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Research Symposium Utilization of Genomic Information for the Sheep Industry

Introduction

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During the ASI Annual Convention in Scottsdale, Ariz., January 26, 2012, a research symposium ***Utilization of Genomic Information for the Sheep Industry*** was co-sponsored by the American Sheep Industry Association (ASI) and the American Sheep and Goat Center (ASGC). The Symposium Program Planning Committee consisted of Paul Rodgers, ASI; Will R. Getz, Fort Valley State University; and Larry R. Miller, ASGC, who also served as Moderator. The symposium was somewhat different from previous ASI research symposia, in that it more comprehensively focused on a single topic, involved speakers from different perspectives and engaged participants in more in-depth discussion.

Especially in the past two decades, volumes of new genomic and genetic information have been generated by means of new research approaches, techniques, and tools. This information created a challenge to harness, interpret, and utilize the wealth of new genomic/genetic information by drawing upon disciplines, such as biochemistry, genetics, statistics, computer science, animal breeding, and several other sciences associated with the biology of the animal.

The speakers addressed the symposium topic from the following points of view, reflecting their different expertise and experiences: *Genomic Information Available for Use by the Sheep Industry*, Noelle E. Cockett, Utah State University; *Application of Genomic Information for Improvement of Quantitative Traits*, David R. Notter, Virginia Tech University; *Utilization and Potential of Estimates of Genetic Value from an Industry Perspective*, David L. Thomas, University of Wisconsin-Madison; *Utilization from a Producer Perspective*, Chase T. Hibbard, sheep producer, Helena, Mont.; and *Genetic Selection Specifically Utilized for Evaluating the Introduction of Outside Breeds and Measuring Their Potential*, John Helle, sheep producer, Dillon, Mont.

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Genomic Information Available for Use by the Sheep Industry

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Summary

Sheep contribute significantly to food and fiber production across the world through locally and globally distributed meat, milk, and wool markets. In addition, sheep are used in biomedical research as a model organism for heart, lung, and musculoskeletal diseases. A better understanding of the genetic makeup of sheep will lead to improvements in the efficiency of meat, milk, and wool production and contribute to a better understanding of health and disease issues in humans. While several genetic regions associated with economically and biologically important traits in sheep have been identified, the number of known causative mutations is relatively small. However, the development and application of a high-density ovine SNP array and the availability of the whole genome assembly for sheep will undoubtedly lead to more discoveries. It should be noted that the application of genetic markers for selection of quantitative traits in sheep is still in the distant future.

Key Words: Sheep, Genomics, Genome-wide Association Study, SNPs

Introduction

During the past twenty years, several traits in sheep have been mapped to specific regions in the sheep genome using a genetic-linkage analysis, which involves tracing the segregation of marker alleles through pedigrees of animals with known phenotypes. These linkage-analysis studies usually result in very large genetic regions, which contain hundreds of genes, being associated with one or more traits. To dissect these large intervals and ultimately narrow down the region of interest, additional experiments are required. The experimental steps are usually directed towards a higher resolution of the location of the mutation in the genetic region, followed by DNA sequencing of animals differing in performance for the trait of interest. While some causative mutations have been identified utilizing these steps, other genomic regions of suggested importance have not been explored. The cost of these experiences escalates with the complexity of the trait, requiring increasing numbers of animals that are characterized for the trait of interest.

Since the early 1990s, linkage analysis has been used to identify genomic regions that contain causative mutations for several binary traits, including the Booroola fecundity gene (Montgomery et al. 1993), callipyge (Cockett et al. 1994), Spider Lamb Syndrome (Cockett et al. 1999) and muscularity in Texel sheep (Clop et al. 2006). These regions were sequenced in animals within the study populations to eventually determine the causative mutation for the trait. In contrast, only a few mutations that are causative for quantitative traits in sheep have been identified to date. As discussed in a companion paper (Notter, SGRJ, Research Symposium 2012), quantitative traits are more challenging than single gene traits because a large number of genes are involved and the manifestation of the trait is dependent on the animal's environment. In addition, thousands of animals within large pedigrees are needed in the linkage analyses of quantitative traits and many researchers do not have access to those animal numbers. Almost all of the causative mutations for quantitative traits discovered to date have had a major influence on the trait, such as the myostatin (GDF8) gene affecting muscle depth in Charollais sheep (Hadjipavlou et al. 2008) and the calpain and calpastatin genes involved in meat tenderness (Knight et al. 2012). Mutations with minor effects on quantitative traits have been much more elusive, most likely because of the difficulty in detecting differences, given the number of animals and genetic makeup of the study populations. In addition, genetic regions associated with a quantitative trait have differed between studies when different breeds or genetic lines are used in the analyses. For example, recent publications that report genetic regions influencing parasite resistance in sheep (Dominik et al. 2010; Marshall et al. 2009; Matika et al. 2011; Silva et al. 2012) report a total of 10 highly significant QTL on six autosomal chromosomes, with only one genomic region that was identified in more than one study (Dominik et al. 2010; Silva et al. 2012).

Genome-wide association studies (GWAS)

While it is possible to localize the genetic region associated with a trait using a genetic-linkage analysis, an alternative approach developed in the last few years has been used extensively by sheep researchers. The genome-wide association study (GWAS) is a method that tests for differences in the frequencies of alleles or genotypes between groups of animals or people who are distinctly different for a trait, disease status, production value, etc. No pedigrees are required for GWAS; instead, associations between genetic marker alleles or genotypes and the trait of interest are analyzed in large samples of unrelated individuals. Assuming that the trait allele of interest has descended from one or a few ancestors (so that the "ancestral" segment of DNA contains the trait allele because of linkage disequilibrium), a GWAS analysis will reveal influential genetic regions.

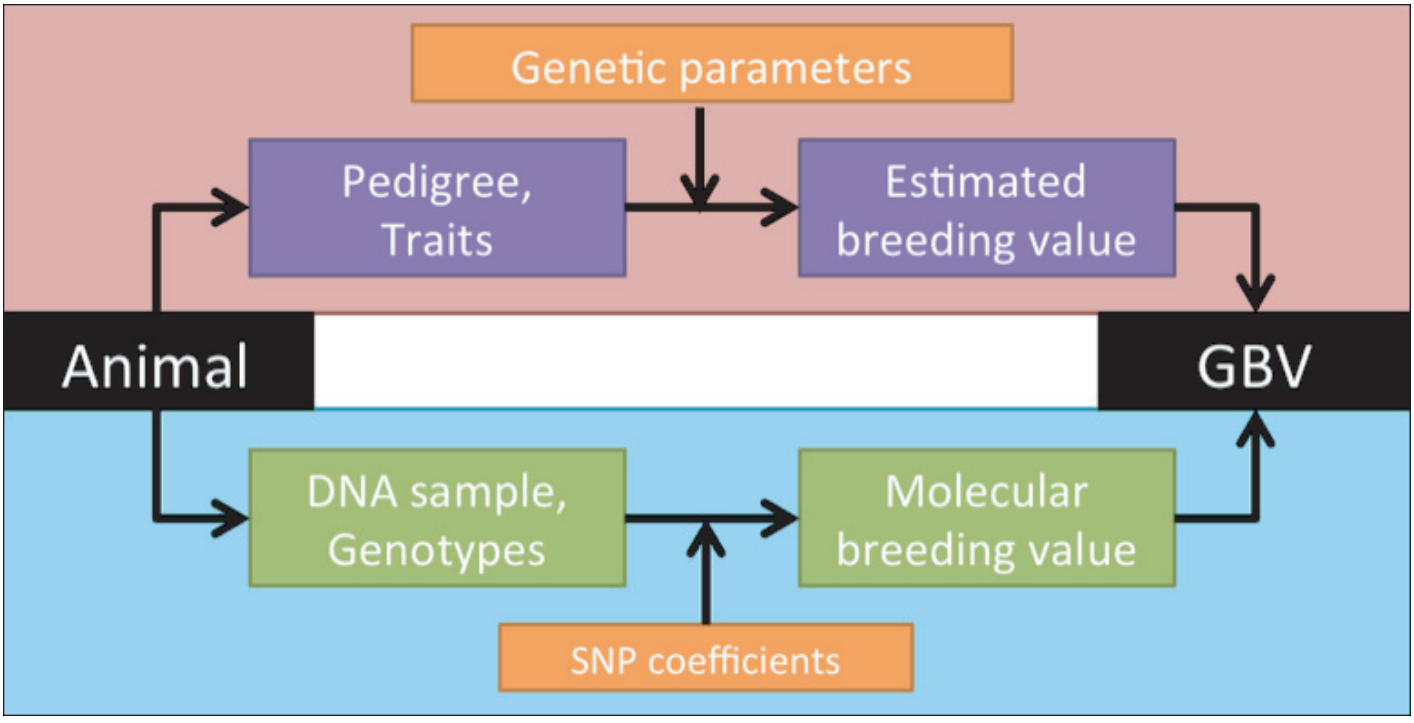
The detection of genetic regions containing the trait allele using the GWAS approach is possible because of "selective sweeps", which are regions that have allele frequency differences because of historical selection for or against the trait (Sabeti et al. 2006). An important aspect of the selective-sweeps analysis is to include genetic-marker genotypes for several closely related species (such as the thin horn Ovis dalli for sheep) in order to determine the ancestral allele of the genetic markers (called SNPs). If multiple breeds are included in the study, the data also can be used to explore the degree of diversity between and within breeds, and make more informed choices about how to best manage and conserve genetic resources. Genetic markers identified in a genome-wide, association analysis must be verified in additional populations, as described by Notter (2012). Verification is necessary because of the likelihood of spurious associations when testing large numbers of SNPs for significance, such as the recently released ovine SNP50 BeadChip, which contains more than 50,000 SNPs. In addition to verification of significant associations, the significance values are adjusted for multiple comparisons when the genotypes from high-density, SNP chips, such as the ovine BeadChip, are analyzed.

