DNA MARKERS REVOLUTION OR EVOLUTION?

DNA markers and their use for genetic advancement has been a hot topic lately, we have asked some of the leading people in the industry for their thoughts on the role of DNA markers in genetic evaluations.

Dr. Denny Funk, Group Chief Scientist, ABS Global Inc. and Genus, plc.

How are genomics being used in the dairy industry?

Genome-enhanced predicted transmitting abilities (ge-PTAs) are now routinely calculated by USDA for dairy cattle in the United States. All young bulls that are being progeny tested by the major A.I. organizations are now genotyped using the Illumina 50k SNP chip, and the genotypes are sent to USDA for inclusion into ge-PTA calculations. All traditional traits, such as milk yield, protein yield, conformation traits, and health traits are "topped off" with genomic results, and ge-PTAs have essentially replaced traditional PTAs. Similar to traditional PTAs, the ge-PTAs include pedigree and performance information on the individual plus its relatives, but now also include genomic results from the individual trait-SNP association research undertaken by USDA for each trait summarized.

Although ge-PTAs are now routine, the amount of information that genomics adds to the accuracy of the breeding values is equivalent to about 10-20 progeny. In dairy cattle, a traditional progeny test would include information from about 100 offspring. Therefore, almost all young bulls are still progeny tested by the A.I. companies to obtain a higher accuracy PTA than can be achieved from pedigree and genomics alone. Results from the three USDA evaluations in 2009 (January, April, and August) clearly show that ge-PTAs can still change a great deal as progeny information is added into the genetic evaluations.

Having ge-PTAs for young bulls has allowed the dairy industry to more intensely screen which bulls are the best candidate bulls to progeny test, but it has not replaced progeny test. Results to date indicate that ge-PTAs for young sires are much closer to traditional parent average PTAs than they are to ge-PTAs that include progeny information.

Traits with lower heritability estimates, such are fertility traits and fitness traits, are traits where higher accuracy breeding values would be most beneficial, and in theory, genomics could help increase the accuracies for these low heritability traits substantially. But it also takes much more data to get accurate genomic estimates for these low heritability traits than for higher heritability traits, and having lots of performance data for these low heritability traits will be essential to achieve accurate genomic estimates. We face the same challenge with tradition breeding values, where it always has been difficult to obtain the volume of data necessary to achieve high accuracy breeding values for these low heritability traits.

Lastly, we must remember that mother nature is constantly reshuffling the genetic "deck of cards" via chromosome crossover and other wonderfully complex genetic mysteries that we don't fully understand, and therefore we must re-estimate the genomic effects every couple of generations to ensure that the genomic results observed in previous generations are still applicable to current generations. That will require a diligent commitment to collect performance information on lots of individuals moving forward. This continual collection of large volumes of performance data is crucial to making genomics applicable both today and in the future.

How are genomics being used for genetic selection in the pig industry?

Unlike the dairy industry where USDA calculates breeding values in the U.S., all genetic evaluations for pigs are done by the individual breeding companies. PIC, (the pig breeding company owned by Genus) has been incorporating genomics into their breeding values for over 15 years, but it is only recently with the development of the 60k pig SNP chip in 2009 that genomics have started to have any appreciable impact on the accuracy of estimated breeding values (EBVs). Prior to the dense 60k chip, PIC had upwards of 50 significant markers for some traits, but the increase in EBV accuracy from this small number of markers was small.

Similar to dairy cattle, PIC is now adding the genomic results from the 60k SNP chip to the traditional breeding value information (pedigree and performance data) to arrive at ge-EBVs for each trait summarized. Hence these ge-EBVs replace traditional EBVs, and selection of individuals to use as parents remains the same as before: Rank the animals based on ge-EBV, and use the accuracy of the ge-EBV to determine how heavily to use that individual in the breeding program.

Bill Bowman, Chief Operating Officer and Director of Performance Programs, American Angus Assoication:

Explain the vision that AGI has for incorporating genomics in the genetic evaluation process?

We have continued to follow the development of DNA technology and how that technology could ultimately be used in genetic improvement. Historically incorporating the use of science and technology to provide the beef industry with reliable information characterizing Angus genetics has remained the focus. The scientific community's thought process has moved from developing independent selection tools and using the genomic information to incorporating the genomic information into national cattle evaluation procedures and EPDs. The Beef Improvement Federation has provided some guiding philosophy on the use of genomic information….

"BIF believes that information from DNA tests only has value in selection when incorporated with all other available forms of performance information for economically important traits in NCE, and when communicated in the form of an EPD with a corresponding BIF accuracy. For some economically important traits, information other than DNA tests may not be available. Selection tools based on these tests should still be expressed as EPD within the normal parameters of NCE."

