Use of genetic marker information in beef cattle selection

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Introduction

Genetic markers can be used for several purposes in selection decisions. These include parentage determination, avoidance of genetic conditions, marker-assisted selection for specific traits, or as a way to develop genomic-enhanced EPDs (GE-EPDs). The value of testing is dependent upon which animals in the breeding herd are being tested and for what purpose (e.g. selection, sale, culling, flushing).

There are a number of different companies offering DNA tests, and testing is being done to answer a number of different questions. I have sometimes heard producers say they "DNAed" their cattle, but that is little bit like saying I vaccinated my cattle – the important question is "for what"? DNA is present in every cell and so DNA can be extracted from a number of different tissues including blood, semen, hair follicles, and an ear notch. Before going ahead to perform DNA testing there are a number of questions you need to ask as detailed below.

Step 1: What do you want to test?

There are several different types of DNA tests, including parentage tests that can determine a particular animal's sire, single trait tests that evaluate simple traits like coat color or inherited defects/diseases and SNP chip tests which can be used for genomic selection of complex traits such as weaning weight and calving ease. Some testing platforms can simultaneously provide parentage, single trait and information to enable the calculation of genomic-enhanced EPDs (GE-EPD) which can improve selection accuracy.

The value of DNA testing to an individual operation depends on a number of factors. These include the breed(s) and number of animals that will be tested, and sometimes the availability of health records, pedigrees and EPDs. The ultimate goals for testing results are also important to consider. DNA testing can be used for a variety of purposes such as aiding in selection and breeding choices, sorting into management groups, pedigree verification, and marketing based solely on the test result. The successful use of DNA tests for these purposes requires a basic understanding of how they work and how the results should be applied.

Parentage and paternity tests

Parentage tests work with a variety of sample types, including blood, hair and tissue. They require that the breeder/producer identify at least one potential parent that has DNA on file or that can have a sample included with the offspring's sample. The quickest and best results are available if DNA is available from both the dam and all potential sires. This is best accomplished by taking a DNA sample from all potential sires BEFORE they are turned out with the cows. Parentage tests generate DNA profiles for the offspring and the presumed parent(s) using multiple genetic markers. Parental status is determined based on exclusions (Figure 1). Parentage tests are required by many breed registries and are useful for ensuring accurate pedigrees which increases the accuracy of genetic evaluations. Paternity results are also useful for evaluating the performance and prolificacy of new bulls in multiple-bull breeding pastures.
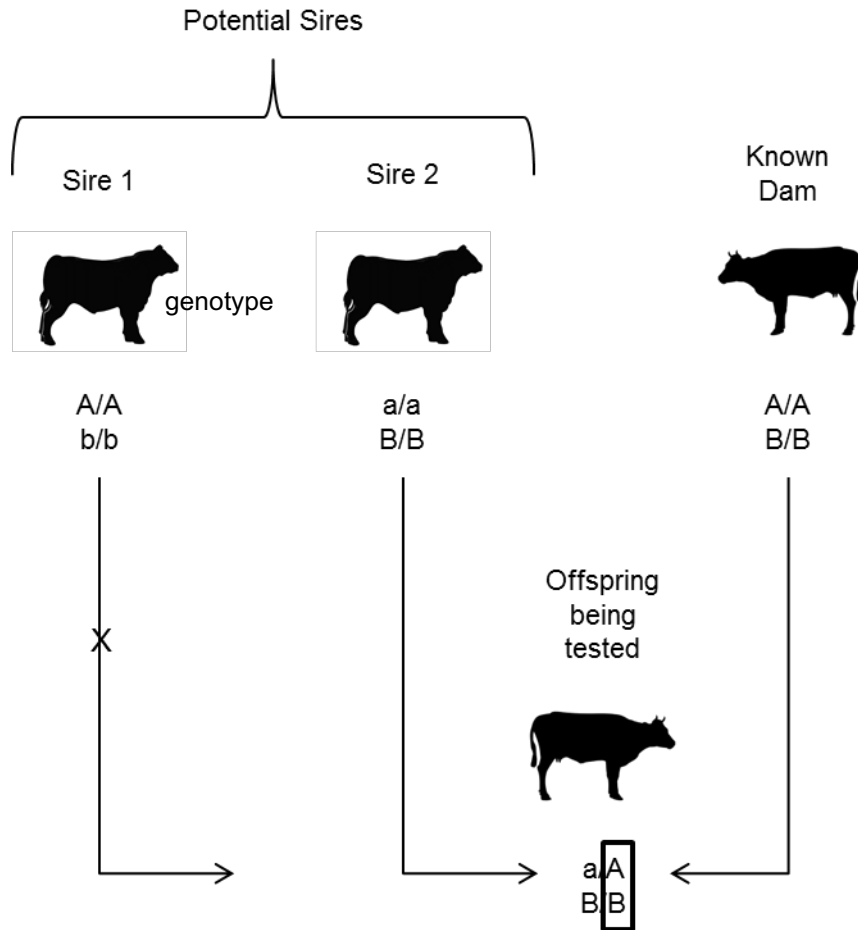
Figure 1. Example of sire exclusion using 2 genetic markers, A and B. The offspring being tested received one form of the gene (allele) at each marker locus from each parent. In this case, the offspring had to receive an "A" allele from one parent and an "a" allele from the other parent and a "B" allele from each parent. Since the known dam has two "A" alleles and no "a" alleles, the offspring's "A" had to come from the dam. This means that Sire 2 had to contribute the "a" since Sire 1 only has "A"s. The same is true for the "B" allele since Sire 1 only has "b" alleles and the offspring has no "b" allele. Sire 1 is excluded at 2 loci in this example, meaning that Sire 2 is the most likely sire for this offspring based on these two genetic markers.