Discovery of the causative mutation requires additional steps (Ron and Weller, 2007), such as the physiological manifestation of the trait in transgenic animals that carry the mutation. However, production of transgenic animals for confirmation of the mutation is expensive. Also, appropriate control of the transgene does not always occur, so absence of the trait in the resulting animals does not necessarily mean the mutation is not causative, only that the transgenic animals do not display the trait.

Genetic markers that have been verified can then be incorporated into the calculation of molecular breeding values (MBV) for individual animals. The MBV can be combined with estimated breeding values (EBV) into what is referred to as a genetic breeding value (Figure 1). This approach, which combines the underlying genetics of a trait with pedigree information and the animal's own trait measurement, will lead to more informed genetic-selection decisions.

Some progress has been made in identifying genetic markers for disease traits using a GWAS approach. A recent publication (Heaton et al. 2012) reports a risk factor of 2.75 for the incidence of ovine progressive pneumonia (OPP) in sheep carrying at least one of three mutations in the TMEM154 gene, located on chromosome 17 (OAR17) in sheep. These investigators collected genotypes from the Ovine SNP50 BeadChip from 69 animals that had serum OPPV antibodies (considered a reliable measure of OPPV infection) and 69 con-

Figure 1. Information that is used to produce a genetic breeding value (GBV). (John McEwan, personal communication)



trol animals matched for breed composition, exposure, and environmental factors (sex and age), and all animals were from a research flock maintained at the USDA, ARS Meat Animal Research Center in Clay Center, Neb. Analysis of the data associated a specific gene (TMEM154) with OPP infection. Heaton and his colleagues pointed out that the matched control design using older sheep (5 years old to 9 years old) was "key in reducing variation in the management conditions, environment, breed composition, and pathogen exposure." They said that "the use of older sheep increased the chances that sufficient natural exposure had occurred so that a high proportion of susceptible individuals could become infected". They also noted that "the inclusion of different breed compositions increased the likelihood that the association observed in the 69 matched pairs was not limited to one breed".

While no form of the TMEM154 gene is known to be resistant to OPP-virus infection, the ability to identify animals with an increased risk of infection should lead to improved management in sheep flocks. This same approach for designated management of animals with specific genetic markers could be applied to production and carcass traits. Some success has occurred in using genetic-marker panels to assign beef cattle to specific feeding regimens in feedlots in order to reach a certain carcass endpoint (B. Woodward, Merial Limited, personal communication).

Genomic Resources in Sheep

The availability of a high-density, SNP array specific for the sheep has dramatically impacted the search for important genomic regions using the GWAS analysis. The Illumina Ovine SNP50 BeadChip *(http://www.illumina.com/documents//products/datasheets/datasheet_ovinesnp50.pdf)* was developed by the International Sheep Genomics Consortium and released to the public in January, 2009. Researchers can now obtain genotypes for over 50,000 SNPs for hundreds of animals in a single analysis.

A large, international-sequencing effort was undertaken to generate the information needed for development of the SNP50 chip. The first source of sequence data (9.7 Gbp) was generated from six sheep breeds (Romney, Texel, Merino, Dorset, Rambouillet and Suffolk) using funding from the International Science Linkage Program (Australia) and Ovita (New Zealand). The second source of sequence data used for SNP mining (3 Gbp) was generated from a pool of DNA comprised of 60 genetically divergent animals. These sequences were compared to identify single nucleotide differences (i.e. SNPs) that differed in at least 5 percent of the sequenced animals.

To date, at least 10,000 sheep have been genotyped with the SNP50 chip, and analyses of the genotypes are ongoing in a myriad of research projects across the world. For example, SNP genotypes of 3064 sheep from 64 breeds have been combined with genotypic data from seven species of wild sheep and nine outgroup species as part of the world-wide ovine HapMap project *(http://www.sheephapmap.org/)*. Results from the HapMap analysis indicate that domestic breeds diverged from their wild ancestors about 11,000 years ago, and modern breeds started to differentiate around 200 years ago (Kijas et al. 2009). Although not unexpected, the data also indicated that American breeds are most closely related to European and Middle Eastern breeds rather than to Asian or African breeds.

Another important genomic resource that is now available for sheep is the whole-genome-reference assembly (Dalrymple et al. 2007). The assembly is a compilation of all known information about the sheep genome into a searchable database that is publicly available on the internet on a site maintained by CSIRO Livestock *(http://www.livestockgenomics.csiro.au/sheep/oar2.0.php)*. The assembly contains a myriad of details, including the location of genes and genetic markers from the linkage (Maddox et al. 2001), radiation hybrid (Goldammer et al. 2009; Wu et al. 2008, 2009) and physical (Goldammer et al. 2009) maps, and the location of SNPs from the Illumina chips. Improvement and additions to the assembly are discussed and approved continually by the ISGC, whereas updates are released publicly about every 12 months. The currently available version (Oarv2.0) was released in February, 2011, and an updated version (Oarv3.) is scheduled for release in Summer, 2012 (Y. Jiang, CSIRO Livestock Industries, personal communication). Full annotation of the genes within the genome (Oar v3.0) will be done by NCBI (B. Dalrymple, CSIRO Livestock Industries, personal communication).

A key component of the genome assembly is the reference genome sequence (Jiang et al. 2011), which is the linear order of DNA nucleotides found in the sheep genome. The assembled reference sequence contains approximately 2,710,000,000 of ordered nucleotides assigned to specific chromosomes and covers approximately 92 percent of the ovine genome. Sequence data for the whole-genome-reference sequence were generated at two sequencing facilities (Beijing Genomics Institute and the Roslin Institute) from DNA of a Texel ewe and a Texel ram, respectively. The first step in assembling the reference sequence involved de novo assembly of 75X reads from the Texel ewe into contigs, scaffolds and super-scaffolds. Once that was completed, sequences from both animals were used for gap filling. Information from the sheep linkage, radiation hybrid and physical maps has been used to refine the assembly of the reference sequence. In order to define the expressed portion of the genome, mRNA-seq was performed on seven tissue samples (heart, liver, ovary, kidney, brain, lung, and white fat) of the Texel ewe. This information is being used for annotation of genes within the ovine genome. In addition to the reference assembly, about 5 million SNPs were identified in separate analyses of the male and female Texel sequences.

The whole-genome assembly for sheep will significantly accelerate searches for genetic regions and genes influencing phenotypes in sheep. The assembly also will provide a backbone for the interpretation of low-pass sequences of individual animals expected within the next few years. Without a reference assembly, identification of differences among animals in genome organization, including rearrangements and duplications, will be difficult to interpret.

Considerations for Genomic Research in Sheep

The availability of a high-density, SNP chip for sheep has revolutionized researchers' ability to locate genetic

regions influencing economically traits. The number of animals needed for identifying a mutation responsible for a single-gene trait has been reduced from more than 100 (with linkage analyses) to 5 to 13 affected animals along with a similar number of controls. Hundreds of animals are still needed for identifying regions containing quantitative trait loci (QTL) but the time to test markers across a population is reduced from years to just a few months. The cost-per-genetic marker is reduced greatly with the SNP chip, but given the number of animals that are needed for QTL discovery, the cost of a QTL search may still be prohibitive, particularly for lowly heritable traits because more animals are needed in the study. A genotype-imputation approach (Hayes et al. 2011) can reduce the cost because a small select group of animals is genotyped with the more expensive high-density chip (50,000 SNPs), while the bulk of the animals are genotyped with a cheaper lower density chip (> 5,000 SNPs). The accuracy of imputation is dependent on the amount of genetic diversity in a breed, with lower-genetic diversity resulting in more accurate imputation. After the identification of significant SNPs, the DNA of key individuals could be sequenced and compared to key ancestors within the breed to reveal interesting mutations associated with the analyzed trait.

The volume of data generated within the high-density chip (50,000 genotypes per animal) can be an issue, requiring increased computer capacity and new analysis methods. However, the density of markers that are tested on the high-density, SNP chip means that the genetic regions identified through GWAS are typically of higher resolution than those identified in linkage studies. This higher resolution helps limit the size of the region in which one needs to search for the causative gene or mutation, leading to a quicker turn-around in the identification and characterization of genomic regions. However, the discovery of genetic markers suitable for genetic selection of quantitative traits is still elusive. At this point in time, there are only a few sheep populations worldwide with appropriate numbers (in the thousands) and appropriate trait measurements. In addition, the genetic markers identified in these populations must be tested in other populations to determine the utility of the markers across genetic lines.

