Update on Holstein Haplotype associated with Cholesterol Deficiency (HCD) for August Genetic Evaluations

Information on a newly discovered unfavorable haplotype in Holstein cattle, known as haplotype associated with cholesterol deficiency (HCD), will be made available with next week's official genetic evaluation release. Calves who are homozygous for the unfavorable form of the haplotype only survive for a few months after birth. This new haplotype was identified by German researchers and first reported at the July 2015 Interbull meeting.

According to reports from German researchers, calves inheriting the homozygous form of the unfavorable haplotype presented with chronic diarrhea, did not respond to any treatment, and tested negative for pathogens that may cause those symptoms. The calves became very thin, depleting all fat reserves in the body, and in their weakened state, sometimes developed secondary diseases such as pneumonia. In the majority of cases, death occurred between three weeks and six months after birth, from apparent starvation, or from complications of a secondary disease. Economic impact of HCD is estimated to be approximately $450 per case, including the value of the calf, cost of raising until death, and medical treatment. There is no treatment or cure for affected calves.

Since the genetic variant causing this genetic defect is relatively new, the haplotype carrying the defect is difficult to track because both the normal version and the unfavorable version occur frequently, especially in Canadian Holsteins. The earliest known carrier of the unfavorable haplotype is Maughlin Storm-ET (HOCAN000005457798), born in 1991. The primary source of the normal form of the haplotype is Willowholme Mark Anthony (HOCAN000000334489), born in 1975.

The exact genetic variant causing this inherited condition has yet to be identified. Researchers have been able to narrow down the search to a haplotype which encompasses the precise location of the genetic defect. The two haplotype versions look identical when examining only the surrounding marker genotypes. Pedigree information, combined with knowledge of the haplotype status of earlier ancestors, allows for an accurate determination. An animal's true HCD status is simple to determine when only one of those two ancestors appears in the pedigree, but is more difficult to ascertain when both appear, which is not uncommon for younger animals. This leads to different coding than what has previously been used for Haplotypes Impacting Fertility, with two new codes denoting "suspect" animals. USDA-AGIL, CDN and Germany's VIT are cooperating to improve the precision of HCD tracing.

"The discovery of HCD is an example of how genomic testing, coupled with excellent data collection, good pedigree data and rigorous scientific investigation has led to valuable genetic information," says Dr. Tom Lawlor, Executive Director of Research at Holstein Association USA. "However, the lack of a gene test indicates that more work needs to be done in obtaining a more complete genetic map of the full sequence of our cattle, as well as obtaining a better understanding of the metabolic pathways involved. Labeling this haplotype as a Cholesterol Deficiency indicates our knowledge of this genetic condition today. The actual name of this inherited disorder could change when the precise error in lipid (fat) metabolism and/or the actual gene involved is discovered."

Holstein Association USA encourages breeders to pay attention to pedigrees, work to learn the status of their animals, be mindful of the status of service sires in their herd, and avoid mating carriers of individual

unfavorable haplotypes to carriers of the same haplotype. Discovery and labelling of these haplotypes is a benefit of genomic testing, and gives breeders the opportunity to improve the genetic quality of the breed through careful mating.

Codes of 0 to 4 are being used to denote an animal's status, with approximate percentages of animals in each category shown below, as of July 2015. Animals with missing pedigree were coded as non-carriers (0) in the counts below, but will have code 3 in the future if they carry a haplotype but lack the pedigree to determine its source.

Haplotype Code	% Affected Animals	Description
0	94.0%	Non-carrier: free of HCD
1	4.4%	Carrier: haplotype confirmed with pedigree information
2	0.03%	Homozygous: confirmed on both sides of pedigree
3	1.6%	Suspect carrier: haplotype origin could not be confirmed from pedigree
4	0.02%	Suspect homozygous: probable carrier and may be homozygous; origin of haplotypes could not be confirmed from pedigree

HCD results will be available for all animals who have been previously genomic tested, after the August 2015 genetic evaluation, and Holstein Association USA is making this information available in a variety of places. Lists of tested animals will appear on the Holstein Association USA web site, and HCD status will also appear on the Family Tree Search results in the haplotype section. Breeders using Enlight™ may use the Genetic Conditions report to view the status of all tested animals in their herd, and the haplotype result will be available on Holstein Association USA's preliminary and interim genomic reports after the release.

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