Genomic testing of female Holsteins: a resource for selection and improvement

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INTRODUCTION

The strategic use of genomic selection for economically important traits will support the sustainability of the U.S. dairy industry. Although genomic testing is a common tool used in sire selection, this technology is now beginning to be implemented for selection of superior females (Hansen Axelsson et al., 2011; Weigel et al., 2012). The identification of females with the most promising genetic potential in a herd can influence selection decisions such as identification of replacement and cull animals early in the animal’s life, which can save feed and other costs associated with heifer raising. The selection of replacement heifers with superior economically important traits, such as daughter pregnancy rate (DPR) and longevity, will increase profitability of the herd (König et al., 2009; Weigel et al., 2012; Bouquet and Juga, 2013).

Despite the potential benefits of genomic testing of females to the producer, genomic selection technology is not commonly used for selection of superior females. Each dairy may have slightly different production goals, and trait emphases, for genetic selection. The University of Idaho (UI) dairy management selects replacement heifers heavily on reproductive traits to maximize timely pregnancy and calving. We hypothesize that genomic testing of female animals in the University of Idaho herd will be an effective way to identify replacement and cull animals to increase the genetic merit and profitability of the herd. The objectives of this study are to 1) confirm and correct pedigree information with genetic parentage to ensure each animal is correctly identified, 2) identify and document females that carry a disease-associated allele to prevent the mating of 2 carrier animals, and 3) analyze production trait data for selection indices and identify individuals with the highest and lowest performance potential for replacement and cull considerations, respectively.

MATERIALS AND METHODS

This study was conducted at the UI Dairy Research and Extension Center located in Moscow, ID, and all animal handling procedures were approved by the UI Animal Care and Use Committee. Holstein cows, heifers, and heifer calves \((n = 162)\) were sampled by ear punch using an Allflex (Dallas, TX) Tissue Sampling Unit (TSU). Tissue samples were stored in a vial with preservation solution and shipped to Zoetis (Florham Park, NJ) to conduct the low-density CLARIFIDE genomic test. Females were first tested to determine whether they were at least 7/8 Holstein before proceeding.
Of the 162 animals sampled, 143 animals were confirmed to be at least 7/8 Holstein. The CLARIFIDE genomic test, a 19,000 SNP panel, was used to analyze parentage, carrier status, and specific production traits on confirmed Holstein females. Twenty genetic conditions, 36 production and type traits, and 14 composite indices were evaluated as part of the genomic test. Phenotypic trait values were compared to Holstein breed averages and assigned a relative value. Merit indices formulated by the USDA were calculated and included in the results. Data were analyzed and interpreted to make replacement and cull decisions for the UI dairy. The top 85% of animals were recommended to be kept as replacements and bottom 15% of animals recommended to cull.

RESULTS AND DISCUSSION

Correcting Pedigree Parentage Information With Genomic Parentage Testing

To address the first objective of this study, genomic parentage results were compared with pedigree information. The UI Holstein herd pedigree records had an 18.2% (n = 26 animals) parentage misidentification. The majority of parentage misidentification was due to sire misidentification, approximately 13.3% (n = 19 animals), whereas 4.9% (n = 7 animals) was due to dam misidentification. The dam and sire for 0.6% of animals sampled (n = 1 animal) were both unable to be confirmed because the parents were not reported by the UI dairy or genomically tested. Animals with no reported sire (n = 5 animals, 3.5% of animals tested) were believed to be sired by a clean-up bull that was not genomically tested. In addition, the animals with no reported dam (n = 5 animals, 3.5% of animals tested) were in third or greater lactation, and their dams left the herd prior to testing. Data entry errors of both sire and dam can contribute to parent misidentifications, including service sire data entry error by AI technician, and calf to dam matching error.

