How might DNA-based information generate value in the beef cattle sector?

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Abstract

Using DNA information for parentage determination and recessive carrier status is an often undervalued benefit of genomics research. These "simple" applications enable the management of recessive conditions and the correction of pedigree errors which result in an improved rate of genetic gain. The promise of using DNA information to directly make better selection decisions is a tantalizing prospect. Value has been clearly demonstrated in the dairy industry and adoption had been rapid. However the beef industry presents a number of challenges when it comes to using DNA-based information to improve the accuracy of selection. The beef stud sector tends to include a small number of disperse nucleus breeders operating in the absence of records for many economically important traits (fertility, disease resistance). The industry makes extensive use of natural service bulls and there is significant value associated with the hybrid vigour derived from cross breeding. Additionally, the industry is segmented (breeder, producer, processor) and there is often little transfer of information and/or profit between sectors. This limits the availability of phenotypic records for many economically important traits and the value proposition associated with DNA testing. There is limited value associated with the improved genetic gain resulting from increasing the accuracy of genetic evaluations for yearling natural service bulls destined to sire fewer than 100 progeny over their lifetime. Commercial farmers could use DNA tests to improve the accuracy of replacement female selection. This assumes the development of low-cost DNA tests that perform well for the low heritability traits that affect maternal performance (e.g. heifer pregnancy). Genomics would most benefit the beef industry if it results in selection approaches for hard-to-measure, economically relevant traits that are currently omitted from breeding objectives due to the absence of selection criteria upon which to base breeding decisions.

Keywords: accuracy, DNA testing, EBV, genetic defect, genomics, marker-assisted management, parentage, recessive, selection, SNP, value

Introduction

DNA-based information is becoming increasingly important to beef cattle producers. Single-gene tests for various genetic defects and qualitative traits (e.g. coat colour) and parentage testing are being used routinely, and some breeds are using singe nucleotide polymorphism (**SNP**) chips to improve the accuracy of genetic merit estimates. Adoption of this technology will require a clear market signal that the value derived from testing outweighs the costs involved. To date, the cost of DNA testing has tended to exceed the value that is returned to any single sector. The costs associated with performing DNA-based analyses continue to drop precipitously. The following paper examines how DNA testing is currently being used and how an era of low-cost genotyping might seed change.

Parentage

The value of paternity testing is multifaceted, and depends upon whether tests are being used in the breeding sector or the commercial sector. In the breeding sector it is well known that correct pedigree information is necessary for the accurate estimation of breeding values (**EBV**), and incorrect records are known to reduce genetic progress. In the absence of pedigree information, the assessment of an animal's breeding value can only be based on its own performance record. The accuracy of an EBV based on an animal's own performance record is equal to the square root of the trait heritability (e.g. if trait $h^2 = 0.25$; accuracy = 0.5). Historically breeders have managed paternity assignment by using known AI sires or single-sire natural service bull pastures in their breeding program. Assigning new born calves to their correct dam is not an identity problem in beef cattle but is labour intensive and may be hazardous. These management considerations have negated a strong need to use DNA information to identify parentage, although many breed associations require parentage "verification" as a condition of registration. At the nucleus level pedigree information can also be used to manage inbreeding. There are some benefits associated with the use of multiple-sire mating pastures (no need for fencing and space required for single sire pastures, elimination of bull failure, and a tighter calving season) that should also be considered when assessing the value of using DNA-based parentage testing.

At the commercial level, larger operations often use multisire mating pastures, and have no way to correctly assign paternity to a given calf. In some countries it is not even common practice to individually identify cattle precluding genetic improvement. One of the proposed uses of parentage assignment on commercial farms includes the development of on-farm genetic evaluations (Dodds et al., 2005). This offers the opportunity for large commercial farms to produce their own young sires by developing a bull-breeding herd and testing their bulls in multi-sire settings, and using DNA to resolve the offspring paternity at a later date (Pollak, 2005). Candidate herd bulls are selected on the basis of their progeny test data. The returns from the progeny test are achieved by the increased revenue generated by response to selection generated by that information. This benefit can outweigh the costs involved with collecting and analysing DNA for progeny testing.

This technique is widely used in the New Zealand sheep and deer industries, but has seen limited uptake in the beef industry. One of the reasons for this is the time lag associated with obtaining progeny phenotypes and developing the on-farm genetic evaluations. If we assume that a commercial bull is used for 4 breeding seasons and that his calves are finished in a feedlot and typically killed at 15 months of age, then the information on the carcass performance of his progeny will not be collected before that herd sire has completed his third breeding season (Figure 1).

Month-Yr	Year 1	Year 2	Year 3	Year 4	
Mar-Yr 1	**Breed**				← **Purchase bulls**
Jan-Yr 2	Calve				← **Calculate on-farm EBV for birth traits**
Mar-Yr 2		**Breed**			
Aug-Yr 2	Wean				← **Calculate on-farm EBV for weaning traits**
Jan-Yr 3		Calve			
Mar-Yr 3			**Breed**		
Apr-Yr 3	Harvest				← **Calculate on-farm EBV for carcass traits**
Aug-Yr 3		Wean			
Jan-Yr 4			Calve		
Mar-Yr 4				**Breed**	
Apr-Yr 4		Harvest			
Aug-Yr 4			Wean		
Jan-Yr 5				Calve	
Mar-Yr 5					
Apr-Yr 5			Harvest		
Aug-Yr 5				Wean	
Jan-Yr 6					
Mar-Yr 6					
Apr-Yr 6				Harvest	
Bull Age at breeding	1.5	2.5	3.5	4.5	

Figure 1. Time delay in obtaining beef cattle progeny records to develop on-farm genetic evaluations for sires in the commercial sector.

