behavior and erratic feed intake by cattle. This perception is based on the belief that variability in intake of high grain diets compromises the maintenance of ruminal pH at levels high enough for optimal fibre digestion and rumen function (i.e., >5.6 to 5.8). Periodic abundance in starch availability allows amylolytic bacteria (e.g., *Ruminobacter amylophilus*, *Streptococcus bovis*, *Lactobacillus* spp.) to proliferate and produce excessive quantities of fermentation acids. It has been proposed that heightened VFA production stimulates satiety receptors in cattle, which in turn results in the commonly observed "off-feed" or low intake syndrome. Despite this well accepted relationship, comparatively few studies have actually demonstrated that variability in ad libitum feed intake impairs growth performance of cattle. Ruminal pH profiles differ substantially among cattle, even among those with identical diet composition, feed quantity and delivery schedules. It is apparent, therefore, that factors other than meal size and feeding regime determine an animal's susceptibility to subclinical acidosis and ultimately, its growth performance. Feedlot management practices developed to regulate feeding behavior and reduce variations in feed intake by penned cattle include programmed feeding, multiple feed deliveries per day, and consistent timing of feed delivery. However, the efficacy of these practices is assessed largely on the basis of intake per pen, with little or no appreciation of the variation in feed intake among individuals. Further characterization of this variability in feeding behaviors among penmates could provide the foundation for effective refinement of present feeding practices.

Key Words: Acidosis, Bunk Management, Rumen

448 Controlling variation in feed intake through bunk management. R. H. Pritchard*[1], [1]*South Dakota State University*.

Controlling variation of daily feed intake stems from the obvious concern that a significant aberration in grain intake can lead to clinical acidosis or death. Less dramatic aberrations also occur when cattle have unrestricted access to feed. A cyclic pattern of higher and lower daily DMI can cause gain efficiency to be less than that predicted from the mean DMI since ADG responses to changes in DMI are not linear. If bunk management (BM) is a means of ameliorating either of these events, it is presumed that management ascribed to the pen is affecting variability in daily DMI by individuals within the pen. Two likely mechanisms are limiting availability of feed to prevent overconsumption events, or affecting animal behavior so that daily intake is more consistent. BM approaches that have been evaluated for their impact on production rates and in some instances on day to day variability in DMI include: limiting the quantity of feed available or the amount of time feed is available each day, the timing and frequency of feed deliveries, linear bunk space allocation, and mixed diet or segregated ingredient feeding. When BM approaches do alter responses, it may be that the approach has a direct biological and/or behavioral impact on the animal, or that the approach itself involves less variation, which is consequently favorable to the animal (or the data). The causes of variable results in BM research can be ambiguous. Management and feeding systems are difficult to standardize which can cause the definitions of controls, the characterizations of treatments, and the context of responses to be inconsistent. A rudimentary limitation is that in systems where individual daily DMI is known, competition for access to feed is usually not comparable to typical pen feeding. There is evidence of favorable responses to some BM approaches that could be used commercially. Impact on production efficiency in these studies is of significant biological and economic importance. These mechanisms must be more fully characterized to allow broad application.

Key Words: cattle, management, feedlot

Breeding and Genetics
Applications of Functional Genomics in Animal Breeding and Genetics

449 Novel approaches for complex trait analysis. B Bowen*, *Lynx Therapeutics, Inc.*

Complex traits include the majority of human diseases and commercially important targets of selection in agriculture, such as yield or hybrid vigor. Unlike monogenic traits, they are controlled or influenced by the interplay of multiple genes and environmental factors. Although it is not clear to what extent complex traits are controlled by alleles that qualitatively affect the function of proteins or quantitatively affect gene expression, both types of genetic variation are likely to be important. Lynx's Massively Parallel Signature Sequencing (MPSSTM) technology is a gene expression profiling system that can help understand the genetic architecture of complex traits at the molecular level by addressing two fundamental questions in quantitative genetics:
1. How much variation in gene expression between individuals is controlled by cis-acting alleles vs. segregation of trans-acting factors? 2. How many genes that differ in expression between parents and offspring behave non-additively?
I will demonstrate how an understanding of these two questions can be exploited to help identify candidate genes for quantitative trait loci controlling a complex trait in a model plant species on the one hand and candidate genes for heterosis in a poorly characterized animal species on the other.