We are following this approach as we move forward with the implementation of genomic enhanced EPDs.

How would you advise breeders to use the new genomics panels in their programs?

We encourage the breeders to use genomic enhanced EPDs from our National Cattle Evaluations as a part of their selection strategies. Genomic enhanced carcass EPDs are the first traits to be released. In a timely fashion, genomic, carcass and ultrasound databases can be used to produce these carcass EPDs. We still encourage breeders to measure phenotypic traits as much as possible because these records have great long term value in the evaluation of economically relevant traits.

Dr. Wade Shafer, Director of Performance Programs, American Simmental Association:

How much benefit or accuracy from current DNA markers should producers expect when selecting yearling bulls, replacement and donor females or A.I. sires?

First, genomic test results should only be used if: 1) estimates from traditional genetic evaluation (EPDs) are not available for the trait of interest or 2) the genomic data are incorporated into traditional genetic evaluation.

For traits where EPDs are not available, most current genomic panels will produce genetic predictions with BIF accuracies equivalent to the low end of pedigree estimated EPDs (less than .10). For traits where they are available, genomic data will provide a slight increase in accuracy when included in the evaluation of low accuracy animals (e.g., non parents). They will not enhance the accuracy of evaluation for mid- to high-accuracy animals.

The industry is rapidly moving toward an infrastructure capable of incorporating genomic data into National Cattle Evaluation (NCE). Also, several entities are feverishly working on genomic panels that will provide more information to NCE.

If you were king for a day what traits would you like to be able to use DNA markers to select for and why?

I would like to see DNA markers used in the evaluation of all traits.

Though currently available genomic panels do not provide a great deal of value, as the technology evolves genomic data will become an integral component in genetic prediction. The value of the technology will only be fully harnessed when genomic panels and the NCE infrastructure capable of utilizing them are developed for all economically relevant traits.

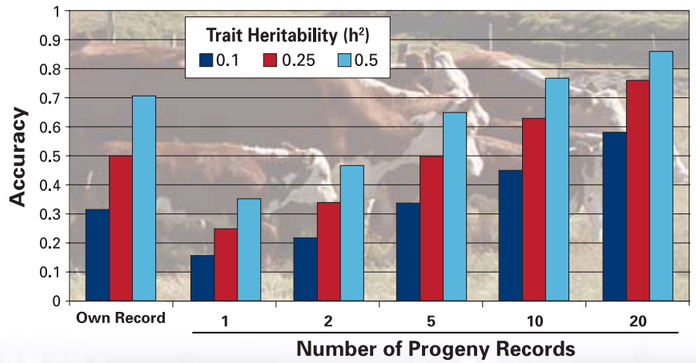
Alison Van Eenennaam, Animal Genomics and Biotechnology Extension Specialist, University of California, Davis:

Can you help put DNA markers and progeny testing in perspective – how many progeny would a DNA marker test be equal to?

That depends on how accurate the test is, and also on the heritability of the trait. Accuracy is defined as the correlation between the estimated breeding value (e.g. EPD) and the true value. Note that BIF accuracies that are listed in U.S. sire catalogs are more conservative than this definition and tend to be lower for a given amount of information. In a perfect world the accuracy value would be 1, and it does in fact approach that for well-proven sires with many progeny records. However, on young animals there is less information available upon which to estimate genetic merit.

Continued on page 7

Effect of Number of Progeny Records on Accuracy



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Progeny testing provides a way to obtain this information, although it involves waiting for an animal to reproduce prior to obtaining an accurate genetic merit estimate. For traits that are highly heritable, offspring strongly resemble their parents and so only a few progeny are needed to give an accurate indication of genetic merit. Simply put the higher the heritability, the more the trait is influenced by genetics. The figure on the previous page shows how progeny test information influences the accuracy of genetic merit estimates for traits of different heritability.

So, now to answer the question that was asked – and that is – how many progeny would a DNA marker test be equal to? That depends on the accuracy of the DNA marker test and the heritability of the trait it is predicting. If a DNA test has an accuracy of 0.5 for a trait with a heritability of 0.25, then from the graph above that test would be equivalent to having 5 progeny records from the animal that was DNA tested, or to having the animal's own record for that trait. A DNA like this would be very useful for traits that are hard to measure (e.g. carcass traits).

So, what is the accuracy of tests that are currently on the market for beef cattle? The only independent source of that data is at the Australian beef CRC website (http://www.beefcrc.com.au/Aus-Beef-DNA-results) where the relevant value is the rg (genetic correlation). At the current time, tests on the market have variable accuracies ranging from 0 to 0.25, with the notable exception of meat tenderness tests which have consistently been shown to have higher accuracies (0.13-0.55). Tenderness has a heritability of ~ 0.3.

