

Breeding and Genetics: Applications of Genomic Analysis

403 Validation of multiple marker DNA profiles for carcass merit across multiple populations of beef cattle. J. D. Nkrumah* and B. W. Woodward, *Merial Limited, Duluth, GA.*

Genomic information can be employed in the management and selection of beef cattle to increase profitability and genetic progress. Advances in livestock genomics have resulted in the detection of numerous polymorphisms that putatively show associations with a range of economically relevant traits in beef cattle. The goal of DNA marker validation work is to re-evaluate and potentially confirm the proposed effects of genetic markers reported by the research community, usually in an experimental population, by utilizing information from commercial herds that are unrelated to the original herd(s) in which the initial discovery was made. Genetic markers discovered to date generally have small effects, which may not be economically relevant unless used in combination. Most reported associations are also based on markers that do not cause the phenotypic variation but are linked to, and therefore serve as surrogates for yet to be detected causal mutations. The significance and the sign of marker effect estimates, or which genotype combination is favorable may vary from population to population. To ensure broad applicability across the industry, DNA marker effects need to be tested across multiple populations and evaluated for the value in profile. Not all markers will provide statistically significant associations across all populations evaluated, but a profile could continue to remain instructive for determining differences among animals in as many herds and breeds as possible. As an example, we have created DNA profiles using a set of markers for beef carcass marbling score (effect = 96.0; $P = 10^{-12}$) and percent choice (effect = 43%; $P = 10^{-06}$), as well as multiple marker panels for carcass rib eye area (effect = 13.0 cm²; $P = 10^{-20}$), yield grade (effect = 1.20; $P = 10^{-27}$), and carcass backfat thickness (5.8 mm; $P = 10^{-18}$) based on assessments in multiple commercial populations with more than 6,000 steers and heifers. We have subsequently confirmed these profile associations using EPDs for similar traits and genotypes from a repository of about 2,000 beef bulls representing the major beef breeds used in North America.

Key Words: Beef Cattle, Carcass Merit, SNP Profile Validation

404 Genetic prediction of beef tenderness using a multi-marker SNP panel. S. P Miller*¹, M. J. Kelly¹, and D. J. Nkrumah², ¹*University of Guelph, Guelph, ON, Canada,* ²*Merial Limited, Duluth, GA.*

Beef tenderness is the most important quality attribute contributing to the consumer acceptance of beef. However improvement of beef tenderness has not been included in traditional beef breeding programs due to cost and difficulty of measuring this trait. The standard measurement used to assess tenderness of beef is the shear force, which is the force required to shear a standardized cooked meat sample. Recently commercial DNA tests have been developed that explain some of the variation in shear force. We have used the Merial/Igenity large SNP panel to screen for associations between SNP and beef tenderness in a multi-breed beef population that were assessed for shear force (n=648). This population consisted of progeny of mainly crossbred dams mated to terminal sires. The predominant breeds were Angus, Simmental, Limousin, Charolais

and Piedmontese. The effect of each marker was fit individually in a mixed model that included breed proportion, contemporary group and a polygenic effect. Markers that were significant in the single marker regressions were used to develop a multiple marker panel. Each of the markers that remained in the panel was explaining a significant proportion of the variation in shearforce ($P < 0.05$) and the marker effects ranged from 0.14kg to 0.49kg. The multi-marker panel explained 12% of the phenotypic variance. Given that the heritability of tenderness from this dataset is approximately 20% the current panel explains a large proportion of the genetic variance within this population. Selecting animals based on this panel will shift the mean tenderness from 4.92kg to 4.59kg which is slightly lower to that achieved selecting the best bulls based on their across breed expected progeny difference (4.47kg). These results indicate the growing power of SNP panels to explain significant genetic differences for beef tenderness and their practical application in the beef industries efforts to improve consumer demand.

