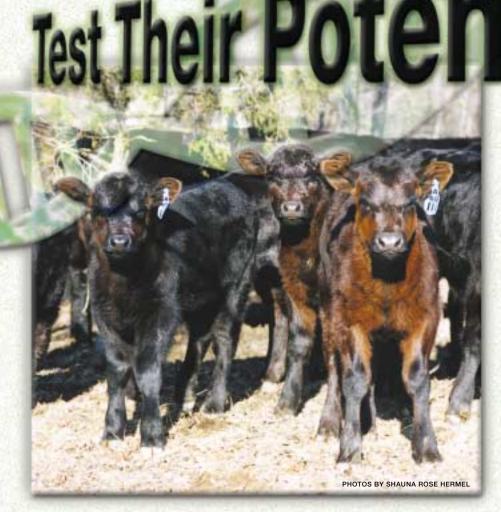
# GENETIC TECHNOLOGY:

Marker-assisted selection offers the ability to determine an animal's genotype—its genetic potential for a number of traits.



#### BY MAGGIE MARTIN

Technological advances aren't new to the seedstock industry. Artificial insemination (AI), estrus synchronization, expected progeny differences (EPDs) and embryo transfer (ET), to name a few, have each earned useful roles in beef-cattle breeding and have made substantial contributions toward breed improvement or production efficiency.

Marker-assisted selection (MAS) — using genetic markers in cattle selection — is the newest attempt to help producers compete in an aggressive marketplace. As each technology before it had to go through phases of research and development, industry introduction, refinement and adoption, so too will MAS.

"Producers have to be looking at information and making decisions about bulls as fast as an auctioneer can sell them," says Dan Moser, professor of beef cattle genetics at Kansas State University.

"The biggest benefit [from gene-marker tests] is that we're going to know exactly what genetic material an animal has. This is particularly true for traits, such as carcass characteristics, that otherwise can't be measured in an animal."

Although genetic-marker tests currently exist for only a few traits in cattle, Moser thinks the industry will see more in the next five to 10 years.

#### Know your cattle better

"Marker tests enable us to know more about the animals, be more accurate in our evaluation of them and use them accordingly," he says.

Moser explains that EPDs are calculated for yearling bulls by using their own measurements and the measurements of related animals. But lacking direct measurements for yearling carcass traits, producers must calculate them by averaging those of the sire and dam. Yet each animal receives a random half of the genetics of each parent. With genetic marker technology, a producer with a group of calves from a good carcass-trait bull could test the calves to see which half brothers received the preferred genetics.

When DNA results become available, Moser suggests, producers will need a system that they can digest easily, understand and use to make decisions.

"It can't be a system where we have 30 different tests and a bull has 15 pluses and 15 minuses," Moser says. "That's just not a useful kind of system. But that's what we have now."

Moser explains that the GeneSTAR marbling test, developed by Australian government researchers and recently purchased by GenomicFX of Austin, Texas, is the only test marketed to beef producers at this time. If a breeder submits a DNA sample for testing, test results would indicate if the animal possessed two, one or zero copies of the favorable gene.

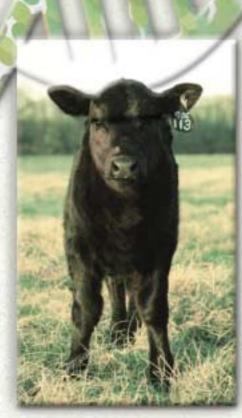
#### What's it mean?

"That's just fine for one test, but with 20 tests, that's information overload," Moser says. "We need a way to convey not only what tests the animal had and what the results are, but also the effects of each of those results. Producers want to know what the results realistically mean about an animal. There are many genes that influence marbling, fat thickness, growth and maternal traits. The industry will need to know which tests have what effect."

Moser says the system most geneticists envision incorporates marker information into EPD calculations. The models used for EPD calculations already are finished, Moser says. They have been published and peerreviewed.

"That's the easy part," Moser says. "The hard part is getting the data. If marker information is used in EPD calculations, then all the results need to be in the associations' databases."

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Certified Angus Beef LLC is funding research at Ohio State University (OSU) that focuses on genetic-marker tests.

