ARSBC 2012: Genetics

DNA Testing

What we know, what we don't know and how to use it.

by **Troy Smith,** *field editor*

PHOTOS BY TROY SMITH

►"To know if a DNA test is any good, we need to know what percentage of genetic variation is explained by the test," stated Michael Gonda. "No DNA test can explain all the genetic variation for a trait, but the percentage needs to be high."

It's a blueprint for life, an instruction manual for everything that functions in a living thing. That's how geneticist Michael Gonda described DNA to an audience gathered for the 2012 Applied Reproductive Strategies in Beef Cattle (ARSBC) symposium in Sioux Falls, S.D. A South Dakota State University (SDSU) assistant professor and researcher, Gonda reviewed the development and application of DNA testing to aid genetic selection of cattle for breeding.

> **"DNA tests can be developed for most traits for which there are EPDs, and genomic-enhanced EPDs are going to be the standard for most breeds because of their higher accuracy."**
> *— Michael Gonda*

Gonda explained how a single gene can be responsible for the expression of certain simply inherited traits, while multiple genes influence complex traits. A DNA test for the presence of a gene known to be associated with a simply inherited trait may be highly accurate. A test for a gene associated with a complex trait may not be particularly accurate, because the complex trait is controlled by perhaps hundreds of genes. Consequently, not all DNA tests predict genetic merit with equal accuracy.

"To know if a DNA test is any good, we need to know what percentage of genetic variation is explained by the test," stated Gonda. "No DNA test can explain all the genetic variation for a trait, but the percentage needs to be high."

According to Gonda, some DNA tests are breed-specific, while others can be applied to cattle of any breed. Generally, breed-specific tests are more accurate. Ideally, he added, more highly accurate DNA tests applicable to multiple breeds will be developed in the future.

Gonda said the best practical application of DNA tests is to incorporate results in the calculation of expected progeny difference (EPD) values for respective genetic traits. The result, a genomic-enhanced EPD, then includes information representing an animal's pedigree, individual performance information, available progeny performance information and DNA test information. The significant advantage over traditional EPDs is the higher accuracy of genomic-enhanced EPDs as predictors of genetic merit.

"DNA tests can be developed for most traits for which there are EPDs, and genomic-enhanced EPDs are going to be the standard for most breeds because of their higher accuracy," said Gonda.

Gonda spoke during Monday's ARSBC session focused on genetics. Visit *www.appliedreprostrategies.com/2012/SiouxFalls/newsroom.html* to view the accompanying PowerPoint slides and proceedings paper.

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Who Got the Job Done?

DNA testing can help determine performance, economic value of bulls in a multi-sire breeding pasture.

by **Troy Smith,** *field editor*

►"The data suggest 72% of ranch income comes from calves born during the first 42 days of the calving season," said Alison Van Eenennaam.

According to geneticist Alison Van Eenennaam, the number of progeny produced by a given natural-service sire likely is the most dominant factor influencing ranch income. That was one take-home message shared during the University of California–Davis researcher's presentation to the 2012 Applied Reproductive Strategies in Beef Cattle (ARSBC) symposium. Based on results of a study led by Van Eenennaam, the ability to predict sire prolificacy would offer ranchers a significant economic advantage.

"What we'd like to see is bulls getting a large number of cows pregnant early in the breeding season. The data suggest 72% of ranch income comes from calves born during the first 42 days of the calving season," said Van Eenennaam.

Toward that end, it appears, some bulls can and will do their part. Other bulls can't do it, or maybe they just don't try.

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Van Eenennaam described the California Commercial Ranch Project, which evaluated nine calf crops from three different ranching operations using primarily Angus bulls in multi-sire breeding pastures. DNA paternity testing was applied to the roughly 6,000 calves evaluated.

Results indicated bulls sired from 0 to 54 progeny per calving season, Van Eenennaam shared. Even though all bulls had passed breeding soundness examinations (sometimes referred to as BSEs) prior to the breeding season, some bulls sired no calves. At the other extreme were the superstars.

The wide range of bull prolificacy resulted in large differences in the bulls' contribution to total ranch income, whether calves were sold as feeder cattle or ownership was retained until harvest. However, some bulls sired calves that were more profitable when marketed as feeders, while progeny of other bulls were more profitable when ownership was retained.

Noting that scrotal circumference has previously been linked to fertility traits in males and females, Van Eenennaam said the study results suggest size also matters to sire prolificacy.

