

Potential Contribution of Genomics and Biotechnology in Animal Production*

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Introduction

Integration of Latin American countries into international agricultural markets requires animal production systems to be competitive. Demand of animal products is increasing due to population growth, and changes in lifestyle of some countries. This will demand modifications to the production systems to increase efficiency of animal production. The use of genomics will offer new opportunities to improve animal production that is sustainable and highly competitive in world markets.

Selection has been useful to increase productivity in livestock. Conventional selection schemes used to increase milk, beef, pork, and other livestock products have been implemented by using quantitative genetics. Selection programs have mainly focused on quantitative traits; this is, traits controlled by many genes. Animal breeding schemes have been successful when implemented. Their objective is to determine which progenitors have the best combination of genes to improve the trait of interest by producing improved offspring. Establishing which animals have the best combination of genes for a given trait has been accomplished by using pedigree information (parents, grandparents, cousins, and/or offspring).

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The use of animal breeding schemes is difficult in many production systems because no pedigree information exists.

There are several biotechnology techniques currently being effectively used world-wide in livestock production. These include artificial insemination, vaccine production, *in vitro* fertilization (IVF), and multiple ovulation and embryo transfer (MOET). These techniques have allowed the use of high quality genetic material to be used. The impact of these techniques has been mostly in dairy cattle production, and to a lesser extent in beef cattle and swine. Genomics, genome-wide association studies, and genomic selection are additional biotechnological techniques that have been recently developed, and will be further discussed.

Genomics is the discipline that studies the genome, and was first coined by Thomas H. Roderick in 1986. The word "genome" is the consolidation of the words "gene" and "chromosome" (McKusick, 1997). The genome refers to the genetic material contained within the chromosomes; therefore, genomics is the study of the genetic material, its sequencing, and analysis. The development of genomics was prompted by the availability of the human genome sequence (Lander *et al.*, 2001; Venter *et al.*, 2001), and since then, the genome sequence of most livestock species is available or will be available in the near future.

A genome-wide association study (GWAS), or whole genome association study, is the use of thousands of genetic variants, known as single nucleotide polymorphisms (SNP), to examine the genome and identify if these variants are associated with a trait of interest. These studies compare variation at each SNP to determine if alleles are associated with binary or continuous traits. The process is repeated for each SNP (Goddard and Hayes, 2012).

Genomic selection was defined by Goddard and Hayes (2007) as a form of marker-assisted selection in which markers covering the genome are in linkage disequilibrium with all quantitative trait loci, so estimated breeding values (EBV) can be predicted with high accuracy in further generations using genetic markers. Genomic selection uses the information derived from GWAS to produce genomic estimated breeding values (GEBV). These values can be used in animal breeding schemes.

This chapter is divided in two sections. In the first section we will briefly discuss what are genomics and genomic selection, and its potential implementation in animal breeding schemes. In the second section, advances made in genome-wide association studies and their potential use in genomic selection will be described for dairy and beef cattle, pigs, sheep

and goats. Producers need to be aware these procedures can be used or are being used in livestock to improve production.

Genomics

The bovine genome is comprised of 29 autosomal pairs of chromosomes and the sex chromosomal pair. The bovine genome has a minimum of 22 000 genes, of which 14 345 are orthologues shared among different mammalian species. The estimated size of the bovine genome is 2.87 Gigabases (Bovine Genome *et al.*, 2009). The swine genome covers 18 autosomal chromosomes and the sex chromosomal pair. Its size is estimated to be 2.6 Gigabases, and there are currently 21 640 annotated genes in the genome sequence (Archibald *et al.*, 2010). The sheep genome comprises 26 pairs of autosomal chromosomes and the sex chromosomal pair. The sheep genome is estimated at 2.61 Gigabases in length (International Sheep Genomics *et al.*, 2010). The goat genome sequence is underway and will likely be available in the near future (www.goatgenome.org). The availability of the genomic sequences for livestock is important because it is now possible to identify the genes, and to understand the role of these genes (known as functional genomics), in the productivity of the species of interest.

The availability of high throughput sequencing not only enabled the development of the genome sequencing projects for livestock, but also allowed for the development of microarrays with thousands of single nucleotide polymorphisms (SNP). Such is the case of the BovineSNP50 BeadChip with 50 000 SNP, and the BovineHD BeadChip with 777 000 SNP (Van Tassell *et al.*, 2008). The PorcineSNP60 BeadChip is comprised of 60 000 SNP (Ramos *et al.*, 2009). Both, the SheepSNP50 BeadChip (Kijas *et al.*, 2009), and the GoatSNP50 BeadChip (Tosser-Klopp *et al.*, 2014) contain 50 000 SNP each. These microarrays have been produced by one company (Illumina Inc., San Diego, CA), and other companies may produce their own. These microarrays are important tools in genomic selection because allow genome-wide association studies.

The development of high density BeadChips using SNP has allowed for the simultaneous scanning of the entire genome. Studies with this objective are known as Genome-Wide Association Studies (GWAS). Their objective is to identify genomic regions or genes associated with traits of interest in livestock. These studies have different objectives according to the species or the trait of interest within the species, but in all cases, the objective is to improve productivity using the animal's genetic potential.

Genomic selection

The process of genomic selection (GS) is shown on Figure 1. This process initiates by measuring economically important traits (Phenotypes) in a population (training population), and at the same time collecting genomics information (Genotypes based on SNP), based on Bead-Chip information. This information is used to estimate marker effects in the population. Genotypic information is attained from the progeny, or test population, without obtaining phenotypic information. BeadChips are used in the test population, and genotypes are imputed from the training population. Genomic expected breeding values (GEBV) are generated for the test population. Similarly, it is possible to generate GEBV for other generations (Goddard and Hayes, 2009; Goddard *et al.*, 2010).

