DNA Technologies and Production Markers

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Overview

- Background information on genetic improvement and DNA marker technology
- Improvements in genetic gain possible from including DNA information into genetic predictions
- Genetic tests that are on the market for production traits
- DNA testing for recessive genetic defects
Traditional animal breeding on the basis of phenotype (appearance) can be very successful.
However breeding based on objective performance recording has been spectacularly successful.....

Average milk production per lactation of US Holstein cows has nearly doubled during the past 40 years

Should you use this bull?
In the absence of any other information selection can only be based on appearance or reputation...
But what you would really like to know is the future performance of his unborn calves!!
What if I told you these calves belonged to the bull?
What if I told you these were his daughters’ calves?
What if I told you this was a typical steak from his progeny?
Animal breeders use records of an animal's own performance and that of its relatives to predict an animal’s genetic merit or estimated breeding value.

\[ \frac{1}{2} \times EBV = \text{Expected Progeny Difference (EPD)} \]
**What is an EPD/breeding value?**

An animal’s **breeding value** is an estimate of its genetic merit, half of which will be passed on to its progeny (EPD). While we will never know the exact breeding value, for performance traits it is possible to make good estimates based on performance records of the animal and its relatives. These are called Estimated Breeding Values.

**Calculating EBVs**

In the calculation of EBVs, the performance of individual animals within a contemporary group is directly compared to the average of other animals in that group. A contemporary group consists of animals of the same sex and age class within a herd, run under the same management conditions and treated equally. Indirect comparisons are made between animals reared in different contemporary groups, through the use of pedigree links between the groups.
Challenge for breeders is to accurately identify those individuals that have the best true breeding values

- Records – more are better
- Would ideally like records before selection
- Need to know genetic relationship between what you are measuring (e.g. an ultrasound scan) and the trait you get paid for (e.g. marbling)
- Perhaps DNA information can help improve the accuracy of breeding values if they have been shown to work in Wagyu!
The genome age

PROTEINS ARE THE BUILDING BLOCKS OF LIFE AND COLLECTIVELY ACT TO DETERMINE PHENOTYPE

GENES CONTAIN INSTRUCTIONS FOR MAKING PROTEINS
SNP (Single Nucleotide Polymorphism)

A DNA sequence variation that varies sufficiently between individuals that its inheritance can be tracked through families.
What is a Genetic Marker?

A DNA sequence variation that has been associated with a given trait in one or more populations.
What is needed for develop a DNA test?

**TRAINING**
- Population
- Phenotypes
- Genotypes

**Training** = Need a population where genetic markers have been associated with production traits in BREED of interest

**Prediction** = the results of training can then be used to predict the genetic merit of new animals based on their DNA genotype alone.
There are DNA-markers for simple traits

- DNA test result is highly predictive
  - Coat color
  - Polled/horned status
  - Certain genetic diseases (e.g. "curly calf")
  - SCD (Prescribe Genomics, $90 per test)
  - "Exon 5" (Prescribe Genomics, $100/test)
Wagyu-specific DNA-makers for simple traits

SCD - Stearoyl-CoA desaturase (AA, VA, VV)
- “the percentage of beef that is “not delicious” has increased as a result of increased fat of a high melting temperature
- ~ 18% AA, 74% VA, 8% VV

Exon 5 – growth hormone (AA, AB, BB, BC, CC)
- Only found in Wagyu,
- Purportedly associated with marbling
- No more information on frequency
SIMPLE TRAITS
- e.g. Coat Color
- Double muscling

COMPLEX TRAITS
- e.g. Marbling ($h^2 = 0.37$)

100% GENETICS

37% GENETICS

63% ENVIRONMENT

Animal Genomics and Biotechnology Education
Merial, Quantum sign leptin test pact. (Business Report)

Publication: Feedstuffs

Publication Date: 04-AUG-03

Ads by Google

B-Bridge International  ELISA Assays for Metabolic Studies Adipocytokines, esRAGE, HGF

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SASKATOON, SASK., and DULUTH, GA. -- Quantum Genetics Inc. and Merial Ltd. announced July 23 that they have entered into a global marketing agreement to provide Merial with exclusive rights to market Quantum's new patent-pending DNA test to determine an animal's leptin genotype.

The leptin protein has been demonstrated...

Igenity L was a single T/C SNP test for Leptin

Advanced technology. Advanced knowledge.

What if there was a test that could tell you – in advance – an animal’s genetic potential for energy utilization or carcass quality? You’d have the advantage of knowing an animal’s potential now, instead of discovering it later through success or failure in the milk string or when the animal goes to market.

Researchers have discovered the specific gene that carries the code for the production of a protein called leptin. Leptin is associated with an animal’s potential for appetite and energy utilization, among other things.