Therefore the information on the genetic merit of a bull for carcass traits is typically not available until the final breeding season of that sire. At that time there is limited opportunity to generate value from that information through improved response to selection. Conceptually a very good sire might be kept for an extra year, or a very poor sire could be culled a year ahead of schedule. Some large beef operations in the US are using DNA testing to develop on-farm genetic evaluations of sires. In a simulation study, Weaber (2005) found that the return on investment that results from such progeny testing was greatly influenced by the cost of parentage determination (i.e. DNA testing), proportion of calves sampled, subsequent years of service of selected bulls, and whether the operation had two breeding seasons per year, i.e. both a spring and fall breeding season. In this latter situation weaning data is available prior to the second year's breeding in the alternate season. For example August weaning data collected in Year 2 could be used to provide weaning weight EBVs prior to the alternative breeding season in September of Year 2. It was found that the sale weight superiority of the progeny of bulls selected in this way was sufficient to offset the costs associated with progeny testing.

Traditionally, highly polymorphic microsatellite markers have been the choice for parentage inference but there is increasing interest in using SNPs for this purpose due to their abundance, potential for automation, low genotyping error rates, and relative ease of standardization between laboratories. The low resolving power of biallelic loci means that SNP panels need to include more loci than microsatellite panels to achieve similar discriminatory power. Early panels made up of <50 SNP loci were not sufficiently powerful to assign paternity in field situations where factors including variable calf output per sire, large sire cohorts, relatedness among sires, low minor allele frequencies, and missing data often occur concurrently (Van Eenennaam et al., 2007). In herds with large numbers of natural service sires in a breeding group, low resolution panels may result in multiple bulls qualifying to a single calf. Given the rapid evolution and precipitous drop in the price of SNP genotyping, having too few SNPs to assign parentage will likely relegate this problem to a concern of the past. Panels of approximately 100 SNP markers developed by Heaton et al. (2002) the US Meat Animal Research Centre (**USMARC**) with an exclusion probability of >99.99% are being commercially offered for US$10, and are being routinely used on some commercial farms. Harlizius et al. (2011) reported that 100 SNP loci in combination with criteria allowing $\leq$ 1 mismatches, and specific values associated with the logarithm of odds (LOD) score for assigning the first and second most likely sire, gave accurate results and a practical trade-off between false negative and false positive assignments when using SNP data for paternity testing. Although it is likely SNP genotyping will be the paternity assignment method of choice in the future, the considerable costs involved in transitioning breed society records and laboratories from microsatellite- to SNP-based parentage assignments remain a barrier to implementation. This is further complicated by the need to decide which of the competing SNP genotyping platforms will ultimately prove to be optimal.

Recently there has been an effort to develop an approach to impute historical microsatellite calls for the main International Society for Animal Genetics (**ISAG**) markers based on SNP haplotype data for the four main dairy breeds. The approach used a training population consisting of 347 dairy animals with both Illumina 770K genotypes and microsatellite call data. The microsatellite and SNP data were phased in the training population, and then the minimum SNP haplotypes associated with one or a small number of microsatellite alleles were identified. These imputations were then tested for accuracy using a validation population of ~ 1,300 animals. It appears that some haplotype-MS allele associations hold true across all four dairy breeds, but that some others are breed specific (McClure et al., 2012). This information suggests an analogous training population

containing 770K genotyped animals with microsatellite data from all the major beef breeds will be required to develop a set of SNP haplotypes that can be used to accurate impute ISAG microsatellite alleles for the different beef breeds. Approximately 400 SNPs for this ISAG imputation purpose are currently included on an 8.5K multipurpose SNP chip product that is being offered to the dairy industry for a cost of approximately US$ 35-40. (http://www.neogen.com/GeneSeek/pdf/Catalogs/DairyGenomicProfiler.pdf).

There may be an opportunity to use DNA-based parentage assignments to facilitate programs to select for traits with low incidence (e.g. genetic defects or disease that is only evident at slaughter) which require records from a large number (>100,000) of cattle. For these traits retrospective assignment of the true sire is only required for affected animals, and this offers a substantial cost savings over identifying the sires of all animals in the population (Harlizius et al., 2011). This may be of particular utility in Ireland, where the integration of mandatory individual cattle identification, the Irish Cattle Breeding Federation Society Ltd. cattle breeding database, and the animal events data collection system (Wickham and Dürr, 2011), presents an opportunity to identify animals with rare phenotypes for traits of interest and use the database, potentially in conjunction with DNA-based parentage determination, to identify the genetic basis of these traits with low incidence. Others have argued that one of the requirements for widespread adoption of DNA testing technology will likely be the development of systems that simplify DNA collection and seamlessly report data of integral importance back to livestock producers (McEwan, 2007). In New Zealand DNA collection is linked to electronic tags, which are being implemented as part of a national identification system. The DNA samplers are labelled with bar codes and this in turn offers the opportunity for all subsequent steps to be automated including the incorporation of the results directly into the appropriate genetic evaluation databases. Collecting DNA samples on all cattle as part of mandatory individual animal identification offers an approach to potentially derive an additional valuable resource from the costs involved with individual animal identification. It is not hard to envision a time when all of this information will be managed in a smart phone application!