This process has been successfully applied in the dairy industry of the United States (VanRaden *et al.*, 2009). VanRaden *et al.* (2009), using genomic selection, were able to increase the reliability of milk production traits up to 23 % when compared to reliabilities of parent averages without using genomic selection. Genomic selection in dairy cattle was possible because of the structure of the dairy industry in the United States. This is, the dairy industry uses mostly Holstein cattle, and selection of this breed has limited the founding sires used in the industry, thus, most dairy cows are related. In beef cattle, the use of genomic selection has been less successful. Snelling *et al.* (2010) produced genomic information from a training population, and this information was used to predict GEBV in a different population (Kuehn *et al.*, 2011). The reliabilities from this prediction were less than expected. Genomic selection allows the prediction of breeding values of young animals, or animals without phenotypic information, but relationship between populations needs to be established if genomic selection is to be successful.

Potential contribution of genomics to dairy cattle

In 2013, Latin American countries had approximately 44 million heads of dairy cattle producing 85.1 million tons of fresh milk. This production represents approximately 13.3 % of the world's fresh milk (FAO, 2013). The countries with most production are Brazil, Argentina, Mexico, Colombia, and Ecuador. These countries produce 82.3 % of fresh milk in Latin America. The other countries combined produce the remaining 17.7 % (Table 1).

The national milk production average per cow is very different among countries (Table 1). Milk production systems are inconsistent, so it is difficult to classify them. In some countries, it is possible to find highly technified dairies with intensive milk production systems; however, it is also possible to find production systems where a small herd is pastured and manually milked. In Brazil, there are approximately 1.35 million dairy farms with an estimated average

herd size of 17 cows. There is an uneven distribution of milk production among producers, because there are small-scale low production farms (*i.e.*, < 20 kg of milk/farm/day), but the majority of the country's milk (75 %) is produced by 20 % of the largest dairy farms.

Milk is mainly produced in farms located in moderate or temperate climates in some Latin American countries, as is the case in Argentina (95 % of the national milk production come from the Pampas region). In this region of Argentina the dairy farm size distribution is different when compared to other regions. There is an average of 192 dairy cows per farm in Argentina. Small size farms (farms producing 845 kg of milk/farm/day), comprise 40 % of the total number of dairy farms, producing 17 % of the country's milk. The remaining 83 % of the milk is produced by middle and large size dairy farms, corresponding to 44 %, and 39 % of the total number of farms, respectively (Taverna, 2010).

After the 1980's the most common dairy breed in Latin America became the Holstein, after a process known as "Holsteinization". Countries with temperate and moderate climate regions in the southern hemisphere are the main buyers of Holstein semen and embryos from the United States and Canada. In Argentina, approximately 65 % of dairy cows are inseminated. In 2013, 96 % of semen traded was Holstein and 4 % of semen was from Jersey or other breeds (CABIA, 2013). Currently the dairy herd composition in Argentina is 77 % Holstein and 23 % of other breeds or crossbred. Recent tendencies incorporate Jersey to improve milk quality (Bretschneider and Cuatrin, 2015). In Brazil most of the milk is produced by large dairy producers from the southern states. The total marketed dairy semen last year was 59 % Holstein imported from the United States and Canada. In 2014, Brazilian semen production from Gyr and Girolando (5/8 Holstein x 3/8 Gyr) was 86.7 %, showing increased use from these breeds in recent years (ASBIA, 2014). Up to 24 % of milk production was produced from Gyr and Girolando.

Regardless of the country, the main focus is to improve the milk yield, efficiency of production and quality traits of milk. Due to the range in climates, geographic and cultural variations, systems to produce milk vary greatly throughout the continent. As a consequence, the genetic resources used in high technological dairy farms and traditional pasture cattle systems are diverse in Latin America. To date, genomics has not been used in comparing GWAS of high performing dairy breeds and crossbred animals for milk production in Latin America.

Genomics of Milk Production

As previously indicated, the assembly of the cattle genome (Bovine Genome *et al.*, 2009), together with the development of high-throughput SNP genotyping, opened the possibility

of using genomic information in animal breeding. The dairy industry has taken advantage of these developments, and today breed associations and artificial insemination companies are making selection decisions based on GEBV. The use of genomic selection approach proposed by Meuwissen *et al.* (2001) was rapidly adopted and adapted for the Holstein. The use of these tools allows breeders to identify genetically superior animals at an earlier age and improve the rate of genetic gain. Nevertheless, the accuracy of GEBV depends on the size of the training population, the heritability of the trait, and the relationship between selected candidate sires and dams, and the training population (Scheifers and Weigel, 2012). There are concerns on the intensive use of genomic selection. One of them is how to maintain genetic diversity when most of males and females used were descendants of the same donor dams derived from MOET and IVF programs from the same population. The effect of superior Mendelian sampling contribution in genomic pre-selection of young bulls was studied by Patry and Ducrocq (2011). They concluded that breeding values of preselected young bulls and daughters, and their accuracies, would be underestimated if preselection is unaccounted for in the evaluation. Preselection of young bulls and daughters need to account for relationships when genomic evaluations are being implemented.

Genomic selection has become the standard in dairy cattle in the United States (Wiggans *et al.*, 2011). The United States and Canada have shared genomic information since the BeadChips became available (Wiggans *et al.*, 2009). Given the structure of the dairy industry in other countries, and standardization of commercial SNP microarrays, it has been possible to share genomic information with other countries using the United States Holstein population as a reference (VanRaden *et al.*, 2012; Zhou *et al.*, 2013). Genomic information has also been used to identify relationships among Holstein, Jersey, and Brown Swiss (VanRaden *et al.*, 2011). Genomic information from Jersey has been shared between the United States and Denmark to improve accuracies in both countries (Wiggans *et al.*, 2015). The use of genomic information used to improve milk production in Latin American countries has been initiated. Garcia-Ruiz *et al.* (2015) used Holstein genomic information from the United States and Mexico to determine the effect of establish the relatedness of animals in the reference population and the Holstein population in Mexico. A similar process can be pursued by other Latin American countries to improve dairy production.