In addition, all the results will need to be included because it's not enough to have only the favorable outcomes reported, Moser says.

To check for genetic markers now, a producer collects and submits a DNA sample — hair, blood or semen, depending on the test. The lab involved calculates the data and sends the results back to the breeder. Breeders choose what information to share with their breed associations and other producers.

Moser foresees a system similar to the kind associations use for blood-typing or DNA-marker-typing for parentage verification. When producers want to sell semen from a bull or use a cow for ET, they send a blood or DNA sample to a lab. The lab relays the results to the association, thus making it aware of any parentage problems. That system also would be useful for looking at DNA samples to determine if an animal carries any of the selected genetic markers.

### Cost vs. benefit

As with most technological developments, producers want to know how this will affect their bottom lines. Currently, technology's cost is highly variable. For example, the GeneSTAR marbling test is \$80/animal. "I think the cost of doing multiple tests will have to come down for this technology to be used," Moser says. "In the past, developing and running genetic-marker tests was university

running genetic-marker tests was university territory. Now, for-profit companies and industry groups are getting involved in DNA-marker research."

For example, labs may propose a marker they think influences marbling. They need to show the data that affects marbling, as well as how it affects fat; kidney, pelvic and heart (KPH) fat; growth; and maternal traits, Moser says.

"This includes the favorable and unfavorable effects associated with that marker," he says. "Then the associations will have to have some way to determine which are the meaningful tests to use."

Moser says the tests are patented because the sequence, or the chromosomes' locations, being tested is proprietary information. Researchers use a lot of resources to determine this information, so they want to keep the results secret.

A problem could occur if two different labs develop a test for marbling; it may actually be the same test, he continues. They do not share information because they don't want another lab conducting the same test at a cheaper price. This lack of sharing and potential duplication leads to intellectual-

# **Gene-mapping technology**

"The genes of cattle are responsible for their performance potential. Achieving that potential also depends on management, nutrition and the environment," Ohio State University research scientist Francis Fluharty says. "Detecting animals with the potential to have superior performance requires identification of the genes controlling the desired traits. Since we lack the technology to identify all the genes responsible for specific performance traits, genetic markers are used to identify a specific location (loci) on an animal's chromosome."

Dan Moser, professor of beef cattle genetics at Kansas State University, explains that chromosomes are structures in the nucleus of cells that store and transmit genetic information. A gene is the basic genetic code that causes an organism to have a certain characteristic. The precise locations of genes on chromosomes are unknown, justifying gene-mapping research.

Chromosomes are arranged into homologous pairs, being similar in size and structure. They also contain genes for the same traits. For example, cattle have 60 total chromosomes and 30 homologous pairs of chromosomes. Thus, they have two of each of the 30 different types of chromosomes, he says.

Moser states that each gene can take on two or more different

forms, called *alleles*, which result in different characteristics. For example, all Angus cattle have two genes for either black or red coat color, one on each member of a homologous pair of chromosomes.

Also, traits can be classified as either *qualitative* or *quantitative*. Qualitative traits are those that can be named. You can see traits like red vs. black coat color, diluted vs. non-diluted color, and horned vs. polled. One or a few genes determine these traits, and they fall into distinct classes.

"All performance traits of cattle are quantitative traits," Moser says. "Many, perhaps hundreds of genes, with each gene having a small effect, influence these traits. Because quantitative traits are the result of genes for factors that control growth, development, reproduction, lactation and other biological processes, they can't be seen just by looking at an animal.

"Genes that influence weaning weight may actually control production or recognition of hormones and other factors," he says. "Most economically important traits in beef cattle are quantitative. Genes that have a measurable effect on quantitative traits are [found at] *quantitative trait loci*, or QTLs. The gene likely turns on or off the synthesis of a hormone or other factor affecting the trait." property issues that create challenges for the industry.

Moser believes a central lab would help solve some of the problems.

"As a breeder, I would not want to send separate DNA samples from the same animal to Australia, Texas and California to have tests done," he says. "We need some kind of centralized lab that would run all the tests, regardless of who owned the samples."

