Genomics Tools for Improving Health and Production Performance of Canadian Pigs

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ABSTRACT: Although the pig industry around the world has benefited much from application of BLUP, new genomics tools are promising more benefits. Studies on production, health and meat quality traits have demonstrated the power and potential of genomics. For successful application of genomics, dense enough marker panel and thousands of genotyped animals to build a large reference population are needed. Despite the benefits of genomics, large-scale application is very costly due to the high price of genotyping. Previous studies have shown that using imputation can help to decrease genotyping costs, however, successful validation models and protocols are needed to define strategies for selection of genotyping candidates and for choosing the appropriate SNP panel density. This study provides an overview on the current status of genomic evaluation research in pigs and tools required for application of the technology by the swine breeding industry.
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Traditional BLUP Evaluations for the swine industry

The Canadian Swine Improvement Program (CSIP) has been using the Best Linear Unbiased Prediction (BLUP) in genetic evaluations since 1985 (Hudson and Kennedy (1985)). At the apex of the swine industry are Canadian purebred swine breeders that produce top genetics, which are exported or flow from breeders down to commercial producers. Good Canadian genetics are also key in helping the country maintain its status as one of the largest pork exporters in the world. One of the most noticeable advantages observed since the implementation of BLUP is the genetic progress made on the litter size in Landrace and Yorkshire breeds since 2000. Since that year, there has been about a +0.25 piglet increase in litter size per year. Before then, there wasn't any change in litter size herd average in Canada despite some of the herds practicing phenotypic selection for this trait (CCSI (2013)). One of the important benefits of changing genetics through selection is consistency over time. For example the average backfat thickness had decreased approximately 0.3 mm every year since 1980 and reached an optimum level of 10 mm in 2010. At that time, backfat was removed from selection objectives thus removing the selection pressure on this trait; since then, phenotypic backfat levels have been maintained almost unchanged (CCSI (2013)). These successful examples of BLUP application in pigs have led to progress on different traits. Genomics is the next game changer and it has even greater potential than BLUP.

Power and Potential of Genomics Technology

Although molecular genetic technologies have been around for several decades, commercial application of genomics technology to animal breeding only began in early 2000s with the introduction of GeneChip® Bovine Mapping 10K SNP Kit (Affymetrix, Santa Clara, USA). Following a decade of intensive research by the dairy cattle industry, official genomic estimated breeding values (GEBVs) now exist for almost every top bull around the world. Schaeffer (2006) predicted that genomics could double the rate of genetic progress in dairy cattle. It has been 5 years since the implementation of genomics in dairy cattle; the industry is now reaping the benefits of using genomics (Van Doormaal (2014)). Genomics has not been as extensively implemented in the pig industry as in dairy cattle. One reason for this is the fact that the PorcineSNP60 panel (Illumina, San Diego, USA) was only made available to the industry about four years ago. The other reason is the cost of this panel in comparison to the economic benefit obtained from genotyping an individual animal. With more than 10 piglets per litter and about 2.2 farrowing each year, genotyping all young piglets with high-density panel can be very expensive. In 2012, the GeneSeek Genomic Profiler for Porcine (GGP-Porcine) LD (GeneSeek, Lansing, USA), containing about 8.5K SNPs was made available to the industry. The cost of this technology was still relatively high, which remains the main limiting factor for the application of genomics. Providing an official GEBV for animals doesn't only depend on the price of the SNP chip. There is also the cost associated with sampling, DNA extraction, genotyping, data handling and storage, GEBV estimation and publication.

While GEBVs have not yet been widely used commercially by the pig industry, there is evidence that this technology can be very beneficial. One of the recent challenges facing the pig industry is emerging diseases such as porcine reproductive and respiratory syndrome (PRRS). The nature of diseases can be very complicated but there is hope that genomics can help. One such example is reported by Boddicker et al. (2012) where crossbred pigs exposed to a PRRS virus challenge were monitored and sampled over several weeks post-infection and genotyped using the 60K Beadchip. The authors found a SNP associated with viral load and post-infection weight gain, which explained a large proportion of observed genetic variance. The porcine 60K panel has been also used to study the potential of genomics for improving meat quality, which generally cannot be measured *in vivo*. As part of a validation study led by the Canadian Centre for Swine Improvement (CCSI)