- For dairy cattle this translates directly into maximum dry matter intake (DMI) and peak milk production.
- For beef cattle it relates to days on feed and carcass quality.

The IGENITY™ L Test identifies leptin genotype (L-tt™, L-ct™ or L-cc™). Now you have another important resource to help you breed, feed, sort, manage and market cattle at an optimum level.

- The IGENITY L Test identifies an animal’s leptin genotype at the DNA level, with 100% accuracy.
**GeneSTAR**

**MARBLING**

**GeneSTAR** Marbling is a DNA genetic marker test offered by Bovigen Solutions, LLC for a major gene (Thyroglobulin) associated with marbling. This marker provides beef producers the opportunity to determine an animal's potential for improved marbling more accurately and at an earlier age.

<table>
<thead>
<tr>
<th>Marbling Results (% Choice)</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yearling Fed</td>
<td>58% 62% 74% 16%</td>
</tr>
<tr>
<td>Calf Fed</td>
<td>34% 41% 53% 19%</td>
</tr>
<tr>
<td>NBCEC Trial¹</td>
<td>47% 54% 64% 17%</td>
</tr>
</tbody>
</table>

In independent trials on over 1500 head, 2-STAR animals produced 16-19% more choice carcasses than 0-STAR animals. Equally important was the effect that the proportion of carcasses qualifying for premium Quality Grades doubled (21% vs. 10%) in 2-STAR carcasses versus 0-STAR.

¹ Trial was a study conducted by an independent third party.


**HOW DO I USE THIS IN MY BREEDING PROGRAM?**

Using 2-STAR sires is the quickest way to influence the presence of these genes in a herd. In addition, selecting 2-STAR females will more rapidly increase the frequency of the positive forms of these genes. Overall, selecting 2-STAR animals with appropriate EPDs and good structural and breeding soundness is the recommended way forward.

**LEGEND**

The results of the GeneSTAR™ tests are reported as:

- 🌟🌟🌟 2-STARs = two copies of the desired gene
- 🌟🌟 1-STAR = one copy of each form of the gene
- 🌟 0-STARs = no copies of the desired gene

**Mating Design**

<table>
<thead>
<tr>
<th>Sire is</th>
<th>Dam is</th>
<th>% of Progeny</th>
</tr>
</thead>
<tbody>
<tr>
<td>🌟🌟🌟</td>
<td>🌟🌟🌟</td>
<td>100%</td>
</tr>
<tr>
<td>🌟🌟🌟</td>
<td>🌟🌟</td>
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</tr>
<tr>
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</tr>
</tbody>
</table>
Which would you rather have???

- A bull that is ‘homozygous’ for a positive genetic variant with a low-accuracy marbling EPD of +3, or

- Or an unrelated bull carrying no copies of that genetic variant with a low-accuracy marbling EPD of +3
Both are important!!

- The ‘homozygous’ bull is a source of favorable alleles (genetic variant) of the gene. Can eventually be used to create homozygous calves.
- The other bull contributes favorable unmarked alleles of other genes, which will improve the frequency of other desirable alleles for the trait.
- Breeding the marker-associated form of the gene into the bull that has no copies should improve the trait by combining all of the good forms of the genes together in one animal.
DNA TEST FOR MARBLING EXPLAINS SOME % ($r^2$) OF GENETIC VARIATION

DNA TEST: 37%
OTHER GENES: 63%
ENVIRONMENT: 63%

EPD estimates all genes

Wagyu 10/27/2011
Animal Genomics and Biotechnology Education
Recap of early product offerings

- Single gene tests reported as actual results of genotyping (**) or AT
- Great deal of explanation of what the gene was and how it had its effect
- DNA-test billed as 100% accurate
- The need for third-party validation of commercial tests becomes evident
- A lot of emphasis was put on a single SNP
First multi-gene test arrives

**TENDERNESS**

*GeneSTAR* Tenderness was the first multi-gene single trait DNA test commercially available to the beef industry. It combines test results for several markers and genes for the same trait. The test is based, in part, on two genes involved in the post-mortem tenderization process: Calpastatin and Calpain. Calpain is an enzyme which weakens muscle fibers thereby making the fibers more tender. Calpastatin is an enzyme which inhibits the post-mortem tenderization process by inhibiting the effects of Calpain.

**Genetic Progeny Difference**

<table>
<thead>
<tr>
<th>SIRE IS</th>
<th>DAM IS</th>
<th>% of Progeny</th>
</tr>
</thead>
<tbody>
<tr>
<td>★★★</td>
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<td>100%</td>
</tr>
<tr>
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<tr>
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<td>★★</td>
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<tr>
<td>★</td>
<td>★</td>
<td>100%</td>
</tr>
</tbody>
</table>

This Mating Design illustrates Mendelian Heredity and the probability of results from mating a 0, 1 or 2 STAR Sire and Dam.

