Breeding & Genetics and Physiology & Endocrinology Symposium: Bridging the Gap Between Physiology and Genomics

287 Spanning research from QTL to functional unit of a gene. J. M. Reecy*, *Iowa State University*, *Ames*.

Since the dawn of modern genetics, researchers have been working toward the elucidation of genetic pathways that control variation in traits of interest. Along the way, new breakthroughs in technology have lead to new insights. The determination of the structure of DNA and the subsequent explosion in molecular biology, enabled researchers to identify genes responsible for many processes in a cell (e.g., glycogenesis, transcription, etc). Eventually, geneticists began to utilize these new molecular techniques to identify regions of the genome that contain genetic variation that was associated with phenotypic variation (quantitative trait loci; QTL). To date, molecular geneticists have identified almost 10,000 QTL in cattle, pigs and chickens. The speed with which new QTL are identified is ever increasing. Unfortunately, the identification of quantitative trait nucleotides (QTN) lags significantly behind. However, now that the genomes of all major livestock species have been sequenced a new suite of techniques have been unleashed. New genotyping and statistical techniques have made it possible to not only identify QTL and fine map them, but to also account for a large amount of total genetic variation associated with a trait of interest. For some traits there are a large number of small effect QTL (i.e., infinitesimal model), while for other traits there appear to be a limited number of QTL. In addition to genotyping and statistical breakthroughs, whole, or even partial, genome re-sequencing and transcriptomics (RNA-seq) are providing new insights into genome and gene structure. We can now combine phenotype, genotype and gene expression data to understand the mechanisms underlying traits of interest in greater detail than ever before. We have entered an era where molecular/quantitative genetic techniques need to be directed beyond production to consider animal health, animal welfare, climate change mitigation, and consumer health traits.

Key Words: genomics, transcriptomics, whole genome association

288 Advancing toward functional genomics. H. L. Neibergs*, *Washington State University*, *Pullman*.

Complex traits are difficult to identify at the molecular level. Because many genes are involved, many with modest effects, it is difficult for them to be detected in genomic studies. To identify loci responsible for complex traits, multidisciplinary collaborations between genetics and physiology are essential. Integration of computational biology, molecular biology and physiology enhances the genomics discovery process because the connections between the functions of the gene products will lead us to the genes involved in the phenotype. To make the link between genome and phenotype, tools such as gene set enrichment combined with single nucleotide polymorphism analysis offer approaches to evaluate biological pathways in the context of genomic variation. Evaluation of the unique transcription profiles of a cell at different points in the life of the animal, whether conducted with microarrays or RNA sequencing, adds information about the transcription regulation of the genome. Proteomics extends the transcriptional message to the proteins being produced in and around the cell and the post-translational modifications that affect the protein′s function. The identification of alternative splicing of the mRNA transcripts and the interaction of proteins with other protein and RNA molecules must also be investigated to determine how a phenotype is expressed. By understanding the biological process of transcription, translation, and interactions of the proteins, the variation present in the genome is placed in context to the phenotype. Progress toward solving the basis of complex traits may well begin with the biological process, rather than the QTL. Genetics may be the foundation of animal improvement, but true genetic progress will be made when we expand our field of view to include gene function.

Key Words: functional, genomics

289 Genomic analysis of data from physiological studies. D. J. Garrick*, *Iowa State University*, *Ames.*

Physiologists have long been undertaking research to discover and elucidate the mechanisms involved in particular metabolic processes such as maintenance, growth, reproduction, and disease. Animal breeders have focused their research endeavors on understanding genetics, the study of inheritance, to implement breeding programs that can systematically advance the genetic merit and phenotypic performance of food animal systems, by exploiting selection of above-average candidates to be the parents of the next generation. Prerequisite characterization of the genetic merit of selection candidates has principally been achieved by visualizing the genomes of the candidates solely through measurement of phenotypes on the candidate itself, or on its close relatives. The resulting artificial selection has made use of those genes that are responsible for variation in performance, without requiring or taking advantage of any knowledge of causality, in the same manner that natural selection can alter populations. Accordingly, selection could rightfully have been described as resembling a black-box. Leveraging on sequencing activities undertaken in various livestock genomes, high-density genotyping systems have become available that allow inheritance of individual genome fragments to be traced from one generation to another and related to variation in performance by quantifying their substitution effect. Genomic selection can then be undertaken by predicting merit by summing up the values of an individual's chromosome fragments. A by-product of this approach is that it identifies genomic regions contributing to variation in performance that can be queried in bioinformatic databases that accumulate knowledge of gene location and function. Collectively this information can extend the scope of physiological studies beyond the underlying mechanisms of average performance to explain the causes of variation in performance.

Key Words: genomic selection

290 Genomic information for physiologists. M. G. Thomas*, K. L. DeAtley, S. O. Peters, G. A. Silver, and A. M. Clayshulte, *New Mexico State University*, *Las Cruces*.

Furthering knowledge of genes and understanding their mechanistic-role is a focus of physiology research. Specifically, this research furthers understanding of transcripts that are translated into proteins and considers their relevance in the whole animal. Development of tools to work with genomic data have enhanced gene discovery for physiology and molecular biology research. Some of these tools also provide data for estimating genome-assisted breeding values for livestock improvement programs. For example, SNP-chip data can be used for QTL detection as well as genetic prediction. Once a QTL is discovered or queried from a database, the process of fine mapping to determine the DNA sequence inferring the physiology from the underlying genes involves numerous

strategies. These include resequencing and denser DNA marker association studies and (or) investigation of transcriptome and proteome reference resources to reveal candidate genes, which can be visualized in pathway software to help design studies to investigate their functions. An example of such a process involved detection of a QTL on chromosome 2 for heifer pregnancy (n = 830 and BovineSNP50 genotypes). Bioinformatic tools (animalgenome.org) were used to visualize 10 QTL and 10 annotations in a 4 Mb region flanking the SNP inferring this QTL. Since hypothalamus is part of the reproductive endocrine axis, RNA was harvested from this tissue of pre- and post-pubertal heifers and deep sequenced (RNA-Seq). Transcriptomes were aligned with the bovine genome (ver. 4.0) to evaluate presence and level of expression of candidate genes with Alpeus. Three genes with differing levels of expression were identified and their ontology suggested neuron function and cell signaling. Most importantly, these genes were new discoveries for this research program and provide opportunity for their visualization in pathways and consideration in design of experiments to decipher their physiological relevance. These considerations could also include evaluation of allele-specific variation. Advancements in genomics have expanded the ability of physiologist to discover genes and explore their functions.

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Key Words: candidate gene, physiology, RNA-Seq