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Application of Genomic Information for Improvement of Quantitative Traits

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Summary

Use of genomic information in livestock breeding can allow direct assessment of genetic merit of potential breeding animals. Genomic information is particularly valuable for managing the expression of simply inherited genetic defects and for using genes with large effects on prolificacy, disease resistance, and muscularity. Use of genomic information to support genetic improvement in quantitative traits has, however, progressed more slowly. The hypothesis, that a few genes of relatively large effect control these traits, has been shown to be incorrect, and the classic hypothesis involving control by many genes with small individual effects appears to be correct. High-density SNP (single-nucleotide polymorphism) arrays allow assessment of differences among individuals at 50,000 or more sites along the genome and can provide genomic breeding values (GBVs) based on observed relationships between these SNPs and performance. However, performance records on large numbers of animals are required to determine the relationships between genomic information and performance that are necessary for effective use of GBVs to select future descendants of these founder animals. To date, correlations between GBVs and performance-based Estimated Breeding Values (EBVs) in progeny-tested sires have been positive and significant, but well below the desired 1.0, and careful attention is required to optimize resources devoted to collection of phenotypic data versus those devoted to collection of genomic information. However, the U.S. sheep industry needs a baseline capacity to collect and utilize genomic information, particularly on progeny-tested rams, and this review will describe options to develop this baseline capacity.

Key Words: Sheep, Genomic improvement, Quantitative traits, Selection

Introduction

The expanding availability of genomic tools in livestock species provides opportunities to utilize genome-based strategies to improve animal performance. Use of these tools to identify, monitor, and limit the spread of simply inherited genetic defects and to identify and appropriately utilize genes of major effect, such as the Booroola fecundity gene and various mutations associated with enhanced muscularity is already common. Rapid identification of the mutation causing the curly-calf syndrome in Angus cattle (Van Eenennaam, 2009) is a particularly compelling example of the power of molecular techniques to identify mutations of major effect.

Use of genomic approaches to identify risk factors for human diseases is an explosive area of research, and these same tools are being applied in animal medicine. The genetic basis of susceptibility to scrapie has long been recognized and genome-based diagnostics tests of susceptibility are the centerpiece of most programs to control this disease (Smit et al., 2002; Baylis and Goldman, 2004). Recent studies of the genetic basis of susceptibility to Ovine Progressive Pneumonia (OPP) (Heaton et al., 2012) demonstrate the power and sophistication of these techniques.

Against this background, there are similar levels of enthusiasm for development and use of genomic strategies to improve quantitative traits, such as growth rate, wool production and quality, reproductive and maternal performance, and carcass yield and quality that are fundamental contributors to profitability in the sheep industry. Despite the presence of a few genes of major effect on litter size and muscle development, control of these traits mainly reflects the actions and interactions of many genes with moderate or small effects, thereby requiring additional levels of sophistication and creativity for their detection and use in breeding programs. This review considers the potential use of genomic strategies to improve these quantitative traits.

The Genetic Model for Quantitative Traits

The classic model for genetic control of quantitative traits is generally referred to as the "infinitesimal model". It assumes that many genes, each with small effects, control these traits. In its literal formulation, the infinitesimal model assumes that each trait is controlled by a near-infinite number of genes, each with a vanishingly small individual effect but cumulatively accounting for the heritable genetic differences observed among individuals. Superior individuals have larger numbers

of favorable genetic variants than inferior individuals and are anticipated to pass larger numbers of favorable variants to their progeny, with resulting correspondence ("heritability") between performance of parent and progeny. This "black box" model of genetic control of quantitative traits is the basis for derivation of Estimated Breeding Values (EBVs) in genetic evaluation programs, such as the U.S. National Sheep Improvement Program (NSIP), and, despite its lack of specificity regarding genetic mechanisms underlying animal performance, has been a powerful tool for genetic improvement.

The ability to sequence the DNA of individual animals provides potential to associate genetic variants at specific sites within the DNA with observable differences among animals. This potential has been realized for many simply inherited conditions such as animal color, scrapie susceptibility, the Spider syndrome, and several others, resulting in simple, commercially available, diagnostic tests. Extension of this approach to quantitative traits is conceptually straightforward, but operationally challenging. The sheep genome contains approximately three billion base pairs and approximately 30,000 structural genes that define the molecular structure of the enzymes, hormones, regulatory and structural proteins, and transcription factors associated with variation among individuals. These structural genes are distributed across 26 ovine chromosomes. Each is surrounded by a variety of associated regulatory DNA sequences that permit interactions with other genes and with the environment to control the expression level of the gene. These regulatory sequences may themselves differ among individuals in ways that create individual differences in extent and timing of gene expression. A substantial proportion of the genome does not have a clearly defined role in creation of genetic differences among individuals. These seemingly nonfunctional sequences for a long period of time were derided as "junk DNA", but their role is being continuously reassessed. For example, DNA regulation involves the binding of various regulatory molecules to the DNA, a process that can be modified by the physical orientation of the DNA molecules. If genetic variation in these "nonfunctional" DNA sequences affects the physical orientation of the DNA molecules, they may also affect gene regulation and function.

Detection of Genetic Markers for Quantitative Traits

If a quantitative trait (e.g., the diameter of the wool fiber) is controlled by 50 genes (an arbitrary, and likely conservative, assumption), then we might anticipate that genetic differences in DNA sequences at those 50 sites (or their associated regulatory regions) are directly associated with heritable differences among individuals in fiber diameter. Identification of the differences in DNA sequences at these sites associated with differences in performance would thus permit development of a DNA-based diagnostic test of genetic merit for fiber diameter. The challenge is how to identify these sites and the variants within them that are associated with differences in performance.

The first step is to identify sites along the genome that are polymorphic in the population of interest. A polymorphic site is one at which the DNA sequence differs in a detectable manner among individuals and can therefore potentially serve as a genetic marker. In most populations, there are millions of polymorphic sites, but only a few are anticipated to be associated with differences in performance. Detection of informative associations between these polymorphisms and quantitative traits allows identification of regions in the DNA that impact the quantitative trait. From this point, more rigorous and detailed analysis of additional polymorphisms within these regions can be used to search for causal mutations associated with differences in performance. This approach is particularly relevant for single genes of large effects and was used to identify the causal mutation involved in the Spider syndrome in Suffolk sheep (Cockett et al, 1999).

A common experimental design to detect genomic regions of interest for quantitative traits involves the crossing of highly divergent sheep types (e.g., prolific Finnsheep and other less-prolific breeds, or parasite-resistant Gulf Coast Native and parasite-susceptible Suffolk sheep). The resulting F_1 (first-cross) lambs always carry one chromosome from each parent. However, when F_1 lambs are mated together to produce the F_2 generation or backcrossed to one of the parent breeds, chromosome segregation in offspring results in individuals with either one, two, or no copies of each of the ancestral genes from the two founder types. From an available catalog of genetic markers, a subset of informative markers can be identified as those that appear **only** in one form, in one breed and exclusively in a different form in the other breed. These breed-specific markers thus identify regions of the DNA with regard to their breed of origin. Screening of performance levels in segregating offspring permits identification of associations between performance and genetic markers derived from the parent breeds. The goal is to find genetic markers from the Finnsheep parent that are associated with more "Finn-like" performance (i.e., larger litters) in crossbred progeny in which these genes and markers are segregating.

Several implicit assumptions in these studies may limit their utility in practical breeding programs. Chief among these is the anticipation that a relatively small number of high-impact regions will emerge as exerting control over the trait(s) of interest. In most cases, the initial results of these marker studies will identify relatively broad regions of control, but if the number of regions is small, then further study (usually involving more advanced generations of mating or detailed study of individual families) is warranted to "drill down" to identify the presumptive causal mutations that underlay observed-breed differences.

Unfortunately, this approach has enjoyed only limited success for most quantitative traits. Several studies have been conducted to attempt to identify genes that influence resistance to GI helminth parasites (Marshall et al., 2009; Silva et al., 2011). A few consistently impactful regions of the genome have been identified, but the common result has been to detect relatively large numbers of potentially important regions and to find different regions of potential interest in different studies. With regard to parasite resistance, the current view is that this trait is behaving as a classical, quantitative trait, with genetic control associated with many genes, most with small effects, and with different genes in different populations. Similar conclusions have been reached for other quantitative traits in a wide range of studies. However, some useful regions involved in tenderness and marbling have been identified in beef cattle (Davis et al.,

2008; McClure et al., 2012) and, more recently, in sheep (Knight et al., 2012).

Generation of Molecular Breeding Values from Genome-wide Association Studies

Development of high-density single-nucleotide polymorphism (SNP) arrays allows characterization of individual animals for very large numbers of genetic markers. SNP arrays containing 50 thousand to 60 thousand individual SNP have been used in cattle, sheep, swine, chickens, and horses, and arrays with up to 750,000 SNP are being used in cattle. Even larger arrays of 2 million to 3 million SNP are available for humans. Thus we now have the capacity to characterize individual animals at 50,000 or more locations spread across the genome. This tool can be used to detect qualitative trait loci (QTLs) using techniques described in the previous section, but also allows for other approaches for estimation of breeding values (BV) for quantitative traits.

Focus has changed from emphasis on detection and characterization of a small number of high-impact regions to the prediction of genomic breeding values (GBV) derived from the cumulative effects of all, or at least many, of the SNPs. In many ways this approach represents a return to the infinitesimal model, with its assumption of many causal genes, each with small effects. Differences in performance associated with individual SNPs are expected to be small, but, when cumulated across the entire SNP array, are anticipated to give a useful predictor of the animals' overall genetic merit for the trait(s) in question.

