"What the Beef Industry Can Learn about Genomics From Another Livestock Industry"

Thomas J Lawlor, Director of Research, Holstein Association USA

Introduction

Genomic evaluations have been a great benefit to the dairy industry. And to my friends in the other livestock groups, it seems as though everything has been easy. Phenotypes are easy to obtain. Our main trait of interest, milk production, is measured two to three times a day. And we have millions of animals who are genotyped.

Hardly a week goes by without some type of popular press article reporting on another genomic tested dairy calf selling for a high price. A recent article from Australia (www.beefcentral.com) stated "will we ever see a $251,000 12-week-old calf? Maybe genomic testing is the answer?"

Even in the scientific Journal of Animal Breeding and Genetics, Jerry Taylor et al (2016) stated "As it turns out, Genomic Selection was a technology waiting to be invented for the US dairy industry." Well, that is partially true. We have certainly welcomed it and we do ask ourselves "what would we do without it?"

So, let's review the dairy genomic journey. You may be surprised that your dairy friends had to "cowboy up" several times to the bumps and challenges along the way.

The science of utilizing genomic information.

As in life, scientific pursuits often start off with some grand "what if" ideas. In genomics, our question was…. What if we had a lot of genetic markers equally spaced across the genome? How would we use that information to better select animals? Two noteworthy papers addressing this question were Nejati-Javaremi et al. (1997) and Meuwissen et al. (2001). It was the latter paper that stimulated the thinking of others on just how important genomic selection could become. Recognizing that affordable large scale genotyping would soon become a reality, Schaeffer (2006) discussed its benefits, which included a reduction in the costs of traditional progeny testing, having more accurate predictions on young animals, selecting them earlier and using them intensively, thereby decreasing the generation interval and increasing the rate of genetic improvement.

Curt Van Tassell was our cheer leader, motivator and sometimes arm-twister in getting the scientific know-how, funding and industry support behind the development of the Bovine SNP50 Van Tassell et al. (2008) and Matukumalli et al. (2009). The work of VanRaden (2008) provided the framework for genomic predictions which launched the genomic selection revolution in the dairy industry. Unofficial genomic predictions were first provided to the owners of genotyped animals in 2008, with an official public release and start of routine evaluations in January 2009.

The management and storage of the growing amount of genomic data was described by Wiggans et al. (2010). Although USDA had complete access to tremendous resource for research, it was beginning to become apparent that running a complete genomic evaluation required a large amount of time commitment for maintenance of this growing database, and the necessity to provide a service to the individual breeders and private breeding companies. Additionally, there were growing concerns about the privacy of sensitive traits, such as, incidence of disease and other health events. And the large amount of financial investment in genotyping and

Availability of genomic information has changed the dairy industry forever. Along with a renewed interest, enthusiasm and appreciation of genetic information came the commercialization of the genetic evaluation system and increasing discussion over the financial commitment to obtain genotypes and phenotypic data, the ownership of that data, and who and when others can have access to the resulting genomic information. The initial introduction of genomic evaluations were a bit controversial, as only members of the original seven AI companies who agreed to genotype their bulls and provide access to USDA, were permitted to obtain a genomic evaluation on bull calves for a 5-year-period.

In 2014, the running of the national genetic evaluations moved from being publicly funded and run by USDA-AIPL to the privately funded Council on Dairy Cattle Breeding (CDCB). In addition to paying for a genotyping service, breeders must now pay for the genomic evaluation. Prices vary depending upon sex - with the logic that bulls have the potential to provide a large financial return to the owner; as well as, the amount of phenotypic data that the farm or organization has contributed to the national database or more specifically to the reference population. Countries, such as Canada and Germany, have followed this open system with differential pricing. Some other countries run an exclusive system where an owner of animal must belong to a domestic organization, in order, to submit a genotype and obtain a genomic evaluation.

Protection of intellectual property in the form of many genotypes tied to a large amount of phenotypic data has become a concern. Countries with long time marketing relationships with one another have formed alliances and pooled their reference populations together. Currently three major international consortiums are in place. The needs of the international dairy community which has had a long-time tradition of pooling data, obtaining a genetic evaluation with a higher accuracy, and having an evaluation expressed on each country's domestic scale has changed.

The within-country genomic evaluations of the major exporting countries provide more accuracy, are available on a more frequent and timely basis, and access can be governed by a country's own domestic policy. Interbull, the international organization which has provides a service of performing the task of running a Multiple Across Country Evaluation (MACE) for our traditional (pedigrees and phenotypic data only) has struggled to find the proper business model in the genomics era.