"We saw a positive correlation for increased prolificacy with scrotal circumference EPD (expected progeny difference). I don't want to overstate it, but at least 5% of total variation (in prolificacy) was explained by scrotal circumference. Cow Energy Value Index ($EN) also was positively correlated, explaining about 3% of the variation," said Van Eenennaam, adding that milk and carcass weight EPDs were negatively correlated.

Based on market prices at the time of analysis, according to Van Eenennaam, the research suggests that each unit increase (1 cm) in scrotal EPD would be associated with 8.2 more progeny, and in excess of $7,000 more ranch revenue, per sire, when calves are marketed as feeder cattle or when ownership is retained. Each unit increase in $EN index would be associated with 0.45 more progeny and a little more than $350 more income, per sire. Income estimates are based on cattle prices at the time study results were analyzed.

"Collectively," concluded Van Eenennaam, "this suggests scrotal circumference EPD, and possibly $EN, should be included in bull selection decisions to increase prolificacy and total income under natural-breeding systems similar to these ranches."

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Genetics of Reproduction

Differences in ovarian morphology exist at birth, but trying to find genetic markers for traits so heavily influenced by environment proves difficult.

by ***Shauna Rose Hermel,*** *editor*

Assisted reproductive technologies, or ARTs, can increase the rate of genetic improvement in beef cattle, but there are some cautions to keep in mind, Robert Cushman said. A reproductive physiologist at the Roman L. Hruska U.S. Meat Animal Research Center (USMARC) in Clay Center, Neb., Cushman explained that reducing the number of influential parents increases the risk of propagating a lethal recesssive gene, and placing embryos in culture during *in vitro* fertilization (IVF) can actually change the way genes are expressed and the way they function.

►"A true inherent failure of fertility doesn't happen very often," said Robert Cushman, noting that only about 1% of heifers will fail to conceive in two consecutive breeding seasons. Most of the time, failure to breed is a result of environmental factors.

While cautions, these are not reasons to fear ARTs; they are reasons to incorporate genomic technologies into ART, Cushman said. "If we continue to understand what the genome is telling us and how we can use the genome, then we can potentially improve our assisted reproductive technologies."

Cushman explored what is known about the genetics of reproduction during the 2012 Applied Reproductive Strategies in Beef Cattle (ARSBC) symposium in Sioux Falls, S.D.

We know that reproductive traits are lowly heritable, Cushman noted. They are polygenic, meaning many genes have small effects. In addition, there are large environmental effects, including nutrition and animal health, that contribute to whether a cow conceives.

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"A true inherent failure of fertility doesn't happen very often," Cushman said, noting that only about 1% of heifers will fail to conceive in two consecutive breeding seasons. Most of the time, failure to breed is a result of environmental factors.

Cushman agreed with other ARSBC speakers who said genetic markers for production traits would likely be adopted first because they provide economic benefits more quickly. However, in adopting those genetic markers, cattlemen need to keep an eye on how they affect fertility.

We don't know that in stacking genes for production traits we won't negatively impact fertility, Cushman said. Whether talking panels of genes or ascertaining net merit with indices, he encouraged inclusion of whatever markers are available for fertility — even if the goal is not to improve fertility, but to make sure we don't negatively impact fertility.

"Genetics are not easy," Cushman added, pointing to the low heritabilities of pregnancy (7%) and stayability (15%). Heritabilities of traits related to heifer development are higher (see Table 1), offering potential to find genetic markers to foster improvement.

Differences in ovarian morphology exist at birth, Cushman said. In studies looking at ovaries removed from newborn heifers, some heifers had ovaries twice as heavy with more antral follicles (the large follicles visible by ultrasound that contain an egg) than others. That begs the question, when does heifer development start?

"Heifer development starts when the undifferentiated gonad actually starts to turn her into a female," Cushman said, referring to cellular development of the reproductive tract. There are a host of growth factors that affect sexual differentiation from an undifferentiated gonad to a very infantile tract to a more mature male or female tract.

"If you start deleting certain genes at the upper end before the gonad has differentiated, you can have a double effect," Cushman said, noting results of small testes and fewer sperm in males, and small ovaries and fewer or no follicles in females. "If you are at a high enough region in that genetic path and you turn genes off or alter their effect, you can influence gonadal development no matter which direction they're going in (male or female), which to me is that connection that we see, at least genetically, between scrotal circumference, age at puberty and female performance."

