DAIRY VETERINARY NEWSLETTER

September 2017

Genomics in Dairy Cattle Selection and Mating - the Accelerating Pace of Change

The dairy industry is experiencing an increasing pace of change in how dairy cattle are selected, mated, and more likely to have longer productive life within herds than cleanup bull sired herdmates on average. Genomics is revolutionizing the selection of the parent cows and bulls, and progress in many production, reproduction and milk composition parameters.

A series of articles summarizing this was published in Progressive Dairyman's August 25, 2017 issue. Below I will describe single nucleotide polymorphisms (SNPs, "snips") and then report on the articles mentioned above.

Single Nucleotide Polymorphisms (SNPs, "snips")

Then most common type of genetic variation within bacteria, insects, humans, cows, etc. is in single nucleotide polymorphisms (SNPs, "snips"). Within any sequence of the 4 nucleotides that make up DNA, adenine (A), thymine (T), cytosine (C), or guanine (G), <u>for many nucleotide positions in a DNA strand, there is one nucleotide that the majority of the species has (major allele), and at least one other nucleotide in that position that the minority of the species has (minor allele). This single nucleotide change (polymorphism) is a SNP</u>.

For example, for this very short nucleotide sequence from the genome of 2 Holstein cows, Cow 1 and Cow 2:

Cow 1: ATTCGAGGCCTATGAATCCCGGTAGGCCATTGCCCATAAGGATGCGGATC
Cow 2: ATTCGAGGCGTATGAATCCCGGTAGGCCATTGCCCATAAGGATGCCGAAC

There are two SNPs shown both above and below. <u>Above, they are hard to see, but if a genetic sequencer detects it and shows that nucleotide in color, as below:</u>

Cow 1: ATTCGAGGCCTATGAATCCCGGTAGGCCATTGCCCATAAGGATGCGGATC
Cow 2: ATTCGAGGCGTATGAATCCCGGTAGGCCATTGCCCATAAGGATGCCGAAC

You can see the guanine and adenine, G and A, SNPs in this part of the genome of cow 2 above. <u>This assumes that in those positions, Cow 1 has what most Holsteins have there, and Cow 2 has one of the minority nucleotides there</u>.

- Some SNPs are lethal or cause major disease problems

- Some SNPs appear to be very protective against a disease or harmful condition

- Many SNPs have no effect or are associated with either a slight increase or slight decrease in a disease

- The effect, if any, of most SNPs is unknown. We all have millions of SNPs in our genome, like cows

- SNP information is not applicable across all breeds - Holsteins, Jerseys and other breeds differ

- SNPs are often found - in every species - in groups of 8 to 12 nucleotide changes that always go together, often on many different chromosomes. This is called linkage disequilibrium, and many of these groups of SNPs found together far apart in the genome are conserved in many species over millions of years

- Cost of bovine genome testing is decreasing, and the number of SNPs tested for is increasing. Many bovine genome tests now cost $100 to $125 and test for more than 777,000 SNPs

- We have done research at Utah State using genome-wide association study (GWAS). GWAS compares two extremes of the cow population (our research was on highly mastitis-susceptible vs. completely mastitis-resistant cows during a nearly year-long study). Any associations between SNPs and whether they are commonly found in either susceptible or resistant individuals for a disease or condition are evaluated for statistical significance. For example, we found 100% of cows with some SNPs to be mastitis resistant, with no abnormal milk or bacteria of any kind found in multiple milk samples, with mean SCC of 93,000/ml. In contrast, 94% to 100% of cows with other SNPs in the same gene were highly mastitis susceptible, acquiring an average of 6.1 cases per lactation.

Advances in Dairy Cattle Genomics

The first article, "Dairy genomics research update: New aspects of selection for health and fertility", is by D. Moore and H. Neibergs. "Genomic selection has its highest value when selecting for traits that are difficult or expensive to measure, occur late in life or when the animal has no or few offspring. Milk production is pretty easy to select for because it is easier to measure. Traits more difficult to measure include health and fertility traits." state the authors.