Some dairy breed associations in Latin America began to genotype dairy bulls and cows with different BeadChips. Results are preliminary and the link between animals with genomic information, methodologies used, and the reference population, is unclear. This hampers the process to accomplish significant results. In some countries most of the dairy production is

done using dual purpose cattle and/or multi-breed. For these populations, the interaction genotype x environmental should be carefully analyzed for genomic selection. The availability of large databases that include phenotypic and genotypic information, the different approaches to predict the response of genomic selection can affect its success as indicated by Bouquet and Juga (2013), and should be considered when implementing genomic selection. In Latin America there are countries that have large dairy cattle pedigrees and phenotypic information, mostly from Holstein, and also expertise in genetic evaluation methodologies (i.e., Argentina, Brazil, Colombia, Mexico, and Uruguay). The basic infrastructure to run breeding programs exists in these countries to perform genomic evaluations.

Recently, there has been scientific contribution from Latin America to the understanding of dairy genomics resources (Garcia-Ruiz *et al.*, 2015). The first quantitative trait locus (QTL) report in *Bos indicus* dairy breed affecting milk production traits was reported by Silva *et al.* (2011) in a Gyr population. Liao *et al.* (2013) used a whole genome sequence of three Gyr bulls from Brazil and found several potential genomic regions putatively associated with adaptation to tropical conditions. Utsunomiya *et al.* (2013) used the BovineHD in Angus, Brown Swiss, Gyr and Nellore, and detected loci under positive selection using different genome-wide scan methods. One putative pathway under selection was the ganglioside deposits in milk globules in Gyr. In a sample of 476 Gyr sires from commercial partner breeders in Brazil, Da Silva *et al.* (2014) described the analysis of Copy Number Variation Regions (CNVR) to have a better understanding of the organization of the *B. indicus* genome. In a Holstein population raised under tropical conditions, Lung *et al.* (2014) identified four SNP associated with somatic cell score (SCS). Nani *et al.* (2015 a; 2015 b), studied SCS and others traits associated with mastitis in a Holstein and Holstein x Jersey population in Argentina using a candidate gene, and a GWAS approach. In one study (Nani *et al.*, 2015 a) they identified two SNP associated with SCS. In the GWAS (Nani *et al.*, 2015 b) they detected at least five chromosomal regions associated with different mastitis-related traits. This showed they identified that different mastitis-related components were associated with SNP in these studies. Beribe *et al.* (2014), using 23 paternal half-sib families derived from Holstein and Jersey x Holstein crossbred parents, detected an association within the region that encompasses the DGAT1 gene. This is considered as a validation test for the genetic marker in this gene associated with fat yield in milk (Thaller *et al.*, 2003a). Beribe *et al.* (2014), besides detecting a QTL on chromosome 14, detected two additional regions associated with fat yield (chromosomes 1 and 27).

A genomic selection approach would be useful if implemented, but it would be limited to countries with large Holstein herds in temperate climates and technically advanced dairy

farms. Much work and effort is needed to collect phenotypic and pedigree information from small size dairy farms which use crossbred or dual purpose breeds. An exception is Brazil which is implementing genetic evaluations in domestic zebu breeds. Brazil has been evaluating the Gyr and Guzarat breeds and the Girolando synthetic breed for more than 18 years (EMBRAPA, 2001; 2014).

Several countries and international organizations in Latin America recognize the importance of food security. As international demand for dairy products is expected to increase along with global population and a growing global middle class, the expectations for Latin America countries are promising if genomic selection is implemented in dairy cattle. The potential contribution of genomics and biotechnology to the dairy industry will be coupled with the political decisions and investment in basic and applied research efforts. This will potentially produce a growing, sustainable, and profitable dairy production system in this region of the world.

Potential contribution of genomics to beef cattle

Genomics of Beef Production

Growth rate and feed efficiency are two important components in beef cattle production. QTL for growth traits were initially identified in different populations using microsatellite markers (Casas *et al.*, 2004a; Gutierrez-Gil *et al.*, 2009). The results from these markers had limitations, given that large families needed to be designed and developed. Single nucleotide polymorphisms allow the identification of loci associated with growth traits in outbred populations without the need to develop large families. Several efforts have been made to identify genomic regions associated with growth traits in beef cattle. As example, Snelling *et al.* (2010), using the BovineSNP50 BeadChip, identified several regions on chromosomes 6, 7, 11, 14, and 20, associated with birth weight, pre- and post-weaning weight gain, and yearling weight. A similar association of SNP with growth traits was detected on chromosome 6 by Lu *et al.* (2013 a). The region identified on chromosome 6 overlapped with another region associated previously identified by Casas *et al.* (2000) and Gutierrez-Gil *et al.* (2009). Buzanskas *et al.* (2014), studying the Canchim breed in Brazil, identified SNP associated with growth traits. Chromosomes 4 and 9 harbored SNP associated with birth weight; chromosomes 6 and 11 harbored genes associated with weaning weight, SNP residing on chromosomes 7, 22, 25, and 27 were associated with yearling weight. It will be important to ascertain if similar regions are associated with growth traits in cattle populations from different Latin American countries to make use of the information currently available.