DNA tests should be considered additional information to be used in conjunction with available performance data for each animal. When comparing two bulls with similar EPDs, GeneSTAR GPD results can be used to further evaluate an animal's true genetic potential.
IGENITY® TenderGENE™
A practical, powerful tenderness selection tool.

IGENITY® TenderGENE™
The inside track to tender beef.

IGENITY® TenderGENE™ profiles the tenderness potential of an animal and is:
• A powerful and comprehensive tenderness selection tool
• Fully validated by the National Beef Cattle Evaluation Consortium (NBCEC)
• Informative in all breed types, including Bos indicus

IGENITY TenderGENE analyzes multiple markers associated with the calpain and calpastatin genes. Both of these genes are important for profiling an animal’s potential for tenderness:
• Calpain enzymes weaken muscle fibers during the post-mortem aging process.
• Calpastatin interacts with the calpain enzymes to impact overall tenderness.

Together they have a significant effect on tenderness as measured by Warner-Bratzler Shear Force (WBSF). In fact, in independently validated research, the calpain and calpastatin markers included in IGENITY TenderGENE are associated with improving tenderness as much as 2.3 lb.

The benefits of IGENITY TenderGENE are proven.
• IGENITY TenderGENE includes markers discovered by researchers at the U.S. Meat Animal Research Center (MARC) and the University of Guelph.
• IGENITY TenderGENE is a powerful tenderness test that is fully validated by the NBCEC.
• Validation work involved cattle from the NCBA National Carcass Merit Project.
• Research included more than 1,200 animals, representing all breed types.
• Because of the favorable effect on WBSF of up to 2.3 lb, selecting for tenderness using IGENITY TenderGENE can help ensure a quality eating experience for consumers.

Learn how this inside information can give you a competitive edge. Call 1-877-IGENITY.

What do you bring to the table?
In this example, the results describe an animal for Feed Efficiency. The genes identified for Feed Efficiency thus far, identify cattle with lower Net Feed Intake (NFI). Cattle with lower NFI will eat less without sacrificing ADG or any other performance trait. The animal in this example will consume 3.2 lbs less feed per day and still have the same ADG and Marbling potential as the rest of his contemporary group. Simply put, the more STARS for Feed Efficiency, the less feed consumed without sacrificing any performance!!!

In this example, the results describe an animal for its Tenderness potential. Nationwide, tenderness is measured by Warner-Bratzler Shear Force, or the pounds needed to cut a core sample from a ribeye. The animal in this example will produce a ribeye that is 2.0 pounds more tender than an animal without the STARS for tenderness.

The GeneSTAR Tenderness panel continues to lead the industry in identification of markers for one of the most valuable traits for producing a quality eating experience. GeneSTAR animals that are homozygous for all the Tenderness markers (T1, T2, T3) show a difference in Tenderness that virtually eliminates the “unsatisfactory eating experience” that plagues nearly 25% of all carcasses compared to an animal devoid of these genes.

In this example, the results describe an animal for Quality Grade. The genes identified thus far for Quality Grade work across all breeds and identify animals with a greater chance of grading Choice or higher. The animal in this example has a 27.42% greater chance of grading Choice or higher than an animal with out the STARS for Quality Grade.
One in a series of break-through products that will advance breeding practices in the cattle industry, Tru-Marbling™ is a powerful and comprehensive DNA selection tool that can determine the genetic potential of animals to express marbling. In a collaborative research program between Cargill and MMI Genomics, an innovative scientific approach was used on over 4000 feedlot animals to identify the majority of regions throughout the bovine genome that have an effect on this economically important trait.

Tru-Marbling™ is a DNA-based genetic test that contains a panel of 128 unique DNA markers, each one highly associated with the expression for marbling score and quality grade. By measuring the cumulative effects for each of these 128 markers, Tru-Marbling™ accounts for a significant proportion of the total genetic variation for this complex metabolic trait—the first DNA-based product to do so.

Tru-Marbling™ is an advanced and revolutionary tool that will allow cattle producers to make early breeding decisions that increase the accuracy of selection and decrease the age at which animals can be selected.

The results: Rapid improvement of marbling within herds and the ability to determine the "Tru" genetic potential of animals.

Explains 70% of the genetic variation in marbling with 128 markers.