Genetic Correlation (r)	BIF Accuracy	# of progeny records required: Low Heritability (0.10)	# of progeny records required: Moderate Heritability (0.30)
0.1	.01	1	1
0.2	.02	2	1
0.3	.05	4	2
0.4	.08	8	3
0.5	.13	13	5
0.6	.20	22	7
0.7	.29	.29	12
0.8	.40	70	22
0.9	.56	167	53
0.99	.93	1921	608
0.995	.99	3800	1225

Accuracies of estimated breeding values based on (A) the correlation with true breeding values (r) and (B) the BIF standard, and the number of progeny test records required to obtain these accuracy values for traits of low (0.1) and moderate (0.3) heritability.

Source: Cattle Network, Cattle Breeding: Marker-Assisted Selection, Alison Van Eenennaam, University of California Department of Animal Science

As DNA technology advances how do you see the tests benefiting commercial and purebred cattle producers?

The hope is that as the technology advances, the tests are going to become more accurate, and also encompass a range of difficult to measure traits (e.g. female fertility). Ideally tests will be for traits for which data are hard to get or expensive to measure, and which contribute greatly to the bottom line. Feed efficiency would be a good example of such a trait. This will give producers a way to obtain genetic merit estimates for these otherwise difficult traits. There are a number of issues that need to be resolved before the power of DNA tests will be useful for the beef industry. It is not clear how well tests work in different breeds, and therefore effects need to be examined in a range of breeds. This is not something that is easily done, and many breeds do not have data to determine if DNA tests work in their populations. Additionally it seems that discovery populations might need to be very large (thousands of animals) to increase the accuracy of tests and it is an expensive proposition to develop large populations of animals with thousands of measurements on difficult or expensive to measure traits! Although current tests do not have very high accuracies, it is hoped that this will increase in the future with the development of new markers. For the seedstock producer DNA tests offer the opportunity to increase the accuracy of selection and hence increase their rate of genetic gain. This means they can sell better bulls (i.e. more valuable bulls) to commercial cattle producers. Higher accuracies on yearling bulls will also provide some peace of mind to bull buyers, because accurate EPDs change little over time compared to low accuracy EPDs where there is greater potential for the values to change as more data becomes available.

Doug Frank, ABS Global Beef Product Manager

What role do DNA markers play in the current selection of bulls entering the ABS Beef program? In the next 3 to 5 years?

To this point, DNA markers have played very little role in the selection of young bulls entering the ABS lineup. We've agreed with the Beef Improvement Federation stance that the genomics piece needed to be included as part of the overall genetic prediction through EPDs to be truly effective.

With improving chips and the advent of genomic enhanced EPDs we would expect this technology to play a larger role in what we do in coming years. As part of an EPD, genomic information will become another tool in the toolbox allowing us to have better and more accurate predictions on the young bulls that we sort through each year.

Just as we do with individual performance data, we will have to be careful to not to get too hung up on one component and risk overvaluing it in the process. That's where the inclusion of genomic information as part of the EPD and corresponding accuracy will be extremely helpful.

Depending on the trait and markers that have been identified, we would initially expect the genomic component to contribute a modest amount to overall accuracy depending on the trait – somewhere in the range of what individual performance measures contribute or up to the accuracy value of 5-10 progeny records.

ABS has always held fast to the principles of progeny testing, do you see the role of progeny testing diminishing in the future? How will DNA markers fit into the progeny testing scheme?

We still see progeny testing as the key component of delivering high accuracy, fully proven bulls. That proving process is similar to a long journey. DNA technology holds the potential of fine tuning the direction that we take and speeding up the start of that trip. However, it is very unlikely that it will provide a short cut or eliminate the journey. It will still take a lot of miles or evaluated progeny to fully understand a bull's true transmitting ability.

ABS will certainly use DNA technology to fine tune our selection process to get a better handle on the young bulls we evaluate and the cows behind them. At the same time we think it is imperative "to put in the miles" to progeny test and validate the complete genetic profiles of our bulls in real world environments. And, today it remains the only way to deliver the high accuracy Rock Solid sires that our customers have come to expect.

Also, as it relates to DNA technology, progeny testing will continue to be critical to providing the largest and most up to date datasets for training and validation of future genomic developments.