Genomics of Feed Intake in Beef Cattle

An important trait in beef production is feed intake. Feed intake is an economically important trait, given that feed represents one of the greatest costs in beef cattle production. The traits used to ascertain feed efficiency have been Residual Feed Intake (RFI) and Dry Matter Intake (DMI). Several studies have been conducted to establish genomic regions associated with RFI or DMI (Bolormaa *et al.*, 2011; Lu *et al.*, 2013 a; Santana *et al.*, 2014). The objective of these studies was to identify SNP associated with RFI or DMI, to support further studies related to the identification of causal genomic differences associated with the traits of interest. Bolormaa *et al.* (2011), using crossbred animals under tropical conditions, found association of SNP with feed efficiency traits on chromosomes 3, 5, 7, and 8. Lu *et al.* (2013 a), using a mixture of purebred and crossbred animals of *Bos taurus* descent, detected the association of SNP with RFI and DMI in several chromosomal regions. Nellore is an important breed in Brazil. A study done using this breed identified SNP on chromosomes 4, 8, 14, and 21, associated with RFI and DMI (Santana *et al.*, 2014). Chromosome 8 seems to be consistent across studies of harboring genes associated with RFI and DMI in beef cattle. Khansefid *et al.* (2014) estimated GEBV for RFI in beef cattle using animals derived from *Bos taurus* descent. Khansefid *et al.* (2014) indicate it is possible to estimate GEBV from a multi-breed training population to identify SNP associated with RFI and use them to estimate GEBV in another breed.

Genomics of Carcass and Meat Quality Traits in Beef Cattle

Carcass and meat quality traits are of importance in beef cattle production. These traits are targets for genomic selection because they are obtained in sacrificed animals and data for these traits are expensive to collect. Genomic selection can be an alternative for breed improvement without the need to collect data for every animal. As with growth traits, carcass and meat quality traits have been the focus of studies designed to identify QTL (Casas *et al.*, 2003; 2004 b; Gutierrez-Gil *et al.*, 2009).

Genome-wide association studies have been done for carcass and meat quality traits. Kim *et al.* (2011), using the BovineSNP50, identified an SNP associated with marbling score on chromosome 3, SNP associated with backfat on chromosomes 11 and 13, and SNP associated with rib-eye area on chromosomes 6 and 16. Lu *et al.* (2013 b), using a crossbred population identified seven SNP associated with hot carcass weight on chromosome 6, and twelve SNP on chromosome 20 associated with rib bone. Genome-wide association studies for carcass traits have also been done in Brazil. Mokry *et al.* (2013) identified genomic regions harboring genes associated with backfat thickness in the Canchim breed. It is important to notice that results from Mokry *et al.* (2013) are different from those in other regions of the world. It would

be important to establish if these differences are due to breed, or to differences in production systems and/or climate.

Genomics of Reproduction in Beef Cattle

Reproduction is an important component of beef production. The initial studies for reproduction traits focused on ovulation rate (Blattman *et al.*, 1996). Blattman *et al.* (1996) identified QTL on chromosomes 5 and 7 associated with ovulation rate in cattle. After these studies, the identification of QTL associated with twinning rate was pursued (Kappes *et al.*, 2000; Cruickshank *et al.*, 2004). Kappes *et al.* (2000) identified a QTL on chromosome 5 associated with twinning rate in beef cattle. Cruickshank *et al.* (2004) identified QTL for twinning rate on chromosomes 5, 7, 19, and 23. From these studies, it can be summarized that chromosomes 5 and 7 potentially harbor genes associated with reproductive traits in cattle. Recently, McDanel *et al.* (2014), using a large population and the BovineHD BeadChip, identified SNP associated with reproductive efficiency on chromosomes 1, 5, 21, 25, 29, and X. McDanel *et al.* (2014) used a binary trait (pregnant/non pregnant) to identify the genomic regions associated with reproductive efficiency. Although populations used to identify genomic regions associated with reproductive traits in females are diverse, results seem to identify few chromosomal regions. The field of genomics for reproductive traits in cattle is open for study and implementation in Latin American countries.

Genomics of Respiratory Disease in Beef Cattle

Respiratory disease in cattle is the major cause of economic loss, and the leading cause of death. Given that cattle is continuously exposed to pathogens, it has been proposed that genomic selection could be used to select for enhanced resistance to disease. Additive genetic variation is known to exist for tolerance or resilience to disease. For example, it has been estimated that heritability for bovine respiratory disease ranges from 0.04 to 0.2 (Snowder *et al.*, 2006). The moderate heritability of disease resistance and high cost of measuring the phenotype makes it suitable for being a candidate for genomic selection implementation. Several studies have identified genomic regions associated with diseases in beef cattle; the most relevant being respiratory disease.

Identification of genomic regions associated with respiratory disease was done using microsatellite markers in reference populations (Casas and Snowder, 2008; Neibergs *et al.*, 2011). Regions on chromosomes 2, 20, and 26 were identified as harboring genes associated with respiratory disease in cattle; although candidate genes responsible for the condition were unidentified. Recently, genome-wide association studies have identified genomic regions

on chromosomes 1, 2, 6, 8, 10, 15, and 18, associated with persistent infection of bovine viral diarrhea virus (PI-BVDV), which is considered a respiratory disease pathogen (Casas *et al.*, 2015). Similarly, a large study was conducted to identify genomic regions associated with respiratory disease, in which more than 370 SNP, residing throughout the genome, were associated with the trait (Neibergs *et al.*, 2014). Results from these studies suggest that genomic selection should be successful in limiting respiratory disease in cattle if it were to be implemented.