Single Gene Traits

Naturally-occurring recessive genetic defects are common in all species, including humans. The average human carries approximately 2,000 deleterious recessive alleles, of which one to two are thought to be lethal (Sunyaev et al., 2001). Such numbers are likely true for cattle. To date the beef cattle industry's approach to deleterious recessives has been to overtly avoid the mating of carrier animals, sometimes without regard of the genetic merit of the animals. In fact, some breed associations will not allow carrier animals to be registered leading to their removal from breeding populations regardless of their genetic merit for all other economically relevant traits. This approach is not optimal from the perspective of genetic improvement since, in some cases, the overall breeding value of carrier animals outweighs the economic penalty of their carrier status (Charlier et al., 2008). Furthermore, such an approach is likely to become untenable as more deleterious recessives are identified through whole genome sequencing of key industry AI sires.

Genetic defects are often propagated as a result of specific trait selection. Perhaps the most famous example of a genetic defect in 20th century beef breeding was "snorter" dwarfism which became an issue in Angus and Hereford cattle during the 1940s and 1950s. A detailed history of snorter dwarfism and the efforts to eliminate it from the Hereford breed is described in a book entitled "The Battle of the Bull Runts" (McCann, 1974). This genetic defect was uncovered as a result of strong selection pressure for animals with small stature. Ultimately the cause of this mutation was traced back to a bull

named St. Louis Lad, born in 1899. Through detailed pedigree analysis and test crosses, the American Hereford Association virtually eliminated the problem from the breed. Because carrier status was difficult to prove and required expensive progeny testing, some entire breeding lines were eliminated. This situation can be contrasted to the speed with which genetic testing has allowed 21st century breeders to quickly and accurately determine the carrier-status of their animals.

The Angus breed has had to manage three simply-inherited, single locus recessive genetic conditions in the past few years. These include two lethal conditions Arthrogryposis Multiplex (**AM**; "Curly Calf Syndrome"), and Neuropathic Hydrocephalus (**NH**). The first is caused by a chromosomal deletion that occurred in a bull referred to as 9J9 born in 1979. The second occurred as a result of a single DNA base pair mutation in his grandson, the widely-used GAR Precision 1680 born in 1990. A third non-lethal autosomal genetic defect is called Congenital Contractural Arachnodactyly (**CA**; "Fawn Calf Syndrome"). Genetic tests for AM, NH, and CA became available 1 January 2009, 15 June 2009 and 4 October 2010, respectively. As of May 2011; 148,677 AM, 110,215 NHC, and 35,162 CA tests, respectively, had been performed by American Angus Association members since testing for these defects began (B. Schumann, American Angus Association, pers. comm.). Assuming these tests cost US$25 each, a conservative number as some tests are more expensive; this amounts to over US$7.35 million in testing costs in the US Angus population alone. While these testing costs are substantial, they are dwarfed by what it would have cost to eliminate all of the descendants of Precision and 9J9 from the Angus breed that tested free. The speed with which these genetic tests were developed demonstrates the power of having access to the bovine genome sequence

It is important not to overemphasize the relative importance of deleterious recessives in selection programs, and to understand the impact of gene frequency on management decisions. If the frequency of the allele is very low there is a relatively low likelihood of carriers interbreeding. For example, in the Australian Angus population the frequency of the AM allele never reached 0.05 (Allen and Teseling, 2011). In a random mating population ($2pq = 2 \times 0.05 \times 0.95$) ~ 9.5 animals in 100 would be expected to be a carrier when the frequency of deleterious allele was 0.05, and so the probability of mating carriers would be approximately 9 in 1000, of which ¼ of the offspring would be affected (i.e. 2.25 dead calves in 1000 matings), 4.5 would be carriers, and 2.25 would be homozygous free.

To illustrate the impact of allele frequency on economics, a cow-calf operation with 1000 cows and 40 bulls (25:1 cow:bull ratio) was modelled and a US$200 dead calf cost was assumed. A scenario was crafted where randomly-selected yearling bulls entering the self-replacing herd in a single year were either all tested and carrier bulls were eliminated, or none were tested. The frequency of the deleterious allele in the herd was then varied from 0.0001 to 0.5 (Table 1). The breakeven cost of the test was then calculated for each deleterious allele frequency. This was the point where the costs of testing and eliminating carrier bulls was equal to the loss in dead calves that would result from not testing the bulls and potentially introducing a carrier bull. We took the effect of the gene flow resulting from this testing out over a 20 year planning horizon using a 7% discounting rate (Van Eenennaam and van der Werf, unpublished data). At deleterious recessive allele frequencies ≤ 0.04 the cost of testing all of the two year old bulls at US$25/test outweighed the benefit in terms of reduced numbers of dead calves. In other words, the probability of a random bull being a carrier and being mated with a carrier cow to produce a dead calf was increased so slightly as a result of not testing, that saving the US$338 testing cost in the first year outweighed the discounted value of the increased number of dead calves over the 20 year period in the scenario where testing was not used. On the other hand, if the allele frequency of the lethal recessive was 0.5, the breakeven price of the test was very high (US$3663)!