"Over the last 50 years, selection has been primarily focused on producing progeny with greater milk production without regard to fertility. Subsequently, we saw a rise in milk yield but a drop in fertility. Although fertilization rates are high, 40 to 56 percent of lactating dairy cows lose their pregnancy within the first month."

The article describes how in recent years, selection indices have added Daughter Pregnancy Rate (DPR), Heifer Conception Rate (HCR) and Cow Conception Rate (CCR). "The new Fertility Index combines several reproductive components into one overall index: a maiden heifer's ability to conceive, a cow's ability to begin cycling, show heat and conceive while lactating, and her ability to maintain a pregnancy."

The authors continue, "Our current research is looking at high-fertile (100 percent CR) and sub-fertile (less than 25 percent CR) heifers and the changes along the DNA associated with CR. We are using a genome-wide association analysis [GWAS] to identify specific regions highly associated with fertility. About 26 loci were identified as associated with HCR with a heritability estimate of 0.46 or 46 percent. Our colleagues in Florida found areas (SNPs) that could select for fertility without impacting milk yield. - - We have - - disease traits we can select for, such as metritis, retained placenta, displaced abomasum and ketosis."

The authors also make an excellent point. In monitoring any disease of dairy cattle or any species, within herds, practices, regions, or in genetic selection, it is imperative to have a practical but standardized case definition of exactly how any animal is classified as having that disease. (E.g. what defines "mastitis", "metritis", etc.?). This is one of the challenges of genomics, trying to define disease on all participating farms, detected by whomever records the cases of disease, using the same criteria. Those of us who have been using DC305 for over 30 years know that trying to standardize disease detection and data entry (how many ways can someone spell metritis or *Staph aureus*?) even by one person is not easy at all. The genetic testing for SNPs is becoming very precise, but defining diseases or conditions that are tested for association with the genetics, the fundamental basis of GWAS, remains a major challenge.

The article adds, "Many individual PTA and selection indexes are available for genomic selection for fertility and health traits, and more are in development. - -Where should a producer go with this information?" To me, this leads into the next article in the series:

Genomics and Dairy Sire Selection

The next article, "Effective use of genomics in commercial farms: sire selection", is by F. Peñagaricano. It begins with a nice summary about the faster turnaround time and younger age of bulls identified by genomic testing compared with the many years needed to test daughters of bulls. One thing it does not mention is something that has always struck me as a challenge ever since I learned about AI proving programs 40 years ago. Progeny testing attempts to control for differences between farms, feeds, pens, herd disease outbreaks, etc. among daughters of bulls or cows. However, it is not reasonable to think that all or much of the difference in how offspring of bulls or cows produce milk, become pregnant, avoid musculoskeletal problems, etc. is related to genetics.