Potential contribution of genomics to pig production

With over a billion head of pigs on the planet and over a hundred million metric tons of pork produced annually, pork is the most widely eaten meat and accounts for about 38 % of all meats consumed worldwide. Latin and South American pork production has increased in recent years along with growing local demand reducing the amount available for export. With an increase in urbanization, disposable incomes and more intensive agricultural practices, pork consumption has increased globally. Pork production in Latin America has recently been dominated by Brazil (50 %) followed by Mexico (18 %), Chile (8 %), Argentina (4 %) and Colombia (3 %). Production has increased from 15 % (Argentina) to 18 % (Colombia) and consumption has raised from 30 to 100 %, respectively. Due to the abundance of crops in South America, feed costs for livestock have been reduced as well. With increasing world population and improved living conditions, meat production and consumption is expected to double and per capita consumption to increase by about 30 % in the next few decades (Wu *et al.*, 2014). Therefore it is critical that world meat production through the development of stable, efficient and sustainable agriculture is substantially increased to meet this need. Challenges to this are increased production costs, an effective infrastructure, reduction of the environmental foot print to produce livestock and disease. Improvements in dietary protein (meat) yields can be made through superior genetics for meat quality, feed and reproductive efficiencies and resistance to disease.

Much of the genetics used for swine production is supplied through semen or live hogs by global swine breeding companies based in Europe, the United States and Canada, such as, PIC, Genesis, Topigs Norsvin and Smithfield. Genetic improvement programs incorporating genomics, pedigree and performance evaluations can enhance genetic progress. These companies have competed to supply superior genetics through traditional selection, pedigree-based BLUP and more recently GS based on GEBV, using SNP due to the availability of high-density genotyping platforms. The main benefits of genomic selection are increased selection accuracy and reduction of cost, and labor to collect phenotypic data. This is

especially useful for traits that difficult or costly to measure, such as meat quality or sex-limited traits that can only be measured in females, *i.e.*, reproduction and litter traits. Since the current pig genomic sequence assembly released in 2011, discovery of large numbers of SNPs in pig genomes by sequencing (Wiedmann *et al.*, 2008; Bianco *et al.*, 2015), and the development of the PorcineSNP60 BeadChip (Ramos *et al.*, 2009), genotyping large numbers of phenotyped animals or breeding animals from nucleus herds on a consistent platform has become a feasible and cost-effective way to collect a large amount of genomic data. This tool has been available for the pig since late 2008 and has been used for numerous genome-wide associations for litter and reproductive traits, meat quality, growth, feed intake and efficiency, and infectious and inherited diseases. The current high-density versions contain over 60 000 SNP and a lower density version containing a fraction of those has over 10 000 SNP. While many whole-genome scans using microsatellite markers have identified many QTL for multiple traits over the last two decades, the dense coverage of high-throughput SNP genotyping has provided much greater resolution to detect associations. Traits selected by breeding companies for genetic improvement include carcass and meat quality, lean growth, feed intake and efficiency, litter size, pig vitality, lactation efficiency and herd health. While selection for these traits can be incorporated into a genetic suppliers breeding program, many of these traits are too costly or difficult to collect on large numbers of breeding animals in nucleus herds and requires large numbers of genotyped and phenotyped animals in production settings. Although the original goals of high-density genotyping was for genome-wide selection using genomic estimated breeding values based on cumulative SNP effects, the genotypes have been used extensively for association testing and mapping QTL. Therefore, additional genome-wide association studies by academic and government researchers have provided genomic information and identification of genes that would be cost prohibitive or threaten industry herds. Examples of this would be genetic evaluation of detailed meat quality on production animals, anestrus behavior in gilts or postpartum sows, ovulation rate in sows or viral disease challenges. Some of the progress gained from genome-wide associations is discussed below.

Genomics of Host Resistance to Disease in Swine

The most costly and devastating threat to livestock production is infectious disease. Genomic studies in pigs have identified host resistance or susceptibility genes or loci for Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) and porcine circovirus 2b (PCV2) challenges, pneumonia and enterotoxigenic *Escherichia coli* F4ac diarrhea. PRRS probably has the most severe impact on pig production worldwide. Using the PorcineSNP60 BeadChip to genotype PRRS-challenged feeder pigs, markers on chromosome 4 (SSC4), the

most significant in the interferon-induced guanylate-binding protein (*GBP1*), were associated with viral load and body weight gain after infection (Boddicker *et al.*, 2012). This region accounted for nearly 16 % of the genetic variance and was confirmed in five other unrelated commercial populations (Boddicker *et al.*, 2014 a; Boddicker *et al.*, 2014 b). Other regions on chromosomes 1, 7, 17 and X were also associated with viral load and weight gain (Boddicker *et al.*, 2012). The region on SSC7 near the major histocompatibility complex (referred to as MHC or SLA) was confirmed in an association of PRRSV IgG during a PRRSV outbreak in a commercial multiplier sow herd (Serao *et al.*, 2014). Other regions on SSC1 and SSC7 were also associated with number and proportion of stillborn during the infection. These studies both indicate that the traits measured were moderately heritable and have a strong genetic component, the favorable alleles were at low to moderate frequency, and that marker-assisted selection could reduce the impact of the host response during PRRSV infection.

Similarly, a genome-wide association analysis was performed for viremia, antibody response and weight gain during experimental infection of PCV2 in commercial lines (McKnite *et al.*, 2014). Porcine circovirus 2 is the primary cause of post-weaning multisystemic wasting syndrome and is frequently co-infected with other pathogens such as PRRSV. Similar genomic locations were associated with viral load and antibody response on three chromosomes. As with PRRSV challenge, a region on SSC7 near the swine leukocyte antigen II cluster (SLAII) was associated with viral load.

