Calf Recumbency: What to know about this trait and ongoing research

Summary

- The science underlying the description of the genetic mutation as the causal mutation for Recumbency is reliable and is supported by substantial evidence. This mutation is indeed a true lethal mutation.
- Genetic Visions-ST™ has developed an accurate genetic test for this mutation, and STgenetics® is systematically testing all of our genetic nucleus animals.
- Given the severity of the issue and the substantial scientific evidence, and in an effort to eradicate this mutation from our population, STgenetics® has decided to phase out all carrier bulls and cows from our genetic nucleus effective immediately.
- Genetic Visions-ST™ has secured a licensing agreement with Pennsylvania State University which will allow the genetic test for Recumbency to be accessible for the dairy industry worldwide.
- Producers can manage this genetic mutation in their herd by testing their females to identify carriers and utilize Chromosomal Mating® to ensure that carrier females are not mated to carrier bulls

Introduction

In a recent study, a new haplotype potentially affecting calf well-being was discovered that may result in calves that are weak and unable to stand at birth or shortly after (Recumbency). Some affected calves in the study were able to recover, but most did not survive beyond 6 weeks of age (C.D. Dechow, et al., 2022). As this is a new discovery, more research is needed to understand how to make decisions based on this mutation. The goal of this paper is to summarize recent scientific findings and state STgenetics® position and actions on this new discovery.

How are negative genetic characteristics discovered?

In order to determine the region of DNA that is affecting animal performance, groups of affected and non-affected animals need to be genotyped so that the region of the genome that is different can be determined between the two groups. Once the genomic region that is different is determined, explaining the performance difference between animals that are affected, or unaffected, a DNA test can be developed to identify other animals that are carriers of the affected region of DNA.

In the case of the newly discovered haplotype that affects calf Recumbency, 18 calves that displayed the inability to stand in the neonatal period were genotyped and compared to 26 unaffected calves from the same family groups. Researchers determined that the 18 affected calves were homozygous or carried two copies of a region of DNA on Chromosome 16 (C.D. Dechow, et al., 2022). A haplotype is a segment of DNA that is inherited from parent to progeny and can change over generations which makes it challenging to identify carriers and non-carriers of the specific region of DNA that is causing negative phenotypes. In the study led by Dr. Dechow, the haplotype or segment of DNA that affects Recumbency was discovered, but more analysis has led to the discovery of the actual gene that causes Recumbency. This discovery has led to increased confidence that animals can be identified as carriers or non-carriers. For more information about haplotypes and markers, please check out this article: https://stgen.com/upload/articles/files/geneSTream_Haplotypes-January%202022.pdf.

Where did the Recumbency mutation originate?

At this time, it is unclear when the mutation first occurred. The earliest known carrier of the Recumbency haplotype was Southwind Bell of Bar-Lee. Southwind inherited the region of the mutation from Osborndale Ivanhoe, one of the foundation sires of the modern Holstein breed. Ivanhoe did not have the mutation, so the mutation occurred someplace in between. It is through Southwind's most prominent descendants, Robust and Supersire, that the gene has spread throughout the breed. For STgenetics®, we were fortunate that Cogent Supershot, the Supersire son who led to Charl and Captain, was not a carrier. Charl and Captain are both non-carriers. STgenetics® was also fortunate that the Robust daughter Miss OCD Robust Delicious, dam of Delta and foundation cow of the STgenetics® program, was a non-carrier. However the Supersire son, Megasire was a carrier.

What is the phenotype called Recumbency?

The term "Recumbency" refers to the condition where newborn calves are weak and unable to stand up shortly after birth. This condition can result from a variety of factors, such as physical trauma during delivery, nutritional deficiencies, or genetic abnormalities. In our opinion, the lack of a clear definition/diagnosis of the new disorder was the main reason for the hesitation to take more direct actions to control the spread of the mutation.

STgenetics®

What tools are available for breeders today from STgenetics®?

Through a collaboration involving STgenetics®, Genetic Visions-ST™, and Dr. Dechow, we have successfully sequenced the genomic region that is associated with the Recumbency disorder. This has enabled Genetic Visions-ST™ to create a stand-alone genotyping test capable of screening for the causal mutation and accurately identify animals as either homozygous-normal (animals that do not carry the mutation), heterozygous or carriers (animals that appear normal but can transmit the mutation to their offspring), or homozygous for the mutation (affected animals that are likely to die or be euthanized shortly after birth).

Utilizing sequencing data in conjunction with the stand-alone assay, STgenetics® has conducted tests on all of our Holstein bulls in the United States, and we are in the process of testing all remaining bulls globally. Furthermore, high-genetic-value females in STgenetics®' herds are also being tested, and measures are being taken to eradicate this causal mutation from our herds.

