Will Genomic Selection be the Key to Improving Feed Efficiency in Dairy Cattle?

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Introduction

The efficiency of feed utilization on dairy farms can be influenced by a variety of practices that are beyond the scope of this paper, including many aspects of the harvesting, storage, mixing, and delivery of feed components, as well as the grouping of animals according to nutritional needs. Two practices that will be addressed are: 1) improvement of the biological efficiency of lactating cows through genetic or genomic selection for enhanced feed efficiency, and 2) reduction of feed costs through genome-guided management of the replacement heifer inventory. Both approaches have potential for improving the production efficiency of modern dairy farms, which will improve the economic viability of dairy farmers, the affordability of dairy products for consumers, and the environmental footprint of dairy operations.

Feed efficiency is a complex trait in all food animal species, but in beef cattle, swine, and poultry it is possible to limit the focus of selection to the efficiency of feed utilization during the growing and fattening periods of meat animals. The dairy cow poses a particularly challenging problem because of the need to balance the competing process of lactation, reproduction, health, maintenance, and (in young cows) growth. Up to this point in time, selection programs for dairy cattle have focused on increasing milk production, improving milk composition, and reducing the incidence of infectious diseases, metabolic disorders, infertility, and premature culling. Improvements in health, fertility, and longevity have been modest, because for many years producers focused their attention on improved physical conformation. However, in the past two decades the quantity and quality of genetic evaluations for functional traits have improved considerably. The next frontier of genetic selection in dairy cattle will be improvement of the biological efficiency of feed utilization, a trait for which cost effective tools and strategies have been lacking.

Impact of increased milk yield per cow on biological efficiency

As noted by VandeHaar and St-Pierre (2006), a modern dairy cow producing 45 kg of milk per day needs 4 times as much energy for milk production than for maintenance, and the net energy for lactation (NEL) of an elite dairy cow producing 90 kg of milk per day is 7 times the 10 Mcal of energy the cow needs each day for maintenance. Improvements in average milk production per cow due to genetic selection and enhanced management are well documented, and these have led to dramatic gains in production efficiency. However, it is important to recognize that, as milk production per cow continues to increase, the marginal savings in feed costs per unit of milk produced are diminishing. For example, assume that a typical dairy cow uses the first 6 kg of feed consumed each day for maintenance. If the cow eats 12 kg of feed per day, with the

remainder going toward milk production (or growth) she is consuming 2X maintenance requirements, and if the cow eats 18 kg of feed per day she is consuming 3X maintenance. As noted earlier, modern dairy cows can consume 4X maintenance throughout much of the lactation, and elite cows often consume more than 7X maintenance during peak lactation. The critical point is that the gain in efficiency associated with an increase from 2X to 3X maintenance is greater than the gain in efficiency when going from 3X to 4X, which is in turn greater than the gain when going from 4X to 5X. Based on this concept, which is known as dilution of maintenance, we are at or near a plateau in efficiency in terms of multiples of maintenance. Furthermore, digestive efficiency may become depressed as cows consume increasingly large quantities of feed. This is an additional barrier to improving feed efficiency, and when coupled with dilution of maintenance, it appears that we have already captured most of the gains that can be achieved in feed efficiency simply by increasing milk production per cow.