One in a series of break-through products that will advance breeding practices in the cattle industry, Tru-Tenderness™ is a powerful and comprehensive DNA selection tool that can determine the genetic potential of animals to produce tender meat. In a collaborative research program between Cargill and MMI Genomics, an innovative scientific approach was used on over 4000 feedlot animals to identify the majority of regions throughout the bovine genome that have an effect on this valuable consumer trait.

Tru-Tenderness™ is a DNA-based genetic test that contains a panel of 11 unique DNA markers, each one highly associated with expression for tenderness. By measuring the cumulative effects for each of these 11 markers, Tru-Tenderness™ accounts for a substantial proportion of the total genetic variation for this complex metabolic trait.

Since tenderness can only be measured in harvested cattle it is difficult, time consuming and expensive to make genetic progress for this trait using traditional genetic improvement tools. Tru-Tenderness™ changes this paradigm by allowing producers to accurately assess the genetic potential of their breeding stock to produce tender meat. In addition, Tru-Tenderness™ also shortens the interval for making genetic progress because it can be used to test animals of any age.

Tru-Tenderness™ is an advanced and revolutionary tool that will allow cattle producers to make early breeding decisions that increase the accuracy of selection and decrease the age at which animals can be selected.

The results: Rapid improvement of tenderness within herds and the ability to determine the "Tru" genetic potential of animals.

Explains 100% of the genetic variation in tenderness.
Results reported on 1-10 scale

The IGENITY profile.

It’s easy to understand an IGENITY profile.
One of the greatest values of the IGENITY profile is that all results are integrated and provided in one single profile, similar to the report shown here.

<table>
<thead>
<tr>
<th>Animal ID</th>
<th>M/F</th>
<th>Breed</th>
<th>Sample Barcode #</th>
<th>Tenderness</th>
<th>Red/Black Coat Color</th>
<th>Heifer Pregnancy Rate</th>
<th>Yield Grade</th>
<th>Ribeye Area</th>
<th>Hot Carcass Weight</th>
<th>Quality Grade</th>
<th>Stayability</th>
<th>BVD-PI</th>
<th>Polled</th>
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</thead>
<tbody>
<tr>
<td>701</td>
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<td>ED/ED</td>
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</table>
Results reported as a MGV

MOLECULAR GENETIC VALUE (MGV) REPORT

<table>
<thead>
<tr>
<th>NAME</th>
<th>LOCATION</th>
<th>REPORT DATE</th>
<th>ORIGINAL REPORT</th>
<th>CASE ID</th>
<th>CUSTOMER</th>
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<tbody>
<tr>
<td>Legends of the West - Angus Farm</td>
<td>13457 Trujillo Creek Road Aguilar, CO 81020</td>
<td>09/23/2006</td>
<td>09/23/2006</td>
<td>MT-0059302S</td>
<td>LWAF - Legends of the West Angus Farm</td>
</tr>
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</table>

CONTACT

Wes Johnson, Foreman

TRU-MARBLING and TRU-TENDERNESS REPORT

<table>
<thead>
<tr>
<th>BREED</th>
<th>NAME</th>
<th>REG #</th>
<th>TAG/ TATTOO</th>
<th>SEX</th>
<th>BORN</th>
<th>SAMPLE ID</th>
<th>MARBLING MGV</th>
<th>TENDERNESS MGV</th>
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</thead>
<tbody>
<tr>
<td>Angus</td>
<td>AF Paul Bunyan</td>
<td>19352178</td>
<td>AZ-105</td>
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<td>05/14/2004</td>
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<td>19352211</td>
<td>AZ-112</td>
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<td>05/29/2004</td>
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All four animals represented in the above test result have Tru-Marbling™ and Tru-Tenderness™ MGVs. All MGVs within a trait have the same accuracy because every animal has the same number of markers in the prediction of genetic potential.

Paul Bunyan and Casey Jones are predicted to grade in the low Select and No Roll USDA grades because of their large negative marbling MGVs. Alamo Rising and Geronimo are predicted to grade in the USDA grades of high Choice and Prime because of their high MGVs for marbling. MGVs near 0 are expected to grade in the high Select USDA grading category.

Paul Bunyan is predicted to produce tough meat with the larger MGV for Tru-Tenderness™. Casey Jones and Geronimo are predicted to produce very tender meat. Alamo Rising is predicted to produce acceptable tenderness, bordering on slightly tough.