Just as EBVs derived from performance records in conventional genetic evaluations are "black-box" calculations with regard to genetic mechanisms, so too are the genomic BVs largely also "black boxes" with regard to the functional characteristics of causal genes associated with individual SNP. However, just as the black-box EBVs derived from performance records have led to significant and substantial improvements in genetic merit, so may these GBVs contribute valuable information for use in genetic evaluation, and with the important additional potential to occasionally uncover individual genes of major, or at least relatively large, effect. Thus SNP markers associated with DGAT, a gene in cattle that has a relatively large effect on milk fat content, contribute strongly to GBVs for fat production in dairy cattle (Grisart et al., 2004) but with substantial additional contributions from many other SNP with smaller individual effects.

Likewise focus has shifted from emphasis on searching for functional mutations of large effect in breeds or families with extreme phenotypes to use of SNP-based approaches within livestock breeds. This approach emphasizes the detection and utilization of potentially large numbers of genomic variants responsible for the heritable genetic variation within each breed. Implicit in this approach is the recognition that those genomic variants, or at least the SNPs associated with them, often will not be the same in different breeds.

Genomic breeding values are not derived from clearly delineated functional characteristics of individual genes, but are instead derived from statistically determined associations between SNP variants and reported animal performance. They thus require both SNP information on candidates for selection and extensive performance records on the genotyped individuals. These performance records provide the basis for estimation of associations between SNP and genetic merit and are absolutely critical to derivation of GBVs. However, once these relationships are derived and validated, future SNP information on descendants may be used to derive GBVs prior to, or in some cases without recourse to, collection of performance data.

Utilization of Genomic Breeding Values

Generation of GBVs from SNP arrays is possible only if detailed performance records for the traits of interest are available for many genotyped individuals. This "training population" is used to determine the relationships between SNPs and genetic merit that will be used to predict genetic merit in future descendants of the training population. For example, Van Raden et al. (2009) used 3,576 genotyped, progeny-tested Holstein bulls to establish GBVs for milk production in dairy cattle. The genotyping of proven sires has emerged as the strategy of choice in dairy and beef cattle, with EBVs from these sires providing the necessary phenotypic information. Most authors suggest that an adequate training population of progeny-tested sires would require a few thousand sires with accuracy levels for their EBVs approaching 0.9. In beef cattle, the American Angus Association utilized an initial training population of over 3,000 bulls (McClure et al., 2010), and the U.S. Meat Animal Research Center developed a DNA repository representing over 2,000 bulls of several breeds to use as a multi-breed training population (Thallman, 2011).

When progeny-tested sires are used as the training population, the number of individuals required for the training population is influenced by the accuracies of the EBVs. Widespread use of AI and a longer history of performance recording in cattle relative to sheep provide greater access to high-accuracy, proven sires for use in training. Accuracies of EBVs in proven sires with many progeny approach 1.0 and thereby minimize the number of individuals required in the training population. At lower accuracies for EBV of 0.6 to 0.7 that are typical of progeny-tested NSIP rams, correspondingly larger numbers of sires are required to achieve acceptable accuracies of resulting GBVs, with requisite numbers of sires in the range of 5,000 to 7,500 (Hayes and Goddard, 2010). Use of individual-animal records to develop training populations is correspondingly even more daunting, with requisite number of animals with genotypes and detailed phenotypes ranging from 10,000 to 15,000 for a heritability of 0.4 up to around 25,000 at a heritability of 0.2 (Hayes and Goddard, 2010).

The exact numbers of individuals required to generate an informative training population is still the subject of debate and continuing research, but the above considerations indicate that:

- EBVs for progeny-tested sires are likely to be the most efficient phenotypes for use in developing GBVs in cattle and sheep;
- Use of sires with high-accuracy EBVs is strongly advantageous, but the number of sires required within a breed is still likely to exceed 1,000;
- Use of lower-accuracy sires is associated with a corresponding requirement for larger numbers of sires, usually at least a few thousand; and
- Use of individual-animal records (as opposed to EBVs) requires very large numbers of individuals and is probably not feasible for most ruminant species.

To put this situation in perspective for the U.S. sheep industry, Table 1 shows average numbers of progeny-tested sires born in each of the five years ending in 2009 and average accuracies of weaning weight EBVs for those sires for the four breeds with the highest rates of participation in NSIP. Among breeds, this number ranges from 22 to 41. Given the small numbers of additional sires tested in other NSIP breeds (Hampshire, Dorset, Columbia, Rambouillet, Dorper, and a few others) and the increasing trend in numbers of progeny-tested Katahdin sires over this period, NSIP is thus currently producing EBVs for 130 to 140 new progeny-tested rams per year. In terms of research institutions, the two main USDA research stations with sheep (the U.S. Sheep Experiment Station and the U.S. Meat Animal Research Station) have a combined ewe inventory of approximately 5,000 ewes and would be expected to generate something in the range of 50 new progeny-tested rams per year, currently spread across 8 to 10 breeds.

Development of GBVs for quantitative traits in U.S. breeds would thus require a major coordinated effort by industry, federal research institutions, and universities. It is not clear, however, that such an effort would be cost-effective for the industry. Van der Werf et al. (2011) concluded that genomic selection for quantitative traits could be cost-effective in the Australian sheep industry, but only with a nucleus breeding structure in which intensive genetic selection (even at relatively high costs) in a few elite flocks is efficiently transmitted through multiplier flocks to serve a commercial industry of one million breeding ewes. Expansion of the nucleus-breeding segment, with more seedstock flocks serving smaller numbers of commercial ewes per nucleus-breeding ram or a smaller commercial-ewe base (both typical of the U.S. industry) reduced anticipated benefits and required, lower break-even costs for genomic testing.

Emphasis regarding benefits of GBVs shifted dramatically in the four years between the 8th and 9th World Congresses on Genetics Applied to Livestock Production in 2006 and 2010, respectively. Speculation that GBVs could replace data-based predictors within a few years was replaced by realization that genomic information would likely supplement, rather than replace, data-based approaches for BV prediction. Interest in genomic prediction increasingly focused on its capacity to provide early-life predictors of genetic merit for traits that cannot be evaluated directly until later in life, with the most notable example being the comparative evaluation of dairy bulls prior to progeny testing. A second key area is the use of GBVs for difficult-to-measure characteristics that are not amenable to improvement under normal production conditions, including traits, such as meat tenderness and resistance to such infectious diseases as foot rot and OPP.

In the beef industry, molecular BV for individual traits are provided mainly by private companies and have been shown to be useful, but imperfect, predictors of genetic merit. These GBVs are currently incorporated into national cattle evaluations as correlated phenotypes, generally with genetic correlations of 0.4 to 0.7 with the actual trait of interest (Kachman, 2008; Spangler and Van Eenennaam, 2010.)

Genomic information also can be used to determine genetic relationship among individuals evaluated in national genetic evaluation (NGE) programs. These relationships are essential for proper weighting of performance records of relatives in derivation of EBVs. Under current methodology, relationships are based on pedigree information. Information from SNP arrays, however, allows direct assessment of animal relationships. Under current NGE procedures, pedigree information is used to quantify relationships as the predicted proportions of alleles shared by pairs of individuals. With genomic information, these proportions can be measured directly as the proportion of the (e.g.) 50,000 SNP variants shared by two individuals, providing a measure of relationship that does not require pedigree information and can therefore be determined between animals in the same flock, in different flocks, or even in different breeds.

Correspondence between SNP- and pedigree-based measurements has yet to be fully validated by comparing genomic relationships in individuals with known, but differing, pedigree relationships. Legarra et al. (2009) showed that pedigree and genomic information may be combined for use in NGE and developed procedures for optimally combining the two sources of information. Hayes et al. (2011) likewise demonstrated use of genomic relationships within and among Australian sheep breeds.

Table 1. Numbers of sires tested and average accuracies for weaning weight EBVs for progeny-tested sires of the four NSIP breeds with the largest numbers of participating flocks. Only sires with at least five progeny with weaning weights were included in the tabulation.

Breed	Average annual number of new progeny-tested sires[a]	Accuracy of weaning weight EBVs[b]	
		Average	Range
Targhee	23	0.73	0.34 to 0.87
Suffolk	29	0.68	0.53 to 0.84
Polypay	22	0.67	0.56 to 0.87
Katahdin	41	0.68	0.39 to 0.91

[a] Average for the 5 years ending in 2009.
[b] Accuracy is defined as the expected correlation between estimated and actual breeding values.

The Way Forward

Consideration of potential benefits of genomic testing must recognize that there are a number of different situations in which DNA-based diagnostic testing may provide useful information for U.S. sheep producers. An immediate benefit of genomic testing and expanding knowledge of the sheep genome is the opportunity to rapidly identify and develop DNA-based diagnostic tests for simply inherited genetic defects, such as the Spider syndrome in Suffolks. Opportunities to manage such defects are now available for all livestock species.

Continued study of the sheep genome using breeds, families, or individuals with extreme performance characteristics will likely result in detection of other potentially useful, simply inherited mutations. A number of major genes affecting quantitative traits have been identified in sheep and are already in use around the world in various specialized-breeding programs. For example, the FecB (or Booroola) gene and the sex-linked FecX (or Invermay) gene result in an increase in litter size of approximately 0.5 lambs in heterozygotes and up to 1.0 lambs in homozygotes (Davis, 2005). Simply inherited genes controlling resistance to scrapie are central to eradication programs in Europe and the Americas, and a DNA-based, diagnostic test for genetic resistance to OPP has been developed (Heaton et al., 2012). A number of major genes influencing muscularity involve mutations in the myostatin gene or in a region of chromosome 18 that included the callipyge, Carwell, and Texel muscling genes (Cockett et al., 2005). Each of these genes is capable of increasing loin weights by 5 percent to 12 percent in heterozygotes.