Key Words: Gene Expression, Quantitative Trait Loci, Genetic Variation

450 Integrating molecular marker information into national beef cattle evaluation. R. L. Quaas*, *Cornell University, Ithaca, New York.*

Information from molecular markers has the potential to increase the accuracy of genetic evaluation, especially for traits for which phenotypes are difficult and(or) expensive to obtain. Several problems remain for this potential to be realized. The purpose of this paper is to discuss some of these and offer some suggestions. Among these problems is the likelihood that the number of animals in the pedigree will exceed the number with phenotypes which will greatly exceed those with genotypes. Suggestions as to how to combine many phenotypic data with limited marker data will be discussed in more detail. Emphasis is on approximations practicable for routine national beef cattle evaluation.

Key Words: Genetic Markers, Genetic Evaluation, National Beef Cattle Evaluation

451 Using gene expression profiling to study disease resistance in the chicken: honing in on candidate genes. J. Burnside*[1], R. Morgan[1], and H. Cheng[2], [1]*Delaware Biotechnology Institute, University of Delaware,* [2]*USDA/ARS, Avian Disease and Oncology Laboratory.*

Poultry disease is a major threat to chickens raised in a production environment, where birds are exposed to a variety of pathogens. Of particular economic importance is Marek's Disease (MD), which is caused by the MD virus (MDV), an oncogenic herpesvirus of chickens that latently infects T lymphocytes and induces T-cell lymphomas. A study of the gene regulatory pathways that control development of the immune system as well as an understanding of the host response to MDV will improve our understanding and our control of this disease. Using a functional genomics approach, we have sequenced over 6,000 ESTs from chicken lymphoid libraries and used a selected subset of these ESTs for the preparation of DNA arrays for gene expression profiling studies. These arrays have been used to assess developmental changes in gene expression in the immune system. Expression of cell surface markers (MHC class I, MHC class II invariant chain, CD8, CD18, and beta-2 microglobulin), and genes involved in the innate immune response (NK lysin) increased with age, and these patterns were consistent with an increase in the immune-responsiveness of young chicks. We also evaluated changes in viral and cellular gene expression that accompany infection of chicken embryo fibroblasts (CEF) with MDV. MIP, quiescence specific protein and MHC class I genes were among the host genes that were induced by infection with MDV. In parallel studies, these arrays have been used to identify genes that confer genetic resistance to MD, by comparing expression profiles in genetically resistant and susceptible birds. Differential expression of candidate genes has been detected, and at least one maps near a QTL conferring resistance to MD. Using

microarray technology to study global changes in gene expression of the immune system will provide considerable insight for improving strategies for MD prevention, and understanding the pathogenesis of this disease.

Key Words: Chickens, DNA array, Disease resistance

452 Power calculation in microarray experiments using Bayesian mixture models. R. Rekaya*[1], [1]*Dept. of Animal and Dairy Science, University of Georgia*.

Comparison of gene expression patterns of tissues or cells under several conditions provides important information to answer several biological questions. Using the simple fold changes in expression based on the ratio of intensities in the red and green channels, as was done in the earlier days of this technology, is unreliable and inefficient. The statistical power or the probability of detecting a given magnitude of expression change in microarray experiments is of crucial interest as a result of the noisy data used. The calculation of power depends on the specified magnitude of change and the false positive rate. Data used in this study consisted of the expression levels of 8,150 cDNA of individuals with and without cutaneous malignant melanoma. Eight arrays under two experimental conditions (4 melanoma and 4 controls) were used. A global normalization was applied to the raw data. A mixture model with 2 and 3 components was implemented and compared with a parametric Gaussian model using Bayesian information criteria (BIC). Both the Gaussian model and the mixture model with two components were superior to the model with three components. Although there was no strong evidence against the parametric Gaussian model, there was around 5% change in the number of genes differentially expressed using both models. Using a Gaussian model and a false positive rate of 0.1%, the power was 0.16, 0.48 and 0.78 for 2, 3 and 4 fold change in expression, respectively. With the same setting, but using a mixture model with two components, the power was 0.15, 0.50 and 0.81 for 2, 3 and 4 fold change in expression, respectively.

Key Words: Gene, Expression, Mixture

453 Detection of quantitative trait loci for mastitis resistance in Canadian Holsteins. J. Moro-Mendez*, J.F. Hayes, and D. Zadworny, *McGill University, Department of Animal Science (Macdonald Campus), Montreal, Quebec, Canada*..