Single gene tests

Single gene and genetic defect tests also work with a variety of sample types and usually test for single, known, genetic variants (Table 1). The results are used to make appropriate breeding decisions to reduce or eliminate genetic disorders/diseases in herds and to optimize beneficial traits.

Table 1. Commercially available single gene tests

Phenotype	Common Abbreviation	Mode of Inheritance	Breed(s)*
Arachnomelia		AR	Braunvieh, Simmental
Arthrogryposis Multiplex (Curly Calf Syndrome)	AM	AR	Angus
Bulldog Dwarfism (chondrodysplasia)	BD	AR	Dexter
Chondrodysplasia	CHO	AR	Angus
Contractural Arachnodactyly (Fawn Calf)	CA	AR	Angus
Coat Color	CC		
Red/Black		Black AD Red AR	Angus, Simmental, Limousin, Gelbvieh, Dexter
Dilution	DL	Incomplete Dominance	Hereford, Charolais
Dun	DN	AR	Dexter
Developmental Duplication	DD	AR	Angus
Deficiency of Urine Monophosphate Synthase	DUMPS	AR	
Digital Subluxation	DS		
Hypotrichosis	HY	AR	Hereford
Idiopathic Epilepsy	IE	AR	Hereford
Alpha-Mannosidosis	MA or MAN		Red Angus
Myostatin			Belgian Blue, Piedmontese, Limousin
Neuropathic Hydrocephalus	NH	AR	Angus
Osteopetrosis	OS	AR	Angus, Hereford, Simmental
Pulmonary Hypoplasia with Anasarca	PHA	AR	Shorthorn, Dexter
Horned/Polled	Polled		
Holstein-Friesian/Jersey	Pf	AD	Holstein, Jersey
Celtic	Pc	AD	Angus, Brahman, Brangus, Blonde d'Aquitaine, Charolais, Dexter, Hereford, Limousin, Santa Gertrudis, Shorthorn, Simmental, Tropical Composite
Tibial Hemimelia	TH	AR	Galloway, Shorthorn

*Animals from breeds with open herdbooks may consider testing for mutations found in other breeds.