The need for research into the modelling of genetic evaluations is at a level not seen in decades. And there is a shortage of well-trained quantitative geneticists to meet this demand. Although there are many ways to categorize research, a simple grouping is accuracy versus bias. Improvements in accuracy have been made by advances in imputation, fully sequencing influential ancestors,

Controlling bias is often connected with evaluating different groups fairly and equitably. For example, young animals versus older, domestic versus foreign, genotyped versus non-gentoyped, selected versus culled, etc.. Identifying a bias in different segments of a population takes a combination of skills; observing differences and forming a hypothesis on why different groups of animals may be handled differently by the current genetic evaluation model. Knowing how to properly categorize the population to address a concern. And having the skill set to develop the theory and a solution which can be programmed and implemented. Some good examples are adjusting cow variances and trait heritabilities (VanRaden, 2016), to control genomic pre-selection ssGBLUP (Aquilar et al, 2010))and incorporating foreign data that may be missing from your domestic genomic evaluation (**Vandenplas, 2017**).

Genomic information allows us to make genetic improvement on the more difficult traits, i.e. lowly heritable traits (Table 1) and those traits that are costly to collect data. Private organizations saw a business opportunity in creating one's own reference population by collecting valuable but costly phenotypes on a limited group of animals and providing an opportunity to access the genomic information. Four different sources of proprietary information on health traits are now available from Zoetis (Wellness Traits), ABS Global (TransitionRight), Genex (Exclusive Health Traits) and Semex (Immunity Plus). The CDCB is developing a national genetic evaluation, but, it's yet to be determined if any of the existing data sets will be pooled together.

As expected, the acceptance, utilization and accuracy of genomic information varies across the dairy industry. Genomic predictions were first officially available for Holsteins and Jerseys in January 2009; followed by Brown Swiss in August 2009, Ayrshire in April 2013, and Guernsey in April 2016. As of May 2017, 1.5 million Holsteins have a genotype; followed by 0.2, 0.03, 0.007, and 0.003 million, respectively for Jerseys, Brown Swiss, Ayrshire and Guernsey.

Presently, the SNP effects are breed specific. Which means greater accuracy in the Holstein breed does not get conveyed to the others. Additionally, the Holstein breed is much larger, on both a domestic and international basis, providing greater selection intensity. The difference in the genetic merit of the top Holstein bulls versus the Jersey bulls continues to widen over time (Table 2). The Holstein breed is pulling away, genetically, from the other breeds.

In addition to genetic evaluations, the dairy industry also receives information on parentage verification and/or discovery; identification of desirable and undesirable alleles; and indication of breed purity. Although, there is a very limited amount of crossbreeding in the dairy industry,

there are differences in the rules on how unregistered animals may enter the different herd books. A percentage value called the Breed Base Representation (BBR) provides a measure of the admixture of genes from different breeds. The BBR values on many of the top Jersey bulls indicate that Jersey breeders have introgressed Holstein genes into their elite cows.

The business of genomics.

Within a breed, breeders must decide on whether to use the younger and genetically superior genomic tested bulls as opposed to the older bulls with milking daughters. Whether they will participate in genomic testing and to what extent. And whether they will use sexed semen, embryo transfer, IVF, IVM or other reproductive technologies. These decisions will influence not only the herd's rate of genetic improvement and its ability to be successful in a competitive industry, but it will also determine their ability to be a provider of elite genetics.

Today's seed stock providers are breeding to young genomic bulls, genomic testing, and using advanced reproductive tools extensively. To obtain an extreme genetic outlier, high additive genetic merit of the parents is required, as well as, high Mendelian sampling. The latter component is simply a matter of the number of matings being made. The more embryoes a breeder obtains from the top parents, the more likely they are to obtain a high sample of better chromosome segments from each parent. A lack of ready access to a large number of recipients is the limiting factor for many of the current elite breeders. Without an opportunity to create a lot offspring, the odds are stacked against them to obtain an extreme outlier. For this reason, we've seen a large shift away from the smaller or moderate size farms to larger ones.

Genomics has changed the business of dairy cattle genetics. As with all technologies, there are early adopters and latter ones. In our industry, different AI companies approached this new technology differently. Several AI companies, were quite aggressive, by using young genomic bulls as sires of sons, buying and owning females, changing the way that semen was released, and establishing closer and often contractual business relationships with farmers. In the last five years, the registration of animals from these more aggressive AI companies, as well as new upstart companies, has grown by 14% at the expense of the more conservative companies. Couple this domestic change with large changes in the international sale of semen and we have a genetics industry in transition.

The growth in the investment in dairy cattle genetics has led to an increase desire to protect that investment and control the distribution of its product. Using the top genetics, early and exclusively, within one's own nucleus breeding program. And then selling sexed-sorted semen is a strategy that some studs have implemented.