Identifying Females That Carry Recessive Genetic Disorders

This genomic test included information on animal carrier status for 14 recessive genetic conditions. With regards to this study, we have categorized recessive genetic conditions as follows: early embryonic death, fetal or early calf loss, and a live animal that fails to be productive in the herd (Table 1). When considering the overall distribution of carriers in the 3 categories, animals that carry a diseased recessive allele for early embryonic death loss comprised the largest group at 17.5% of the animals sampled (n = 25). Next, 11.9% (n = 17) of animals sampled were carriers for a recessive disorder that can result in fetal or early calf loss. None of the animals tested possess a recessive allele that would result in a live calf' affected by Mulefoot or Factor XI Deficiency. However, some animals carry more than 1 diseased allele. 3 animals carry both Holstein Haplotype (HH) 1 and complex vertebral malformation (CVM), 1 animal carries both HH4 and CVM, and 1 animal carries both HH4 and HH5. These animals require more stringent service sire selection criteria to prevent the mating of 2 animals carrying the same recessive disorder.

Identification of animals that carry a recessive genetic condition in a herd can aid in breeding decisions to prevent the mating of 2 carrier animals that result in an affected offspring. It is important to recognize that early embryonic death due to a genetic condition may be mistaken for fertility issues and mislead management decisions. Previous studies indicate that dairy cattle experience a high percentage of early embryonic loss, primarily between 8 and 16 d after fertilization (Thatcher et al., 1994; Dunne et al., 2000; Silke et al., 2002). Holstein Haplotypes 1 to 5 is one such example that is included in the test, and these haplotypes have been associated with early embryonic loss (Cole et al., 2016). If 2 copies of the defective haplotype, one from the sire and one from the dam, undergo syngamy, the resulting embryo will not survive. Identification of carriers can help prevent potential early embryonic mortality, fetal loss, or animals affected by the genetic condition, therefore improving the reproductive efficiency of the herd.

Evaluating Females Based on Production Traits and Merit Indices

The genomic test includes predicted performance values for 36 production traits as compared to Holstein breed base (Table 2). These performance traits are then used to formulate 14 composite indices for each animal (Table 2). Production traits include those associated with milk production, reproduction, and type. In addition to production values for milk production and components, genotypes for milk traits such as beta lactoglobulin, kappa casein I, kappa casein II, and alpha s-1 casein are included in the test. Beta lactoglobulin is
Table 1. The number of University of Idaho Holstein females identified with known genomic recessive conditions using the CLARIFIDE low-density panel

| Genetic conditions categorized by phenotypic consequence | Fetal or early calf loss | Affected animal          |
|--------------------------------------------------------|--------------------------|--------------------------|
| Early embryonic death loss                             | HH1                      | Brachyspina              |
|                                                        | HH2                      | CVM                      |
|                                                        | HH3                      | BLAD                     |
|                                                        | HH4                      | Chondrodysplasia         |
|                                                        | HH5                      | Citrullinemia            |
| DUMPS                                                  |                          |                          |

Number in herd
- n = 25 (17%)
- n = 17 (12%)
- n = 0 (0%)

Carriers of more than 1 genetic condition
- CVM and HH1: n = 3
- CVM and HH4: n = 1
- HH4 and HH5: n = 1

1HH = Holstein Haplotype.
2CVM = complex vertebral malformation.
3BLAD = bovine leukocyte adhesion deficiency.
4DUMPS = Deficiency of uridine monophosphate synthase.

Table 2. Production traits and composite indices reported by the CLARIFIDE genomic test

| Milk traits       | Reproductive traits          | Type traits continued                | Composite indices         |
|-------------------|------------------------------|-------------------------------------|---------------------------|
| Milk yield (lbs)  | Daughter pregnancy rate (%)  | Stature                             | Productive life (mo)      |
| Fat (lbs, %)      | Heifer conception rate (%)   | Strength                             | Net merit ($)             |
| Protein (lbs, %)  | Cow conception rate (%)      | Body depth                           | Cheese merit ($)          |
| Somatic cell score| Sire calving ease (%)        | Dairy form                           | Fluid merit ($)           |
| Beta lactoglobulin| Daughter calving ease (%)    | Rump angle                           | Grazing merit ($)         |
| Alpha S-1 casein  | Sire still birth (%)         | Rump-thurl width                     | Total performance index (points) |
| Kappa casein I    | Daughter still birth (%)      | Rear legs side view                  | Holstein feed efficiency  |
| Kappa casein II   |                              | Rear legs rear view                  |                          |
|                   |                              | Foot angle                           | Calving ability ($)       |
|                   |                              | Feet/legs score                      | Final score type (points) |
|                   |                              | Fore udder attachment               | Udder composite (points)  |
|                   |                              |                                     | Feet and legs composite (points) |
|                   |                              |                                     | Body size composite (points) |
|                   |                              |                                     | Genomic individual inbreeding|
|                   |                              |                                     | Genomic future inbreeding  |