Potential for decreasing maintenance costs by selecting for smaller body size

VanRaden (2004) noted that body size composite, as calculated from linear scores for body traits in the type classification program, has been a component of the Net Merit index (NM$) used to select Holsteins in the USA since 2000. Milk revenues and feed costs associated with differences in milk yield of cows with greater or lesser body size are already considered in the NM$ index, so the economic weight applied to body size composite reflects the marginal costs associated with greater maintenance and housing costs and the marginal revenues associated with greater salvage and calf values. Table 1 shows estimated genetic correlations between metabolic body weight (MBW), dry matter intake (DMI), NEL, and linear type scores for 714 Holstein cows in six research herds (University of Florida, Iowa State University, Michigan State University, USDA-ARS Dairy Forage Research Center, University of Wisconsin, and Virginia Tech University). Genetic correlations of MBW with stature, strength, body depth, and thurl width were 0.71, 0.84, 0.65, and 0.57 respectively, confirming that these linear type traits can serve as an effective proxy for body weight, which is not measured routinely on commercial farms. Several udder traits were positively correlated with MBW as well, particularly udder depth (0.47), which is known to be phenotypically correlated with stature. Genetic correlations of DMI with stature, strength, and body depth were also relatively high, with estimates of 0.40, 0.46, and 0.36, respectively. Presumably this reflects greater feed intake for maintenance among larger animals, as well as a tendency for higher NEL requirements among larger cows, as indicated by genetic correlations of 0.31, 0.41, and 0.42 with stature, strength, and body depth, respectively. Most udder traits had negative genetic correlations with DMI, possibly due to deeper udders and weaker attachments among cows producing very large quantities of milk. As evidence of the latter, genetic correlations between NEL and fore udder, rear udder height, rear udder width, udder depth, and front teat placement were -0.12, -0.27, -0.47, -0.40, and -0.59, respectively. Dairy form was negatively correlated with MBW (-0.22), positively correlated with NEL (0.37), and uncorrelated with DMI (-0.02). Because cows with larger body size have higher DMI but also tend to have greater NEL requirements due to higher milk production, it appears that the solution to improving feed efficiency in dairy cattle is not as simple as just selecting for smaller body size. At the same time, these data provide no evidence that selecting for larger body size will enhance feed efficiency. In reality, selection for larger body size in US Holsteins continues, and at a rapid pace. For example, very few bulls that sire below average stature have semen available for purchase by dairy farmers, and the genetic trend for increasing stature is

consistently greater than that of most or all other type traits. The presence of a negative weight on body size composite in the NM$ index for more than a decade has done little to dampen breeders' enthusiasm for large cattle, and situations in which the cows outgrow housing or milking facilities are common. In addition, a long-term selection project by Becker et al. (2012) reported that Holstein cows selected for large body size had significantly greater health costs than their more moderately sized contemporaries, particularly displaced abomasums. However, attitudes toward selection for body size are unlikely to change unless very large penalties are applied to size-related traits in NM$ and other selection indices.

Challenges in measuring individual feed intakes in dairy cattle

Extensive research on the phenotypic, genetic, and economic relationships between dry matter intake, body weight (BWT), metabolic body weight, milk production, and residual feed intake (RFI) was carried out nearly two decades ago, most notably the work of Veerkamp et al. (1995), Veerkamp and Evans (1995), and Veerkamp (1998). However, the insurmountable costs and challenges associated with measuring individual feed intake data on a sufficient number of animals in a conventional progeny testing program precluded implementation of this work in practical breeding programs. For example, assume that it costs $200 per cow to measure a feed intake phenotype, and that we must measure 100 daughters of each of the 1,500 dairy bulls that are progeny tested in the USA each year. The annual cost of measuring these 150,000 phenotypes would be $30 million, which comes out to $20,000 per bull for a predicted transmitting ability (PTA) for DMI or RFI. Interest in selection for feed efficiency was renewed with the advent of genomic selection, which allows measurement of difficult and costly phenotypes in a reference population of (tens of) thousands of animals, followed by implementation of selection for these traits in the general population. Revisiting our previous example, consider the possibility of spending $200 per cow to measure a feed intake phenotype in an initial reference population of 20,000 cows, with 2,000 new cows added each year. Further assume that genomic testing costs $100 per animal, and that we must genotype all cows in the reference population plus 5,000 young bulls each year. Total cost of the program would be approximately $1.37 million per year or about $275 per bull for a genomic PTA for DMI or RFI. Therefore, it is no surprise that research groups around the world have embarked on studies that aim to facilitate genomic selection for improved feed efficiency.

Genomic selection has already become routine practice in the USA and many other countries, and this has greatly reduced the generation interval, particularly in the "sires to produce sires" and "sires to produce cows" pathways (Schefers and Weigel, 2012). For example, Hutchison et al. (2014) reported that 51 and 52% of inseminations to Holstein and Jersey sires, respectively, in the USA in 2012 involved genome-tested young sires less than 4 years of age. Therefore, if genomic PTA values of young bulls for DMI, RFI, or other measures of feed efficiency become available, widespread implementation by farmers and breeding companies is likely.