In terms of gene function, most simply-inherited genes with large effects on quantitative traits result in loss of regulatory control over some aspect of development, such as ovulation rate or muscle development. These mutations were almost always deleterious in wild ancestors of domestic sheep but may be advantageous under domestication and intensive management and are generally most useful in specific production systems and carefully controlled-breeding programs.

For much of the sheep industry, however, genetic improvement requires steady, modest improvements in several quantitative traits, hopefully in association with a properly configured, multi-trait breeding objective (Borg et al., 2007). Genes of large effect may be useful in terminal-sire breeds or intensive-production systems. However, under the extensive conditions that prevail in much of the sheep industry and in the maternal and dual-purpose breeds that dominate the national ewe flock, sustained improvement in several quantitative traits is the most appropriate strategy. Many of these traits (body size, ovulation rate, muscling, milk production) have intermediate optima that are only occasionally consistent with use of genes of large effect. Existing EBV systems, which focus on use of performance records to assess genetic merit in individual breeds, flocks, and production systems, are an appropriate model for sustained, genetic improvement. The issue then becomes how molecular information can enhance the effectiveness of existing EBV systems.

Development of GBVs for quantitative traits requires a major joint effort by industry, academic, and federal research laboratories. An example of such an effort can be seen in the Australian Sheep CRC *(http://www.sheepcrc.org.au)* but seems unlikely in the United States.

An appropriate direction for the U.S. sheep industry appears to be to establish of a baseline capacity for genomic characterization of breeding animals in U.S. flocks; establish and maintain the international connections and collaborations necessary to take advantage of advances in genomic information; develop structures for testing newly developed and released genomic tools in U.S. sheep populations; continue emphasis on detection of QTLs of large effects, especially for disease resistance and meat yield and quality; study functional genomic relationships between DNA and animal performance; and expand and strengthen traditional, genetic-evaluation systems to build capacity for establishing appropriate reference populations for training. More specifically:

- DNA samples should be collected from all progeny-tested NSIP sires to provide an archive of genomic information on these animals, and genomic characterization of these individuals should be carried out using the currently available 50K chip. This action would provide access to SNP information on a nucleus of influential, progeny-tested sires and link that information to the animals' NSIP EBVs. Benefits to this approach include:
  - Use of empirical, SNP-based relationships among tested animals to quantify and improve genetic linkages among flocks. The incorporation of genomic relationships in LAMBPLAN is anticipated in the near future and will also allow use of genomic relationships in NSIP.
  - Capacity to use genomic information and EBVs to rapidly validate new genomic tools. This capacity is provided for the U.S. beef industry by the National Beef Cattle Evaluation Corsortium (*http://www.nbcec.org*) and is essential to allow objective assessment of prospective genomic tools. For example, existing EBVs for resistance to gastrointestinal parasites in Katahdin sires could be used to assess the association between OPP resistance and parasite resistance.
  - Inceased capacity for international collaboration. Without baseline capacity to relate genomic information to objective measures of animal performance (e.g., NSIP EBVs), the U.S. sheep industry risks being shut out of collaborative international efforts to use genomic information to improve quantitative traits.
  - Possibility to take advantage of future opportunities. The field of genomics will likely continue to develop rapidly, with anticipated access to higher-density SNP chips (750K or larger) and individual-animal-genome sequences. Markers for major genes influencing various performance traits will likewise periodically emerge. Access to DNA and EBVs from a diverse cross-section of U.S. sires will prepare the industry to assess and take advantage of these opportunities.
- At least one additional SY in quantitative genomics of sheep is needed to implement the activities described above. The position could be located at an ARS station or a university, but should have the mandate and capacity to interact with the sheep industry via NSIP, federal laboratories and universities involved in sheep research, and potential international collaborators. Collaboration with scientists working in other aspects of genomics and within other species also is essential. Given the relatively small economic impact of the sheep industry, an appropriate strategy would be to locate an individual with strong training and interest in quantitative-genomics theory in an existing program involving one or more other species, with the expectation that the individual would both address needs and opportunities unique to the U.S. sheep industry and also make broader contributions to the overall science of quantitative genomics.

Conclusions

Genomic information can enhance responses to selection for quantitative traits, but only if seamlessly integrated into existing, genetic-evaluation programs. The actions described in this review would establish a baseline capacity in genomics of quantitative traits for the U.S. sheep industry. The proposed commitment is quite modest. A greater investment to actively develop genomic tools for the industry would be desirable and could be added to the above proposal, but should not be allowed to defer establishment of the proposed-baseline capacity.

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Utilization and Potential of Estimates of Genetic Value from an Industry Perspective

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Background

The U.S. sheep industry is far behind dairy cattle, beef cattle, swine, and poultry industries in the United States and the sheep industries of many other countries in the utilization of estimates of genetic values for the improvement of economically important traits. This situation is due to both 1) a general indifference on the part of the industry to utilize currently available genetic technology, as evidenced by the low number of flocks enrolled in the National Sheep Improvement Program (NSIP) and 2) the slow output of new technology to the industry by research institutions and commercial companies. The second point is due to a small U.S. sheep research effort and lack of significant profit potential for commercial companies from a small national flock.

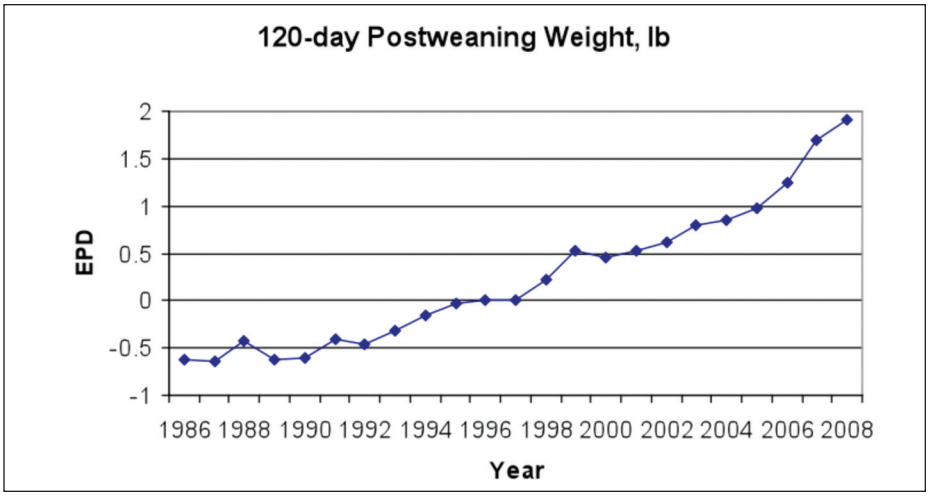
Key Words: Sheep industry, Genetic Selection, Economic value

Moving Forward

There are several examples of the improvement in animal performance that can be made by the selection of replacements, especially males, on estimates of genetic value obtained from phenotypic performance records. Holstein dairy cows in the Dairy Herd Improvement program born in 2009 compared to 1990 had a 28-percent-greater milk yield (26,861 pounds vs. 20,959 pounds) (AIPL, 2011). Fifty-eight percent of this increase was due to increased genetic value of cows born in 2009 compared to cows born in 1990 – annual increases in cow breeding value resulted in a 0.8-percent-per-year increase in milk yield. Angus calves in the Angus Herd Improvement Records program born in 2010 had a yearling-weight-breeding value that was 96 pounds greater than the yearling-weight-breeding value of Angus calves born 20 years earlier in 1991 for an increase of 4.8 pounds per year or 0.5 percent per year (AHIR, 2011). There is widespread use of bulls with estimates of breeding value in commercial cattle herds, so rates of genetic change in commercial dairy and beef cattle herds would be expected to be only slightly less than the rates of change in these performance-recorded, purebred herds.

We have ample evidence that genetic change also is possible in U.S. sheep flocks if performance is recorded and selection is based on estimates of genetic value. Lambs from Suffolk flocks enrolled in the National Sheep Improvement Program born in 2008 had an average 120-day-postweaning weight estimated breeding value (EBV) that was 3.7 pounds more than the average 120-day-postweaning weight EBV of lambs born in 1996 (Figure 1), for an annual change in average, postweaning weight due to genetic improvement of approximately 0.3 percent per year (Notter, 2008). However, genetic change for economically important traits is expected to

Figure 1. Genetic trend for 120-day weight for Suffolk sheep enrolled in the National Sheep Improvement Program (from Notter, 2008). Note: EPD = Expected Progeny difference, 2(EPD) = Estimated Breeding Value.



be much lower for commercial flocks compared to flocks enrolled in NSIP because there is very little use of rams with estimates of genetic value in commercial flocks. This is because there is limited availability of such rams due to the small number of purebred flocks enrolled in NSIP. In 2011, among all breeds of sheep in the United States, data were submitted to NSIP on only 4,146 sheep in 70 flocks (M. Sorensen, pers. com.). One reason for the low involvement in NSIP by purebred flocks is due to the failure of the commercial sheep industry to demand, pay a premium for, and use rams with high estimates of genetic value.