Diarrhea due to enterotoxigenic *E. coli* (ETEC) is the most common and important bacterial infection causing moderate to high mortality in neonatal and weaned piglets. These antigenic bacteria contain F4ab/ac fimbriae bind to an unidentified intestinal receptor(s) and substantial evidence exists that there is genetic variation in ETEC susceptibility that resides in a 1.5 Mb region on chromosome 13 (Jacobsen *et al.*, 2010). This region has been refined to a few hundred kilobases by genome-wide association using the PorcineSNP60 BeadChip and harbors the candidate genes *HEG1* and *ITGB5* (Fu *et al.*, 2012) and *MUC13* (Ren *et al.*, 2012). While QTL studies using linkage analysis of microsatellite genotypes for ETEC susceptibility had identified multiple QTL, genome-wide association studies indicate the possibility of multiple F4 receptors in this narrow region on chromosome 13.

The identification of markers and genetic variation in genes that confer resistance to infection are encouraging, and could provide information on mechanisms of infection (identification of receptors) or clearance and aid in the development of more effective vaccines.

Genomics of Swine Feed Intake, Efficiency, Behavior and Growth

Feed costs typically make up 60-70 % of the total production costs, and small changes in feed intake can change profitability substantially. Therefore feed efficiency and factors such as age, stage of the reproductive cycle for breeding females (breeding, gestation, or lactation), and body condition can all affect the feed requirements of pigs. The fluctuation of grain prices and the availability of alternate feed sources make feed intake and efficiency critical for economical pig production. Also, a desire to reduce the environmental impact of pork production provides an incentive to reduce nutrient excretion (Shirali *et al.*, 2013). Substantial variation for feed efficiency, intake and behavior exists in commercial populations and these traits are moderately heritable (Hoque *et al.*, 2007). While growth is easy to measure and will respond to selection, feed efficiency is costly and labor intensive to measure in large numbers of animals. Numerous genome-wide association studies have been done for feed efficiency traits (Onteru *et al.*, 2013; Sahana *et al.*, 2013; Jiao *et al.*, 2014), residual feed intake, or RFI (Onteru *et al.*, 2013; Do *et al.*, 2014 a), and feeding behavior (Do *et al.*, 2013). Candidate genes for feed efficiency traits were identified that are involved in myogenesis (Onteru *et al.*, 2013; Sahana *et al.*, 2013), metabolic rate (Onteru *et al.*, 2013; Sahana *et al.*, 2013; Do *et al.*, 2014 b), and leptin and insulin signaling (Onteru *et al.*, 2013; Do *et al.*, 2014 b; Jiao *et al.*, 2014), and synapse genes and peptide secretion for feeding behavior (Do *et al.*, 2013). While some of QTL regions overlap with previously known QTL using scans, many novel loci were identified using high-density SNP genotyping. It has been shown that different QTL exist for different stages of the growth cycle and selection could be most efficient at specific stages (Shirali *et al.*, 2013).

Genomics of Swine Reproduction

Reproductive failure accounts for about 30 % of sow removals and most of these in lower parities (Engblom *et al.*, 2007). Genetic improvement of reproductive traits in pigs has been challenging because of low heritabilities, traits are sex-limited and are not realized until late in the animal's life and could be improved by selecting on the genetic variants that affect these traits. Several association studies have evaluated litter or farrowing traits, such as number born, number born alive and stillborn (Uimari *et al.*, 2011; Onteru *et al.*, 2012; Schneider *et al.*, 2012; Bergfelder-Druing *et al.*, 2015), and lifetime productivity (Onteru *et al.*, 2011). While some associations overlap associations from other studies or lie in QTL regions known to affect swine reproduction from genome scans, many other novel QTL have been discovered. These novel associations found in different populations for litter traits indicate differences in genetic architecture, the presence of a large number of loci with small effects and interactions with the environment. Regions associated with other critical components of sow reproduction

that are not routinely measured in industry settings include ovulation rate (Schneider *et al.*, 2014), age at puberty (Tart *et al.*, 2013), and delayed puberty (Nonneman *et al.*, 2014).

These examples represent a fraction of the high-density SNP genome-wide association studies for a multitude of traits in the pig that should provide a gateway for the use of markers for genetic selection. These studies coupled with the many genome sequences capturing the genetic diversity of pigs (Bianco *et al.*, 2015) will lead to the discovery of genes and variation affecting economically important traits and improve the accuracy of genetic selection in swine.

Potential contribution of genomics to sheep and goat

In general, genomic applications in the case of sheep and goats are unlikely to be fundamentally different from a technical point of view from those in other ruminants. The use of genomics in breeding programs will be based on the development of SNP BeadChips that will cover most of the genes that control complex traits, thereby making it possible for such programs to incorporate GS. This approach is based on linkage disequilibrium between the SNP and the genes that control the traits (Stock and Reents, 2013).

In sheep and goats, GWAS may be implemented for two main purposes: 1) To develop programs based on predicting GEBV, and 2) To detect individual SNP closely associated with the putative QTL. The first type of studies focus on the accuracy of GEBV, while the second seeks to identify individual polymorphisms associated with the traits studied.

As sheep and goats are primarily associated with low-income farming systems and their contribution to total production in most countries is moderate, the application of genomics in these species lags behind that for cattle. The potential contribution of GS in small ruminants is further differentiated because in these species the use of progeny testing programs is not as widespread as in dairy cattle; therefore, the possible advantages of using GS would be lower. This is because the main advantage in GS is the possibility of reducing the generation interval by accepting a degree of accuracy that is comparatively lower than that for progeny testing, although increased in comparison to classical parent average Best Linear Unbiased Prediction (BLUP; use of mixed linear models on records and genealogy) evaluations of young animals (Stock and Reents, 2013).

In this section we review a selection of studies to estimate the comparative ability of GEBV to predict breeding values conducted on goats and sheep, as well as studies predicting the potential of GS for increasing rates of genetic improvement in these species.