These results can be used to rank bulls for their genetic potential for marbling and tenderness.
Pfizer Animal Genetics acquired Bovigen – results reported as GPD
Recap of next generation of products

- Multigenic marker panels start to become the norm
- Number of traits and markers grow exponentially
- No longer any emphasis on which genes the markers are associated with, or how those genes function
- No independent validation of many tests
- Multiple different reporting systems that do not allow interchange (1-10, MGV, GPD, Number of Stars) or interpretation relative to EPDs
- DNA information still being presented separately from EPDs
Lead Today with 50K

1. Birth weight
2. Weaning weight
3. Weaning maternal (milk)
4. Calving ease direct
5. Calving ease maternal
6. Marbling
7. Backfat thickness
8. Ribeye area
9. Carcass weight
10. Tenderness
11. Postweaning average daily gain
12. Daily feed intake
13. Feed efficiency (net feed intake)

50K SNP chip assays
50,000 SNPs spread throughout genome
The Power of the IGENITY® profile for Angus

The American Angus Association® through its subsidiary, Angus Genetics Inc.® (AGI), has a vision to provide Angus breeders with the most advanced solutions to their genetic selection and management needs.

Genomic-enhanced Expected Progeny Differences (EPDs) can now be calculated for your animals using the highly predictable American Angus Association database along with IGENITY® profile results to provide a more thorough characterization of economically important traits and improved accuracy on young animals.

Using the IGENITY profile for Angus, breeders receive comprehensive genomic results for multiple, economically important traits.

1. Dry Matter Intake
2. Birth Weight
3. Mature Height
4. Mature Weight
5. Milk
6. Scrotal Circumference
7. Weaning Weight
8. Yearling Weight
9. Marbling
10. Ribeye Area
11. Fat Thickness
12. Carcass Weight
13. Tenderness
14. Percent Choice (quality grade)
15. Heifer Pregnancy
16. Maternal Calving Ease
17. Direct Calving Ease
18. Docility
19. Average Daily Gain
20. Feed Efficiency
21. Yearling Height
22. Scrotal Circumference
GAR Predestined:

From start to finish—conception to carcass—no other bull in the beef business today adds as much real value to cattle as Predestined. Ranking as the #1 bull for $B in the breed—our customers tell us that their Predestined-sired cattle return the most dollars to their pockets—they know that $B works. Unlike any other 036 son, Predestined tones down size, adds depth of flank, superior feet and legs and a pleasant disposition to his offspring. His conception rate is high and he’s been a standout in timed-AI programs. His progeny look good—his bulls are thick and his heifers are fancy—and they always display additional shape and capacity. He ended 2006 as our top-seller and rightfully so—Predestined’s many talents for creating value are for real.

### Production

<table>
<thead>
<tr>
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<td>Beef</td>
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### Maternal

<table>
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<tr>
<th>Registration #</th>
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<th>Fat Thickness</th>
<th>Yield Grade</th>
<th>Ribeye Area</th>
<th>Carcass Weight</th>
<th>Percent Choice</th>
<th>Marbling</th>
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<tbody>
<tr>
<td>13395344</td>
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<td>6</td>
<td>6</td>
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<td>2</td>
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### EPD and MVP

<table>
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<tr>
<th>Trait</th>
<th>EPD</th>
<th>ACC</th>
<th>EPD % Rank</th>
<th>MVP</th>
<th>MVP % Rank</th>
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<tbody>
<tr>
<td>CED</td>
<td>7</td>
<td>0.84</td>
<td>150</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>BW</td>
<td>4.1</td>
<td>0.97</td>
<td>150</td>
<td>-</td>
<td>70</td>
</tr>
<tr>
<td>WW</td>
<td>53</td>
<td>0.96</td>
<td>150</td>
<td>-</td>
<td>10</td>
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<tr>
<td>YW</td>
<td>99</td>
<td>0.94</td>
<td>150</td>
<td>-</td>
<td>10</td>
</tr>
<tr>
<td>ADG</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>30</td>
</tr>
<tr>
<td>DMI</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>90</td>
</tr>
<tr>
<td>NFI</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>90</td>
</tr>
<tr>
<td>CEM</td>
<td>6</td>
<td>0.85</td>
<td>150</td>
<td>8</td>
<td>1</td>
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<tr>
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<td>28</td>
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<td>150</td>
<td>33</td>
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<tr>
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<td>0.82</td>
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<td>55</td>
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<tr>
<td>FAT</td>
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<td>0.81</td>
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<td>0.073</td>
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<td>REA</td>
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<td>0.82</td>
<td>150</td>
<td>0.073</td>
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<tr>
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<td>0.84</td>
<td>150</td>
<td>1.07</td>
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<tr>
<td>TND</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>60.78</td>
</tr>
<tr>
<td>$B/$MVP</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1.0</td>
</tr>
</tbody>
</table>

