opment. Nevertheless, those embryo and uterine responses to B_9 are often more pronounced in multiparous sows than in gilts. This parity effect on B_9 responses could be attributed to the metabolic interaction with another vitamin, B_{12}. Those two vitamins are essential to modulate the transfer of one-carbon groups for protein and DNA synthesis, methylation and gene expression. The metabolic pathway involved is the remethylation of methionine from an intermediary metabolite, homocysteine (Hcy). A deficiency in B_9 or B_{12} may induce a local or systemic accumulation of Hcy, a powerful pro-oxidant known to impair embryo development. It appears that the B_{12} status, which is about 2 times lower in gilts than in multiparous sows, could be a limiting factor to the B_9 action on uterus and embryo metabolisms during the first pregnancy. This B_{12} status is particularly critical since the sow uterus drained in early gestation massive amounts of B_{12}, representing 2 to 3 times the B_{12} plasma pool. Dietary B_{12}, at levels 10 times higher than recommended, maximized B_{12} status and minimized Hcy accumulation in first parity sows. It appears that an optimum ratio B_9:B_{12}, yet to be estimated, would allow the full beneficial response of B_9 on sow prolificacy. In the future, it is likely that the need for updated information on requirements for B-complex vitamins will be enhanced taking into account the "dietary fine tuning" required with the highly producing pigs selected during the last decades.

Key Words: Folic Acid, Vitamin B_{12}, Sow

Genomics: Functional Genomics for Livestock Improvement

12 What is functional genomics? J. Pérez Laspiur* and T. Ferris, *Michigan State University*, *East Lansing*.

In the past, we have attempted to understand the physiological responses of livestock to stressors, such as environmental conditions and husbandry practices, and their impact on performance traits. Further, we have selected livestock using quantitative approaches that involve estimating the effects of all genes affecting these traits without knowing the specific role of any of these genes. Evident phenotypic traits are a combination of internal (genetics) and external (environment) factors working jointly. Although we have advanced in our understanding of the role that external factors play on the occurrence of important phenotypic traits, we lag behind in our understanding of the genetic factors that affect these same traits. With the recent completion of the bovine genome sequence and availability of high-throughout technology, a functional genomics approach can now be used to simultaneously investigate disturbances in expression of thousands of genes in relation to environmental and physiological challenges. This approach allows us to determine what groups of genes and pathways are responsible for, or correlated with, - metabolic changes and how these may be manipulated to improve performance and well-being of cattle. Functional genomics therefore has the potential to highlight significant new candidate genes to improve genetic selection programs and to evaluate the effect of various practices on multiple systems within an animal. A vital contribution of these studies is the integration of physiological, nutritional, and genetic data to develop public resources for cattle. These resources will help answer questions concerning genes involved in milk production, milk quality and composition, and response to husbandry stressors. Eventually, this knowledge will further aid in selection and management of livestock.

Key Words: Functional Genomics, Genetic Improvement

13 Implications of functional genomics for animal breeding programs. J. C. M. Dekkers*, *Iowa State University*, *Ames*.

Current selection programs in livestock are primarily based on selection on EBV for traits of economic importance, that are estimated from phenotypic records. These EBV provide an estimate the collective effects of all genes that affect the trait, without knowing where the genes that control the trait are located in the genome or what their individual effects are. Thus, although this quantitative genetic approach to selection has been effective for many traits, it is essentially a black-box approach. In the past decade, much research has been conducted to locate so-called Quantitative Trait Loci (QTL), which are regions in the genome that contain genes that affect the trait and which can be identified using molecular markers that are linked to the QTL. In most cases, however, the actual location, identity, and functional role of the QTL remains unknown. Thus, QTL mapping has essentially subdivided the black box of quantitative genetics into multiple smaller black boxes. Examples where the causative gene for the QTL has been identified are limited. Although markers that are linked to QTL can be used to enhance genetic progress through marker-assisted selection, there are limitations to such selection. In addition, the ability to identify QTL is limited for traits that are difficult or expensive to record. The purpose of this presentation is to describe and discuss how functional genomics can enhance the discovery of genes that control traits of importance and how the knowledge functional genomics promises to provide on gene function could be used in the future to enhance selection programs, management programs, and the integration of selection and management programs.

Key Words: Functional Genomics, Selection, Marker-Assisted Selection

14 Use of functional genomics in genetic selection programs for environmental stress tolerance in dairy cattle. R. Collier*[1], C. Stiening[1], B. Pollard[1], M. VanBaale[1], and P. Coussens[2], [1]*University of Arizona*, *Tucson*, [2]*Michigan State University*, *East Lansing*.

Selection for tolerance to environmental stress has traditionally been counterproductive in domestic animal production. As animals acclimatize to environmental stressors they reduce or divert metabolizable energy from production to balance heat gain and loss. Thus, it has generally been faster and easier to obtain production increases by altering the environment around animals. However, environmental modification comes at a high cost and in some cases these costs cannot be economically justified. Ideally, one would like to simultaneously select for increased production and thermal resistance to increased thermal load In order to do this the genes associated with acclimatizationon need to be identified. In acclimatization, the body's response to the environment is coordinated in two phases (acute and chronic) over a several week period at the structural, organ, cellular and molecular level to respond the stress or stressors with alterations in the organism's capacity to tolerate the stress. These changes include alteration in gene expression, enzyme activity, cell receptor populations, body organ size, fat deposition, energy consumption and a wide variety of other possible effector mechanisms depending on the stressors. Targets of potential genetic manipulation would include increased efficiency and capacity of thermal effectors and delayed onset of temperature threshold for thermal injury. We have identified a group of genes associated with the heat shock response in bovine mammary tissue. We have also identified factors associated with altered sweating rate in cattle. Presentation will focus on strategies to improve heat shock response and sweating rate to improve thermal tolerance in dairy cattle.