### Leveling the field

Both small- and large-scale producers are interested in new technologies to improve herd development. All breeders could use gene-marker tests, whether they have 40 cows or 400.

"In some ways this technology can level the playing field," Moser says. "If you have superior genetics, here's a way to document it. The EPDs have done this to some extent as well. When you shop for bulls, you can compare different breeders' bulls equitably because the EPDs are unbiased. The more factual, objective information we have on the animal, the less it comes down to perception, opinion and promotion."

Although genetic-marker tests have numerous possibilities for the beef industry, some concerns do exist. It is possible to abuse any technology.

"There's a danger in overselecting for particular traits," Moser says. "We're not going to have markers for all traits, especially right away. Since many genes influence a particular trait, I hope breeders don't discount or throw away genetics because they come up short on one marker test. "I hope breeders don't discount or throw away genetics because they come up short on one marker test. Assuming that many different genes influence marbling, we shouldn't discount a bull with favorable marbling EPDs because of one unfavorable gene test."

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Producers, associations and beef companies need to educate the public about their research.

"When we talk about molecular genetics and marker-assisted selection, the uninformed public could say we're changing things," Moser says. "But we're not. We're still picking a bull and cow, allowing them to mate and produce offspring. We're just measuring them in a different way."

Genetic-marker tests don't entail gene manipulation, Moser says. Researchers are not taking genes from another organism and placing them in cattle.

"We're trying to increase the consistency of our product," Moser says. "With this technology, we have a better chance of getting the animal we want. There are no unfavorable effects, other than the perception."

One example of current research underway to find markers or actual genes that influence economically important traits is the National Cattlemen's Beef Association (NCBA) Carcass Merit Project. The project validates marker tests for economically important carcass traits, says Elizabeth Westcott, associate director of research and technological services for the NCBA.

"The primary goal of the project is to provide the tools and mechanisms to genetically identify superior animals in the U.S. beef population that will produce progeny with the greatest potential for meeting the demands of the consumers of CONTINUED ON PAGE 136

Moser says genes can be found by either direct mapping in the species of interest, such as cattle, or by comparative mapping from other species, such as humans or mice. Livestock species are more difficult to manipulate genetically than mice, and the generation interval is much longer.

He explains one example of comparative mapping benefiting livestock producers is the discovery of the red/black gene in cattle, formally known as the *melatonin receptor gene*. The red/black coat color gene first was mapped in mice. Researchers interested in cattle noted the discovery, and they noted that the location of the gene in mice correlated with a region on Chromosome 18 in cattle. Once they focused on that specific region, they were able to map the red/black gene in cattle. Similar efforts resulted in the mapping of the double muscling (myostatin) gene in cattle, Moser says.

Moser states that a genetic marker is a known DNA sequence that is believed to be located near a QTL. These markers have a statistical association with a particular trait. Markers are a step toward finding the actual genes for a trait, but in some cases, producers could use marker tests for selection before the precise location of the gene is known.

Markers often work well for selection within families, but unrelated

animals may not have the same association between the marker and the gene. The effect of the marker becomes more consistent as the marker gets closer to the actual gene. It is plausible that marker tests might be useful for all animals of a species, only several breeds, or only some families within breeds, he says.

"Gene mapping of traits that are difficult or expensive to measure provide the most benefit. For example, tenderness," Moser says. "This trait is difficult to measure but has economic importance. Using a gene test influencing disease resistance would be easier than selecting for optimum growth rate, since producers would want to achieve maximum resistance but would prefer an intermediate level of growth. If we had 10 gene tests each for disease resistance and growth rate, everyone would want all 10 disease resistance tests to be positive, but there would be disagreement on what level of growth is optimum."

Moser points out that, if genes exist having major effects on traits for which producers currently select, the favorable allele most likely already has been fixed in the population through traditional selection methods. today and tomorrow," she says. "Upon completion of the study, validated markers will be made commercially available to the industry. In addition, the participating breed associations will have generated individual databases, which will allow the development of EPDs for important carcass traits within each breed."