A granddaughter design, consisting of 20 grandsires and 1747 sons, was used to test the hypothesis of associations between genetic markers and mastitis resistance in Canadian Holsteins. The grandsires and sons were genotyped for 10 genetic markers (6 in the growth hormone (GH) region, 2 in the GH receptor region, and 2 in the Ornithine Decarboxilase region). The raw phenotypic information consisted of 1,561,631 lactation records from 969,747 Holstein cows enrolled in the Quebec Dairy Analysis Service (PATLQ). The final data set after editing consisted of 67,908 first lactation records from daughters of 612 sons (19 grandsire families). The response variable was the frequency of culling due to mastitis in first lactation daughters of each son. The GENMOD procedure of SAS was used to fit a model which included year of birth of the son, grandsire, and marker nested within grandsire. The number of informative grandsire families for individual markers ranged from 3 to 17, and the number of informative sons by grandsire ranged from 3 to 77. No effect of marker within grandsire was found ($P<0.05$). These results suggest that in the data under study there is no association between the above genetic markers and quantitative trait loci for the frequency of culling due to mastitis in first lactation. A larger marker data set is being constructed for further studies of associations of markers with mastitis.

Key Words: Genetic Markers, Mastitis Resistance, Holstein

454 Application of daughter and granddaughter designs in a study of microsatellite markers in a large A.I. breeding company. E.B. Burnside*[1,2], Y. Pan[1,2], G.B. Jansen[3], Y. Plante[4], N. Caron[1], and D. Petitclerc[5], [1]*The Semex Alliance, Saint-Hyacinthe, Quebec, Canada,* [2]*L#Alliance Boviteq, Saint-Hyacinthe, Quebec, Canada,* [3]*University of Guelph, Ontario, Canada,* [4]*The Saskatchewan Research Council, Saskatoon, Saskatchewan, Canada,* [5]*Agriculture and Agri-Food Canada, Lennoxville, Quebec, Canada*.

To apply marker assisted-selection (MAS) in a large A.I. breeding company, a study of a Holstein sire's female and male progeny was undertaken to confirm microsatellite markers closely linked to economically important QTLs. Two designs, daughter and granddaughter, were carried out for corroboration of 24 informative markers, first via genotyping approximately 400 daughters of the sire for each informative marker, and subsequently by genotyping 88 A.I. proven sons for the same markers. The daughter design was based on heifers selected for extremely high and low estimated breeding values (EBV) adjusted by regression of daughters' (EBV) on dams' EBV for protein yield and mammary system. When the selected daughters were genotyped, 68.3% and 69.2% of them were informative for protein yield and mammary system, respectively. A logistic regression analysis yielded four of the 24 microsatellite markers that significantly affected protein yield ($P< 0.05$ to 0.008), while one marker approached significance for mammary system ($P = 0.07$). These markers explained from 7.1% to 15.6% of the standard deviation of adjusted EBVs for protein yield. Canadian Test Day Record EBVs for production, conformation, and health traits were also used to analyze the 88 proven sons for the same 24 informative markers. Results from the two designs were compared to throw light on efficacy of the daughter design to provide preliminary information for MAS in A.I. progeny testing schemes.

Key Words: Microsatellite marker, Daughter design, Granddaughter design

455 Development of a cattle population for mapping economic trait loci (ETL) affecting parasite resistance. Tad S Sonstegard*[1], Louis C Gasbarre[2], Curtis P Van Tassell[1], and Terazinha Padilha[2], [1]*Gene Evaluation & Mapping Laboratory,* [2]*Immunology & Disease Resistance Laboratory*.