Table 1. Break even cost of DNA testing to eliminate randomly selected carrier sires from entering a herd over a range allele frequencies for a recessive lethal allele. The value increases substantially if the sire is very likely to be a carrier.

Allele freq. (p)	No DNA testing of random bull from population assuming equilibrium		DNA testing and cull carrier yearling bulls	Cost of calf loss with no DNA testing of yearling bulls (US$)	Breakeven cost DNA test if testing yearling bulls (US$)	
	1st generation affected calves	1st generation carrier calves	1st generation carrier calves		All bulls tested	Carrier bull
0.0001	<0.01%	0.02%	0.01%	<0.01	<0.01	213
0.0005	<0.01%	0.1%	0.05%	0.05	<0.01	216
0.001	<0.01%	0.2%	0.1%	0.20	0.01	219
0.005	<0.01%	1%	0.5%	4.95	0.37	247
0.01	0.01%	2%	1%	19.81	1.47	281
0.02	0.04%	4%	2%	79.24	5.86	350
0.03	0.09%	6%	3%	178	14	419
0.04	0.16%	8%	4%	317	23	488
0.05	0.25%	10%	5%	495	37	557
0.06	0.36%	11%	6%	713	53	626
0.07	0.49%	13%	7%	971	72	695
0.08	0.64%	15%	8%	1268	94	764
0.09	0.81%	16%	9%	1605	119	833
0.1	1 %	18%	10%	1981	147	902
0.2	4%	32%	20%	7924	586	1593
0.3	9%	42%	30%	17828	1319	2283
0.4	16%	48%	40%	31695	2344	2973
0.5	25%	50%	50%	49523	3663	3663

In the situation where there is a high likelihood that a bull is a carrier (e.g. the offspring of a carrier), then the value of testing is quite high even for low allele frequencies (p) in the population as the probability that the son of a carrier will pass on the deleterious allele to his offspring is (0.5+p)/2. In reality it is likely that the allele frequency will vary between the seedstock and the commercial sector, with the frequency typically being higher in the seedstock sector as a result of higher rates of inbreeding. As such, the value of testing is likely greater for the seedstock sector than the commercial sector. Of course culling carrier bulls will decrease the selection intensity which in turn will decrease the rate of genetic gain. It is important to balance the overall breeding value of carrier animals against the economic penalty of their carrier status, as the former may outweigh the later, especially if mate selection can be implemented to minimize mating with carrier females.

The genetic defects in Angus cattle became evident as a result of phenotypically deformed calves. There are likely many more such recessive alleles that are associated with a deleterious phenotype that is not so obvious e.g. embryonic lethals. Early embryonic lethal genes have been suggested, as a class, to be responsible for up to 10% of pregnancy loses in cattle (Humblot, 2001). Such conditions will become apparent as a lack of homozygotes in the offspring of carrier matings, and may be manifest as an increased days to calving interval in carrier animals. This approach has already been used to identify harmful recessive effects on fertility in dairy cattle (VanRaden et al., 2011). It is becoming increasingly obvious that the optimal management of an ever growing list of recessive conditions is going to require computerized decision support software. Angus Australia, in collaboration with the Agricultural Business Research Institute (ABRI) uses GeneProb

(Kinghorn, 1999) to track five genetic conditions with a weekly analysis involving almost 1.3 million animals. This software program determines the probability of each animal in the breed dataset being a homozygote and heterozygote based on segregation analysis (Kerr and Kinghorn, 1996; Thallman et al., 2002). Genotype probabilities are certain for genotyped animals and for progeny of two known normal homozygotes. An important step in this process is to extend the information on genotyped animals to their many ungenotyped relatives. The result is that all pedigree-connected animals have some information on the five genetic conditions. This approach has been successfully implemented in pigs and beef cattle, greatly increasing utility where partial genotyping is carried out, and provides a basis to make rational decisions on which animals to genotype. The use of GeneProb significantly reduced the number of animals that needed to be tested for genetic conditions in the Australian Angus population (Teseling and Parnell, 2011)

As with parentage testing, it is likely that genetic testing for deleterious recessives is going to migrate from expensive single gene tests using microsatellite technology, to SNP-based diagnostic tests. This has already occurred in the dairy industry. However, mate selection software to facilitate the management of this information and optimization of genetic gain given all of the information that is being derived from genomic projects in beef cattle is sorely lacking. It is likely that hundreds of deleterious or suboptimal allele combinations will be identified as genomic research starts to move towards whole genome sequencing. Kinghorn (2011) developed a constrained mate selection algorithm that can be used to optimize selection decisions and mate allocation, and intends to extend the algorithm to methodology with a key objective being to reduce both the phenotypic expression and allele frequency of the deleterious recessives. Equally important, is managing recessive alleles in concert with other important issues such as the management of trait merit, genetic diversity, genome-wide inbreeding, logistical constraints and costs. Decision support software will be an essential part of more widespread industry adoption of DNA technologies by providing a unified approach to appropriately weight the relative economic value of traits in the breeding objective against potential deleterious recessives, and suggest an optimal breeding scheme based on all available information.