Acknowledgements: National Functional Bovine Genomics Consortium (NBFGC) IFAFS/USDA

Key Words: Acclimation, Heat Stress, Functional Genomics

15 Functional genomics of reproductive tissues: Creating new knowledge that can be used to solve infertility in farm animals. M. C. Lucy*, *University of Missouri*, *Columbia*.

Reproductive tissues express mRNA for a large number of genes. The full complement of expressed mRNA is unknown and sequencing projects typically find a large number of unique mRNA within the reproductive tract. The function of the proteins that arise from the expressed mRNA is either unknown or poorly understood. Furthermore, genes with recognized functions may have alterna-

tive functions that may be poorly characterized or completely unknown. Functional genomics is a scientific discipline that links gene expression (manifested at the genome level) to gene product (i.e., protein) function and cellular phenotype. Reproductive tissues are similar to other tissues where tissue and developmental patterns of gene expression is incompletely characterized and the functional annotation of expressed genes is poor. Nonetheless, characterizing changes in gene expression for known genes is a powerful tool that can be used to understand the underlying mechanisms controlling fertility in farm animals. Previously unknown control points are revealed when gene expression patterns are examined globally. These control points can act as avenues to ameliorate mechanisms that lead to infertility.

Key Words: Genomics, Ovary, Fertility

16 What has functional genomics taught us about Johne's disease in cattle? P. Coussens*[1], K. Skovgaard[2], and P. Heegaard[2], [1]*Michigan State University*, *East Lansing*, [2]*Danish Institute of Food and Veterinary Research*, *Copenhagen, Denmark*.

Infection of cattle with Mycobacterium avium supspecies paratuberculosis (MAP) leads to a chronic granulomatous enteritis commonly known as Johnes disease. Once established, infections with MAP typically exist in a subclinical state for several years and are difficult to detect during much of this period. We have used functional genomics to understand more about how the host immune system reacts to MAP, and how this response changes over time. During the course of these studies, our cDNA microarray analyses suggested that inherent gene expression profiles in peripheral blood mononuclear cells (PBMCs) from MAP infected cattle may be different those in PBMCs from uninfected controls, providing a possible gene expression signature indicative of Johnes disease. In collaboration with scientists from the Danish Institute of Food and Veterinary Research we have conducted studies aimed at testing this hypothesis. Our novel results indicate that expression profiles of at least 42 genes are inherently different in freshly isolated PBMCs from MAP infected cattle when compared to similar cells from uninfected controls. Major classes of genes differentially expressed include those encoding cytokines and their receptors (IL-5, TGFb, and GM-CSF), matrix metalloproteinases (MMPs) and their inhibitors (TIMPs) (TIMP1, TIMP2, MMP14, and MMP15), and proteins regulating apoptosis (Bad, CIDE-A, and MCL1). Gene expression differences in each of these categories were verified and expanded upon by Q-RT-PCR. Our results not only provide new information on immune responses to MAP, but confirm that infection with MAP may be diagnosed using the tools of functional genomics. With collaborators from University College Dublin, we have further applied these same findings to infections with M. bovis (bovine TB) and to infections with Brucella abortus.

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Key Words: Functional Genomics, Johnes Disease, Gene Expression

17 Immunogenomics and the transition dairy cow: physiological insights and future possibilities for improving animal health. J. L. Burton*[1], S. A. Madsen[1], L-C. Chang[1], P. S. D. Weber[1], P. M. Coussens[1], G. J. M. Rosa[1], L. K. Matukumalli[2], T. S. Sonstegard[2], and T. P. Smith[3], [1]*Michigan State University*, *East Lansing*, [2]*USDA, ARS, BARC, Bovine Functional Genomics Laboratory*, *Beltsville, MD*, [3]*USDA, ARS, MARC*, *Clay Center, NE*.

Neutrophils are sensitive biomarkers of physiological status and are the main line of immune defense against bacteria that cause mastitis in dairy cows. Neutrophils become defective in some anti-bacterial activities as parturition approaches, but little is known about the gene products responsible for these defects. This reduces our ability to make improvements in postpartum cow health. Development of functional genomics tools for cattle provided the opportunity to rapidly investigate how the expression of thousands of genes in bovine neutrophils is affected by parturition. In our recent studies we used BOTL cDNA microarrays (see http://www.nbfgc.msu.edu) to examine gene expression in neutrophils collected from periparturient cows. Of 302 genes we identified to be induced or repressed around parturition, we revealed 3 key functional categories that were responsive to two blood factors of parturition, glucocorticoid and G-CSF. Phenotyping of the cells subjected directly to these factors painted a picture of neutrophil physiology not previously recognized, showing extended life span and induction of tissue degrading and phagocytic activities. Tissue degrading and phagocytic activities of neutrophils are critical for successful parturition and uterine involution in humans, and our results extend this by suggesting that parturient steroids and cytokines reprogram neutrophils so they can take part in parturition, perhaps at the expense of mammary defense. Because we now know the actual molecules involved in these important neutrophil phenotypic changes, our next steps are to: (1) identify which molecules are suitable drug targets for mastitis prevention; (2) test hormone/cytokine regimes as strategies for timed parturition; and (3) identify useful gene polymorphisms to aid genetic selection decisions for improved calving behavior and mammary health.

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Key Words: Functional Genomics, Immunity, Parturition