Key Words: Beef, Tenderness, Genomics

405 Multiple marker DNA profiles for production, fertility, and functional traits in Holstein cattle. J. D. Nkrumah and B. W. Woodward*, *Merial Limited, Duluth, GA.*

Genetic marker-assisted selection is expected to significantly accelerate the rate of genetic progress through increased accuracy of selection, reduction of generation interval, and increasing selection differentials. A number of polymorphisms with moderate to large effects on economically relevant dairy traits have been reported, including the K232A polymorphism in the DGAT1 gene, the F279Y polymorphism in the growth hormone receptor (BGHR) gene, and the Y581S polymorphism in the ATP-binding cassette sub-family G2 (ABCG2) gene. Other polymorphisms have been reported to show small but economically significant associations on important traits in beef and dairy cattle, but most of these have not received further consideration in terms of validation and application in marker-assisted selection. In the present study, we have assembled a repository of over 2,000 dairy AI sires with high reliabilities for production, functional, and conformation traits, and attempted the validation of the effects of several markers on these traits in Holstein cattle. Current multiple marker association analyses using daughter yield deviations for milk, fat, and protein explain differences of about 700 kg ($P < 10^{-11}$), 30 kg ($P < 10^{-19}$), and 17 kg ($P < 10^{-12}$), respectively, among animals with extreme genotype combinations. We have also developed multiple marker panels using daughter deviations that explain up to 5.0 mo differences in dairy productive life ($P < 10^{-05}$), 2.5 percentage points in daughter pregnancy rates ($P < 10^{-04}$), and 1.8 genetic standard deviations in dairy form ($P < 10^{-15}$). These results show that significant increases in the predicted merit for dairy cattle can be obtained by evaluating models that allow the simultaneous computation of the effects of markers of small or moderate to large effects that are each independently associated with specific traits of economic importance.

Key Words: Dairy Cattle, Production and Functional Traits, SNPs Validation

406 Application of a Bayesian approach to identify candidate markers for marker assisted selection in pigs. M. A. Cleveland* and N. Deeb, *Genus plc, Hendersonville, TN.*

Genome-wide approaches to estimate genetic effects have proliferated due to increased availability and affordability of markers. These methods assume marker density is high and animals can be genotyped for all markers, which may not be feasible. This study investigated the ability of a Bayesian approach that fits all marker effects simultaneously to correctly identify markers in linkage disequilibrium (LD) with quantitative trait loci (QTL), at varying marker densities. A single chromosome of 200 cM containing five QTL was simulated, where effects were 0.2, 0.4, 0.6, 0.8 and 1.0 phenotypic standard deviations. Single nucleotide polymorphisms (SNPs) were assigned to the chromosome, based on gene drops from a small founder population, in five simulations where average SNP spacing was targeted at 0.1, 0.5, 1.0, 2.0 and 10.0 cM, respectively. Phenotypes were simulated for 2,600 animals selected from several generations of a closed population of pigs. The data were analyzed using single marker regression and a Bayesian multiple marker approach. The single marker regressions yielded many significant effects. The results from the Bayesian analysis showed clear signals at markers adjacent to the QTL, where most other markers had effect estimates at or near zero. In some cases there were multiple peaks near QTL where the effect was distributed between flanking markers. The decrease in marker density did not reduce the ability to identify markers adjacent to QTL, even at large distances where LD would be reduced. The Bayesian approach was also applied to a commercial dataset of 1,066 pigs with genotypes for 180 targeted SNPs across the genome. The analysis identified six markers with non-zero effects on a mortality trait. Results from these analyses indicated the Bayesian approach was suitable for identifying markers of moderate to large size for inclusion in marker-assisted genetic evaluation systems. This strategy can be used to identify marker associations when density is not optimal, in situations where genome-wide evaluation is not yet feasible.

Key Words: Pigs, Genome-Wide Association, Bayesian Analysis

407 Genomic selection of purebreds using data from admixed populations. A. Toosi*¹, R. Fernando¹, J. C. M. Dekkers¹, and R. L. Quaas², ¹Iowa State University, Ames, ²Cornell University, Ithaca, NY.

Genomic selection involves using marker genotype and phenotype data in a training population to estimate effects of all markers. These estimates are then used to predict the breeding value (BV) of selection candidates given their marker genotypes. In livestock, genomic selection has been investigated by computer simulation of purebred populations. Traits of interest are, however, often measured in crossbreds with uncertain breed composition. If such crossbreds are used as the training population without proper accounting of breed composition, estimates of marker effects may be biased due to population admixture. On the other hand, if the available markers are in high linkage disequilibrium with the trait loci (QTL), it may not be necessary to explicitly account for breed composition. To investigate this idea, a single chromosome of size 1.5 Morgans was simulated with 5000 evenly dispersed loci, of which 250 loci were assigned as QTL. After 1000 generations of random mating in a base population of effective size 500, two sub populations of effective

size 100 were isolated and random mating was continued for another 50 generations to create two breeds (A and B). These breeds were used to generate an F1, F2, and an admixed population. These populations and breed A were used as the training data set, with a total of 1000 individuals with phenotype for a trait controlled by 100 segregating QTL and heritability of 0.30. A Bayesian method (Bayes-B) was used to estimate the effects of 2000 segregating markers. Using these estimates and genotypes of selection candidates, the BVs of breed A animals eight generations away from the training population were estimated. The accuracy of the prediction was quantified by the correlation between the marker based predicted BV and the true BV. The accuracy was highest (0.85) when breed A was used as the training population. When the crossbreds were used as the training population, the accuracy ranged from 0.75 to 0.79. This demonstrates that, under the simulated conditions, purebreds can be accurately selected for crossbred performance using high-density marker data, without pedigree or breed information.