Genomics of Dairy Does and Ewes

A preliminary study of dairy goat breeds in France using a two-breed reference population of 677 progeny-tested bucks and Illumina GoatSNP50 BeadChip for milk production and udder conformation traits found no advantage of GEBV over parent averages in terms of accuracy when a two-step approach was implemented (Carillier *et al.*, 2013). This was attributed to the small size of the reference population and their structure. Nonetheless, further studies with the same population using a single-step approach found advantages of GEBV over parent averages for the same traits (Carillier *et al.*, 2014). A study in the United Kingdom (Mucha *et al.*, 2014), assessed data comprised of 590 409 milk yield records on 14 453 goats. In total, 1960 animals were genotyped with GoatSNP50 BeadChip. Mucha *et al.* (2014) compared two methods, BLUP-SNP and a single-step approach were performed on the data to estimate accuracies of GEBV. The highest degree of accuracy was obtained with the single-step method. The latter method provides the best accuracy for populations with a small number of genotyped individuals, where the number of males is relatively low, and females are predominant in the reference population. The difference between the accuracy of parent average BLUP and GEBV by single-step was 5.2 %. There was an increase of 3.7 % in the accuracy of young animals with and without genotyping information.

Using data of the French Lacaune dairy sheep breed (Duchemin *et al.*, 2012), compared the accuracies of genomic estimated breeding values using different models (infinitesimal only, markers only, and joint estimation of infinitesimal and marker effects) and methods [BLUP, Bayes C π , partial least squares (PLS), and sparse PLS]. The training dataset included results of progeny tests of 1 886 rams born from 1998 to 2006, whereas the validation set had results of 681 rams born in 2007 and 2008. Three lactation traits were studied (milk yield, fat content and SCS). The inclusion of molecular information, as compared with traditional schemes, increased accuracies of estimated breeding values of young males at birth from 18 to 25 %, according to the trait. Methods that select markers implicitly (Bayes C π and sparse PLS) were advantageous for some models and traits, and are of interest for further QTL studies.

Genomics of meat and wool sheep

Daetwyler *et al.* (2010) sought to determine whether genomic information from a SheepSNP50 BeadChip can be used to predict estimated breeding values for wool and meat traits in Australia. The effects of all single nucleotide polymorphism markers in a multi-breed sheep reference population of 7 180 individuals with phenotypic records were estimated to derive prediction equations for GEBV for greasy fleece weight, fiber diameter, staple strength, breech wrinkle score, weight at ultrasound scanning, scanned eye muscle depth, and scan-

ned fat depth. 540 industry sires with very accurate Australian sheep breeding values were used as a validation population and the accuracies of GEBV were assessed according to correlations between GEBV and Australian sheep breeding values. The accuracies of GEBV ranged from 0.15 to 0.79 for wool traits in Merino sheep, and from -0.07 to 0.57 for meat traits in all breeds studied. The results indicate that an increase in the size of the reference population will increase the accuracy of GEBV. Swan *et al.* (2012) developed a practical approach to blend traditional BLUP genetic evaluations and GEBV for multibreed populations in Australia. The GEBV were estimated on the basis of a SheepSNP50 BeadChip. Small advantages for the blended genetic evaluations were observed for most traits.

Genomics of Goat and Sheep Breeding

Other studies have examined the potential of GS to increase rates of genetic improvement in sheep and goats. Van der Werf (2009) estimated possible increases of 15-40 % in annual rates of improvement for wool and meat sheep; primarily related to the opportunities for more accurate selection at a younger age. Genomic Selection promises considerably genetic improvement for traits such as parasite resistance, slaughter traits, adult wool traits, and female fertility. Feasible concepts may involve collection of relevant phenotypes in selected flocks, such as the Australian Information Nucleus (Fogarty *et al.*, 2007). Shumbusho *et al.* (2013) examined the potential benefits of genomic selection on the genetic gain in current French sheep and goat breeding designs. Traditional and genomic scenarios were modeled with deterministic methods for three breeding programs. Results found that optimized traditional breeding programs provide an annual genetic gain (AGG) of 0.139 genetic standard deviations (GSD) for meat, 0.096 GSD for maternal traits in meat breeds and 0.174 GSD and 0.183 GSD in sheep and goat dairy breeds. With a medium-sized reference population (n_{ref}) of 2 000 individuals, the best genomic scenarios yielded an AGG that was 17.9 % greater than with traditional selection methods with optimized values of decisional variables for combined meat and maternal traits in meat sheep, 51.7 % in dairy sheep, and 26.2 % in dairy goats. The superiority of genomic schemes increased with the size of the reference population and genomic selection gave the best results when $n_{ref} > 1\ 000$ individuals for dairy breeds and $n_{ref} > 2\ 000$ individuals for meat breeds. AGG was increased in optimized traditional selection designs by including genomic information.

Few economic evaluations of alternative breeding programs in sheep and goats are available. Shumbusho *et al.* (2014) estimated the revenues of several programs of phenotypic, genomic and combined selection programs under current costs for meat sheep in France. This study showed that some forms of genomic implementation in small ruminant breeding

programs are slightly more profitable than classic selection. However, these economic gains are lower than annual genetic gains predicted in sheep and goat breeding programs (Shumbusho *et al.*, 2013).

Final remarks

The objective of genetic improvement programs is the identification of superior individuals, to become founders of the following generation. Genomics is a thriving area of research that will assist in understanding the genetic basis of physiological mechanisms and will allow improvement of economically important and welfare traits in livestock. This improvement can now be realized in populations with the use of genomics and genomics selection.

Genomic selection can be used based on linkage between specific alleles of randomly selected SNP. This will allow increasing selection accuracy in young animals compared to that of conventional quantitative selection, based exclusively on phenotypic information. Sufficient genetic variation exists in livestock populations that allow for genetic improvement in economically important traits and adaptation to environmental and consumer demands. Genomic selection is a tool that can be used to develop novel breeding strategies, maintain genetic diversity and adaptation to these challenges in large and small breeding populations. Genomic selection has revolutionized the dairy, beef, and swine industries, and should be applicable to any agricultural species. There is also hope that livestock genomics can ensure the nutritional needs of the human population and safeguard our natural resources and the environment in ways that would support sustainable animal agriculture.