- **CED**: Calving Ease Direct
- **BW**: Birth Weight
- **WW**: Weaning Weight
- **YW**: Yearling Weight
- **ADG**: Average Daily Gain
- **DMI**: Daily Feed Intake
- **NFI**: Net Feed Intake
- **CEM**: Condition Evaluation
- **MA**: Marbling
- **CW**: Conformation Weight
- **FAT**: Fat Percentage
- **REA**: Repeatability
- **MS**: Milk Production
- **TND**: Tail Number
- **$B/MVP**: $B/MVP Ratios
American Angus Association performs weekly evaluations with genomic data

<table>
<thead>
<tr>
<th></th>
<th>Igenity</th>
<th>Pfizer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calving ease (CED)</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Growth (BW WW YW Milk)</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Residual Average Daily Gain (RADG)</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Docility (DOC)</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Carcass (CWT MARB RIB FAT)</td>
<td>✔️</td>
<td>✔️</td>
</tr>
</tbody>
</table>

DNA TEST FOR MARBLING EXPLAINS SOME % ($r^2$) OF GENETIC VARIATION

- 63% Environment
- 37% Genetics
- ?? Other Genes
- EPD estimates all genes
<table>
<thead>
<tr>
<th>Trait</th>
<th>AGI h²</th>
<th>IGENITY® Angus Profile</th>
<th>Pfizer HD 50K for Angus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Included</td>
<td>% Genetic variation (r²)</td>
<td>Included</td>
</tr>
<tr>
<td>Average Daily Gain</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Net/residual Feed Intake</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Dry matter intake</td>
<td>0.31</td>
<td>X</td>
<td>20¹</td>
</tr>
<tr>
<td>Feed Efficiency</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenderness</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Calving Ease (Direct)</td>
<td>0.20</td>
<td>X</td>
<td>22¹</td>
</tr>
<tr>
<td>Birth weight</td>
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<td>X</td>
<td>32¹</td>
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<tr>
<td>Weaning Weight</td>
<td>0.20</td>
<td>X</td>
<td>20¹</td>
</tr>
<tr>
<td>Yearling Weight</td>
<td>0.20</td>
<td>X</td>
<td>12¹</td>
</tr>
<tr>
<td>Yearling Height</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calving ease (maternal)</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Milking Ability</td>
<td>0.14</td>
<td>X</td>
<td>6¹</td>
</tr>
<tr>
<td>Heifer Pregnancy</td>
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<td></td>
</tr>
<tr>
<td>Docility</td>
<td>0.37</td>
<td>X</td>
<td>22¹</td>
</tr>
<tr>
<td>Mature Height</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mature Weight</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scrotal Circumference</td>
<td></td>
<td></td>
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<tr>
<td>Carcass weight</td>
<td>0.31</td>
<td>X</td>
<td>29¹</td>
</tr>
<tr>
<td>Backfat thickness</td>
<td>0.26</td>
<td>X</td>
<td>25¹</td>
</tr>
<tr>
<td>Ribeye area</td>
<td>0.32</td>
<td>X</td>
<td>34¹</td>
</tr>
<tr>
<td>Marbling score</td>
<td>0.26</td>
<td>X</td>
<td>42¹</td>
</tr>
<tr>
<td>Percent choice</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>


What about Wagyu?
Summary

- Selection requires accurate identification of genetically superior animals to become parents of next generation.
- Accuracy of EBVs/EPDs can be improved by:
  - Having performance records on individual and its relatives
  - Maintaining contemporary groups – especially in feedlot
  - DNA tests that have been shown to work in Wagyu breed
- Need training populations of Wagyu cattle with records and genotypes to develop accurate DNA tests for Wagyu cattle.
- If DNA tests could be developed that explain genetic variation in marbling in Wagyu cattle, there would be great potential to increase the accuracy of marbling score breeding values – a trait of great financial importance to Wagyu breeders – and considerable value would be generated by this improvement.
There are a large number of genetic abnormalities in cattle occurring in a variety of breeds.

Images from an article by David S. Buchanan, NDSU
Myostatin: mutations in cattle, mice and humans

Phenotypic comparisons of: “double muscled” bull homozygous for loss-of-function allele at the myostatin (MSTN) locus, mouse, and human.

Economic implications of recessive genetic factors

An early '50's advertisement that superimposed a measuring stick in the picture of this bull who was nick-named "Short Snorter."

Based upon his height and age, he was less than a frame score 1.

Image from https://www.msu.edu/~ritchieh/historical/shortsnorter.jpg
A 1956 survey of Hereford breeders in the USA identified 50,000 dwarf-producing animals in 47 states. Through detailed pedigree analysis and test crosses, the American Hereford Association, in concert with breeders and scientists, 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.
From a scientific standpoint, AM is the complete deletion of a segment of DNA that encompasses two different genes.