SNP chip tests

SNP assays work on multiple sample types and are used to analyze thousands, or tens or hundreds of thousands, of single nucleotide polymorphisms (SNPs). SNPs are single base pair changes in the DNA. Large numbers of SNPs can be rapidly evaluated using SNP chips.

Genomic testing is available through breed associations who have partnered with two companies that provide genotyping services; Zoetis and Neogen/GeneSeek. There are several types of tests which differ mainly by the number of genetic markers that are included in the test. There are the so called high-density chips which have somewhere between 50,000-150,000 single nucleotide polymorphism, or SNP, markers on a single assay. There are also some lower-density chips that are less expensive and can be used for "imputation" up to the high density chip (e.g. Zoetis® i50K and GeneSeekLD).

Many SNP panels often include established parentage markers as well as some single trait or genetic defect tests mutation tests for common genetic abnormalities. This can decrease the cost of these tests quite dramatically when they are ordered as an add-on test, rather than a stand-alone test.

Genomic testing

The incorporation of DNA information into genetic evaluations has been a stepwise evolution since the first genetic tests for cattle were released in the early 2000s. The goal of including genomic information in genetic evaluation is to increase the accuracy of the prediction of genetic merit for potential breeding animals. Theoretically, the accuracy of selection can be substantially increased, especially for young seedstock. Initially, results were presented independently of beef breed genetic evaluations (i.e. EPDs). This was not an ideal situation as it resulted in two pieces of information about the same trait, and if the results differed it was unclear which result was "correct".

For breeders to make the best use of genomic data, it needs to be combined with traditional sources of information (i.e. phenotypes and pedigrees) into traditional genetic evaluations. For this to happen there needs to be a way to determine how predictive the genetic test is for traits of interest in the breed. This has required that breed associations make an effort to invest in developing large phenotyped and genotyped "training" populations to enable the development of genomic prediction equations. Basically, this estimates the effect of each genetic marker on the trait of interest, so that when a new animal is genotyped the effect of each marker it inherited can be summed to get a genomic genetic merit estimate. Bigger training populations allow for the development of more accurate tests. Many breeds now have tens of thousands of genotyped animals in their databases.

The majority of genetic evaluations of beef cattle are carried out by breed associations. These associations use a variety of genetic evaluation providers and methods to calculate their Expected Progeny Differences (EPD), and as a result there are different EPDs reported for different breeds. This means that it is sometimes challenging to compare data from different evaluations. Within a breed EPDs can be directly compared; however, this is not true when comparing across different evaluations as an EPD from one evaluation is not directly comparable to an EPD from another evaluation. Historically this has been resolved by using "across-breed" EPD adjustment factors that are developed by the Meat Animal Research Center (MARC), available at http://beefimprovement.org.

Twelve breed associations (Chianina, Gelbvieh, Limousin, Maine-Anjou, Red Angus, Simmental, Shorthorn, Canadian Simmental, Canadian Gelbvieh, Canadian Limousin, Canadian Angus, and Canadian Shorthorn) have been collaborating under the umbrella of International Genetics Solutions (IGS) to leverage a multibreed database that enables the calculation of EPDs on a common base. This allows commercial producers to directly compare the genetic merit of animals in this genetic evaluation system regardless of breed composition. The cumulative IGS database includes approximately 16 million total animal records, 100,000 genotypes, and over 340,000 new animals are added annually.

One feature of this IGS collaboration is that many of the participating breed associations require or strongly

encourage inventory-based recording. Historically, many beef breed genetic evaluations were based on progeny weaned and/or registered and did not require data to be recorded from females that failed to reproduce or whose progeny were not registered. By contrast, inventory-based reporting requires collection of annual reproductive records on every inventoried female within a herd.

According to the Beef Improvement Federation (BIF), the objective of inventory-based or whole herd recording (WHR) is "to accumulate reproductive and certain performance data on all animals in a breed. It does not, however, seek to control which animals will be registered. That remains a decision of individual breeders. With WHR, performance records (or disposal codes) are required on all calves produced by each breeder, but whether any or all of those calves receive registration papers is the breeder's decision." This enables the collection of phenotypes relevant for the development of EPDs for important traits such as heifer pregnancy and stayability.