Recently, Genetic Visions-ST™ secured a licensing agreement with Pennsylvania State University which will allow the genetic test for Recumbency to be accessible for the dairy industry worldwide. Producers who genomic test their females for Recumbency can eradicate this mutation from their herd by only breeding non-carrier females to non-carrier bulls to make replacements, or manage this mutation by utilizing Chromosomal Mating® to avoid mating carrier females to carrier bulls.

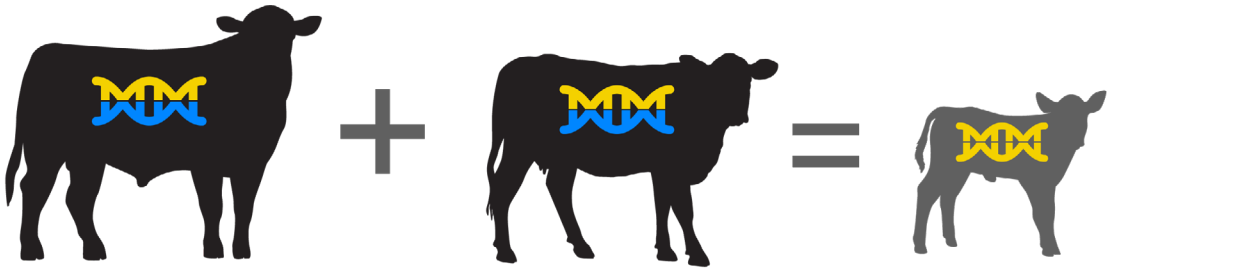
Gene Card: CACNA1S

Mutation is in the coding sequence of the calcium voltage-gated channel subunit alpha1 S gene (CACNA1S).

The CACNA1S gene provides instructions for making the main piece (subunit) of a structure called a calcium channel. Channels containing the CACNA1S protein are found in muscles used for movement (skeletal muscles). These skeletal muscle calcium channels play a key role in a process called excitation-contraction coupling, by which electrical signals (excitation) trigger muscle tensing (contraction).

The mutation changes a conserved glycine residue (in cattle, humans, goats, horses and mice) in the protein to a serine residue, which is predicted to be deleterious to the activity of the protein.

Mutations in the CACNA1S gene in humans and mice are known to cause periodic paralysis.



Recumbency CARRIER + Recumbency CARRIER = Recumbency EXPRESSED

Can animals that were previously genotyped be tested for Recumbency?

There is ongoing research to identify possible carriers based on existing genotypes and pedigree information. The scientific reporting on these efforts have been very scarce, but from what STgenetics® has learned and from our own data analysis, this approach is not going to produce a definite solution in the near future. Significantly more development is needed, and more data is required before a population-wide haplotyping approach becomes commercially feasible. Today, Recumbency can be identified utilizing Genetic Visions-ST™'s stand-alone genetic test.

Let's separate fact from fiction: What do we know today?

1. The science underlying the description of the genetic variation (mutation) identified by Dr. Dechow is reliable and is supported by substantial evidence. As a result, we have a high level of confidence that we are indeed dealing with the correct genomic region and a true deleterious mutation which is a gene that causes the animal to be at risk of developing a certain genetic disorder.

2. The lack of a clear phenotype that distinguishes affected animals from weak newborns has created confusion and hesitancy in labeling all animals with difficulty standing as having Recumbency.

3. The limited success in calling carriers based on historical genotypes has added even more challenges. Today, the industry understands that we have a big problem on our hands, but it does not see an easy way out. This has led to the default position of almost everyone involved to just try to "buy more time"!

4. STgenetics® has been proactive to analyze the data involved in Recumbency research which has allowed Genetic Visions-ST™ to develop an accurate test for the causal mutation, which, when used as a stand-alone test or in conjunction with Chromosomal Mating®, enables farmers to easily manage or eradicate the mutation from their herds.

5. Genetic testing for Recumbency, through Genetic Visions-ST™, is available for everyone, at a reduced price, to help the industry manage this mutation efficiently and effectively.

6. There have been some reports on possible unaffected homozygous animals. If confirmed, this is a well known phenomenon called partial-penetration. STgenetics® is continuing research into other possible variants in the genomic region associated with Recumbency that might impact muscle function as well as running a full evaluation to investigate the effect of this mutation on other traits.

References

Dechow, C.D., E. Frye, F.P. Maunsell. 2022. Identification of a punitive haplotype associated with Recumbency in Holstein calves. J. Dairy Sci. https://doi.org/10.3168/jdsc.2022-0224.