Westcott explains that the NCBA worked on the Genome Mapping Project for nine years. It identified 400 markers for several different traits in one population of Angus and Brahman cattle. In conjunction with four universities and 15 breed associations, the NCBA selected 11 quantitative trait loci (QTLs) — areas on chromosomes at which exist genes that have measurable effects on quantitative traits — to examine more closely. There are seven QTLs for tenderness, three for marbling and one for composition.

"Producers will be able to pull a blood, semen or tissue sample and send it to Celera AgGen for testing," Westcott says. "If testing a sire, the results will determine how many, if any, of the 11 markers that sire could possibly pass to his offspring. If testing the progeny, the results will show how many markers the animal actually has."

Currently, Certified Angus Beef LLC (CAB), a subsidiary of the American Angus Association, is funding research at Ohio State University (OSU) that focuses on genetic-marker tests. The goal of the project is to develop a rapid, low-cost assessment that can detect and identify the DNA markers for marbling and tenderness, says Francis Fluharty, research scientist at OSU.

Fluharty says using DNA technology is beneficial because, when used with ultrasound, it can assure that cattle are marketed with the correct amount of marbling to reach their desired market, whether it's seedstock breeders, cow-calf producers, feeder-calf auctions, feedlot operations or packing plants.

"For seedstock breeders, sire selection could be based on actual genetic potential for the desired customer market," Fluharty says. "Also, lines of cattle with the genetic potential to produce offspring with highmarbled and tender meat will become a reality, and offspring could be tested at birth for genetic potential. Thus, sire selections for the next calf crop could be done prior to mating that year."

Steve Suther, director of industry information for CAB, says the effects of a commercially available test for tenderness and marbling potential will be important to the entire beef industry.

"Producers with access to this DNA test would have a potential market advantage in a quality-based market, to say the least," he says. "A focus on flavor and uniformity could win back more of the consumer dollar to beef, and with the help of this test, a producer could respond quickly with confidence in hitting the target on virtually all of his calves."

Right now, most of the genetic research is in the final stages of testing, Moser concludes. Although a producer might say it isn't that important today, it could be important in one generation of cattle. More information could be available in a short time, he says.

"As a seedstock producer, I would position myself to use this technology," he says. "Producers should at least be educating themselves by reading the popular press. When it happens, it will happen very quickly. Those operations that can take advantage of this technology early will probably increase their success and give themselves a competitive advantage."

# Preserving genetic material

Though not every genetic marker has been discovered, some breeders may want to preserve genetic material to be tested later. If a seedstock producer is using a cow in embryo transfer (ET), a large percentage of the herd may trace back to her genetics in a few years. If in 10 years the cow is dead, it may be beneficial to test her instead of testing all her progeny. The sires to whom she was mated can be tested through frozen semen. Producers can preserve DNA material by taking an ear tissue punch, a blood sample or hair follicles. Because DNA is present in almost all cells of the body, some types of genetic tests can be performed directly on tissue samples without DNA extraction.

Some points to remember:

- Frozen semen—when available, it is an excellent source of DNA. One straw could be used for hundreds of tests. It can be stored in liquid nitrogen.
- Blood spotted on FTA paper a few drops of whole blood can be spotted and dried on a special card and stored at room temperature, presumably for up to 10 years. Each card costs a bit more than \$1 and is sufficient for roughly 100 tests.
- Hair follicles several service labs are accepting tail hairs with the follicle intact. They can be stored at room temperature for a

short term. At least three to five hairs are needed; kits for storing hair follicles on cards are available.

 Frozen blood – blood could be stored indefinitely in syringes or in inexpensive plastic vials.

These methods would allow breeders to keep samples on their ranch because they can be stored at room temperature or in the freezer. They are reasonably cheap to store. Some DNA service labs offer storage as a service or for a fee. Producers should check with each lab to find out what sample method they prefer.

The following is a list of animals from which samples could be taken:

- Sires
- Dams of artificial insemination (Al) sires
- Donor females
- Any progeny groups on which expensive or extensive phenotypes are collected
- In some elite herds, it may be beneficial to collect tissue from all animals, provided the cost of doing so is minimal.

**Source:** Information from Beef Improvement Federation (BIF) Symposium July 2000—R. Mark Thallman, U.S. Meat Animal Research Center, Clay Center, Neb.