The main advantage of including genomic information in EPDs is that it improves accuracy. Accuracy (ACC) is the reliability that can be placed on the EPD; ACC ranges from .00 to 1.0. An accuracy close to 1.0 indicates higher reliability.

This increase in accuracy is dependent upon how much of the genetic variation is explained by the genomic information. In other words, the usefulness of the test is proportional to how well it predicts the true genetic merit of an animal. Genomic testing is most useful for improving the accuracy of EPDs on young animals where there is little other information upon which to base genetic merit estimates. Breed association EPDs are typically associated with Beef Improvement Federation (BIF) accuracies. It takes a lot of progeny records to increase the BIF ACC. Reranking is uncommon among bulls with high accuracy EPDs as there is less possible change associated with well-proven bulls.

Production sale catalogs and breed associations often provide breed average EPDs against which to compare a specific bull's numbers. It is important to consider that, although this is useful information, most commercial herds select bulls that are not the breed average. However, since 87.5% of a calf crop is determined by the previous three sire generations, it is possible to obtain a general sense of a commercial herd's standing for additive genetic merit by evaluating the EPDs of the herd sires used in the recent past.

There are several tests that are being marketed for use on unregistered commercial cattle that are not directly part of a breed association genetic evaluation program. There are two products exclusively distributed by Angus Genetics Inc. (AGI) and marketed by Zoetis® which are designed for animals that are at least 75% Black Angus. These include GeneMax Advantage ($39) and GeneMax Focus ($17). The first test involves tens of thousands of markers and is marketed as a heifer selection and mating test that ranks heifers for net return using three economic indices (Cow Advantage: Predicts differences in profitability from heifer development, pregnancy and calving, to the sales of weaned progeny; Feeder Advantage: Predicts differences in net return of feeder calf progeny due to growth, feed efficiency and CAB carcass merit; Total Advantage: Predicts differences in profitability from genetic merit across all economically-relevant traits captured in Cow and Feeder Advantage index scores). It also identifies genetic outliers for cow cost, docility, marbling and tenderness, and allows for paternity assignment if the sires have been 50K or i50K tested by Zoetis®.

GeneMax Focus utilizes fewer genetic markers and is marketed to provide genomic predictions for feedlot gain and marbling, in addition to sire assignment. These two tests are only intended for use on unregistered, commercial high-percentage Angus cattle. As such, GeneMax predictions do not contribute to Angus breed association genomic-enhanced EPDs (GE-EPDs).

There are also two Angus-specific heifer selection tests available from Igenity; Angus Silver ($25) which includes calving ease maternal, heifer pregnancy, docility, milk, average daily gain, marbling) and Igenity Angus Gold ($40) which additionally includes birth weight, mature weight, residual average daily gain, weaning weight, tenderness, ribeye area, back fat thickness and carcass weight. These two tests can be directly ordered through Igenity. Additionally, there are two breed-specific heifer replacement tests for Red

Angus and Gelbvieh that can be ordered through the breed association. The Red Angus Herd Navigator ($25) test provides results on all traits for which RAAA calculates EPDs and Red Angus' HerdBuilder and GridMaster Indices and parent verification if the potential sires have been tested with the RA50K test. Due to the DNA test being breed specific, the Herd Navigator should only be used on females that are at least 75 percent Red Angus. The Gelbvieh Maternal Edge Female Profile ($26) is a low-density panel to be used by producers as a sorting tool for Gelbvieh influenced commercial females. It includes calving ease, maternal calving ease, weaning weight, yield grade, marbling, and carcass weight.