Peñagaricano says, "Dairy sire selection has dramatically changed with the arrival of genomics. Nowadays, dairy farmers have basically two main options when they make sire selection decisions: use proven (progeny tested) bulls or use young genomic-tested bulls (i.e., young bulls with no progeny that have been evaluated using only their own genomic data). The National Association of Animal Breeders (NAAB) distinguishes these two groups of bulls as the active (A) bulls, progeny-tested bulls with performance information in at least 10 daughters, and the young genomic-tested (G) bulls, young bulls that have not yet milk-recorded offspring. It is important to remark that the number of young genomic-tested bulls currently in the market far exceeds that of progeny-tested bulls. For instance, of the 2,741 Holstein bulls available in the market in August 2016, 2,172 (79%) are young genomic tested bulls. Similarly, in Jersey, 403 of the 534 available bulls have G status. - - on average, these young bulls have greater predicted genetic merit values than the proven bulls. Figure 1 (below) shows the average PTA value for lifetime net merit (NM$) for the group of active (A) and genomic (G) Holstein and Jersey bulls currently marketed to US dairy farmers (August 2016). The difference in the average PTA NM$ between these groups is remarkable: the net merit of young genomic-tested bulls is $270 and $124 greater than for progeny-tested bulls in Holstein and Jersey breeds, respectively."
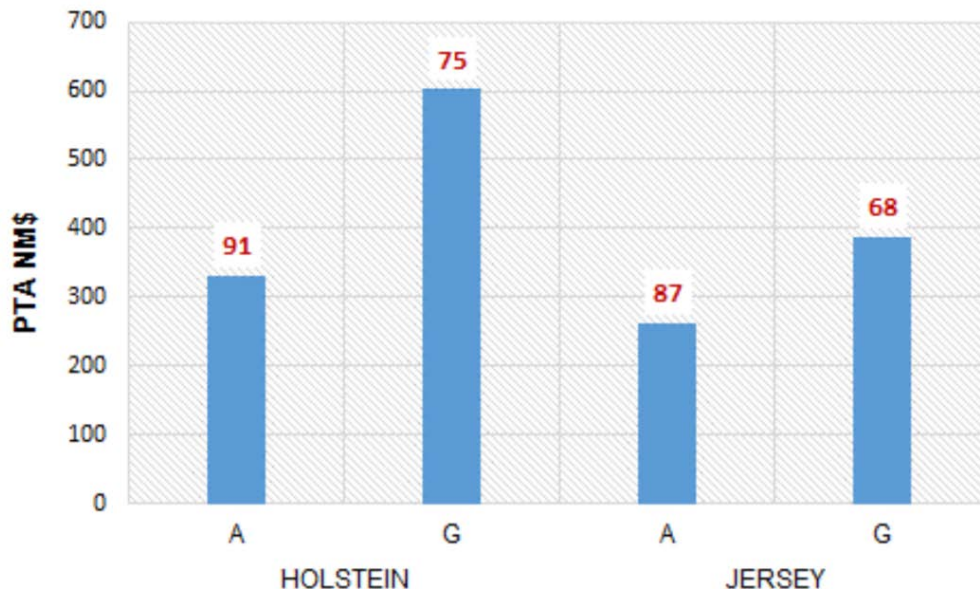

Figure 1. (From Peñagaricano) Average predicted transmitting ability (PTA) values (in the y-axis) and the corresponding reliability (REL) values (above the bars) for Lifetime Net Merit (NM$) for active (A) and genomic (G) Holstein and Jersey bulls marketed to US dairy farmers. Based on August 2016 Council on Dairy Cattle Breeding (CDCB) genetic evaluations.

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The article continues with a good discussion of reliability vs. PTA. PTA is higher, but % reliability is somewhat lower for genomic tested bulls. "The question is how we proceed - - should [we] use young genomic-tested bulls because they have greater PTA values, or instead, we should use proven bulls because they have more reliable PTA estimates? - - sire selection decisions should be always based on PTA values [not reliability]. - - however, we should use reliability as a guide to decide how intensely we want to use a bull. Therefore, - - the best strategy is to use a group or team of young genomic-tested bulls. [If] the REL values of individual young genomic-tested bulls is 70%, then REL of the average genetic merit for a team of three young bulls is about 90%, and if we increase the group size to six or even twelve young bulls, we achieve REL values for the group average between 95% and 98%. - - commercial dairy farmers have now a unique opportunity to capture the greatest benefits of genomics. Now, these G bulls have REL values about 70%, and hence, dairy farmers should manage the risk associated with imprecision in PTA estimates by using a group of young bulls, rather than focusing too heavily on individual animals."

It is clear that genomics, and a flood of new information is coming in the ranking of bulls or cows to be the parents of the next generations of dairy cattle. Dairy veterinarians will be involved in using this information.

Please let us know your comments and also suggestions for future topics. I can be reached at (435) 760-3731 (Cell), (435) 797-1899 M-Tues, (435) 797-7120 W-F or **David.Wilson@usu.edu**.

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