Improving the accuracy of breeding values

The holy grail of genomic information has always been to use DNA information to improve the accuracy of EBVs and rank selection candidates in livestock breeding programs. The theory of genomic selection is based on the prediction of effects of genetic markers. A phenotyped, genotyped training data set is needed to gain information on marker effects and allow for the development of prediction equations. Various methods have been devised to incorporate genomic information into EBVs (Johnston et al., 2011). These include:

1. Use the SNP marker information to fit a genomic relationship matrix that is used to augment estimated relationships based on pedigree information. For this method it is necessary to know the actual SNP genotypes rather than having a single marker score or MBV e.g. US dairy cattle evaluations
2. Include both a molecular breeding value (MBV) derived from genomic information and traditional EBVs derived from pedigree and performance records in a selection index whereby each component is weighted based on the proportion of genetic variation explained e.g. BREEDPLAN is using a multiple-trait selection index to include 12 Pfizer 50K “MVP” genomic predictions into Australian Angus EBVs.
3. Correlated trait approach (Kachman, 2008) e.g. US Angus Association.
4. External EBVs (i.e. EBVs from an animal that is external to the population or breed). This allows for MBVs to influence the accuracy of EBVs differently for each animal

due to the relationship between the animal with the MBV and the training population e.g. US Simmental Association.

In the US, two commercial companies are offering tests for Angus breeders. The Igenity product is a 384 SNP panel, and the Pfizer product is a 50,000 SNP product. Table 2 summarizes the genetic correlations that have been observed between the MBV derived from these two tests and the phenotypic data in the American Angus Association database. At the current time the MBV information is being included in the Angus evaluations as a correlated trait (Kachman, 2008). As the genetic correlation between the MBV and the trait of interest increases so does the accuracy, particularly for low accuracy animals.

Table 2. Genetic correlations (r_g) observed between commercial DNA test results (MBVs) and phenotypic trait of interest in American Angus Association data (Northcutt, 2011).

Trait	Igenity r_g (384 SNP)	Pfizer r_g (50K SNP)
Calving Ease Direct	0.47	0.33
Birth Weight	0.57	0.51
Weaning Weight	0.45	0.52
Yearling Weight	0.34	0.64
Dry Matter Intake	0.45	0.65
Yearling Height	0.38	0.63
Yearling Scrotal	0.35	0.65
Docility	0.29	0.60
Milk	0.24	0.32
Mature Weight	0.53	0.56
Mature Height	0.56	0.56
Carcass Marbling	0.65	0.57
Carcass Ribeye Area	0.58	0.60
Carcass Fat	0.50	0.56
Carcass Weight	0.54	0.48

Genomic predictions rely on both linkage disequilibrium (LD) between markers and quantitative trait loci (QTL), and also genetic relationships between animals in the training data set and those whose breeding value is to be predicted. Within a breed there is often a close relationship between animals in the training data set, typically high-accuracy A.I. sires, and the target population, frequently comprising young offspring of A.I. sires. When animals within a breed are only distantly related to the training data set, the accuracy of genomic predictions are dependent on the size of the training data set (bigger is better), and are inversely proportional to the effective population size (Clark et al., 2012).

Several studies have shown that predictions developed in one breed are not accurate in another. Many breeds do not have thousands of genotyped, highly-proven bulls available for training, and so approaches to develop across-breed predications for beef cattle have been investigated using training data sets consisting of both pooled purebred animals from multiple breeds, or phenotypic records from crossbred animals. Weber et al. (2012) evaluated the accuracy of across breed genomic predictors derived from two training data sets: the USMARC Germplasm Evaluation Project (**GPE**) consisting of adjusted phenotypes on 3,358 crossbred cattle, and deregressed EBV (Garrick et al., 2009) from 1,834 high-accuracy bulls from 13 of the most widely used breeds in the United states (**USMARC 2,000 Bull Project**). In general there were moderate genetic correlations

between MBV and growth traits using the USMARC 2,000 Bull Project MBV in multiple purebred beef breeds, but the correlations were lower when using GPE-derived MBV. Deregressed proofs account for all the information present in an individual's EBV, generating a pseudo-phenotype with a heritability equal to the reliability of the EBV which generated it. When using the EBV of highly used bulls, this may be higher than trait heritability, thereby providing more information than an animal's own phenotype.

In summary, data so far suggest that for traits that are already in genetic evaluations it is possible to get accurate predictions within breed using training populations of (typically >1,000) genotyped bulls with de-regressed EBV as phenotypes. Moderately accurate predictions result from using de-regressed EBV of genotyped bulls pooled from multiple breeds if some representatives of the breed of interest are included in the training population. However, many of the economically-relevant traits in beef cattle production are difficult to measure and are therefore not currently included in genetic evaluations (e.g. feed efficiency). As there are no pre-existing populations with phenotypes for these traits, such training populations are going to have to be developed and will likely consist of individual phenotypes on genotyped animals. This suggests these training datasets are going to need to be large, especially if they include more than one breed. High-density (700K) SNP chips may help to improve the accuracy of across-breed predictions, although it seems increasingly likely that identifying causative SNP, rather than markers in LD with QTL, may be most dependable approach to obtaining accurate across-breed predictions.

