



Interpreting and Utilizing New Holstein Genetic Information

*Prepared by Holstein Association USA Staff
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Genomics has allowed us to learn more information about our cattle at a younger age than ever before. Along with that, geneticists are discovering traits that were previously unknown or unable to be measured because of how they were expressed.

Six **haplotypes impacting fertility** in the Holstein breed have been identified by USDA researchers. A **haplotype** is a combination of alleles (DNA sequences) at different locations on a chromosome that are transmitted together as a group (linked). Referred to as HH0 (the haplotype associated with the previously-identified genetic condition Brachyspina), HH1, HH2, HH3, HH4 and HH5, these haplotypes are believed to cause embryonic or fetal death when present in homozygous form, i.e., the offspring inherits the haplotype from both the sire and dam. In a herd, this would appear as if a cow did not conceive, resulting in greater days open and lower conception rates. Researchers have found that these haplotypes never occur in homozygous form amongst any living animal that has been tested. That scenario is highly unlikely based on population probabilities, unless affected animals did not survive to birth.

We expect, based on theory and experience in other species, every cattle breed (including Holstein) has many different haplotypes impacting various traits that occur at very low frequency. It is likely that additional Holstein haplotypes will be discovered over time as data accumulates. The impact of haplotypes on traits can range from small to large, and it is important that breeders' response to the information is appropriate based on the magnitude of the impact and frequency of the haplotype.

The following material is intended to educate about these haplotypes impacting fertility so Holstein breeders can make more informed mating decisions in their herds.

Testing and Labeling of Holstein Cattle

Haplotypes impacting fertility can be discovered through all genomic testing options available from Holstein Association USA, and the results of these tests are used to designate animals as carriers or non-carriers. The six haplotypes each have carrier frequencies between 0.7 and 6 percent in the current Holstein population.

Since August 2011, carrier status of tested **Available Proven and Genomic Young bulls** has been provided under **Section 5: Reference Information** in the Holstein Association USA Sire Summaries. **A complete list of tested animals (both males and females) is available on the Holstein USA website (www.holsteinusa.com), under Pedigree Information > Genetic Codes/Traits, and will be updated regularly.**

The following labels will be used to distinguish carriers and tested non-carriers of Holstein Haplotypes 0-5 (HH0, HH1, HH2, HH3, HH4 and HH5):

- C = Carrier (HH0, HH1C, HH2C, HH3C, HH4C, HH5C)
- T = Tested Non-Carrier (HH0, HH1T, HH2T, HH3T, HH4T, HH5T)

Inheritance Pattern

It is important to note that each of the haplotypes, HH0, HH1, HH2, HH3, HH4 and HH5, should be treated as separate traits, independent from one another; e.g., for HH1 to cause embryonic or fetal death, the embryo would have to inherit the HH1 haplotype from both the dam and sire. The haplotypes follow a similar inheritance pattern as simple dominant/recessive genes.

Example 1: HH1C cow (carrier = Rr) x HH1C bull (carrier=Rr)

x	R	r	R = normal haplotype r = HH1 haplotype (containing the causative mutation)
R	RR	Rr	
r	Rr	rr	

Resulting offspring: 25% would be homozygous for the unfavorable HH1 haplotype (rr) and would not survive to birth. Of the live offspring, two-thirds would be HH1 carriers, and one-third would be homozygous for favorable haplotypes.

Example 2: Status unknown cow (sire was HH1C) x HH1C bull

If a cow is not genomic tested, but her sire is known to be HH1C, and she is bred to an HH1C bull, the probability is 12.5% that the resulting embryo will express the homozygous form of the unfavorable haplotype and not survive to birth.

Example 3: Mating carriers of different haplotypes impacting fertility – HH1C x HH2C

If you mated two animals that were carriers for different haplotypes – a cow who was an HH1 carrier (HH2T, HH3T), and a bull who was an HH2 carrier (HH1T, HH3T), the following resulting offspring could be expected:

25% non-carriers of both (HH1T and HH2T)

25% HH1 carriers (HH1C, HH2T)

25% HH2 carriers (HH1T, HH2C)

25% carriers of both (HH1C and HH2C)

Statistics for HH1-HH3

Within the available bull population in July 2011, 1,349 bulls were coded as Active, Foreign, Genomic or Limited, meaning semen is available for sale. Of these bulls, 195 are a carrier for one of these haplotypes impacting fertility and one bull has two of them. The probability of a bull having at least one of these haplotypes is 14.45%; or individually, 5.0% for HH1, 4.1% for HH2 and 5.5% for HH3. Despite the relatively high probability of an animal being a carrier for one of the haplotypes, the probability of mating two carrier animals carrying the SAME haplotype impacting fertility is very low. For example, the probability of mating two HH1C animals is 2.5 times out of 1,000.

How Could This Affect Your Breeding Program?

Knowledge is power when it comes to improving the genetics in your herd and working to decrease the frequency of unfavorable haplotypes and recessive traits in the Holstein breed. Given that unfavorable haplotypes exist in virtually all cow families, and that it is likely more will be discovered as genomic testing continues to expand, it is expected that many top bulls and

females will be carriers of one or multiple unfavorable haplotypes. We recognize the value of the desirable genetics those animals possess and what would be lost if breeders eliminated or reduced their usage of those top genetic animals.

As mentioned above, these haplotypes impacting fertility are inherited completely independent of one another. Because the frequency of any one haplotype is low, many potential mates without the same haplotype exist in the Holstein population. Animals with high genetic value that are carrier of a haplotype impacting fertility should still be kept for breeding purposes; breeders should work to ensure she is not mated with a carrier bull. In the instances of carrier-by-carrier matings, we do see a significant reduction in conception rate.

Using Daughter Pregnancy Rate to Improve Fertility

Evaluating Daughter Pregnancy Rate (DPR) is the best method for breeders wishing to improve fertility, and DPR does include effects associated with the newly discovered haplotypes. One potential approach would be to select bulls that best meet the goals of your breeding program as you always have, then use information available on individual haplotypes to avoid carrier-by-carrier matings. If breeders use information about haplotypes alone to make selection decisions, it is likely their impact could be overstated. As the effects of the haplotypes impacting fertility are already included in DPR, breeders both selecting for DPR and eliminating carrier animals completely from their breeding programs would be “double counting” the negative effects of the haplotypes.

Holstein Association USA encourages breeders to pay attention to pedigrees, work to learn the status of their animals, and be mindful of the status of service sires in their herd. **The bottom line is, to reduce negative impacts on conception rate from these haplotypes, avoid carrier-by-carrier matings.**

Holstein Association USA’s Free Genetic Resources

Holstein Association USA offers free resources to help breeders who are looking to reduce the incidence of unfavorable recessive traits and haplotypes in their herds.

Haplotype carrier status of tested **Available Proven and Genomic Young bulls** can be found in **Section 5: Reference Information** in the Holstein Association USA Sire Summaries. In addition, a complete list of tested animals (male and female) is available on the Holstein USA website (www.holsteinusa.com), under Pedigree Information > Genetic Codes/Traits, updated regularly.

Also on that page, breeders can find a list of all bulls who have been labeled as carriers or tested non-carriers of Brachyspina, along with a Family Tree Search tool, which allows you to enter the registration number of an animal and view a family tree, and will display any recessive or dominant genetic codes animals in the family have been given (not including haplotypes; for haplotype status, please refer to the specific lists provided on the website).