The dairy industry in the United States and Canada have adapted genomics and genomic selection to improve accuracy of GEBV, and making efficient and less expensive the production of young bulls. Additional countries (Denmark, China, and Mexico) have shared genomics information with the United States and Canada to initiate studies towards generating GEBV and accuracies of GEBV for their dairy population. Given that several Latin American countries produce milk with Holstein or Jersey cattle, they have the possibility to utilize genomic selection to improve milk production by collaborating with countries that have implemented it. This is an opportunity for Latin American countries with Holstein or Jersey as their basis for milk production.

Implementation of genomic selection in the beef cattle, pig, sheep and goat industries is promising in Latin America. Brazil has initiated the use of this technology for local beef cattle breeds. The objective is to improve GEBV and accuracies of GEBV for growth and carcass and

meat quality traits in *Bos indicus* and Canchim (composite breed developed in Brazil). Brazil is setting up itself to improve in beef cattle production and to compete with external markets in the future.

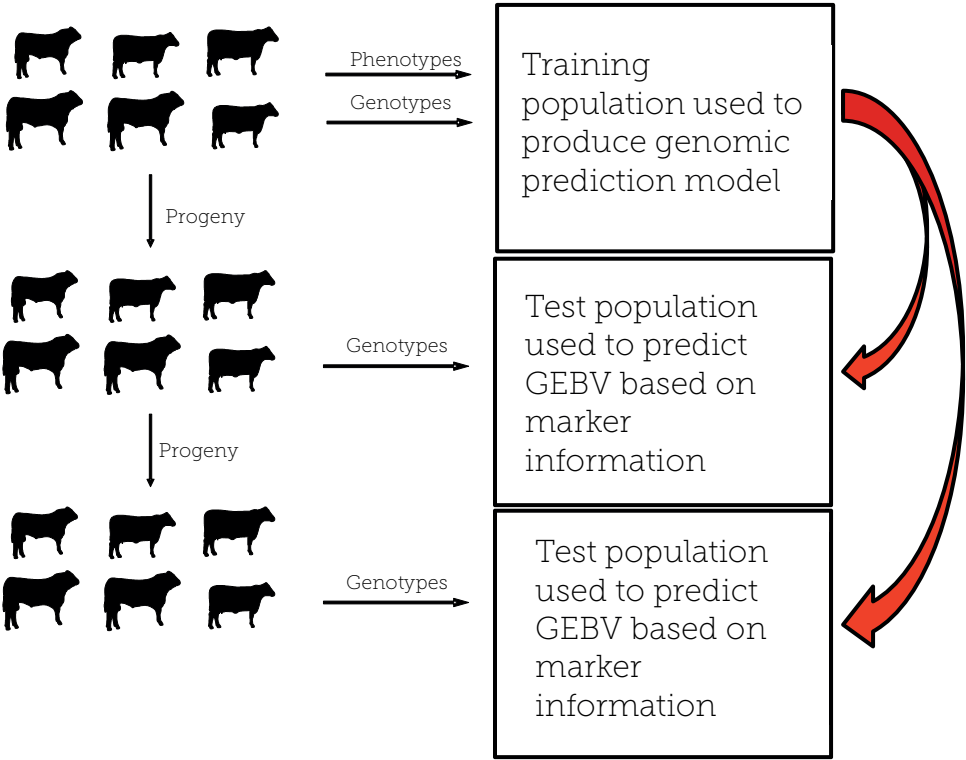
The pig industry is set similar to the dairy industry. Boar studs will be able to use genomic selection and improve economically important traits. Latin American countries that use semen from the United States companies will have the possibility to implement genomic selection as genomics information becomes available.

Resources need to be developed for the sheep and goat industries. Production systems for these species will be able to use genomic selection as information from countries with strong sheep and goat selection programs is shared among other countries. However, it is potentially possible for Latin American countries with a strong sheep and goat production to tap into resources provided by countries working in these species.

Table 1. Fresh milk production and number of dairy cows in Latin American countries in 2013.

Country	Fresh milk (kg)	%	Number of cows	kg/cow/year
Brazil	34 255 236	40.30	22 954 537	1.492
Argentina	11 796 000	13.90	2 193 000	5.379
Mexico	10 965 632	12.90	2 410 000	4.550
Colombia	6 457 398	7.70	5 340 000	1.209
Ecuador	6 262 408	7.50	1 264 000	4.954
Chile	2 675 706	3.20	1 020 000	2.623
Venezuela	2 640 233	3.10	2 151 000	1.227
Uruguay	2 120 000	2.50	760 000	2.789
Peru	1 807 806	2.20	794 500	2.276
Costa Rica	1 066 288	1.30	787 000	1.354
Nicaragua	768 000	0.91	1 015 000	0.756
Honduras	695 000	0.81	560 900	1.239
Dominican Republic	669 193	0.78	440 000	1.521
Cuba	589 100	0.69	400 300	1.471
Bolivia	529 901	0.62	189 000	2.803
Paraguay	518 000	0.61	225 000	2.302
Guatemala	496 245	0.58	679 800	0.729
El Salvador	484 843	0.57	281 000	1.725
Panama	206 000	0.24	165 000	1.248
Haiti	65 000	0.08	212 000	0.306

Figure 1. Representation of the use of genomic selection in livestock. Phenotypic and genotypic information is generated in the training population to generate Genomic Expected Breeding Values (GEBV), in the progeny of the training population (Test population), or further generations. Adapted from Goddard and Hayes (2009).



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