Using genetic tests to increase the accuracy of selection in the nucleus seedstock sector has the potential to generate large returns to all sectors of the beef industry. Improving the accuracy of EBVs on elite young seedstock animals will accelerate the rate of genetic gain and impact the genetic merit of many descendants thereby amplifying the value of each unit of genetic improvement. The value derived from using DNA information to increase the accuracy of beef sire selection was modelled for a closed seedstock herd (Van Eenennaam et al., 2011). Breeding objectives for commercial production systems targeting domestic and export markets were examined using multiple-trait selection indexes developed for the Australian cattle industry. The response to conventional selection based on phenotypic performance records was compared to that obtained following the inclusion of information from DNA tests of varying power. In one case the DNA test explained a percentage of the additive genetic variance equal to the heritability of all traits in the breeding objective and selection criteria (high accuracy), and in the other case to one-half of this amount (intermediate accuracy). DNA testing increased the selection response between 29-158%. The value of this improvement above that obtained using traditional performance recording ranged from AUD$89-565 per commercial bull, and AUD$5,332-27,910 per stud bull. Assuming that the entire bull calf crop was tested to achieve these gains and that the top 3% were selected as replacement stud sires and the sale of the remaining top half as commercial bulls, the value generated ranged between AUD$204 -1,119 per test.

Genetic gain in traits that resulted in direct revenue to the processing sector accounted for 23-85% of the returns generated by the selection of superior commercial sires, depending upon the target market (export versus domestic), selection index (self-replacing versus terminal), and initial index accuracy in the absence of DNA information. These results suggest the development of high-accuracy DNA tests for beef cattle selection could be beneficial from an industry-wide perspective. However, the return on testing to the seedstock operator will strongly depend on efficient transfer of revenue derived from genetic improvement in processor traits up the production chain to the sector incurring the costs of genotyping. This will be particularly true if DNA-based tests are developed that provide previously-absent selection criteria to make genetic improvement in valuable

downstream traits such as feedlot health (e.g. decreased bovine respiratory disease susceptibility), feed efficiency, meat tenderness and/or approaches for profitable marker-assisted management (**MAM**) of feedlot cattle (Van Eenennaam and Drake, 2012).

DNA testing could also be used to help guide commercial replacement heifer selection, which is often undertaken in the absence of EBV information. The beef industry would benefit greatly from improvement in traits directly affecting maternal performance (Roughsedge et al., 2005). Replacement commercial female selection involves a much larger proportion of the national herd than seedstock testing. However, the value derived per test is less because commercial cows produce fewer descendants. In practice, selection for replacement heifers is frequently driven by size and maturity to ensure they are cycling in time for their first potential breeding season. These criteria put indirect selection on fertility traits by selecting heifers born early in the season. Until DNA tests are developed that have high accuracy for maternal traits, they should be used in conjunction with available phenotypic data. Many traits that are of economic value to commercial producers have a low heritability (e.g. age at first calving, reproductive success). Research results suggest that large datasets, especially for low heritability traits being trained on phenotypic records, will be needed to develop accurate genetic tests for such traits, and the development of appropriately phenotyped and genotyped training populations is perhaps the greatest challenge facing the implementation of genomics in the beef industry.

Do bull buyers pay more for high genetic merit bulls?

To consider this question, I examined the relationship between bull sale price and the long fed $Index at six 2011/2012 Australian Angus bull sales (Van Eenennaam, unpublished data). This index estimates the genetic differences between animals in net profitability per cow joined for a self-replacing commercial Angus herd in temperate Australia targeting pasture steers with a 270 day feedlot finishing period for the high quality, high marbled Japanese export market. Steers are assumed marketed at 740 kg live weight (420 kg hot standard carcass weight, and 25 mm P8 fat depth) at 26 months of age. Significant emphasis is placed on marbling and 600 day growth. Figure 2 shows the key economic traits that are important in this selection index. The different trait emphases reflect the underlying profit drivers in a commercial operation targeting the long fed export market.