One of these genes is expressed at a crucial time in the development of nerve and muscle tissue. The mutation results in no protein being produced from this gene and therefore it is unable to carry out its normal function so homozygotes show phenotype
From September 8 – November 3, 2008 identified genetic problem, developed test, and released carrier status of 736 bulls!

- In the 11 months following the release of the test, the AAA posted the results of tests for AM on about 96,247 cattle.

- This amounts to $2.4 million in testing costs

- Of these, 20% (19,529) were carriers of AM. That leaves 23,638 bulls and more than 53,000 heifers which tested as free of AM.

- At $4K/bull and $2K/heifer ~ $200 million of suspect animals shown to be free of RGF allele

Estimates of US and Australia genetic testing costs (Angus)

<table>
<thead>
<tr>
<th></th>
<th>US</th>
<th>AUSTRALIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMF</td>
<td>113,526</td>
<td>12,021</td>
</tr>
<tr>
<td>NHF</td>
<td>77,067</td>
<td>9,936</td>
</tr>
<tr>
<td>CAF</td>
<td>28,837</td>
<td>2,532</td>
</tr>
<tr>
<td>TOTAL NUMBER</td>
<td>294,054</td>
<td>34,991</td>
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<tr>
<td>COST (@ $25/test)</td>
<td>7,351,350</td>
<td>874,775</td>
</tr>
</tbody>
</table>

Numbers kindly shared by Bryce Schumann, American Angus Association; and Carel Teseling, Angus Australia
Angus Australia provides probability data on animal in database

GeneProb used to estimate the probability of every animal in the database being a carrier based on all ancestor and descendant DNA test results

Figure courtesy of Carel Teseling, Angus Australia
Factor XI deficiency (F11) status (usually non-lethal)

Factor XI (F11) is a plasma protein that participates in the formation of blood clots. Factor XI deficiency is an autosomal disorder that is associated with mild bleeding in Wagyu. Affected animals show prolonged bleeding time and abnormal plasma coagulation after trauma or surgical procedures such as castration or dehorning.

PHOTOGRAPH – Affected F11 Female exhibiting no harmful symptoms
Erythrocye Membrane Protein Band Deficiency (Spherocystosis) (Band3)

Cattle that are homozygous (have two copies of the recessive allele) have morbidly anemic (bleeding caused by the abnormal red blood cells). This is a disorder of the surface membrane of the erythrocyte (red blood cells). The calves are typically born weak and small (40-55 lbs birth weight) with labored breathing and are not able to stand or suckle at birth. Death normally occurs within the first 7 days after birth. Some cases live to adulthood but there is a severe retardation in growth.

PHOTOGRAPHS - Icterus in the eyes &, anaemic calf @ 5m (90 kg lw)
Claudin 16 deficiency (CL16) (Type 1)

Claudin 16 or RTD (Renal tubular dysplasia) is a gene disorder on chromosome 1 and causes kidney failure (chronic interstitial nephritis (CIN), often with a build up of excess fibrous connective tissue in kidneys as well as other tissues). This disorder results in terminal kidney failure and the onset can occur any time from late adolescence. Affected cattle typically have short lives (unlikely to live more than 6 years).

*PHOTOGRAPH - Elongated Hooves on an affected CL16*
CHS is a macrophage disorder (a white blood cell that has an important role in the immune response to disease). If cattle have a malfunctioning immune system, this makes them unable to resist bacterial challenge. Blood is slow to coagulate so often the first indicator is unusual umbilical cord hemorrhage at parturition (calving). Cattle with this syndrome often have an unusually pale coat color.

**PHOTOGRAPH – Affected newborn calf with a pale coat**
Factor 13 deficiency (F13) status

This gene contributes to fibrin stability which is an integral part of the blood coagulation pathway (blood clotting ability). Disorders in this gene cause severe hemorrhage (bleeding). In calves hemorrhage is particularly likely to occur in the hindquarters causing blood to pool and stagnate under the hide. In adult cattle any minor trauma (such as hitting the animal) can cause major hemorrhage at the trauma site.

NOTE, this test is still in R&D as a positive control animal has not been identified in the US or Australia. We will continue to run this test and report the results to the American Wagyu Association (the “Association”), and if and when a Positive animal is identified by the test, staff from iGenix will work with the breeder and the Association to validate the results. When the validation is complete iGenix will begin reporting on this disorder to the member. If you have an animal that has symptoms as described above, please collect a blood sample (purple top blood tube) or nasal swab and contact the iGenix lab.

PHOTOGRAPH -
Navel of an affected F13 newborn
Wagyu-breed inherited disorder testing

This test allows you to evaluate your animals for the following recessive genetic mutations that cause:

1. Band13
2. Chediak-Higashi Syndrome (CHS)
3. CL-15
4. F.11-deficiency (mild bleeding disorder).
5. A test for F.13-deficiency (severe bleeding disorder) is still in R&D, and results will not be reported until full validation is completed.