classified into homozygous AA and BB, and heterozygous AB genotypes, with AB genotypes associated with higher milk yield (Tsiaras et al., 2005). The beta lactoglobulin heterozygous genotype AB occurred at the greatest frequency (n = 66), AA at the second greatest frequency (n = 52), and BB at the lowest frequency (n = 24) in UI animals. These milk traits and genotypes can be incorporated into selection decisions to advance the goals of a dairy to produce a particular product, such as fluid milk or cheese. Milk from the UI dairy is sold to Darigold as a fluid product, so the AB genotype is desired for this herd and can be a criterion for replacement heifer selection.

Reproductive traits including DPR and heifer conception rate (HCR) are heavily selected for on the UI dairy. Daughter pregnancy rate values indicate the predicted percent difference that an animal will become pregnant during each 21-d estrous cycle compared with Holstein breed average and ranged from −3.9% to +4.3% in the animals sampled. Of the 143 animals sampled, 58.7% (n = 84) animals had values above Holstein breed base for predicted DPR, 4.2% (n = 6) animals were at breed base, and 37.1% (n = 53) animals were below breed base. Heifer conception rate values are expressed as the percent likelihood of the animal’s daughters to become pregnant in comparison to breed base of 0. Animals above breed base for HCR comprise 55.9% (n = 80) of animals sampled, animals at breed average comprise 2.1% (n = 3) of animals sampled, and animals below breed average comprise 42.0% (n = 60) of animals sampled. These fertility traits can be implemented into the overall
strategies for selection of replacement and cull animals.

Many conformational type traits including Feet and Leg Score, which predicts the overall feet and leg structure of an animal, are also included in the genomic test. The UI dairy heavily selects for adequate feet and legs to extend the longevity and productivity of animals as they are raised in free stalls with concrete floors. Animals above Holstein breed base of 0 for Feet and Leg Score comprised 64.3% \((n = 92)\) of animals sampled, 0.7% or 1 animal had a value equivalent to breed base, and 35.0% \((n = 50)\) of animals sampled had values below breed base. This score can be incorporated in a strategic selection strategy for improvement of longevity in UI animals.

Merit indices formulated by the USDA comprised numerous economically important traits that are weighted for selection purposes (Fig. 1). Merit values for these indices are calculated as part of the CLARIFIDE genomic test. These indices can be a helpful tool for producers to use for selection of replacement animals as they incorporate multiple traits into one value that predicts an offspring’s expected lifetime profit, and producers can rank animals in the herd based on this value. A positive merit value indicates that the animal will make a larger lifetime profit than an average Holstein born in 2010. Merit indices include Net Merit, Grazing Merit, Cheese Merit, and Fluid Merit, which emphasize specific traits to target a particular market. To choose the ideal index for an operation, a number of factors including management style must be considered.

The UI dairy manager is selecting for improved reproduction and longevity. Animals bred using artificial insemination to facilitate 4 calving groups per year based on days in milk. Because of this management strategy, replacement heifers are selected heavily on reproductive traits to maximize timely pregnancy and calving. Fertility as well as adequate feet and legs are both very important to an animal’s success in this operation. Therefore, Grazing Merit was the preferred choice over the other merit indices because this index has greater emphasis on fertility and a similar emphasis on longevity traits to Net Merit. Approximately 77% \((n = 110)\) of animals sampled had higher grazing merit than breed base, 1% \((n = 2)\) of animals had a grazing merit of 0 or breed base, and 22% \((n = 31)\) had a lower grazing merit than Holstein base.

Many components of a genomic test can be valuable tools for selection and improvement of individual dairy herds. First, correct parentage is important for accurate selection, identifying carriers of harmful genetic diseases, and using merit indices to rank animals and select replacements soon after birth can save in feed cost, breeding cost, and increase the advancement of genetic progress in the herd.