Tests being marketed for crossbred cattle

PredicGEN

PredicGEN ($19.50) is a test marketed by Zoetis® as "a heifer selection tool for straight-bred or crossbred British/Continental animals that are less than 75% Black Angus". Data is reported back on a normally distributed 0 to 100 scale, with a mean of 50 based on Zoetis'® database of 20,000 animals. It provides predictions of genetic merit for key carcass traits – marbling score, USDA yield grade and tenderness, as well as an index that predicts carcass grid value The economic importance of these traits for heifer selection will depend upon the individual marketing strategy and value of carcass traits to overall ranch returns.

Igenity Gold and Silver

The Igenity Gold and Silver tests, which include approximately 1000 markers associated with 13 traits of interest and some randomly spaced markers, are being marketed by Neogen® as "DNA profiles for crossbred and purebred cattle." A single prediction equation is used for each trait to give the score or molecular breeding value, irrespective of the breed makeup of the animal being tested. The silver test evaluates six traits (calving ease maternal, stayability, residual feed intake, average daily gain, tenderness, marbling), and the gold test includes an additional 7 traits (birth weight, calving ease direct, heifer pregnancy, docility, milk, ribeye area and back fat thickness). A selection index score is provided for each animal based on the six traits that are in both tests. According to the Neogen brochure, the development of these tests involved large populations with phenotypic data and/or expected progeny differences (EPDs) comprising tens of thousands of animals that represent various biological types. The six main datasets used to form the training data set for this test were from six breed associations: Angus, Hereford, Gelbvieh, Limousin, Red Angus, and Simmental. Data is reported back on a 1 to 10 scale.

These tests were developed with input from researchers at Iowa State University. Unpublished data (Saatchi and Garrick, personal communication) suggests that this reduced SNP panel (~2,300 markers) gives purebred genetic merit estimates of ~ 80-90% of the accuracy of the 50K SNP chip for the six breeds in the training data set. This number dropped to a correlation between the test result and the true breeding value (r) of ~ 0.3 when estimating the genetic merit of commercial crossbred animals. The correlation is likely to be even lower in animals comprised of breeds that were not in the original training set. The lower the correlation (r), the more possible change there is in the ranking based upon that test.

This is analogous to low accuracy "interim" EPDs which are given to young bulls with very little available information where the possible change in the EPD value is high. EPDs with low accuracy are still the single best tool for selecting on the trait of interest; however, they are associated with wide margins of possible change. To explain this concept, consider two bulls that have low accuracy EPDs of 0 and +3, but the possible change at that accuracy is ±4. This means that it is likely that the second bull is better than the other by 3 units, but it is possible the first bull's EPD will improve by up to 4 units with more data, and likewise the second bull's EPD could decrease 4 units reversing their ranking. It is therefore possible that the rank of these two low accuracy bulls could flip with more information. Low accuracy estimates are associated with increased possibilities for changes and reranking.

Unfortunately there are not yet any independent, peer-reviewed papers in the scientific literature documenting the field performance of any of these tests for commercial cattle.

Step 2: Which company do you want to use for testing?

Several companies offer various combinations of mutation tests, and many offer both mutation tests and parentage testing in cattle along with a variety of other species. For a list of companies and currently-available tests, please visit the following webpage at UC Davis: http://animalscience.ucdavis.edu/AnimalBiotech/Biotechnology/Companies.

In order to have genomic information included in breed association genetic evaluations the DNA sample typically has to be submitted through the breed association. The cost for genetic testing the tests that are used in genetic evaluation is ~ $75-90 for the high-density chips, and $45-50 for the low-density imputation chips. Breed associations obtain either molecular breeding values or genotypes from the service provider and work to include that genomic information to provide genomic-enhanced EPDs (GE-EPD) that have improved accuracy due to the inclusion of the genomic information in the EPD calculations.

Neogen's GeneSeek (http://www.neogen.com/Genomics/Beef.html) and Zoetis (http://www.zoetis.com/products-services/animal-genetics.aspx) are currently the companies that are partnering with US beef breed associations to provide the genotypes needed to develop genomic-enhanced EPDs (GE-EPDs).

Step 3: How much do genetic tests cost?