Research projects and extension efforts have validated the advantages of using males with estimates of genetic value, especially in beef cattle (eg. Baker et al., 2003), but very few similar validations with sheep have been conducted in the United States. In a 1999 and 2000 study at the University of Wisconsin-Madison compared growth of lambs sired by seven NSIP Suffolk rams, average, Expected Progeny Difference (EPD) for 120-day weight = +2.6 lb., were compared to lambs sired by four non-NSIP Suffolk rams (Thomas et al., 2000). The 120-day weights of the lambs sired by the NSIP rams were 3.8 pounds greater than the 120-day weights of the lambs sired by the non-NSIP rams (Table 1). That is 380 more pounds of lamb at 120 days of age per 100 lambs or $646 additional potential income per 100 lambs from the NSIP rams if lambs are worth $1.70/lb. live weight. This is not to suggest that all rams with estimates of genetic value from NSIP-enrolled flocks are genetically superior to all rams without estimates of genetic value, but without estimates of genetic value such as EPD or EBV, there is no objective information on which to select rams in order to have a higher probability of genetic ram superiority.

In addition to the need for more validation studies and demonstrations on the advantages to be gained from using rams with desirable estimates of genetic value, there is an immediate need to make the genetic information from NSIP flocks readily available to other purebred breeders and commercial producers so they can locate flocks enrolled in NSIP and identify animals to purchase that have high estimates of genetic value for traits important in their flocks. The logical places for this information are on the NSIP web site (NSIP, 2012) and on sheep-breed-association web sites. The NSIP web site has a list of flocks enrolled in NSIP so that producers know whom to contact to purchase sheep with estimates of genetic value. In addition, NSIP recently added a listing of elite older sires and elite younger rams to their web site. While this is a very positive step, the information would be more useful to prospective ram buyers if the lists could be sorted by all traits and indexes to easily identify sires that meet minimum criteria for several traits. For the most part, U.S. sheep-breed associations have provided very little promotion of NSIP or the use of genetic evaluations in breed improvement.

The success of the Center of the Nation NSIP Sale in Spencer, Iowa is an indication that commercial producers will pay a premium for sheep with high estimates of genetic value if the sheep and their estimates of genetic value are readily available. The 6th annual sale was held on July 30, 2011 and averaged $830 on 74 head ($1017 on 48 rams and $487 on 26 ewes).

The widespread use of DNA tests for scrapie resistance at codon 171 of the prion gene (R = resistant, Q = susceptible) (Hunter, 1997) and for the skeletal deformity of Spider Syndrome (N = normal, S = Spider) (Beever et al., 2006) by the U.S. sheep industry is strong evidence that the industry will make use of new DNA tests for single genes that improve well-being, health, or performance of sheep as they become available. However, it would be desirable if DNA tests for other single genes with known effects were available from U.S. laboratories [e.g. the DNA test for the Booroola gene for increased ovulation rate (Wilson et al., 2001) is commercially available only in New Zealand at Genomnz DNA Testing Laboratory]. In addition, there is a need for U.S. research institutions to validate the effect of single genes or gene markers discovered in other countries in U.S. breeds and under U.S. production conditions to determine if DNA tests for these traits would benefit the U.S. industry. Examples are the gene markers for cold tolerance in lambs and foot-rot resistance discovered in New Zealand with DNA tests available through Lincoln University (2012).

We now have the ability to test individual sheep to determine which nucleotides are present in their DNA at several thousand locations throughout the genome. Quantitative traits, such as average daily gain, feed efficiency, longevity, milk production, and loin eye area are very likely due to the combined action of a few hundred genes, most with a small effect. Specific nucleotides at specific locations in the genome may be related to greater or poorer performance for these traits. Once this is known, sheep can be tested and then selected for the "set" of good nucleotides in order to improve the trait. This is called "Genomic Selection" and is discussed in greater detail by Cockett (2012) in a companion paper.

Genomic selection is currently being used extensively in dairy cattle to improve the rate of genetic improvement (Schefers and Weigel, 2012). It will be used in sheep in the future, but the major hurdle that we have is the lack

Table 1. Body weights (lb.) ± SE of lambs sired by NSIP[a] and Non-NSIP UNITED STATES Suffolk rams.

		Age at weighing, d				
Sire source	**No.**	**Birth**	**30 d**	**60 d**	**90 d**	**120 d**
NSIP	130	12.7 ± 0.22	34.6 ± 0.78	55.8 ± 1.26	79.8 ± 1.62	103.4 ± 1.93
Non-NSIP	115	12.7 ± 0.24	32.9 ± 0.94	54.0 ± 1.51	76.7 ± 1.94	99.6 ± 2.34

[a] NSIP = National Sheep Improvement Program
From: Thomas et al., 2000.

of large numbers of performance-recorded sheep with estimates of genetic value that can serve as a training set to determine the relationship between a sheep's nucleotide profile and its genetic value for a particular, quantitative trait. These relationships are being determined in the countries of Australia and New Zealand, where there are larger numbers of sheep with estimates of genetic value and greater research budgets for sheep than in the United States (e.g. van der Werf, 2011), but it is highly likely that genomic selection criteria developed in these and other countries in their domestic sheep populations will be much less accurate when applied to sheep in the United States. While the U.S. sheep industry may be able to benefit some from genomic selection criteria developed in non-U.S. sheep populations, genomic-selection criteria need to be developed from U.S. sheep populations in order to be of the greatest benefit to our industry. This requires an organized effort by research and industry to record performance, calculate estimates of genetic value, and determine genome nucleotide profiles on large numbers of sheep. This effort will need to start with flocks enrolled in NSIP.

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Utilization from a Producer Perspective: Where We Have Been, Where We Are Now, Challenges and Opportunities for the Future

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Summary

This article is a discussion of the evolution of personal involvement in the sheep business. It is intended to illustrate the evolution from making selection decisions based solely upon look-good, feel-good evaluation, to rudimentary records, all the way to the use of EBVs and profitability indexes. The U.S. sheep industry is challenged to make better use of the genetic selection tools currently available, and the stage is set for moving to the next frontier of gene-enhanced selection.

Key Words: Breeding Values, Performance Testing, Selection, Targhee Sheep

Where We Have Been

The Hibbard family has been in the sheep business since the late 1800s. A great grandfather, who emigrated from Germany and came into Montana on the Bozeman Trail in the 1860s, was a stockman. Although a cattleman at heart, he raised "sheep for the money". By the end of his life, Henry Sieben had established two sheep ranches in west central Montana. The Hibbard family owns and operates one of those ranches today. Initially it was stocked with ten to twelve bands, herded largely by men from the same village in Romania. In those days, record keeping was quite simple. From all indications the important numbers were recorded on the back of a snoose can (smokeless tobacco) or on a leather glove.

In the early 1950s, the decision was made to begin raising rams for use on the ranch and for sale. It was decided to use a new breed ready for release from the U. S. Sheep Experiment Station at Dubois, Idaho. Development had begun in the 1930s and 1940s of a synthetic breed called Targhee, named after the Targhee National Forest just north of the station. To meet the needs of western producers, Targhees were developed as an open-faced sheep with easy fleshing, good twinning potential, foot-rot resistance and easy herding behavior. By 1951, Targhees were ready for release. The Sieben-Hibbard family was one of the first in Montana to receive Targhee rams released from Dubois. Eight hundred ewes were selected from 10,000 Rambouillet-based, western-whiteface sheep that met visual Targhee breed standards, to prepare for the introduction of this new breed. They were top-crossed with the early rams from Dubois, and thus began one of the first Targhee flocks in the United States.

Thirty-six years ago, in 1976 Chase Hibbard took over the ranch, determined to continue the legacy of Targhee sheep. By that time, the ranch had converted to mostly cattle so that the number of purebred sheep was down to about 200 registered ewes. Record keeping was pretty much still on the back of a snoose can, and performance enhancement was inspired by the show ring. In order to progress, it was necessary to make a name for yourself in the ring. Lots of ribbons were won and eventually a National Championship, and it was thought that the ranch was well on the way to meeting the needs of the industry. "On-farm" performance testing had been gaining traction and all of a sudden record keeping began creeping in. As record keeping began to get more sophisticated, with more and more numbers, the snoose can system was actually deserted altogether.

Formal performance testing in the United States began in 1948 in Texas, at the A&M University Sonora Substation. By 1950, the University of Wisconsin began on-farm selection. In 1965, Ohio put the first computerized, record keeping system in place, and by 1980 there were a total of 23 on-farm testing programs and 14 central-ram tests. In Montana, on-farm testing began in the 1960s. As on-farm testing became more prevalent, the use of "ratios" emerged as a tool to select the best of whatever trait was being measured or weighed. Some of the subjectivity of selection was challenged.

This is when the ranch started to make real progress. "Ratios" were a great tool, allowing the user to rank all flock animals against the average for any particular trait. This of course was within your own flock only, with no way to compare a 110 ratio in my flock with a 110 ratio in your flock. Records from one flock to another flock could mean entirely different things. A 100 in Flock A could conceivably be better than a

110 in Flock B. A new ratio called "number of lambs born per ewe exposed" was introduced. An index was developed and another tool was available to make progress. This gave us a way to select the most prolific animals in the flock to move toward greater productivity.

