greatest for traits which are measured later in life. This explains why genomic breeding values have revolutionized dairy cattle breeding. Before genomic breeding values, bulls were selected on the basis of their daughters milk production (progeny test), which meant the bulls were at least five years old before they were used in the industry. Now, genomic breeding values are accurate enough to select bulls for industry use at a young age (http://www.adhis.com.au/) which reduces the breeding cycle by three years. In meat and wool sheep, some similar opportunities exist. For example, the Sheep CRC Pilot II project can already provide genomic breeding values for young Merino rams for adult fleece weight and fiber diameter. Opportunities also exist to now select directly for traits that contribute to profit, rather than indicator traits. For example for meat sheep, genomic breeding values are predicted for lean meat yield.

Even greater benefits will come when genomic breeding values for reproduction are available, as this trait has some similarities to the dairy cattle situation (the trait is measured on one sex only, and measured late in life).

One opportunity to really accelerate genetic gain is to use genomic breeding values in conjunction with reproductive technologies which decrease generation interval. For example, in females there is the possibility of harvesting oocytes from very young females. These oocytes are then fertilised in vitro, and inserted into recipients, in Juvenile In-vitro Embryo Transfer (JIVET). Using JIVET would reduce the generation to approximately half of what it is now. If genomic breeding values were used to select donor ewe lambs, and especially if a reasonable number of embryos could be produced per donor, the rate of genetic gain could be at least doubled. Obviously such a breeding program would be very expensive. For this reason, it is likely to be restricted to a small proportion of the seedstock sector that has very high rates of genetic gain. For breeders who are already using JIVET technology, the marginal cost of genotyping elite ewe lambs is likely to be small. Such breeding programs may be particularly attractive to breeders aiming to rapidly develop lines of sheep with unique attributes, such as high Omega-3 or zinc levels in meat.

In conclusion, the Australian wool and meat sheep industries are well placed to take advantage of rapid developments in genomic technologies, principally because we have a large resource of animals measured for many high value traits (the Information Nucleus). This resource enables genomic breeding values to be calculated for breeders' young rams and ewes. In the near future the value of genomic breeding values to the industry will be even greater, when low density panels and imputation can be used to reduce the cost of the technology for breeders, and genomic breeding values for reproduction become available.

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