The costs for various DNA tests in cattle vary based on the type of test(s) being performed, the company and the number of animals being tested. Costs can range from ~ $13-20 for parentage testing, ~$20-$30 per animal for a single mutation test for a disease or trait, up to $75-90 for the high-density SNP chips for genomic-enhanced EPDs. If multiple tests can be performed on a single DNA sample or a large volume of samples is tested then the cost per test is reduced. Additional costs can include the cost of DNA cards, sample collection, sample storage and shipping and sample processing, again depending on sample type, test and application.

Step 4: What kind of sample do you need to submit?

Most of the DNA testing that has been described here can be performed on a variety of samples. These include tail hairs, blood (in tubes or on blood spot cards), semen, or tissue. Hair samples and blood spot cards are the easiest to submit as they generally do not require refrigeration or any special packaging. The hairs themselves do not contain DNA; it is located in the hair root bulb. Submitted hair samples must contain root bulbs in order to be processed for DNA. Always be sure to follow collection procedures closely and properly label all samples. It is important to note that different preferred sample types may be requested for specific tests, so be sure to carefully review the instructions provided by the testing company.

Step 5: How do you ship the sample?

Many sample types can be shipped at room temperature. Tissue samples may need to be frozen upon collection and shipped in a cooler with an ice pack. Never store samples in direct sunlight or expose them to heat. Heat denatures DNA and will result in a poor sample and potentially inconclusive test results.

Step 6: What do you do with the results?

Parentage and mutation test results often need to be reported to specific breed associations for registration purposes. This is also true for SNP results for breeds that use them for genetic evaluation. Results of disease, trait and coat color mutation tests can be used to manage breeding decisions and mate selection to avoid producing undesirable combinations of genotypes (e.g. double recessive "aa") and phenotypes in the offspring.

Looking ahead

There are a number of breed associations working on developing a suite of new traits for genetic evaluations. There are also several large USDA-funded grants that are working to develop training populations for hard-to-measure traits including feed efficiency, susceptibility to bovine respiratory disease complex, and fertility. These large projects require thousands of genotyped animals with observations on these novel traits. It is anticipated that their results will allow for more traits to be added to the list of GE-EPDs in the future. The interested reader is referred to http://www.eBEEF.org, a website that collates beef cattle genetics information. There are fact sheets located there from which the material in this proceedings paper was drawn. Specifically see: http://articles.extension.org/pages/73798/how-to-get-started-with-dna-testing and http://articles.extension.org/pages/73461/recent-developments-in-genetic-evaluations-and-genomic-testing. Another of particular interest may be: Replacement Heifer Selection http://articles.extension.org/pages/73404/commercial-replacement-heifer-selection.

The application of genomics to improve the accuracy of EPDs is a rapidly developing field. There are ongoing improvements in genotyping and sequencing technologies, statistical methods to increase the correlation between genomic predictions and true genetic merit, and the computing systems to handle the large datasets associated with animal breeding. One thing still remains true in the genomic age and that is the need to collect accurate records. It is essential to ensure performance data, pedigree, and DNA information are recorded and reported accurately. Genomic predictions will only be as reliable as the data upon which they are based. Although it might seem like the genomics era could signal the end of performance recording, the opposite is true. Now more than ever it is important that producers accurately report data, and ensure that animals which are genotyped are correctly identified so that their information can contribute towards improving the accuracy of the genomic predictions of the future.

Conclusion

DNA technologies are evolving rapidly and it is likely that in the future DNA information will play an increasingly important role in beef cattle breeding and management. Even if you are not currently testing it may be prudent to collect DNA samples (e.g. tail hair) on important animals in your herd (e.g. herd bulls) and store them for potential future uses. Many times when performing parentage determinations using DNA information, producers realize they are missing DNA samples from potential sires which typically sired the calves 12-18 months earlier. It is also likely there will be future uses for DNA the technology that have not been thought of yet – like smart phone technology this is a rapidly moving field and it may be wise to have some archived DNA samples on hand to make use of new innovations in the future.

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