on about 500 station-tested Duroc pigs, a correlation of about 60% between direct genomics values (DGVs) and estimated breeding values (EBVs) of animals for Minolta L* and loin marbling score was found. In another study on genomic evaluation for litter size in Canadian Yorkshire pigs, genomic EBVs had 20% greater predictive ability than parental average (PA) EBVs for litter size (Jafarikia et al. (2012)). In another recent paper demonstrating the potential of genomics to improve various traits (Squires et al. (2014)), the authors reported promising results with regards to reducing boar taint via genomics using approximately 100 SNPs across 40 candidate genes associated with the metabolism of boar taint compounds. The authors showed that as the number of unfavourable SNP alleles increased, so did taint levels in fat tissues.

The examples mentioned above show how genomics can help increase the accuracy of genetic evaluations or to select for traits such as disease resistance and meat quality that are challenging to include in traditional BLUP evaluations. It is also possible to use genomics to provide more accurate early evaluations on traits measured later in life and sex-limited traits, such as sow productivity and sow longevity. As an example, for maternal traits such as litter size, it takes about 26 months to have the breeding values of a boar based on the performance of his daughters. However, by that time most of the boars will have been replaced by younger elite boars to increase genetic progress on other traits of interest. Yet, it is possible to have relatively accurate EBVs for litter size and other such traits at a very young age by using genomics technology. This can dramatically increase the rate of the genetics progress for those traits.

Resources Needed for Genomic Application

Linkage disequilibrium. Linkage disequilibrium (LD) is defined as non-random association between markers and usually is quantified by r^2 for SNP (Hill, (1981)). Successful application of genomics requires high levels of LD between markers and quantitative trait loci (QTL) controlling the variation of the trait of interest. Previous research in Canada (Jafarikia, et al. (2010)) and the U.S. (Badke et al. (2012)) have reported high levels of LD in pigs using the current 60K panel SNP chip with average r^2 greater than 0.3 between adjacent SNPs. Meuwissen et al. (2001) reported $r^2 > 0.2$ in their simulation study to obtain a GEBV accuracy of 0.85. The current levels of LD between SNPs on the 60K panel are sufficiently high enough for an accurate estimation of the GEBV in pigs. Though researchers cannot control the levels of LD between markers on a panel, it is possible to use higher density SNP panels if LD levels between SNPs on a given panel are low.

Reference population. Genomic evaluations are calculated through the process of estimating SNP effects in a training population of individuals with genotype and phenotype information and

Figure 1: A schematic view of the application of genomics for selection of the breeding animals at different selection stages
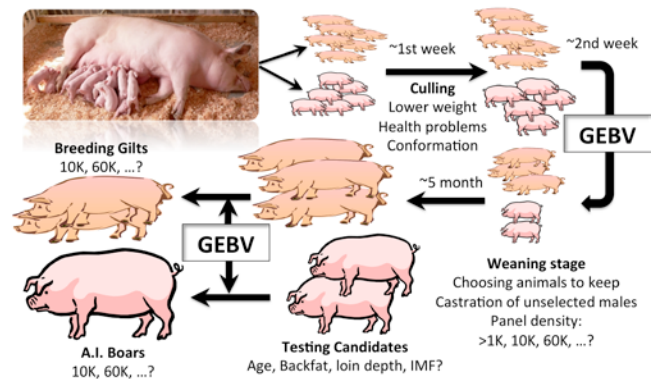

using SNP solutions to predict GEBVs for genotyped individuals in a prediction group. To accurately estimate solutions for thousands of SNPs, thousands of genotyped animals with accurate records are required. Just as important as genotypes are accurate phenotypes which are used to estimate SNP solutions. With thousands of genotyped animals across a given population, there is more chance to capture all haplotypes segregating in the population. The variability of SNP alleles and phenotypes are also important to be able to capture all segregating QTL in the population. The accuracy of GEBVs also depends on the heritability of the trait under study. Genomic evaluation generates more accurate EBVs for traits with higher heritability (Goddard, (2008)).

