

2023 CDCB Industry Meeting

Q&A: Undesirable Genetic Factors and Genomics' Role in Discovery

Due to the strong interest, there was not time to answer all audience questions during this panel at the 2023 Industry Meeting on October 4. Responses to all questions asked in the Slido app appear in this document. Panelists included:

- Spencer Hackett, Melarry Holsteins
- Matt McClure, Ph.D., ABS Global
- J.R. Tait, Jr., Ph.D., Neogen
- Paul VanRaden, Ph.D., USDA Animal Genomics and Improvement Laboratory
- George Wiggans, Ph.D., Council on Dairy Cattle Breeding
- Neal Smith, American Jersey Cattle Association, moderator

How do we get around people trying to patent the gene tests, particularly when public data is used to generate them or validate them?

Data agreements can be used to address this issue specifically. The U.S. Supreme Court did issue a ruling in 2013 against patenting natural variants. Typically, if the work is done by a U.S. federal government employee, it is put into the public domain. On the other hand, universities or other private industry entities will choose a path for the transfer of information as a part of their dissemination plan after they have invested time and resources into their discovery efforts.

What's the cost to a producer to sample and submit a "research" sample on a suspicious animal?

American Jersey Cattle Association will pay all costs for a Jersey animal, and Holstein Association USA will do the same for Holstein animals. Breeders should reach out to their respective breed associations for more details; typically the association will cover the costs.

Who should be responsible for collecting all the reports and initial discovery?

Declaring genetic conditions is the responsibility of breed associations, so reports should be submitted to them through the reporting tools associations have available. CDCB and USDA Animal Genomics and Improvement Laboratory (AGIL) get involved in the process through the haplotype call development after the condition is identified. In all cases, a thorough investigation to eliminate environmental factors and phenotypic expression is important before assuming the issue is an undesirable genetic factor.

Has CDCB or anyone else considered making an app for producers to report undesirable calves born that are suspected of having a genetic condition?

CDCB has not yet explored app development, as genetic condition reports should be made to breed associations.

Do you find reporting to a veterinarian helpful? Who ensures they pass it up the chain instead of just blaming genetics without any proof?

Veterinarians should be involved in the care of animals, regardless of whether their condition is possibly rooted in the environment or genetics. If you believe a condition is potentially caused by a genetic factor, collect a tissue sample and submit it to the respective breed association. If you have affected and unaffected animals with the same ancestry, talk to your breed association as samples from both groups can make a big difference in identifying gene mutations.

Are there plans to use non-SNP measures such as copy number variants (CNVs) for defect discovery?

Yes, AGIL is already using a few insertions and deletions as larger copy number variants (CNVs) may be harder to genotype on SNP chips. While no defect causative CNV has been found, they have been included in such analysis for the past decade.

Do the panelists see gene editing playing an important role in the future? Are we going in this direction at least for undesirable genetic factors?

To date, most gene editing efforts have centered on introducing a favorable mutation into a population more quickly than through traditional breeding methods. As shown in the graphs during the CDCB Industry Meeting, we can quickly reduce a genetic mutation's frequency through breeding strategies once the causative allele is found. There might be more potential in using gene editing as a tool to introduce novel traits and provide immunity for uncontrolled infectious diseases, rather than to remove a genetic defect allele from the population.

Sequencing is great for data, but it may cause problems for data storage. Is there a worry about how to store and process it all?

Storing only the differences from the reference map (using a cram format) or just the genotype calls (vcf) can help reduce the space issue.

What can CDCB do to improve feet and leg issues such as fused rear legs that may be caused by genetic factors?

As with any potential genetic factor, collaboration is key. Breed associations will collect information from breeders and share those genotypes with AGIL and CDCB for haplotype call development. CDCB is then able to provide independent, research-backed information on the condition and status of animals to producers and industry collaborators.

Is there a way to report the percentage of breeds of an animal? Example: HO and JE for dairy cross and HO and AN for beef cross.

[Breed Base Representation](#) (BBR) was introduced in 2016 as an estimate of the percentage of DNA contributed to an individual animal by each of the five dairy breeds genomically evaluated in the U.S.: Ayrshire, Brown Swiss, Guernsey, Holstein and Jersey. CDCB is interested in extending this capability to other breeds including beef breeds to improve screening for participation in crossbred evaluations.

Is muscle weakness being monitored in all breeds? Is the mutation more prominent in a specific breed?

The new mutation causing Early Onset Muscle Weakness Syndrome is in Holstein DNA and not expected to be in DNA of another breed. However, due to crossbreeding, it has the potential like any genetic factor to appear in non-purebred animals that carry Holstein DNA.

Have advances been made about the HH3 and 4 haplotypes about embryonic losses after conception?

Yes, initially HH3 carrier frequency was 6% and is now about 1%. HH4 was only about 1% in the U.S. and is now 0.2%.

Many of these conditions are negative reflections on the increased number of more closely-related animals. Is crossbreeding the real answer?

Agriculture has had to deal with genetic defects since animals were domesticated. As an industry, we are getting better and faster at reporting potential genetic defects, identifying a diagnostic allele or haplotype, and using that data in breeding decisions. Relative to crossbreeding, remember that a purebred animal only needs to consider conditions in that breed, while a crossbred must be concerned about conditions in all breeds present.

Is eradication of every known undesirable genetic factor a necessity?

No. There are often many favorable attributes of individuals who are carriers of undesirable genetic factors. The best way to approach this is to manage the undesirable genetic factor by knowing the status of the animals that will be mated together. Knowing that matings are between free and carrier status and not mating carrier to carrier is the key to leveraging as many favorable attributes as possible without discarding those favorable attributes through an eradication program. An eradication program could be viewed as a form of single-trait selection, which is not often a viable mating strategy.

As an example, it is estimated that Pawnee Farm Arlinda Chief who carried the HH1 allele cost the global industry \$420 million from HH1-related pregnancy losses. On the other hand, Chief's genetics provided the global industry an estimated \$30 billion from improved milk production. Therefore, while he carried an undesirable condition that had a negative economic impact, his net economic impact was \$29.5 billion. More information on this study can be read in the Journal of Dairy Science paper co-authored by CDCB's Applied Geneticist Dr. Heather Adams Enzenauer, [https://www.journalofdairyscience.org/article/S0022-0302\(16\)30352-6/fulltext](https://www.journalofdairyscience.org/article/S0022-0302(16)30352-6/fulltext).

For optimal genetic progress, should we label a defect or include the defect's economic impact in an overall economic index?

This option is currently being considered, but regardless of doing so, the economic impacts should already be addressed indirectly in all four CDCB indices.

What tools/programs do you [Spencer Hackett, Holstein breeder on panel] utilize to manage conditions? What software/programs would you like to see available in the future?

I use genomic information provided by Holstein Association USA's Enlight program and Select Sires bull search. In the future, the more information that can be easily accessible, the better for producers to make profitable decisions.

Do you [Spencer] test all dams kept on your farm to avoid homozygous breedings for known defects?

Yes, as a breeder, we do test all dams, so that carrier-to-carrier matings can be avoided.