Genomic selection for feed efficiency using dry matter intake

Berry et al. (2014) described an enormous multiple-country effort to characterize DMI in Holstein cattle, assess consistencies in trait expression between countries or production systems, and evaluate its suitability as a selection criterion. Data represented 10,068 lactation records

from 6,953 lactating cows in Australia, Canada, Denmark, Germany, Ireland, The Netherlands, UK, and the USA. Predicted DMI was computed for lactating cows at 70 days postpartum using a random regression model; means ranged from 15.6 kg per day in Australia to 24.2 kg per day in the USA. Heritability estimates from a single-step genomic BLUP analysis ranged from 0.11 in Canada to 0.46 in Denmark. Genetic correlations were estimated for DMI in different production systems, including North America (Canada + USA), EU high-input (Denmark + Germany + Netherlands + UK high-input cohort), EU low-input (UK low-input cohort), and Grazing (Australia + Ireland). Estimates between the EU low-input, EU high-input, and North America groups ranged from 0.76 to 0.84, whereas estimates between the aforementioned groups and Grazing ranged from 0.14 to 0.57. However, it is important to note that the number of common sires and maternal grandsires between Grazing and the other three groups ranged from 4 to 28, as compared with a range of 10 to 144 between North American and the two EU groups, and additional data are needed to confirm whether DMI measurements in different management systems reflect the expression of genetically distinct traits. In general, selection for improved feed efficiency using DMI is a reasonable option, and this trait is more understandable to dairy producers than RFI. On the other hand, as shown in Table 1, large positive or negative genetic correlations exist between DMI and many traits that are already included in the breeding goal, so proper accounting for genetic relationships with other traits will be a critical prerequisite to effective use of DMI in a selection program.

Genomic selection for feed efficiency using residual feed intake

Statistically, RFI represents the amount by which a given cow over-consumes or under-consumes feed, as compared with other cows in her cohort, after adjustment for energy sinks such as MBW, change in body weight (ΔBW), body condition score (BCS), and the NEL of the milk she produces. A major effort involving six research stations located throughout the USA, three in The Netherlands, and two in the United Kingdom is currently underway, with the objectives of enhancing our understanding of RFI and its components and developing a resource population of Holstein cows to facilitate the development of a genomic selection program for reduced RFI (Tempelman et al., 2014). At present, the data include 84,645 weekly records from 6,133 lactations of 4,376 Holstein cows. Heritability estimates for RFI during the period from 75 to 175 days postpartum ranged from 0.08 to 0.23, depending on country and stage of lactation, with an estimate of 0.17 for the multiple-country data set at 125 days postpartum. Within-lactation repeatability estimates for weekly RFI measurements ranged from 0.55 to 0.88, with an estimate of 0.74 in the multiple-country data set at 125 days postpartum, whereas between-lactation repeatability estimates ranged from 0.14 to 0.37, with an estimate of 0.30 in the multiple-country data set at 125 days postpartum.

Estimated genetic correlations between linear type traits and RFI based on 714 Holstein cows in the six aforementioned research herds are also shown in Table 1. Genetic correlations between RFI and the body size traits, namely stature, strength, body depth, and thurl width, were all between -0.05 and 0.23, which is expected given that RFI is constructed to be phenotypically independent of MBW. Therefore, selection for RFI should neither increase nor decrease the size and strength of Holstein cattle. Because RFI is also calculated to be phenotypically independent of milk yield and milk composition, those traits should be unaffected, as should traits related to udder conformation, which had genetic correlations that averaged -0.17 and ranged from -0.37 to

0.11. Lastly, genetic correlations between RFI and mobility traits were negligible and ranged from -0.17 to 0.01. While this is encouraging, as regards our ability to avoid unintended correlated responses to selection for improved RFI, it will be important to assess genetic relationships with early postpartum health and female fertility prior to its inclusion in a selection index. If RFI is independent of these traits as well, preliminary selection index calculations suggest that it could warrant a relative economic weight that would represent 10 to 20% of the overall breeding goal.

Relationships with energy balance

Spurlock et al. (2012) estimated genetic parameters for energy balance (EB), energy-corrected milk (ECM), DMI, BW, BCS, and gross feed efficiency (GFE) from calving to 150 days postpartum in Holstein cattle. Conceptually similar to RFI, EB was calculated as the difference between energy consumed as DMI and the energy expended as MBW for maintenance and as NEL for milk production in each of the first five months postpartum. Meanwhile, GFE was calculated as the quotient of the sum of daily ECM and the sum of daily DMI during the first 150 days postpartum, as well as in the first and second half of that time period. On average, EB was negative for the first 60 days postpartum in primiparous cows and the first 70 days postpartum in multiparous cows. Genetic correlations between EB and GFE ranged from -0.73 to -0.99 in a given month of lactation. Genetic correlations between ECM and GFE averaged 0.59 and ranged from 0.42 to 0.72 in a given month, whereas genetic correlations between ECM and EB averaged -0.31 and ranged from -0.02 to -0.53. Among the linear type traits shown in Table 1, dairy form is the most indicative of EB, and its estimated genetic correlation with RFI was -0.09.