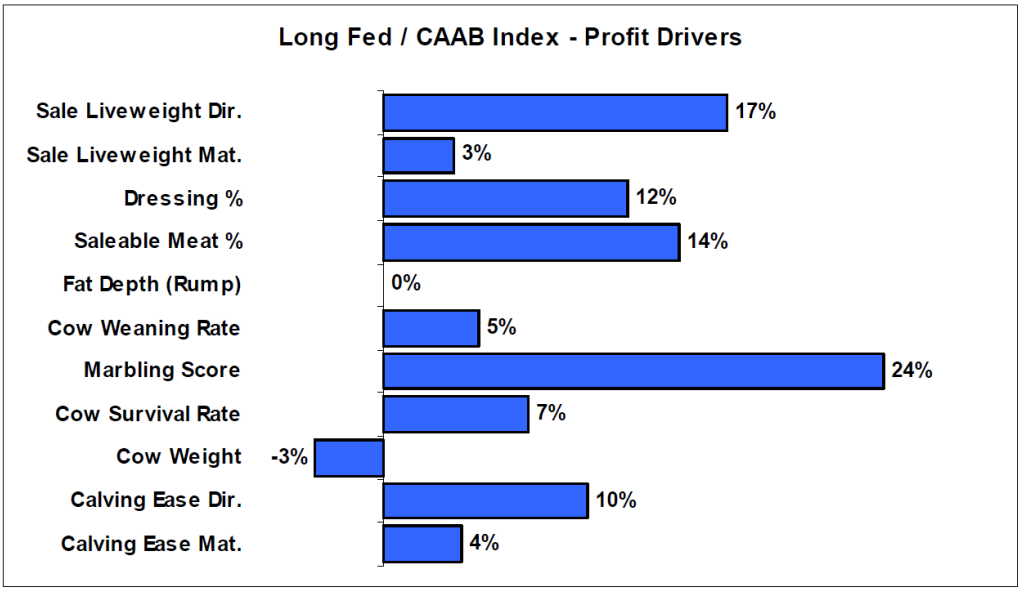

Figure 2. Relative importance (% relative economic value) of traits in the Angus self-replacing herd $Long Fed breeding objective. (http://breedplan.une.edu.au)

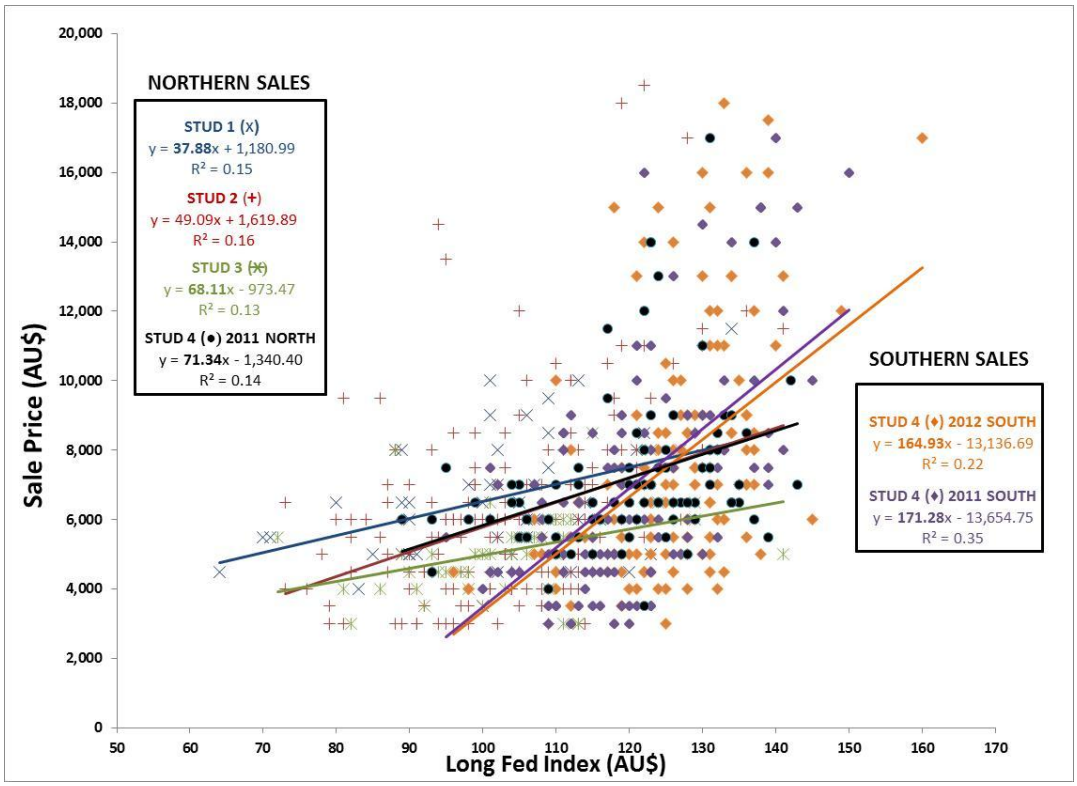

Figure 3. Bull sale prices plotted against $Index for four Australian Angus studs selling bulls to cattle producers in Northern and Southern Australia, 2011-2012. The slope of the regression lines is the dollar ($AU) increase in bull price for every unit increase in $Long Fed Index. Four of these sales took place in New South Wales (NORTH) targeting mostly commercial buyers, and two in Victoria (SOUTH) targeting mostly seedstock buyers.

