Interpretation of Haplotypes Impacting Fertility

Starting with the release of the December 2011 genetic evaluations, Canadian Dairy Network (CDN) will be making results available for the recently discovered haplotypes that impact fertility. These include three for the Holstein breed, labelled as HH1, HH2 and HH3 (i.e.: Holstein Haplotypes 1, 2 and 3, respectively) and one each in the Jersey (JH1) and Brown Swiss (BH1) breeds. As usual with any new piece of information available, it is important for dairy producers to understand how "Haplotypes Impacting Fertility" will be identified and published and how to use this new diagnostic tool in their breeding programs.

What Are Haplotypes?

As part of the North American agreement to share all DNA genotypes for dairy cattle in Canada and the United States, the databank of genotypes now counts over 130,000 for Holsteins alone and thousands are added each month. These genotypes are not only the basis for genomic evaluation calculations but breed associations such as Holstein Canada use them for confirming parental information for registered animals as well as discovering parents when they are not known or recorded.

While it is clearly understood by most that DNA is transmitted from parents to progeny, with half from the sire and half from the dam, the specific details of gene transmission remain vague. Simply stated, the DNA strands are transmitted in short sections which are called "haplotypes". The haplotypes received by an animal from each parent are combined to create its genotype. Since a specific haplotype can vary in length, one or more genes may be included in that section of the DNA strand.

The new "Haplotypes Impacting Fertility" discovered in each breed by researchers at USDA in the United States have been found to have an association with reduced fertility stemming from embryonic loss at some stage of pregnancy. These haplotypes are not exact genes and they are also not genetic recessives with a known biological impact.

Publication of Results for These Haplotypes

Given that haplotype results are not yet exact and they may change for a small proportion of animals, CDN and Holstein Canada have agreed to not publish specific "Carrier" versus "Free" codes. Instead, a unique approach developed at CDN will yield a "Carrier Probability" value for every animal in the CDN database. For Holsteins, since there are three new "Haplotypes Impacting Fertility", each animal will receive a separate Carrier Probability for HH1, HH2 and HH3, expressed as a simple percentage value between 1 and 99. To compute the probability values for each animal, the starting point will be the haplotype results for the males and females with a 50K genotype, which currently count over 75,000 for Holsteins. From these genotyped animals, a relatively small group of non-genotyped animals will also have their haplotype result inferred when they have a genotyped progeny determined to be a Carrier and the other parent is genotyped but is not a Carrier. The 50K genotyped animals and those with an inferred result will receive a published Carrier Probability of 99% if results indicate they are a carrier or a published Carrier Probability of 1% if the result indicates the animal is not a carrier. Therefore published probabilities of 99% and 1% will not be assigned 100% or 0% values to account for the possibility of haplotype inaccuracies and/or improvements in methodology over time.

All Carrier Probability values for the new "Haplotypes Impacting Fertility" will be publicly displayed on the CDN web site within each animal's "Pedigree Tree" page, which is directly linked to its Genetic Evaluation Summary page. The animal's own Carrier Probabilities will be displayed in the top section immediately below the usual line of various codes including coat colour and genetic recessive tests (i.e.: ET, BW, BLF, CVF, BYF, etc...). Within the Pedigree Tree, the Carrier Probabilities will be presented for the animal's parents and grandparents, whether genotyped or not.

Usage and Importance

Earlier this year, the discovery of new "Haplotypes Impacting Fertility" stirred up some interest as well as confusion regarding their importance and usage in breeding programs. There are three critical points to remember when considering the new Carrier Probability values published by CDN effective December 2011:

(1) Although these haplotypes are clearly associated with reduced fertility, there is no knowledge of the underlying biological processes that result in the observed embryonic loss.

(2) Given the recessive nature of these haplotypes, embryonic mortality will only occur for one-quarter of all pregnancies resulting from two known carrier animals being mated together. For all other matings, the risk of embryonic loss is not affected.

(3) Given that CDN already calculates and publishes genetic evaluations for female fertility traits, both individually and within the Daughter Fertility index, extra attention to exclude carrier males or females from a genetic selection strategy would lead to some level of double counting the impact of the "Haplotypes Impacting Fertility".

In addition to publishing the Carrier Probability values on its web site, CDN also plans to collaborate with industry partners in terms of promoting the appropriate use of this additional information. In particular, the intention is that any breed association involved would also provide the same Carrier Probability values on their respective web site. Also, CDN will provide data files that include Carrier Probabilities to A.I. organizations offering mating programs in Canada to give producers the opportunity to establish criteria for excluding matings between animals that have a high Carrier Probability.

Summary

Effective December 2011, CDN will be publishing Carrier Probabilities, expressed as a value between 1% and 99%, for each of the new "Haplotypes Impacting Fertility". This additional information may be useful for inclusion in A.I. mating programs to reduce the frequency of breedings between carrier animals. Caution is warranted not to place too much focus on these results in terms of genetic selection criteria. Undoubtedly, the discovery of these influential haplotypes will some day lead to the identification of the specific genes (rather than haplotypes) underlying the observed embryonic loss as well as an understanding of the affected biological processes. ■

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