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Recumbency in Holstein Calves

April 3, 2023 – Researchers at Penn State University have been collaborating with colleagues at USDA's Agricultural Research Service to study a new genetic defect in Holstein cattle. This defect is characterized by otherwise healthy animals that are unable to stand.

This condition, currently called **calf recumbency**, has proven to be more complex than other known genetic defects. Considering the animal welfare aspect of this defect, the development of a reliable diagnostic tool is very important to consumers, farmers and the dairy genetics industry.

The industry position
The industry acknowledges that this defect must be addressed quickly. The priority is to provide access to accurate diagnostic tools with transparent and wide communication of carrier statuses of affected males and females.

Two commercial gene tests are currently available at Genetic Visions and Feanix Bio to determine carrier status of this defect. Artificial Insemination (AI) bulls are actively being tested and the industry is working on a defined system to get the test results from the laboratory to the Council on Dairy Cattle Breeding (CDCB) and Holstein Association USA, so they can be made public as soon as possible. USDA's Animal Genetics and Improvement Laboratory (AGIL) and CDCB are working on a more accurate haplotype test. There will not be a haplotype publication for calf recumbency at the April 2023 sire evaluations. Any updates on the availability of that test in the coming months will be shared promptly.

Research summary on calf recumbency, from region to mutation
Identifying a genetic defect with enough certainty for publication is a long process. This is especially the case when the phenotypes (observations) are subjective or when calves are euthanized before accurate phenotyping took place.

When a genetic defect causes embryonic death, the defect can be detected at CDCB by lack of homozygous genotypes for that DNA location in our national cooperator database. This was the case for the Holstein HH1-HH6. When the mutation causes death of calves that may be genotyped before dying, such as with Holstein Cholesterol Deficiency (HCD) and this new defect, the reporting of abnormalities in calves is the first step in identifying the causal defect.

We thank all the breeders that have come forward to researchers or industry organizations with observations and samples and we encourage others to do so in the future.

DNA samples of affected calves must be collected for genotyping, as well as the genotypes of as many family members as possible. By genomic association studies and pedigree analyses, a DNA region (haplotype) was identified that was common among affected calves. Pedigree analyses allows tracing the haplotype up the paternal and maternal pedigrees to find common ancestors. Tracing the identified haplotype through the known pedigrees was done by both Penn State and the researchers at the USDA Animal Improvement and Genomics Laboratory (AGIL). The identified haplotype is common and traces back many generations, but the number of homozygous calves in the national database is lower than expected. This points to a recent mutation within the haplotype, just like HCD. Recent mutations make tracing a haplotype back to a clear source animal difficult because we deal with a large number of normal haplotypes and a smaller number of mutated haplotypes, but they have the same ‘signature’ of genetic markers.

Sequence analyses allows for the potential identification of the causal genetic mutation within the haplotype. Using sequence data, Dechow et al 2023 identified a mutation within the *CACNA1S* gene on chromosome 16. When a possible genetic mutation is pinpointed, the next step is to validate the mutation by genotyping a large number of affected and unaffected animals for the mutation. This is currently ongoing. However, collected data supports the hypothesis that the identified mutation is causal to the phenotypes of the affected calves.

Haplotype Test

The team at USDA's AGIL are developing a haplotype-based test that can be applied to all genotyped animals. The test is not available yet.

The concordance between the DNA test results from Dechow et. al. and the haplotype test currently is fairly low. In addition, the research by Dechow et al. as well as by the USDA AGIL team identified a number of animals homozygous for the haplotype that show no symptoms. Both these findings may be explained by the haplotype not accurately identifying and tracking the recent mutation. This reminds us of HCD, in which there were two different pieces of DNA with the same SNP "fingerprint". This happens with new mutations because there hasn't been sufficient time and data to differentiate the mutated haplotype from the original and normal one.

More validation between the data from the available gene tests with the haplotype data must take place to remove uncertainty and increase reliability so the haplotype test can be routinely applied for all genotyped animals. This will also give us better estimates of carrier frequency in the Holstein population.

Available gene tests

Two commercial gene tests are currently available at Genetic Visions and Feanix Bio for bulls and cows and other labs are exploring the development of a gene test for the defect. AI companies are currently testing their bulls, and it is the industry's intention to publish carrier statuses as soon as possible. Due to chance in families sampled, some companies will have more carrier animals in their bull and donor cow populations than others.

Next Steps

The immediate next step is to develop a defined system to get test results from laboratories to Holstein USA and CDCB/AGIL so carrier statuses can be published, and the national haplotype test can be improved. The naming structure must also be confirmed to identify and label if the result is a gene test or from a future haplotype test.

Long term, as an industry, there is a need to further develop strategies for continuous monitoring of the population to identify emerging genetic defects and ensure that high-quality biological samples and phenotypic information are collected. Collaboration with government and university researchers will enable continuity of efforts and ensure access to any resulting diagnostic tools. Individual farmer reporting of abnormal calves remains essential to identify defects accurately and quickly.

References

[1] Dechow, C.D., E. Frye, and F.P. Maunsell. 2022. Identification of a putative haplotype associated with recumbency in Holstein calves. JDS Comm. 3:412–415. https://doi.org/10.3168/jdsc.2022-0224.
[2] Dechow, C. 2023. Mutation sometimes leads to calf recumbency. *Hoard's Dairyman*.