Several points of interest can be observed in Figure 3. First there is positive slope between sale price and $Index, and this slope tends to be steeper when the target market is breeders (Southern sales), rather than the commercial bull market (Northern sales). For stud 4 there was a significant stud by location of sale interaction. If it is assumed that a commercial bull will breed 100 cows over his life (25 cows/season for 4 years), then in a perfect market the regression coefficient would be expected to be 100 x 0.5 for each unit increase in $Index for a commercial bull. The regression coefficient for all of the Northern markets was approximately 50 (average ~ AUD$56). This suggests commercial buyers are paying approximately the value of the genetic improvement encompassed by the $Index value. It also appears that there is a higher slope associated with high $Index bulls, with those over $110 being perhaps destined for the bull multiplier sector. A multiplier bull might breed 100 cows, have 80 progeny, of which 20 will be sold as sons. For every $Index in the sire, those sons would be improved 0.25. If we further assume those sons all breed 100 cows then the added value per index point in the bull would be 20 x 0.25 x 100 = $500. So for these multiplier bulls the buyer could theoretically bid up to AUD$499 per $Index (in a perfect market). Some component of bull price is also driven by other factors (e.g. the average bull price is strongly dependent on prevailing cattle prices). These data indicate that bull buyers are paying the breeder some of value associated with a unit increase in $Index, and suggest that if a breeder is able to produce bulls with $Index values substantially above breed average, they can move into the higher-value multiplier bull market. Accurate genetic tests could help improve the rate of genetic progress towards such a goal, especially for traits where individual phenotypes are not available at the time of selection.

The Future

At the current time the costs of genomic testing tend to exceed the value that is returned to any single sector. Seedstock producers are using DNA information for pedigree verification, genetic defect testing, and genomic enhanced EBVs. Sometimes these analyses are sent to three different laboratories, and costs can be in excess of $200 per animal. This is inefficient and extracting DNA multiple times from the same animal in different laboratories for different applications will likely become a relic of the past. As a result of industry segmentation, DNA information is frequently not available to downstream industry sectors. For example, feedlots wanting to use DNA information for marker-assisted management are faced with the prospect of collecting DNA again at feedlot entry and using that information at some later time, neither of which is cost-effective. Already genomic technology providers are starting to develop multipurpose SNP-based panels so that a single DNA sample can be used for parentage, genetic defects, single gene traits (e.g. polled), and imputation to high density genotypes. Concurrently the cost of genotyping continues to fall steeply, and continuous innovation seems likely to deliver extremely low cost (<$5/sample) testing platforms to the industry in the near future. Low testing costs could enable new models of data collection to develop. For example, if a large feedlot incentivized DNA collection and genotyping of animals *prior* to feedlot entry through breeder and producer partnerships and then routinely collected feedlot phenotypes on those animals, large training datasets for these traits would soon accumulate.

There is also the tantalizing prospect of low cost (<$1,000) whole genome sequencing on the horizon. Individual bull sequencing may accelerate the discovery of causative SNP for quantitative trait loci and recessive defects. This will allow for new concepts to be considered such as individual mate selection and even improved models for genetic evaluation based on marker, rather than pedigree, information. It may be that low-cost DNA testing and the combined value derived from using DNA information for multiple purposes across the value chain will push the economics of genomics over the tipping point towards widespread industry adoption (Van Eenennaam, 2011).

An analogy comparing beef cattle genomics applications to the burgeoning mobile communication market is depicted in Table 3. The cost column is hypothetical and represents a guess as to what costs might be assuming continued genotyping innovations.

Table 3. Mobile communication market analogy for the type of genomics products that are likely to be required by different segments of the beef cattle industry and projected costs.

Cattle industry Sector	**Mobile Device// Data Access Plan**	**Type of DNA product // DNA information access required**	**Cost? (US$)**
Nucleus seedstock/AI bulls	ipad	Full genome sequence	$250
Seedstock/bull multiplier	iphone	HD 770 K genotype	$50
Registered females and bulls for commercial sector	Talk and text smart phone	50K genotype + parentage + single gene traits/recessives	$25
Commercial cattle – MAM, replacement heifer selection	Prepaid cellular phone	Imputation chip + parentage + single gene traits/recessives	$10
Feedlot cattle purchasing, sorting, and MAM	Pay as you go contract	Access genotypes from supplier (subset of imputation chip).	<$1
Traceability for voluntary labelling e.g. Angus beef	Friends and family plan	Access genotypes from supplier (subset of imputation chip).	<$1
Traceability for disease outbreak/contaminated meat	Emergency only phone (911 calls)	Access genotypes from supplier (subset of imputation chip).	<$1

Summary

Groups that can organize themselves technologically and structurally to obtain and seamlessly marry phenotypes of importance to the entire supply chain with genotypes to capture the cumulative value derived from using genomic information for multiple purposes (selection, parentage, genetic defects, marker-assisted management, product differentiation, traceability) will be ideally positioned to fully realize the nascent potential of genomic information.

Acknowledgements

The author would like to thank Dr. Julius van der Werf, Professor in Animal Breeding and Genetics, and Wayne Upton, Retired Extension Specialist, Animal Genetics and Breeding Unit, University of New England, New South Wales, Australia; Dr. Rob Banks, Meat and Livestock, Australia; Dr. Matthew McClure, Research Geneticist, USDA ARS, Beltsville, MD, USA; and Kristina Weber, Ph.D. candidate, UC Davis, CA, USA for helpful discussions, ideas, and/or sharing data for the preparation of this manuscript. The author acknowledges support from the National Research Initiative Competitive Grant No. 2009-55205-05057 from the USDA National Institute of Food and Agriculture.

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