The natural genetic variability of the bovine immune system provides an alternative means to control gastro-intestinal (GI) parasite infection without anthelmintics. However, the paradigm of traditional selection has not been applied to parasite resistance due to the difficulty and expense of gathering accurate phenotypes. To validate the potential effectiveness of selection and create a population amenable for mapping, divergent selection was initiated using founder animals from the University of Maryland Wye Angus herd previously observed to be segregating for GI nematode resistance and susceptibility to *Ostertagia ostertagi*. After nine years of selection, five generations of half-sib progeny ($N>350$) with phenotypic records from controlled infections have been produced. These progeny fall into three distinct phenotypic classes based on response as measured by eggs per gram (EPG) of fecal matter: innately immune, acquired immune, and immunologically non-responsive. The respective ratio of these calves in the first generation was approximately 1:2:1. Selection based on expected progeny difference (EPD) values for EPG has effectively increased the fraction of innately immune and non-responsive calves. In addition, the range of EPD values has been reduced to half the mean EPG value for calves tested to date, further supporting the role of host genetics in parasite transmission. Currently, this phenotypic data and genotypic data generated using microsatellite markers ($N=199$) is being analyzed using a multiple locus allelic peeling algorithm (GenoProb) designed to identify the genomic locations of ETL segregating in looped, complex pedigrees. Analysis of the individual pedigrees revealed that $> 90\%$ of the test progeny were paternally descended from a single historic sire, and marker genotypes from 68 sires spanning 8 generations in this paternal pedigree have been added to the ETL analysis. Preliminary analysis of marker information ($N=103$) revealed an expected heterozygosity index of 50% and polymorphic information content of 45 with an average of four alleles per marker. Although power of ETL detection in this population is limited by half-sib family size, genetic analysis of the historic pedigree will provide additional statistical power for refining map position of potential ETL.

Key Words: Economic Trait Loci, Parasite resistance, Mapping

456 Genetic variation among sheep breeds at the insulin-like growth factor-1 receptor locus. C.J. Otieno and A. Farid, *Nova Scotia Agricultural College*.

Heterologous polymerase chain reaction (PCR) primers based on the mouse insulin-like growth factor-1 receptor (IGF1-R) gene sequence amplified a 601 bp fragment in sheep consisting of exon 21 and the 3' UTR. Sequencing of the PCR products revealed a polymorphic GC repeat 29 bp 3' to the stop codon and a mononucleotide deletion. A new pair of primers was designed to amplify the polymorphic region, and genotype of animals was determined using an ABI 377 DNA sequencer. The 216 bp fragment contained a (GC)5, and the combination of an additional GC and the deletion generated 215, 217 and 218 bp fragments. Genotypes of 182 sheep from 13 breeds with diverse developmental histories and production performance were determined at this locus. The breeds were Romanov (RO), Suffolk (SU), Finnsheep (FI), Scottish Blackface (SB), Cheviot (CH), Icelandic (IC), Border Leicester (BL), Black Welsh Mountain (BW), Hexham Leicester (HL), Karakul (KA), Red Masai (RM, Kenya), Newala (NE, Tanzania) and Djallonke (WD, Nigeria). Except RO, all the breeds were polymorphic and allele frequencies were different ($P<0.01$) among the breeds. FI, NE, WD and MAS had lower frequency (0.41 to 0.50) of allele 216 and high frequency (0.31 to 0.56) of allele 217, while other breeds had high frequency of allele 216 (0.65 to 1.00) and low frequency of allele 217 (0.0 to 0.29). The allele 218 was detected only in FI, KA, MAS and WD, and allele 215 was not detected in BW, FI, IC, RO and SU. There was no clear relationship between allele frequencies and the evolutionary histories of the breeds. Most of the breeds that have been intensely selected for production traits (SU, RO) had only 216 and 217 alleles, while all four alleles were segregating in the less intensely-selected breeds (KA, MAS, WD). The data suggest that the IGF1-R gene may be linked with other genes that contributed to the differences in production performance among the breeds.

Key Words: IGF1-R, Sheep breeds, Polymorphism

457 Genetic diversity of Chinese indigenous pig breed resources by microsatellites and near-complete mitochondrial genome. K Li*, *Huazhong Agricultural University, Wuhan 430070, China*.

Over 100 indigenous pig breeds currently exist in China, comprising almost one-third of the pig breeds in the world. Some Chinese local breeds are known internationally, particularly for their high prolificacy and meat quality. However, both the number of Chinese local breeds and the population sizes of the remaining breeds have decreased dranatically in recent years, because their performance, particularly in growth rate, food conversion efficiency and lean meat percentage, is much lower than that of commercial breeds of European and Amercian origin. Special efforts are therefore required to conserve the genetic resources of these Chinese local breeds. A total of 1,581 Chinese indigenous pigs, which belong to 30 Chinese local breeds have been genotyped using 27 microsatellite markers recommended by FAO and ISAG. Twenty breeds, one sample from each breed, have been studied using the nearly complete mitochondrial genome. The genetic variation between breeds and within breed variation have beed caculated. NJ dendrogram based on Nei standard genetic distances between the breeds studied has been obtained. The systematic evaluation of genetic diversity of these important breeds will enable us to better understand the relative distinctiveness of these animal genetic resources and to assist in developing a rational plan for conservation.