About this time, a further challenge was received from Charles Parker, who was then at the U.S. Sheep Experiment Station. His message was that U.S. producers were getting trounced by our overseas competitors and by other meat- and milk-producing industries. In his view, we weren't being competitive with either costs of production or pounds of lamb raised per ewe. This really set us on our ear. Comparisons were made to New Zealand, where the average sheep raising family raised something like 2600 ewes, fed no hay, pasture lambed, and had little or no extra labor. And to add insult to injury, when the sheep-industry's productivity was compared to the progress that had been made in terms of pounds-of-product-produced per female, or the increases in pounds-of-milk per milk cow, the sheep industry remained way behind.

At the time, selection strategies were based upon visual evaluation, better known as "best guess", plus "performance records". This meant selection was based upon how the animal looked and felt, plus the animal's own, in-flock-performance records.

Enter genetic evaluation. The National Sheep Improvement Program (NSIP)1, introduced around 1986, gave us a vehicle to take us to the next level and really begin focusing on true genetic improvement. Through Best Linear Unbiased Prediction (Henderson, 1975), we now had the ability to make genetic comparisons through Expected Progeny Differences (EPDs). EPDs are calculated as one-half Estimated Breeding Values (EBVs, which are now reported in LAMBPLAN). They are a prediction of how an individual's offspring will perform or an estimate of the animal's genetic value. EBVs and EPDs are calculated using the animal's individual performance, the animal's family performance, and the animal's offspring performance. In other words, they provide a 360-degree view of an animal's potential.

The big advancement made by introduction of EPDs was the ability to make across-flock evaluations, something not previously possible. Across-flock comparison allowed the best animals for any given trait to be identified. No longer was it necessary to scratch our heads when my ram has a weaning weight (WW) ratio of 110 and my neighbor's WW ratio is 98 and it is not known whose is better. A powerful tool was now available to begin making much more rapid genetic improvement.

NSIP really caught on in the Targhee breed, and those using it found that the show ring began to take on a different meaning. The breed association attempted to accommodate both schools of thought and it began sponsoring an NSIP class in addition to the open show classes. NSIP records for the entered animals were analyzed and ranked upon their merit. The animals were not allowed to be fitted, but otherwise were shown in traditional show-ring fashion. A formula was devised to rank both the NSIP-performance-record results and the show-ring-judging placement. A judging template included:

- Rams ranked upon individual EPDs (EBVs after 2009),
- Rams visually placed in NSIP class by show judge, and
- NSIP score doubled and combined with show ranking.

It was likely for the top-NSIP ram to win overall unless he placed near the bottom of the show class. The winner then went on to show in the open class against the fitted-range sheep. Occasionally an NSIP ram would win the open class, but he would need tremendous phenotype to beat fitted-show rams. This dual system persists to this day at Targhee shows, and is a good example of the "art" of animal breeding, since it addresses both the objective and measurable animal-performance traits with the visual, structural, aesthetic and subjective traits, the ones you can see and feel.

Where We Are Now

Most recently, NSIP has evolved into LAMBPLAN, which is processed in Australia. Traits that are important to commercial producers have been added, and the result is a huge number of EBVs. There is so much information reported that most breeders export only the most relevant numbers to a spreadsheet in order to simplify the process. In our case, we export nine genetic traits, plus spinning count, actual micron, actual and adjusted ribeye area, scrotal measurement, and genotype for scrapie resistance (codon.) The question for most of us now s — how do I make actual decisions with all this information, particularly when some of the traits are antagonistic?

How should the following traits be sorted out: weaning weight, maternal milk, milk + growth, yearling weight, ribeye, fleece weight, fiber diameter, staple length, number of lambs born, genotype? Fortunately, selection indexes had been crafted to synthesize and measure the most important criteria. Most cattle breeds have them. Now, with LAMBPLAN, several selection indexes are available. Selection indexes weigh the most important traits in a formula according to their importance toward the breeding goal selected. Typically, the goal focuses on "profit." Index values give us an estimate of economic merit for the breeding animal. In other words, profitability indexes provide an economic filter to help sort out the traits that will positively influence income from increased production, and traits that will negatively influence income from increased expenses. An example is, selecting for increased weaning weights, which seems desirable, yearling weight of mature ewes also goes up and the overall size of mature animals increases, thereby increasing the carrying costs of the flock. A good profitability index should sort these things out by applying an economic standard. The economic value would be the difference between the increased income from the trait and the increased expense associated with the trait.

For Targhees, two profitability indexes have been designed to fit two production scenarios. The Western Range Index fits a typical Montana range, marketing system. The Farm Flock Index fits a system in which extra market-lamb weight is valued through retained ownership. A Profitability Index:

- Simplifies what is too much data, reducing it to one number, focusing on profitability;
- Eliminates "analysis paralysis"; makes production decisions easier at home; and
- Makes purchasing decisions easier for buyers.

Have these tools made a difference? The short answer is "yes, they have."

There has been a great deal of improvement since the inception of NSIP and a huge amount of improvement since the application of profitability indexes. Both weaning weights and number of lambs weaned have seen significant increases when graphed, and depending on how they are weighted, other traits are improving as well. From 2009 to 2011, the time during which our Western Range Index has been in place, progress in profitability is at an ever-increasing pace.

Personal experiences of the ranch and evolution in the sheep business have been discussed as an example of how genetic improvement has evolved over time. In summary the ranch:

- Started making selection choices almost entirely on how the sheep looked and felt,
- Progressed to keeping crude records, was influenced by the show ring,
- Moved forward utilizing in-flock testing,
- Used central ram tests,
- Was inspired by Charles Parker's Holy Grail to raise more pounds of lamb per ewe exposed or be left in the dust, and finally
- Utilized genetic evaluation made possible by NSIP, EPDs/EBVs, across flock analysis, and profitability indexes.

This brings us to where we are today. Gene-enhanced selection, or genomics, is the next frontier. Are we ready to go there? I am sure a question that most will ask is "what will it do for me?" In short, with these more advanced tools, the possibilities should include the ability to:

- Select at an earlier age, even selecting replacements or rams as lambs;
- Use shorter generation intervals with more confidence in my selection process; and
- Select for hard-to-measure, impossible-to-see traits, such as:
  - livability
  - female reproduction
  - disease and parasite resistance
  - more efficient feed conversion
  - omega-3 health component
  - eating quality.

There are some impediments, which include:

- Lack of acceptance
  The Hibbard Ranch has been using EPDs for 25 years. For the first several years at the Montana Ram Sale, we spent time explaining what the numbers meant, and buyers eyes would glass over, they would nod politely and climb in the pen to make a visual evaluation. The central ram test winners sold well, with no promise that their offspring would perform anything like their daddy. In the last 5 or 6 years, EBVs have really caught on and now, finally, the first and sometimes the only questions buyers ask is: "What is your best indexing sheep?", or "Which has the best ribeye?", or "Which will increase my number of lambs born?" It would be difficult to sell rams at the Montana Ram Sale at all anymore without EBVs, but it has taken a very, very long time to get to that point.
- Most producers don't use the proven tools currently available. Is there support to move forward to the next level?
- Cost
  In Australia, producers are talking about $5 a sample. This is a fraction of the current cost.
- Turnaround time
  Again in Australia, producers are talking about less than 10 days.

There are great tools out there that work, but producers have to use these tools in order to benefit from them. As a purebred producer, the ranch is making better selections in the flock, and selling animals that will improve the bottom line for my customers in the commercial sheep industry. Most sales of commercial breeding rams around the country don't require or even post EBVs. Buyers have not recognized their value. A challenge is made to the industry to use these tremendous tools—commercial producers to require their ram suppliers to enroll in NSIP and purebred producers to take the leadership to use the proven tools available.

Enhanced selection through performance records is here now, it is real, and the results are tangible. Gene-enhanced selection is the next step. It has the potential to take us to the next level. Most of the industry is flying around in a DC-8. Those using EBVs are flying in a 747. A rocket ship for Mars is currently in the dock being fueled for the next frontier. Do you want to be on it?

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Genetic Selection Specifically Utilized for Evaluating the Introduction of Outside Breeds and Measuring Their Potential