According to USMARC data, females that calve early as heifers will be more likely to stay in the herd to 5 years of age, and they will continue to wean a heavier calf through their

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Table 1: Heritability of reproductive traits

Trait	Heritability	Reference
Age at first ovulation	0.28	Mialon et al., 2001
Age at first progesterone	0.38	Mialon et al., 2001
Age at puberty	0.14	Snelling et al., 2012
	0.24	Morris et al., 2000
Reproductive tract score	0.30	Martin et al., 1992
Yearling uterine horn diameter	0.20	Johnston et al., 2009
Antral follicle count	0.44	Snelling et al., 2012
Age at first calving	0.28	Minick Bormann and Wilson, 2010
Heifer pregnancy rate	0.21	Doyle et al., 2000
	0.28	Thallman et al., 1999
Pregnancy rate	0.07	MacNeil et al., 2006
Stayability	0.15	Doyle et al., 2000

Sources: Cushman et al., 2008. *R Bras Zootec* 37:116

Cammack et al., 2009. PAS. 25:515

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fifth or sixth calf. That affects your bottom line, Cushman said. But how do you select for heifers that will calve early other than by selecting the biggest — and theoretically oldest — heifers, which can have negative repercussions on cow size.

One option is to breed all the heifers, then pregnancy-check them by ultrasound at 21 days and keep those that conceive. Another option is to limit the breeding season to 21 days, keeping only those that conceive. Reproductive tract scores (RTS) provide another good way to analyze reproductive development.

Using ultrasound to assess the antral follicle count (AFC) can also provide an idea of reproductive capacity, Cushman said. Heifers are born with about 100,000 primordial follicles. Studies have shown that heifers with more than 100,000 primordial follicles also had more secondary follicles and more antral follicles than heifers born with fewer than 100,000.

In his research, Cushman used ultrasound to classify heifers as low-AFC (fewer than 15 antral follicles) or high-AFC (more than 25 antral follicles). The difference in subsequent pregnancy rates was 85% for the low-AFC heifers and 95% for the high-AFC heifers.

While a 10% difference in pregnancy rate is substantial, it doesn't mean that the low-AFC heifers were infertile, Cushman emphasized. An 85% pregnancy rate means those heifers were fertile. The high-AFC group was just more fertile — and for reasons still to be discovered.

In another study comparing AFC of heifers calving in the first, second or later 21-day period, heifers calving in the first 21 days had a four-follicle advantage in AFC.

While there is a correlation between AFC and histology, AFC only predicts about 30% of the variation in ovarian reserve, Cushman said, pointing to the need for other predictors, preferably combined in a panel of traits that can explain a larger percent of the variation in fertility.

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— Robert Cushman

"Variation in the genetic sequence that results in a change in the function of the encoded protein makes the best genetic markers because their identity and function can be clearly understood," Cushman explained in his proceedings paper. "However, the identification of functional polymorphisms within a gene is the most difficult aspect of this work."

Progress is being made, especially in human research, in the area of pharmacogenetics — a concept that you can tailor hormonal or medicinal doses to a person based on their genetic makeup, Cushman noted. Common hormones used in synchronization and superovulation — gonadotropin-releasing hormone (GnRH), follicle-stimulating hormone (FSH) and prostaglandin F2α (PG) — all work through protein receptors. Different genotypes for a receptor may function differently, changing the dose of hormone needed.

To explain variation in ovulatory response due to superovulation, USMARC researchers conducted a whole-genome scan and worked their way down to a gene on chromosome 6. The polymorphism in the ionotropic glutamate receptor AMPA1 (GRIA1) had previously been reported by Sugimoto et al. as a functional polymorphism, changing the amino acid sequence. The researchers reported that animals homozygous for the serine amino acid and heterozygotes had antral follicle counts up around 20. Cattle homozygous for asparagine, which changed the receptor, had lower AFC. The researchers proposed the change to asparagine changed the binding affinity of the hormone receptor. They reported decreased GnRH secretion, a decreased luteinizing hormone (LH) surge after synchronization with PG and decreased AI conception.

A USMARC study found no difference in the AFC of beef cows carrying the polymorphism vs. those that didn't; however, when they compared repeat breeder cows (cows that failed to conceive in two breeding seasons) to cows that had calved throughout their lifetime, the repeat breeders had fewer follicles. There was no difference in age at first breeding, but the repeat breeders were about 40 days older at first calving. Their ovaries were smaller and the diameter of the uterine horns was smaller.

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