Holstein Haplotype for Cholesterol Deficiency (HCD)

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A new defect was discovered in Holsteins that causes young calves to die if homozygous and was reported at the July Interbull meeting in Orlando by Kipp et al. (2015) at VIT in Germany. They concluded that heterozygous animals have reduced cholesterol, but homozygotes have no cholesterol and survive only a few months. The particular haplotype carrying the defect is difficult to track because a normal version and a recently mutated version are both very frequent, especially in Canadian Holsteins. The exact mutation has not yet been determined, and the two haplotype versions look identical when examining only the surrounding marker genotypes.

The defective haplotype traces to HOCAN000005457798 MAUGHLIN STORM born in 1991. Storm's sire and maternal grandsire are genotyped and do not carry HCD. Storm's maternal great grandsire HOCAN000000299855 FAIRLEA ROYAL MARK born in 1966 is not genotyped but is the sire of HOCAN000000334489 WILLOWHOLME MARK ANTHONY born in 1975, the primary source of the normal version of the haplotype. The mutation causing HCD must have occurred in the 3 generations between Royal Mark and Storm. Mark Anthony must have a normal version of the haplotype because the following bulls received his haplotype through their maternal lines, and homozygous calves descending from these bulls live normal lives: (HOCAN000005319769 COMESTAR LEADER, HOCAN000005757117 COMESTAR LEE, HOCAN000006026421 COMESTAR OUTSIDE, HOCAN000006663935 COMESTAR LHEROS). HCD status is easy to determine for animals with only Storm in their pedigree, but is more difficult if both Storm and Mark Anthony appear, and that happens often with young animals. AGIL, CDN, and VIT are cooperating to improve the precision of tracing HCD.

VIT released carrier status with label CDH instead of HCD and using a 2-code system along with similar codes for HH1 through HH5:

IN = noncarrier

IV = suspect carrier

Codes of 0 to 4 are proposed for reporting HCD in USA, CAN, ITA, and GBR, with numbers and percentages of animals in each category shown below. Animals with missing pedigree were coded as noncarriers (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.

0	772,675	94.0%	Non-carrier: free of HCD
1	35,793	4.4%	Carrier: haplotype confirmed with pedigree information
2	286	0.03%	Homozygous: confirmed on both sides of pedigree
3	12,996	1.6%	Suspect carrier: haplotype origin could not be confirmed from pedigree
4	198	0.02%	Suspect homozygous: probable carrier and may be homozygous; origin of haplotypes could not be confirmed from pedigree

Codes from VIT were matched with the codes above calculated from June 2015 CDCB data, after combining proposed codes 1 and 3 to mimic VIT code IV. A total of 2,344 bulls had genotypes in both datasets, and results were:

2,113 were noncarriers in both VIT and CDCB data

203 were carriers or suspect carriers in both VIT and CDCB data

23 were suspect carriers in VIT but noncarriers in CDCB data

5 were noncarriers in VIT but suspect carriers in CDCB data

Some bulls differed because VIT checked only if Storm is in the pedigree, whereas AGIL checked if the pedigree paths leading to Storm or Mark Anthony were blocked by noncarriers. This AGIL strategy ruled out more suspects. The bulls matched above had nearly complete pedigrees, whereas commercial cattle with incomplete pedigrees or with fewer maternal ancestors genotyped may give less consistent results.

HCD caused calf loss in Germany and also within the Storm descendants based on USA data. A list of homozygous Storm descendants that had no Anthony in their pedigrees included about 100 calves born > 2 years ago. The earliest 11 homozygous USA females had no breedings recorded and no lactations (we did not check the younger ones), and none of the homozygous males entered an AI company or had any daughters, consistent with the calf loss hypothesis. Termination codes were available for 5 of the 11 heifer calves, and they had 2 code 6's (died), 2 code 2's (sold for dairy, perhaps to a heifer grower), and 1 code 5 (left herd for other reasons). Many owners and processing centers do not provide termination codes for calves. However, HCD did not always cause early losses in Canada, with some suspect homozygous females living to 2 years of age. Later investigation found that the US pedigrees for these were incomplete, and one of their haplotypes could have been the normal version from Mark Anthony.

Calf losses have more economic impact than most of the other haplotypes that cause early embryo loss. Thus, HCD may be more similar to BLAD, BH2, or the new FH2 and FH3 calf loss defects discovered in Fleckvieh (Simmental) by Pausch et al. (2015). Calf survival has low heritability, but recessive defects should be avoided by selection and mating programs.

More information:

http://www.vit.de/index.php?id=milchrinder-zws-online&no_cache=1&L=1#c2493

Pausch, H, H Schwarzenbacher, J Burgstaller, K Flisikowski, C Wurmser, S Jansen, S Jung, A Schnieke, T Wittek, and Ruedi Fries. 2015. Homozygous haplotype deficiency reveals deleterious mutations compromising reproductive and rearing success in cattle. BMC Genomics 16:312. [similar Fleckvieh defects]