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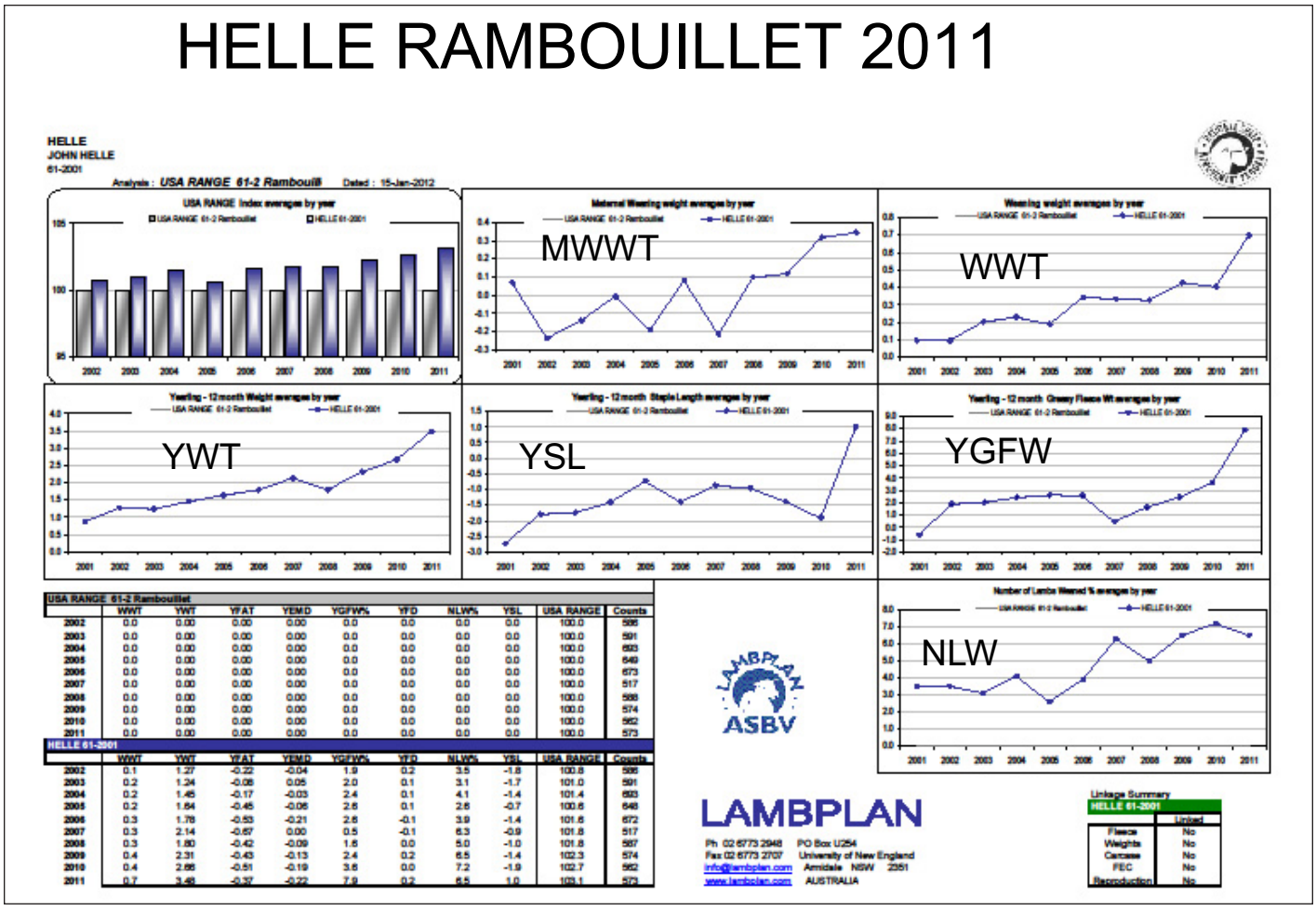
Background

Helle Rambouillet has utilized extensive record keeping for a number of years, placing a large emphasis on wool and maternal traits since the beginning. New traits of interest were added each year. This has been a confusing and complicated process, as data are maintained for each purebred animal; however, it has been rewarding because significant progress has been made for improved genetic selection.

Key Words: Genetic Selection, Traits, Breeds, Rambouillet

Figure 1. Progress over time in USA Range Index, weight traits, staple length, greasy fleece weight and number of lambs weaned in the Helle Rambouillet Flock.



Forward Progress

The use of genetic records has allowed fine-tuning and careful monitoring of the genetic-selection progress. The summary report (Figure 1) from the National Sheep Improvement Program (NSIP) allows the monitoring of progress over time for some of the more important traits. In this case, the flock is a single flock in NSIP with really no genetic ties to other flocks so all analyses are within flock.

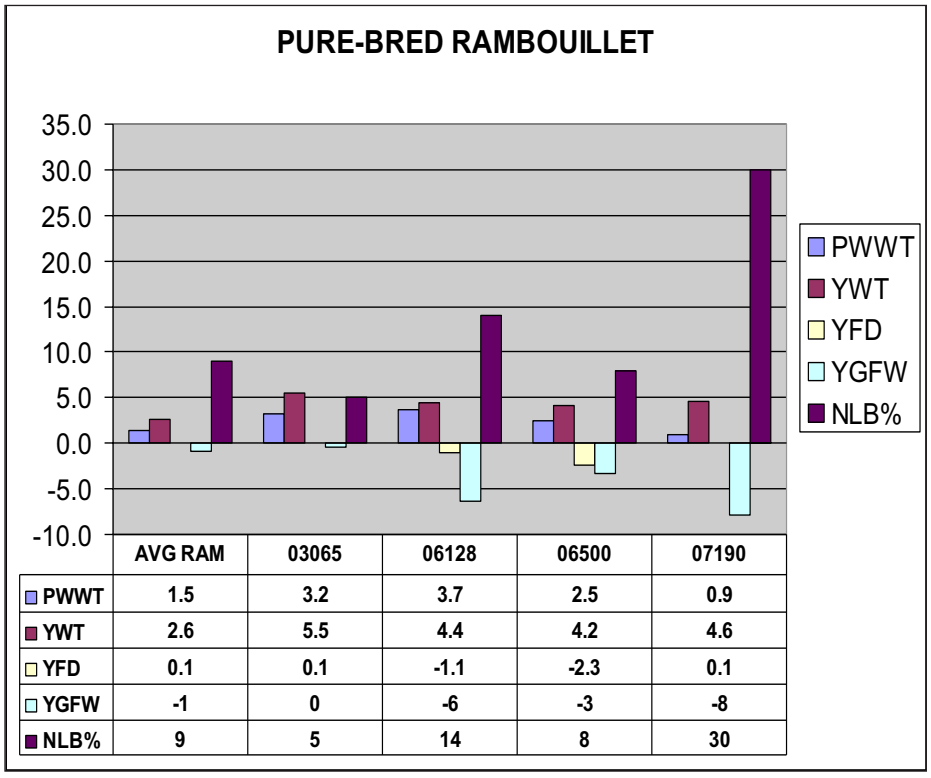
In recent years, Australian genetics was incorporated through artificial insemination. Three Merino, four SAMM (South African Mutton Merino), and two Dohne rams were selected to improve the Helle Rambouillet flock through the use of outside genetics to improve traits of interest. The use of NSIP has allowed the comparison of these rams to each other and to the pure-bred Rambouillet flock (Figures 2 and 3). It is apparent that some choices were better than others. The role of Australian genetics is still being evaluated for use in the breeding program.

The Helle Rambouillet records are now incorporated into the Australian database, and comparisons are made between rams within the Australian system, which is viewed as a huge advantage. There are some differences in adjustment factors and correlations used in the U.S. analysis versus the Australian analysis, so interpretations must be guarded, but some of the comparisons are of value.

Conclusion

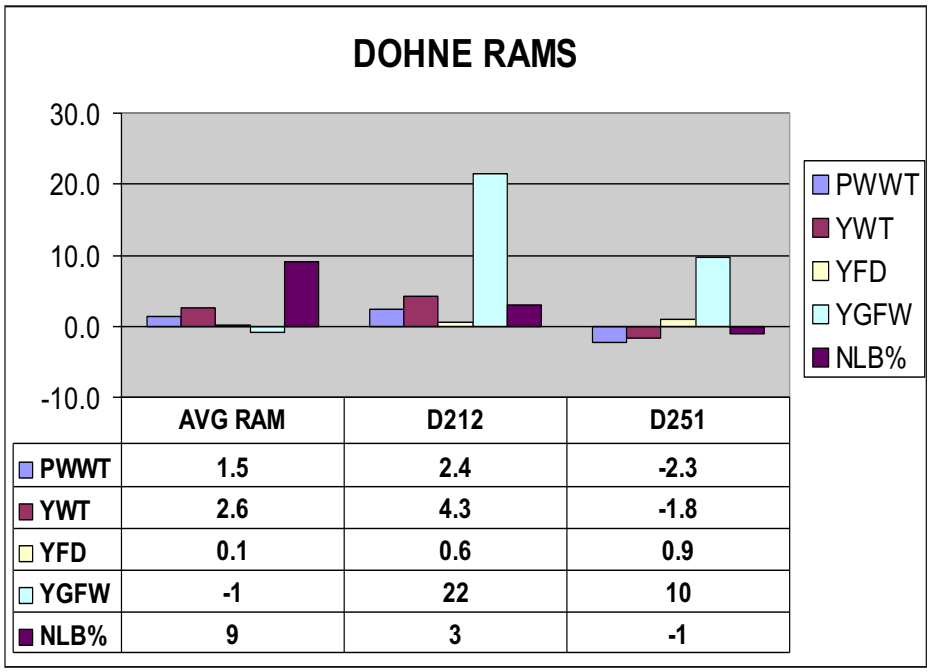
Through NSIP, Helle Rambouillet was able to more accurately interpret production data for use in a selection program. It is helping make decisions as to how Australian genetics might be effectively utilized in a selection program.

Figure 2. Comparison of selected Rambouillet rams to the average ram in regard to post-weaning weight, yearling weight, yearling fiber diameter, greasy fleece weight and number of lambs born.



	AVG RAM	03065	06128	06500	07190
PWWT	1.5	3.2	3.7	2.5	0.9
YWT	2.6	5.5	4.4	4.2	4.6
YFD	0.1	0.1	-1.1	-2.3	0.1
YGFW	-1	0	-6	-3	-8
NLB%	9	5	14	8	30

Figure 3. Comparison of selected Dohne rams to the average ram in regard to post-weaning weight, yearling weight, yearling fiber diameter, greasy fleece weight and number of lambs born.



	AVG RAM	D212	D251
PWWT	1.5	2.4	-2.3
YWT	2.6	4.3	-1.8
YFD	0.1	0.6	0.9
YGFW	-1	22	10
NLB%	9	3	-1