Identification of major genes associated with feed efficiency

Most genome-wide association studies (GWAS) in dairy cattle consider only additive allele substitution effects, in part because deregressed sire PTA values or daughter averages are often used as the input phenotypes. However, it is unlikely that all genes affecting RFI act independently and in an additive manner, and building the aforementioned genomic reference populations for feed efficiency necessitates genotyping and phenotyping large numbers of females. In a recent study involving 395 Holstein cows with 42,275 SNP genotypes, Yao et al. (2013) used a random forest algorithm to study possible epistatic interactions between pairs of SNPs that were associated with RFI. By analyzing the structure of decision trees within the forests, the authors were able to identify descendant pairs of SNPs that showed up repeatedly within the same branch in various trees. In many cases, the SNPs that occurred most frequently in descendant pairs were not among those with the largest additive effects in a Bayesian regression analysis that ignored possible interactions. Furthermore, many of the SNPs implicated in the random forest analysis were in common with SNPs associated with RFI in a previous study in beef cattle (Sherman et al., 2009). It is important to consider that RFI is a composite trait that represents the sum of several other traits and numerous underlying physiological processes. Furthermore, other than DMI, most of the individual traits that make up RFI (with the exception of DMI) have been the subject of dozens of GWAS that aimed to identify SNP or microsatellite markers with large effects. Therefore, one might expect that the current GWAS for RFI will lead to candidate SNPs or haplotypes that tend to be fairly numerous but with relatively modest effects on RFI.

Using genomic predictions to manage heifer inventories

The cost of raising dairy replacement heifers represents 20 to 25% of the total cost of producing milk on a typical commercial dairy farm, and feed costs constitute 60 to 65% of total heifer rearing costs. At the same time, the availability of gender-enhanced semen, coupled with the widespread implementation of sand bedding and other advancements in animal housing and husbandry, have led to an excess of potential replacement heifers on many farms. Therefore, for the first time, many farmers are faced with the decision of whether to rear all of the available heifers or to cull some potentially inferior heifers in order to reduce feed costs.

Due to availability of inexpensive low-density genotyping platforms, coupled with accurate imputation to high-density using established reference populations (Weigel et al. (2010a), Weigel et al. (2010b)), genomic testing of young calves and yearling heifers has increased dramatically in the past three years. Weigel et al. (2012) showed via simulation that using genomic testing to identify inferior heifer calves for early culling can be a cost-effective way to improve the production potential of dairy replacements, not to mention the corresponding savings in foregone feed costs.

Do genomic predictions at 2 or 3 months of age provide enough information about future phenotypes to allow confidence in culling decisions at this early stage? Figure 1 shows the relationship between genomic PTA values at 12 months of age and projected or actual 305-day mature-equivalent milk yield phenotypes for 309 first lactation Holstein cows in the University of Wisconsin herd. Average milk yield for the lowest quartile of heifers, as ranked by genomic PTA at 12 months of age, was 11,790 kg, as compared with 12,091, 12,754, and 13,623 kg for heifers in the second, third, and highest quartiles. On average, heifers in the lowest quartile produced 3.4 kg less milk per day than their counterparts in the other three quartiles, and as such they would have been good candidates for early culling.

Figure 1 also shows the regression of 305-day mature equivalent milk yield on the genomic PTA from 12 months of age. The value of 3.2 kg of milk per kg of genomic PTA exceeds its expectation of 2.0, and in general one can use this regression coefficient as an assessment of whether the management level on a given farm is sufficient to fully capitalize on the herd's genetic potential. Closer inspection of Figure 1 shows that individual cows that deviate widely from their expectation tend to be those for which management has failed, most notably protocols for managing animal health in the early postpartum period.

Although the coupling of low-density chips and genotype imputation as made genomic predictions more affordable, routine genomic testing of all heifer calves is limited to a small minority of commercial dairy farms. A significant reduction in the cost of genomic testing is unlikely without another technological breakthrough in chip design or processing capacity. Work by de los Campos et al. (2009) and Vazquez et al. (2010) showed that prediction accuracy using a subset of several hundred selected SNPs that have strong associations with the NM$ index could be beneficial, but the cost of such testing would have to be substantially reduced in order to compensate for the loss in prediction accuracy relative to the current strategy of low-density genotyping and imputation to higher density.