Benefits from investment on genomics can differ based on the amount of money spent and structure of the population under selection. In a paper by Lillehammer et al. (2013), they showed how the break-even point (minimum number of market hogs to cover the costs of genotyping) could be changed based on different factors. Genetic gain can be changed by choosing which animals to genotype. Consequently, genomic selection could change current industry practices where across litter selection of young piglets could be used instead of within litter selection. A schematic view for a potential use of genomics is presented in Figure 1.

Imputation. Although there is no doubt about the benefits of genomics, a significant barrier to adoption of genomics by the industry is the cost of genotyping. Development of imputation procedures to impute untyped genotypes from cheaper SNP panels to higher density ones is a promising option that can help decrease genotyping costs. Research has shown that the Canadian pig industry can significantly decrease genotyping costs through imputation. Kinsman et al. (2012) showed that it is possible to impute 60K SNP genotypes from a 10K panel with more than 95% accuracy using 658 Yorkshire pigs in a reference population. Further research on imputation using a larger reference population (Lee et al. (2013)) also demonstrated that it is possible to obtain high levels of accuracy of imputation using a low-density SNP panel (Figure 2). Lee

Figure 2: Accuracy of imputation for different panel sizes in major Canadian pig breeds (adapted from Lee, 2013).
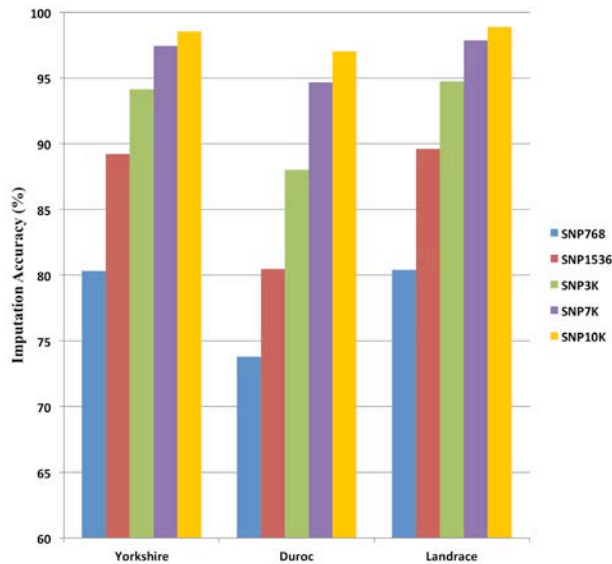
et al. (2013) used reference population sizes of 866 Duroc, 1,469 Landrace and 1,941 Yorkshire pigs. In that particular study, a total of 200 animals were included in validation groups in each breed. Within breed imputation accuracies of 60K genotypes from a 10K chip were 97% in Duroc, 99% in Landrace and 99% in Yorkshire. Imputation accuracy of a 3K panel was 88%, 94% and 95% in Duroc, Landrace and Yorkshire, respectively. Other studies (Huang et al. (2012); Cleveland and Hickey (2013)) showed that the accuracy of imputation and GEBV from imputed data depends on the panel density and population structure. Results from these studies suggest that to reap the benefits of genomics, strategies for choosing genotyping candidates and a panel with an adequate density are required. Wellman et al. (2013) suggested genotyping selection candidates using a very low-density panel (384 SNP) where at least one parent is genotyped using a high-density panel. Huang et al. (2012) recommended genotyping sires using high-density panels, dams with lower-density ones (e.g. 3K SNP) and young candidates using a panel consisting of 384 SNPs. Lillehammer et al. (2013) proposed genotyping dams using high-density panels if progress on maternal traits is more of interest than production traits. They also reported that genotyping females instead of males would lower the inbreeding rates.

Methods of evaluation. There are different methods available to estimate GEBV such as GBLUP (Legarra, et. al., (2009); VanRaden, (2008)) or Bayesian methods (Gianola, et al. (2009)). Each method has its own strength. Different methods need to be validated for different traits using enough genotyped animals.

Implications

By using imputation technology, the very low-density SNP panels (384 SNPs) should be accurate enough and affordable to start selecting animals at a very young age. Putting the theory into practice, however, requires some guidelines and successful validation models. Besides the need for building a large resource population by genotyping thousands of purebred animals, emphasis should be placed on defining strategies for developing low-density panels and protocols for a genomic evaluation program. Collaboration between different breeding suppliers could increase the size of the reference population. By doing this, the swine industry could benefit from collaborative research on a strategy for application of genomics.

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