Key Words: Genetic diversity, Chinese indigenous pig breeds, Microsatellites

458 A novel and highly effective method to generate transgenic cows and goats: linker-based sperm-mediated gene transfer (LB-SMGT). J. Qian*[1], K. Chang[2,3], C. Lai[2], C. Chen[2], T. Keng[2], C. Huang[2], F. Wu[3], H. Huang[1], and K. Wang, [1]*BioAgri Corp., City of Industry, CA, USA,* [2]*BioAgri Corp.-Taiwan Branch, Taipei, Taiwan,* [3]*Dept. of Chemistry, Soochow University, Taipei, Taiwan*.

Genetic modification of domestic animal traits can be used to improve productivity and quality or to produce bioreactors for modern medicine. DNA microinjection, the current method to produce transgenic livestock, is time consuming and requires extensive training and special equipment. More importantly, except in mice, microinjection has reported only limited success in larger or higher species. Sperm-mediated gene transfer has been recognized as a potentially powerful alternative method, but the original results have been difficult to duplicate. We have developed a linker (mAb C) to bind with sperm and DNA. Using flow cytometry, it has shown cross-reactivity with sperm cells from all tested species including pig, mouse, chicken, cow, goat, sheep, and human. We have successfully applied a novel linker-based sperm-mediated gene transfer method (LB-SMGT) in mice, pigs, and chickens at a high germ-line transmission rate (30-40%). We report here the use of LB-SMGT to successfully generate transgenic cows and goats. Sperm from bulls or goats were treated first with mAb C and then combined with a linearized DNA fragment containing the human interferon β gene or lactoferrin. The sperm-linker-DNA complexes were used in standard artificial inseminations. The transgenic gene was detected in 4 of 5 calves (F0 generation) and in 4 of 9 kids (F0 generation) by PCR and verified by a ^{32}P-labeled 3rd oligo. The expression of human lactoferrin in sera was also detected in 1 of 10 kids (F0 generation) by ELISA. We expect a high germ-line transmission rate, based on our results in transgenic pigs, mice, and chickens. Our data demonstrate that LB-SMGT can efficiently generate transgenic goats and cows.

Key Words: Transgenic, Cow, Goat

459 Generation of transgenic pigs at a high efficiency by linker based sperm-mediated gene transfer. K. Chang[2,3], J. Qian[1], C. Chen[2], C. Lai[2], I. Ho[2], M. Wu[4], and K. Wang*, [1]*BioAgri Corp. City of Industry, CA, USA,* [2]*BioAgri Corp-Taiwan Branch, Taipei, Taiwan,* [3]*Dept. of Chemistry, Soochow University, Taipei, Taiwan,* [4]*Dept. of Physiology, Taiwan Livestock Research Center, Tainan, Taiwan*.

Sperm-mediated gene transfer (SMGT) has been recognized as a potentially powerful method to make transgenic animals for many years. The current method of gene transfer, microinjection, used widely in transgenic mouse production, has had only limited success in producing transgenic animals from larger or higher species. Last year, we reported a linker based sperm-mediated gene transfer method (LB-SMGT) that greatly improves the production efficiency of large transgenic animals. The linker protein, a monoclonal antibody (mAb C), is reactive to a surface antigen on sperm of all tested species including pig, mouse, chicken, cow, goat, sheep, and human. Sperm from pigs were treated first with mAb C and then combined with a linearized DNA fragment (pSEAP-2 control from Clontech Laboratories Inc.). After surgical oviduct fertilization of the egg, the DNA is shown to successfully integrate into the chromosome genome of viable pig offspring with germ-line transfer to the F1 generation at a highly efficient rate, 37.5%, by Southern blot analysis. Expression of the transgene was detected in 60% of transgenic pigs (F0 generation). We report here that the integration of the transgene is further demonstrated by FISH. The transgenic pigs have also been bred into the F2 generation to demonstrate that the transgene is stably transmitted. Standard artificial insemination can also be used with LB-SMGT to generate transgenic pigs (F0 generation) at a similar efficiency as surgical oviduct fertilization. These results demonstrate that transgenic pigs can be generated with a very simple protocol at a significantly improved efficiency by sperm-mediated gene transfer using the linker protein, mAb C.

Key Words: Transgenic, Pigs, Linker based sperm-mediated gene transfer(LB-SMGT)