Just Because You Have a Genetic Test Doesn't Mean You Can Throw Away Your Tape Measure

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"It's not like we can take one DNA test and have it tell us everything and remain accurate forever," says Dr. Alison Van Eenennaam, PhD. "We're going to always need phenotypes to keep training [genomic] prediction equations. They're not mutually exclusive things."

Van Eenennaam is a Cooperative Extension Specialist in Animal Genomics and Biotechnology at University of California, Davis, specializing in the use of DNA-based biotechnologies in beef cattle production. She explains what it means to "retrain" genomic equations.

"DNA markers are developed using a large population of animals that have genotypes and phenotypes of whatever trait we're interested in - a population of animals that has ultrasound and possibly carcass records – their own or their progeny's. To predict marbling, for example, that large population of phenotypes is combined with the genotype information to tell you whether or not a particular genetic marker has a positive or negative association with marbling."

Dr. Alison Van Eenennaam

Van Eenennaam continues. "Let's say at one particular marker TT is good for marbling and CC is bad for marbling. And if you do that throughout thousands of locations on the genome, you can start to get what's called a prediction, based on an animal's genotype, as to what its likely marbling phenotype is going to be. But, it's based on that training, or discovery, population.

"And what the data seems to be showing is that yes, you can train and then you can predict an animal just based on its genotype with no phenotypic information, but every generation the accuracy of how well that prediction works tends to go down. And so, it seems continual retraining of the prediction equation every generation is required. So, there's going to be a need to continue phenotyping. According to Van Eenennaam, the data shows the accuracy of that genomic prediction equation decreases as much as 50 percent every generation.

"It'll depend a little bit on the density of the markers, and whether you have a causative or associative marker," she explains. "If you have a DNA marker that is actually *causing* the marbling, the accuracy wouldn't change very much from generation to generation. But what has been found is that we've not actually got the causative marker, but rather a marker that's "linked to" the causative marker. It's like a little flagpole saying, 'it's over here somewhere.' As a result of recombination, there's a possibility that it might not be associated with that particular causative marker in the next generation. And so, you tend to get a drop off in the accuracy of those equations over time, as the generations move away from the training population."

There are thousands of genes associated with a complex trait like marbling, not one single marker that can be considered causative, as is the case with most carcass traits.

"To be honest, we haven't found that many actual causative genes for complex traits," says Van Eenennaam. "Despite all the work we've done there's only really a handful where you can show that an animal that didn't get a mutation, or genetic variant, had one particular phenotype and one that does have the variant has that phenotype. Myostatin, or double muscling is an example. Van Eenennaam explains if a mutation is caused in that particular gene and that protein is not formed, the result will be a double-

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muscled phenotype. But it's more complex with traits like marbling that are not controlled by a single gene.

Different Breeds, Different Animals

Currently the Angus breed leads the way in utilizing genetic markers. "DNA can be an indicator for economically important carcass traits," says Bill Bowman, President of Angus Genetics, Inc. and Chief Operating Officer of the American Angus Association. "The AAA has made it a priority to utilize genetic selection tools to serve the breed and the industry."

Hereford breeders are developing genomic tools for their breed, and others are following suit. But, as Van Eenennaam further explains, what works on one breed does not carry over to another.

"The data shows quite clearly that if you train on one breed using the 50,000 or 50K SNP chip, those predictions don't work in another breed. The hope was that if we went up to a denser genotyping platform - an 800,000 SNP chip - the marker would be situated immediately adjacent to the causative allele, such that the relationship would be so tight that it would be in common between say Angus and Hereford. At the current time there are insufficient data to determine whether this is actually the case. "It may be that we have to go to actually sequencing animals and there are a couple of labs now that are starting to sequence entire genomes to find the causative mutations in order to get right on top of where the change is that's affecting the phenotype. Hopefully that will be useful across breeds. And it typically will be, although not every breed is going to be what's called polymorphic for that particular mutation. For example, if I get something that's causing an increase in marbling in Angus it may be that particular mutation doesn't exist in Herefords or maybe it's already fixed to unity in Herefords so there's no genetic variation there to play with. So, let's just say, in one particular location, a "T" is a good thing, it may be there's no Herefords with a "T" at that location, or maybe *all* the Herefords have a "T" at that location and so there's not genetic variation to select for.

"At the moment the best approach seems to be to use multiple breeds in the training population. There are some data to suggest that can actually help obtain accurate predictions for all the included breeds.

Predicting Profit

Van Eenennaam says genomic tests offer the most promise for traits that display low heritability. Those with a high heritability, such as birth or weaning weight, are visually obvious and can be measured before the animal produces offspring, thus reducing the need for genomic prediction. But traits that don't appear until later in life, such as carcass traits, are very well-suited to genomic selection because it gives an indicator of how that animal's going to perform before selection decisions are made.

"Now, having said that, that's exactly what ultrasound does," says Van Eenennaam. "DNA tests give you a genetic merit estimate, and ultrasound gives you a phenotypic prediction as to the likely carcass quality attributes of a live animal. And we need new phenotypes every generation to keep the genomic tests accurate."

Bowman agrees the need for ultrasound generated phenotype data is ongoing. "We still need to look at the phenotypic evaluation," he says. "Ultrasound is a valuable information source that enhances the accuracy of the breed's EPDs. It continues to play an integral role in generating reliable predictions."

"And that way," adds Van Eenennaam, "producers can make decisions based on the genetic merit of the animals in their herd with some level of accuracy."