Do DNA Tests Work?

DNA tests hold tremendous promise. But questions remain.

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Sales literature claims DNA tests can be used to accurately evaluate genetic potential of cattle at birth, and ultimately improve your bottom line. While it is evident that animals can be genotyped at a young age, producers often ask me, "Do DNA tests work?" The answer to that question is, as with many questions, "It depends."

It depends on your motive for testing, and what you mean by "works." DNA-based tests can be used for various purposes: selection and breeding decisions, feedlot sorting, pedigree verification, and as a marketing tool. Their utility for these applications requires knowledge of both how well they work in cattle populations where they are to be applied, and the cost of testing. In the absence of these two pieces of information, it isn't possible to evaluate the costs and benefits associated with the use of these tests, and so it's not possible to determine if they "work."

Some seedstock producers are testing their bulls to provide potential buyers with DNA information. The value of that information to the buyer is determined by the market. If the value is deemed to be more than the cost of testing and is reflected in the bull purchase price, then the test "worked," at least as a marketing tool.

However, many people are interested in using DNA test results for marker-assisted selection (MAS) — using the results of DNA-marker tests to assist in selecting individuals to become parents of the next generation. Therefore, as a geneticist, I interpret the real question being posed when producers ask whether DNA tests work as whether they "work" to improve the accuracy of genetic predictions sufficiently to justify the expense.

The answer to that question is again, "It depends" — on which trait is being examined, which test is being used and how much it costs, and in which breed or population the test is going to be used.

Breed differences

Traditional methods of DNA marker discovery have focused on finding genetic markers in locations on chromosomes that are experimentally known to have an effect on the trait of interest. Rarely has the marker been the actual DNA sequence causing the effect; rather, the marker flags the approximate location of the causative or "good" sequence.

However, the relationship between the marker and the good sequence may differ among breeds. For one breed, a marker might be linked to the DNA sequence causing the desirable effect on the trait; in other breeds, there may be no effect of that marker on the trait, or the marker might even flag the "bad" sequence. The predictive value of a DNA test decreases when markers are incorrectly associated with the trait of interest in a given breed or animal.

The U.S. National Beef Cattle Evaluation Consortium (NBCEC) has been involved in the process of independently validating commercial DNA tests for quantitative beef quality traits since their first appearance on the U.S. market in the early 2000s (results are posted at www.NBCEC.org). Validation is a critical activity to test the strength of support for the genotyping company's published claims based on independent data. This process sometimes revealed that tests did not perform as expected; in certain cases, companies chose to withdraw those tests from commercialization.

Problems arose as the DNA-testing industry matured from single marker tests to multiple-marker "panels" with effects on numerous traits. The NBCEC and DNA testing companies struggled to find appropriately phenotyped populations that were not involved in the discovery process for validation studies. Such populations are rare, as they are expensive to develop and phenotype.

Additionally, results from different breeds and cattle types (e.g., *Bos taurus, Bos indicus*) genotyped with the same single-nucleotide polymorphism (SNP) panel were often inconsistent with respect to the significance of the association between the test and the trait(s), and sometimes even with respect to the direction of the association (i.e., a good DNA test result in one breed was the least desirable result in a different breed).

This complicated the interpretation of validation results, and created confusion as to whether “validation” meant a test “worked” (was significantly associated with the trait) in all or some breeds, or whether the test had simply been evaluated by an independent third party. This exposed the process to marketing zeal and left producers confused and somewhat stymied because the data reported (significance of the association) did not really help to inform decisions about the value associated with investing in specific DNA tests.

Accuracy

The accuracy of a DNA test at predicting the true genetic merit of an animal (improving accuracy) is primarily driven by the amount of additive genetic variation accounted for by the DNA test. Current estimates of the proportion of genetic variation accounted for by existing tests are generally low (0.0-0.10), although this number is not readily available for all tests.

A key criticism of the currently available tests is that their ability to predict genetic merit is limited. The exception is tenderness DNA tests, where available estimates for the proportion of genetic variation range from 0.016 to 0.299 (www.beefcrc.com.au/Aus-Beef-DNA-results). Over time, it's envisioned that genetic tests will have markers associated with the majority of important genes influencing a trait. In other words, it is hoped that in the future, genotyping results will be highly predictive of the true genetic value of an animal.

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In the interim, however, from the user's perspective, perhaps the most useful information that could be provided is how much accuracy improvement can be expected from adding DNA test information to EPDs. Publishing traditional EPDs and marker information separately, as is currently the case, is confusing and can lead to incorrect selection decisions when marker scores predict only a small proportion of the genetic variation.

Creating an approach to developing marker-assisted EPDs seems to be a logical next step in the implementation of DNA tests into national genetic evaluations.

A paper recently submitted to the *Journal of Animal Science*, entitled “Genetic Evaluation of Angus Cattle For Carcass Marbling Using Ultrasound and Genomic Indicators” by M.D. MacNeil, J. D. Nkrumah, and S. L. Northcutt, examined the impact of including DNA-marker data from a 114-marker panel that was calculated to have a genetic correlation of 0.37 with the marbling (i.e., the test explained (0.37)2 = 0.137 of the additive genetic variation) in Angus cattle.

For animals with no ultrasound record or progeny data, the marker information improved the Beef Improvement Federation accuracy of the Angus marbling EPD from 0.07 to 0.13. So this test “worked” in Angus cattle (there was a correlation between the genetic test result and the trait of interest) and the test was associated with 13.7% of the genetic variation in marbling.

It isn't clear how the marker panel examined in this paper relates to the version of the test that is currently on the market. This is an important point as companies are constantly developing new, and presumably improved, marker panels. These panels are proprietary and which markers are used in various versions is confidential.

This creates an obvious problem for entities charged with developing EPDs. The genetic parameters required to incorporate DNA information into EPDs need to be re-estimated for each new marker panel, and correspondingly, DNA results using a specific version of a test will have to be incorporated into genetic evaluations using the appropriate values for that test version.

This is a logistical problem for genetic-evaluation providers, and at the current time it also appears that these parameters may have to be individually determined for each breed. This is quite a daunting prospect given the imminent commercialization of a multiplicity of products derived from high-density, SNP assays.

Do they work?

So do DNA tests work? At the current time, tests on the market explain 0-30% of the genetic variation associated with various traits. A test that explains 0% of the variation is of little use. A test that explains 30% may be very useful for improving the accuracy of genetic predictions, although its worth is dependent on the economic value associated with the trait it predicts.

DNA tests for traits that are collected after culling decisions are made are likely to be of greater value than tests for traits that can be easily measured early in life. Details of how DNA tests perform in representative populations are needed to enable an informed decision regarding the use and value of these tests. Currently such details (proportion of genetic variation accounted for by a DNA test panel) are not reported on the NBCEC validation site, although they will be reported for all future validations. This will assist with plans to incorporate DNA data into the existing genetic evaluation infrastructure to develop marker-assisted EPDs with an associated accuracy.

Such an approach is appealing as it presents results in a format that is familiar to producers, and it eliminates the choice that is implicitly associated with the current practice of publishing traditional EPDs and marker information separately.

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