ABS continues to be committed to real world progeny testing of our bulls even for traits that are expensive and difficult to measure like feed efficiency and tenderness. The Angus Sire Alliance program is one of the key components of that commitment along with relationships with groups like Power Genetics and breed association programs like the American Simmental Association Carcass merit project. ■

Take home points for producers on the evolving use of DNA markers in genetic selection

The most effective use of DNA marker data is through genomic-enhanced EPDs

- Genomic data needs to be combined with traditional pedigree information, individual performance and progeny performance data
- Genomics will increase EPD accuracies the most for young cattle or animals with few progeny records
- Progeny proven sires remain the best source of high accuracy genetics

Don't stop progeny testing and measuring phenotypic traits

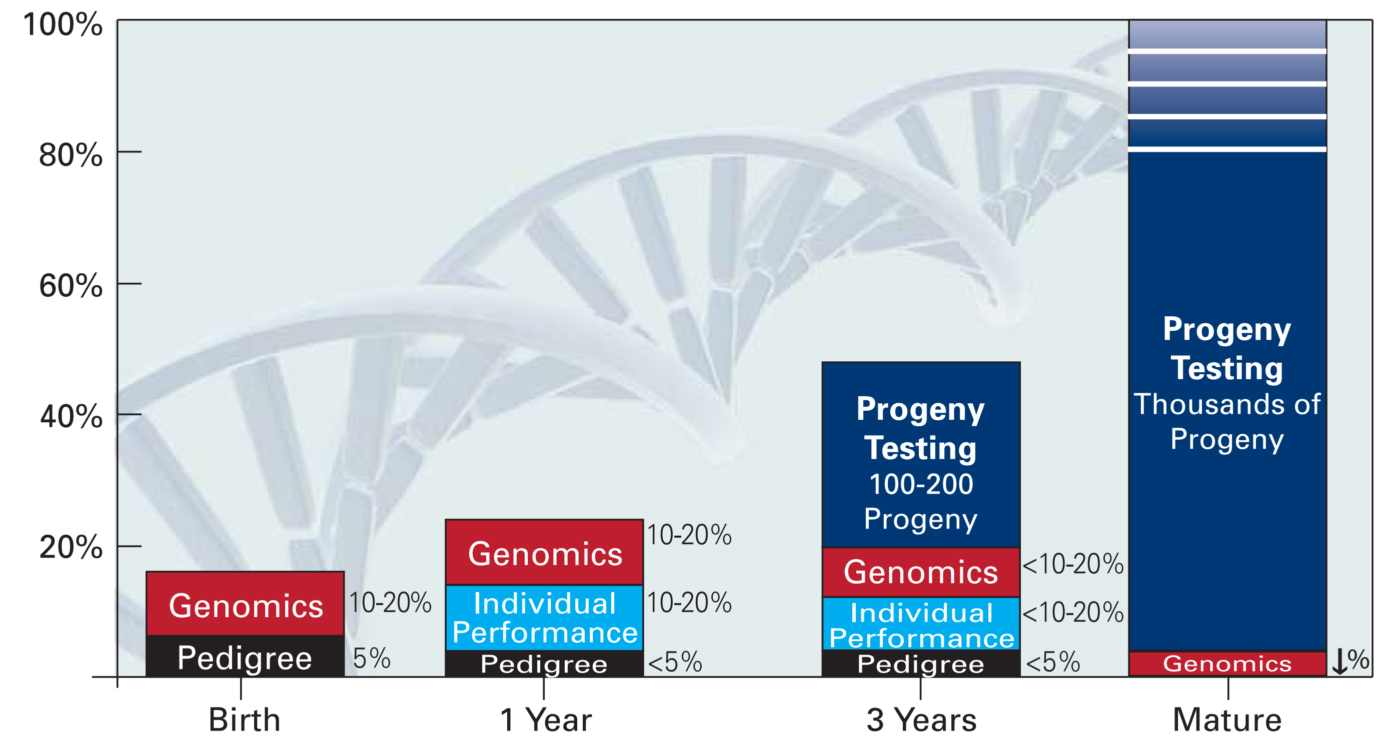
- Individual phenotypes will continue to have significant impact on individual EPDs
- Progeny testing will continue to be the biggest accuracy driver for heavily used sires and donor dams
- Expanding the use of DNA technology to new (and more difficult) traits will require large volumes of phenotypic data for these traits
- Phenotypes will be needed on an ongoing basis to update and "retrain" existing marker effects

There will be multiple sources of genomic information

- The most effective genomic data will be breed specific with training data sets very similar to the target populations
- It will be difficult to obtain accurate genomic results for small breeds with limited data sets
- Challenges remain in providing effective across-breed marker panels

Example Accuracy Contributions

Over a Bull's Lifetime



Pedigree and genomic data have their largest relative impact on young animals. As successive components are added, overall accuracy increases, but the contribution of each individual piece declines. Progeny data is the key component of high accuracy proofs and in large enough numbers eventually overwhelms pedigree, individual performance and genomic information.

* Actual contributions are dependent on heritability of the trait, the available ancestral information and the genetic correlation of the DNA markers used.