Figure 1 shows the registration of male and female offspring from one of the breed's top young sires. All of the bulls born during the pre-release period are either owned by the AI company or under contract for first right of refusal at a set price. Then the commercial product that is sold is sexed-sorted semen, which is good for the commercial farmer looking for dairy replacements and

not so good for seed-stock producers or competing AI companies looking for bulls. This strategy does provide the owner with early access to the sons of an elite sire, but, given enough breeding by others, elite sons are still available to their competitors with a six-month delay in availability.

The current time in the business of genetics is quite exciting. Companies who were either slow in their initial uptake of an aggressive genomic breeding, or, were aggressive at the beginning and are being fueled by initial success and the desire to capture more market share are paying large prices for elite genetics. Seed-stock breeders are putting IVF facilities on their farm, negotiating their own contracts with AI companies, consulting with geneticists, studying consumer and economic trends, and trying to predict where our industry is headed.

However, the real driver behind the pursuit for faster genetic gain are the improved genetics they bring into their herd. These large farms realize that the occasional lucrative sale is merely frosting on the cake. The real money is made from milking those elite genetics. This is the true success of the genomic era. Farmers are more convinced than ever of the importance of good genetics in their herds. Many are investing heavily in it and are convinced that their herd will be more profitable due to their genomic breeding program.

The use of genetic advisors has increased within the dairy industry. A frequent request is for the design of a genomic breeding program whereby a small percentage of the elite females will be put into an IVF program. The next tier of females will be breed with sexed semen followed by females that will be used as recipients or bred to beef bulls, and finally the low end who will be culled. Many farms have become quite adept at producing embryos and are achieving high transfer rates. The cost of purchasing high genetic level embryos has dropped to the point where many believe that embryos will soon rival semen as the most economical way of disbursing genetics throughout the industry.

The future:

Information on sequence data available from the 1000 Bull Genome Project has identified informative SNPs in close linkage to causative genetic variants. These SNPs are being included on next production run of SNP chips.

Personalized nutrition is becoming more popular. With a growth in genotyping amongst both humans and cows, the ultimate personalized nutrition program is one where the genotype of the consumer is matched with a dairy product that best complements their needs. Dairy farms have grown to where several tanker trucks of milk per day will be filled. If a certain milk protein is deemed desirable by a certain portion of consumers, farmers can easily genotype their cows, segregate them into subgroups, and fill a complete milk-tanker with a specified milk protein.

The dairy cattle breeding industry has a history of being open to new technologies. For example, gene editing and cloning have been successfully demonstrated in dairy cows. Their acceptance

and utilization is ultimately dependent upon its cost effectiveness, long-term sustainability, and consumer acceptance.

Citations

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Table 1. Lowly heritable traits benefit more from the addition of genomic information.

Trait	Extra Daughter Equivalents from SNP effects
Production	25
Conformation	25
Calving Ease	38
Somatic Cell Score	58
Productive Life	80
Fertility	140

Table 2. USDA Sire Summary, April 2017. Genomic tested young bulls being marketed

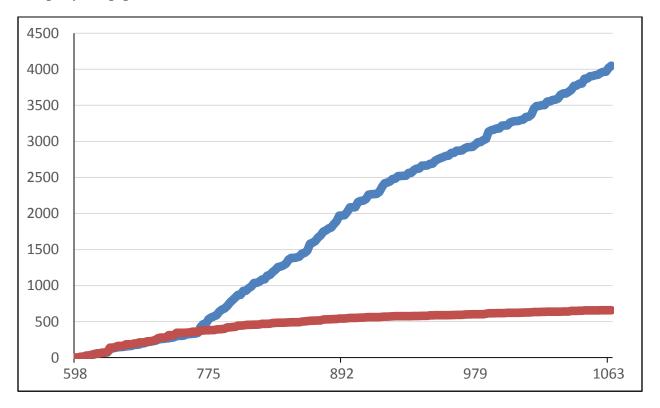| Breed	Number	PTAM	PTAF%	PTAF	PTAP%	PTAP	SCS	PL	DPR	NM$	FM$	CM$
Holstein	2215	1105	0.06	58	0.03	42	2.81	5.2	1.6	635	586	656
Jersey	394	691	0.08	48	0.05	33	2.93	4.2	0	445	387	469
Ayrshire and Red	39	981	0.06	51	0.04	40	2.92	1.3	1.1	392	344	412
Brown Swiss	51	749	0.01	32	0.02	28	2.87	3.5	0.9	364	332	377
Red and White	28	335	0.05	25	0.04	21	2.88	2.8	0.7	332	278	354
Guernsey	8	504	-0.02	20	-0.02	12	2.96	1.4	-0.3	169	178	165

Figure 1. Use of restricted access to pre-release unsorted semen, followed by the commercial sale of sex-sorted semen, in an effort to control the access and usage of an AI company's top genetics.