Prediction of future phenotypes using SNP genotypes and heath history phenotypes

As noted earlier, a calf's future phenotype for milk yield and other economically important traits is influenced by its health history as well as its genetic predisposition. Therefore, farmers will need to develop holistic replacement management protocols in which the decision to keep or cull a specific calf, to breed a certain heifer with conventional or gender-enhanced semen, or to make a given animal an embryo transfer donor or recipient depends on its genomic test result, birth weight, growth rate, and health history. With regard to genomic prediction of RFI and other future phenotypes, we may not be interested in only the animal's PTA or estimated breeding value (EBV), but rather the sum of the animal's EBV and its permanent environmental effects. This quantity is commonly known as predicted producing ability or estimated relative producing ability, and it refers to the animal's total broad-sense genetic effects (additive, dominance, and epistatis) plus carry-over effects associated with its management, nutrition, and health history. In our recent work, information regarding 57,541 SNP genotypes for 465 Holstein cows was combined with data regarding the incidence of 13 health disorders during the rearing period and early postpartum period (Yao and Weigel, 2014). Future phenotypes for NEL, DMI, RFI, and MBW were predicted from SNPs only or SNPs plus health history using random forest and support vector machine algorithms. Several health-related traits, including birth weight, calving weight, mastitis, metabolic disorders (ketosis, milk fever, and displaced abomasum), respiratory disease, and scours affected future phenotypes significantly. Correlations between predicted values and future phenotypes averaged 27.5% with SNPs only and 27.8% with SNPs and health history. It is likely that the small magnitude of improvement reflected a lack of precision in the diagnosis or reporting of health problems, coupled with the fact that whole-genome SNPs already contain substantial information about an animal's predisposition for traits such as body weight and susceptibility to infectious diseases and metabolic disorders.

Conclusions

Improvements in average milk yield per cow due to genetic selection and enhanced management have resulted in substantial gains in efficiency over the past half-century, but additional gains will be modest unless individual animal intakes are measured directly. Genomic selection has allowed renewed interest in breeding for feed efficiency, because genomic predictions for DMI and RFI derived from deeply phenotyped reference populations are roughly 100-fold cheaper than predictions derived from conventional progeny testing schemes. Due to the limited size of these reference populations, reliability values for feed efficiency will be lower than reliabilities for milk production and most other important traits. However, the high economic value of feed efficiency will necessitate a large relative weight in the breeding index. Preliminary research suggests that RFI may be an attractive choice for improving biological efficiency, due to its apparent genetic and phenotypic independence from milk production, milk composition, body size, udder conformation, and mobility. However, more research is needed to confirm associations between RFI and functional traits, such as early postpartum health and female fertility. Lastly, strategies for using genome-based predictions of future phenotypes to manage heifer inventories appear to be cost effective, particularly in herds with low rates of involuntary culling or significant use of gender-enhanced semen.

Conclusions

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Table 1: Genetic correlations between linear scores for type traits and metabolic body weight (MBW), dry matter intake (DMI), net energy of lactation (NEL), and residual feed intake (RFI).

Trait	MBW	DMI	NEL	RFI
Stature	0.71	0.40	0.31	0.13
Strength	0.84	0.46	0.41	0.23
Body Depth	0.65	0.36	0.42	0.06
Dairy Form	-0.22	-0.02	0.37	-0.09
Rump Angle	-0.04	-0.06	0.25	-0.33
Thurl Width	0.57	-0.03	-0.41	-0.05
Rear Legs Side View	-0.27	0.13	0.34	-0.06
Rear Legs Rear View	0.27	-0.01	-0.38	0.01
Foot Angle	0.11	-0.14	-0.42	-0.17
Fore Udder	0.03	-0.09	-0.12	-0.17
Rear Udder Height	0.24	-0.23	-0.27	-0.23
Rear Udder Width	0.28	-0.37	-0.47	-0.08
Udder Cleft	0.03	-0.01	-0.17	0.11
Udder Depth	0.47	-0.24	-0.40	-0.27
Front Teat Placement	0.03	-0.55	-0.59	-0.37
Teat Length	0.44	0.19	0.53	-0.18

Figure 1: Relationship between genomic predicted transmitting abilities for milk yield at 12 months of age and daily milk yield phenotypes in first lactation.