Cost to Benefit Example Analysis for the UI Dairy

A simple cost to benefit analysis in an example scenario relating to the operation will aid in determining if continued use of genomic testing in females is economically feasible (Table 3). In this example, 100 heifers are born into the herd over 1 yr, and 85% are kept as replacements. The cost of feeding a heifer in the UI herd (averaged from birth until calving) is approximately $2.00 per day. The cost of the CLARIFIDE genomic test as of 15 June 2017 is $39.50 per test (Zoetis, 2017). Typically, heifers are kept until the third breeding (approximately 17 mo) and are culled if not pregnant. Considering the 15 animals that are culled this year, the feed cost to raise them to 17 mo is $1,036 per animal. In addition, drug and semen costs for breeding is approximately $18.00 per breeding or $54 per heifer for 3 synchronizations and inseminations (Overton, 2006). Cull price is $0.90 per pound (USDA 2016) or approximately $810 based on animals that are 17 mo old and 900 pounds, which lessens the total cost to raise each animal to $280. In total, it will cost $15,540 for feed, $810 for drug and semen costs, and $12,150 will be recovered in the cull price for 15 animals. Therefore, it will cost approximately $4,200 to raise 15 heifers and cull at third breeding if not pregnant.

If animals are genomically tested shortly after birth and culled from the herd after weaning at 6 wk, feed cost equals approximately $84 per heifer. The genomic test costs $39.50 per test (CLARIFIDE genomic test as of 15 June 2017 is $39.50 per test). In this scenario, the cost of raising heifers and cull at weaning is approximately $0.90 per day. The cost recovered for selling a weaned heifer is approximately $100 each (Lancaster Weekly Cattle Summary Report, 2017). Therefore, the cost of raising each female to weaning age is approximately $23.50 including the sale income. In total, the cost of raising 15 heifers and culling at weaning is $3,710. This includes the genomic test for 100 heifers, which costs $3,950 in total.

In this scenario, the cost of raising heifers and culling at third breeding (17 mo) is $490 higher than genomic testing 100 heifers and culling animals at weaning. However, this does not include the higher merit and profitability of animals selected using a genomic test. Therefore, from this example scenario, use of a genomic test is in the UI dairy manager’s best interest to accelerate genetic progress and
increase profitability. For other dairy operations, a cost analysis is needed to determine whether genomic testing fits into that specific management style.

**IMPLICATIONS**

There are numerous strategic and effective uses of genomic testing; however, it is only beginning to be used for selection of replacement and cull females in the dairy industry. Correcting parentage eliminates animal misidentification and provides more accurate selection of replacements and culls. Identifying females that carry diseased alleles will aid in making breeding decisions to prevent reproductive losses due to recessive disorders. Selecting replacements and culls based on predicted phenotypic traits and merit indices will accelerate the genetic progress and overall productivity of the herd. Genomic tests could also be implemented in an embryo transfer program by identifying superior females to be donors early in life. The sustainability of the dairy industry will become more dependent on the strategic use of genomic selection in females to capitalize on genomic information from both parents to accelerate genetic progress and productivity of the dairy industry.

**Table 3.** Cost to benefit analysis breakdown for using genomic testing in the University of Idaho dairy herd to select replacement and cull animals

| Item                                                                 | Cost per animal | Total cost for the herd |
|---------------------------------------------------------------------|-----------------|-------------------------|
| Total feed cost until 17 mo                                        | +$1,036         | +$15,540 (15 cull animals) |
| Drug and semen costs for 3 breedings                               | +$54            | +$810 (15 cull animals)  |
| Cull price at $0.90/lb                                            | −$810           | −$12,150 (15 cull animals) |
| Total cost of raising                                              | +$280           | +$4,200                  |

| Item                                                                 | Cost per heifer | Total cost for the herd |
|---------------------------------------------------------------------|-----------------|-------------------------|
| Total feed cost for cull heifers until weaning (6 wk)               | +$84            | +$1,260 (15 cull heifers) |
| Cost of genomic test for all heifers                                | +$39.50         | +$3,950 (100 heifers in herd) |
| Sale price for weaned heifers                                      | −$100           | −$1,500 (15 cull heifers)  |
| Total cost of raising                                               | +$23.50         | +$3,710                  |
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