2011 Test prices:

<table>
<thead>
<tr>
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<tr>
<td>Band13</td>
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<tr>
<td>CHS</td>
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<tr>
<td>CL-15</td>
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<tr>
<td>F.11</td>
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<table>
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<th>Bundled Tests</th>
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<td>Any 2 tests</td>
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<td>Any 3 tests</td>
<td>$135.00</td>
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<tr>
<td>All 4 tests</td>
<td>$145.00</td>
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Genetic Testing Status and Offspring Distribution Predictions

The genetic status of each tested animal will be reported as one of the four following results:

- **Free (F)**
  - Means the animal has two copies of the normal gene
  - Also referred to as Normal and Unaffected

- **Carrier (C)**
  - Means the animal has one copy of the normal gene and one copy of the mutated gene
  - Also referred to as Positive

- **Affected (A)**
  - Means the animal has two copies of the mutated gene

- **No Result (NR)**
  - Means the DNA sample was good but did not yield a result under the applicable test protocol

The Science of Genetics Predicts the Following Results from Each Type of Mating:

<table>
<thead>
<tr>
<th>Mating</th>
<th>Offspring Distribution</th>
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<tbody>
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<td></td>
<td>Free</td>
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<tr>
<td>Free x Free</td>
<td>100%</td>
</tr>
<tr>
<td>Free x Carrier</td>
<td>50%</td>
</tr>
<tr>
<td>Carrier x Carrier</td>
<td>25%</td>
</tr>
<tr>
<td>Free x Affected</td>
<td></td>
</tr>
<tr>
<td>Carrier x Affected</td>
<td></td>
</tr>
<tr>
<td>Affected x Affected</td>
<td></td>
</tr>
</tbody>
</table>
If you breed a curly calf carrier cow (AMC) to an curly calf free bull (AMF), what is the chance that the offspring will be stillborn as a result of being curly calf?

1. 0
2. ¼ (25%)
3. ½ (50%)
4. 2/3 (66%)
5. ¾ (75%)
6. 1 (100%)

Results from a typical producer meeting
Genetic implications of recessive genetic factors

“Carrier animals….their overall breeding value worth may outweigh the economic value of carrier status”


Should the market decide or should this choice be directed by industry (e.g. disallowing registration of known carriers)?
Important Registration Information and Testing Policy

Registration Information
Effective October 1, 2010, offspring from animals required to be tested in the section below, will not be eligible for registration until such time that the applicable testing has been completed and the results are received by the Association.

Required Testing Effective October 1, 2010
All fullblood, purebred, and percentage AI sires and embryo donor dams are required to be tested for all five genetic disorders. All live cattle and genetics sold at Association sanctioned production sales must be tested as well and the results must be published in the sale catalog for all potential buyers to review prior to the sale. As an exception to Required Testing, if both the sire and dam of the offspring are Free from all five of the genetic disorders set out above, the offspring will be exempt from testing and will be given “Free” status by the Association for all five genetic disorders.

Annual Association Sales
Only cattle and genetics from cattle testing Free for all five genetic disorders are allowed to be sold through these sponsored events.

Publication of Test Results
All test results will be added to registration certificates and will be posted on the Association website. Once the Breedplan implementation is complete the information will be tracked in the database which is available to the public. Test results will be published in all public sale catalogs.

Fullblood, Purebred, and Percentage Cattle Not Tested
Effective January 1, 2011, any animal that traces to a known Carrier or Affected tested animal will be classified in Association records as a “Potential Carrier” until such time that the animal is tested and the status will be updated as applicable.
Some questions that remain about recessive genetic defects

- If all animals carry recessive genetic factors/defects – how should “defects” be managed

- Can 50K or 800K data be also used to identify carrier status to spread the costs of DNA extraction. If so does it infringe on diagnostic test patents/IP

- Can we use genomics to better manage recessive genetic factors/defects

- Are appropriate decision support tools available for producers
Ideally cattle would be genotyped once early in life and genotypes shared among production sectors to derive the maximum value from the fixed DNA collection and extraction costs.

From the USDA National Institute of Food and Agriculture

National Research Initiative Grant no. 2009-55205-05057

From the USDA National Institute of Food and Agriculture
DNA tests are most valuable for traits that are:

- **low heritability** (influence that genetics rather than environment has on a trait)
- **are difficult or expensive to measure** (feed efficiency)
- **cannot be measured until after selection has occurred** (carcass data)
- **are currently not selected for due to lack of available phenotypic data** (tenderness)