Key Words: Admixed Populations, Genomic Selection

408 A marker-assisted assessment of genotype by environment interaction: SNP-mortality association in broilers in two hygiene environments. N. Long¹, D. Gianola¹, G. J. M. Rosa*¹, K. A. Weigel¹, and S. Avendaño², ¹University of Wisconsin, Madison, ²Aviagen Ltd., Newbridge, UK.

An interplay between genetic and environmental factors, genotype by environment interaction ($G \times E$), determines phenotypes of complex traits, and implies that some genetic effects may be relevant only in certain environments. $G \times E$ was investigated here by detecting hygiene environment-specific SNP subsets associated with broiler chicken mortality at both early and late ages, followed by an examination of consistency between SNP subsets selected from different hygiene (low and high) environments. The trait was mean progeny mortality rate in 253 sire families, calculated after adjusting records for non-genetic and non-hygiene related environmental effects affecting mortality at the individual bird level. Over 5,000 whole genome SNPs were narrowed down via a machine learning (filter-wrapper) feature selection procedure applied to mortality rates in each of the low and high hygiene environments. For both early and late mortality, it was found that the SNP subsets selected were not consistent across hygiene environments, in terms of either across-environment predictive ability or extent of linkage disequilibrium (LD) between the subsets. Reduction in mortality predictive ability due to $G \times E$ was assessed by the ratio of two PRESS (predicted residual sum of squares) statistics, one associated with using SNPs selected from the same hygiene environment, and the other one associated with the SNP subset from a different environment. The reduction was 30% and 20% for early and late mortality, respectively. In addition, an extremely low level or absence of LD between SNP subsets selected under low and high hygiene also indicated $G \times E$. These findings suggest that there may not be a universally best SNP subset for predicting mortality, and that interactions between genomes and environmental factors need to be considered when attempting to associate genetic variants with complex traits.

Key Words: Genotype by Environment Interaction, SNP-Mortality Association, Hygiene Environments

409 Linkage disequilibrium and persistence of phase in Holstein Friesian, Jersey and Angus cattle. A. P. W. De Roos^{*1}, B. J. Hayes², R. J. Spelman³, and M. E. Goddard^{2,4}, ¹CRV, Arnhem, The Netherlands, ²Animal Genetics and Genomics, Primary Industries Research Victoria, Attwood, Australia, ³Livestock Improvement Corporation, Hamilton, New Zealand, ⁴University of Melbourne, Melbourne, Australia.

Genomic selection across multiple populations is complicated because linkage disequilibrium (LD) between markers and QTL may differ across populations. The objectives of this study were to compare the extent of LD and the persistence of LD phase across multiple cattle populations. LD measures r and r^2 were calculated for syntenic marker pairs using genome-wide single nucleotide polymorphisms (SNP) that were genotyped in Dutch and Australian Holstein Friesian (HF) bulls, Australian Angus cattle, and New Zealand Friesian and Jersey cows. Average r^2 was around 0.35, 0.25, 0.22, 0.14, and 0.06 at marker distance 10, 20, 40, 100 and 1000 kb, respectively, which indicates that genome-wide association studies or genomic selection within cattle breeds would require ~50,000 SNP. The correlation of r values between populations for the same marker pairs was close to 1 for pairs of very close markers (<10 kb) and decreased with increasing marker distance and the extent of divergence between the populations. The correlation of r values between Dutch and Australian HF, was still above 0.80 for marker distances of more than 1 Mb. Between Australian HF and New Zealand Friesian, or between New Zealand Friesian and New Zealand Jersey this correlation dropped below 0.80 for marker distances above ~50 kb, whereas between Australian Angus and New Zealand Jersey, the correlation dropped below 0.80 when the markers were more than 5 kb apart. To find markers in that are in LD with QTL across diverged breeds, such as HF, Jersey, and Angus, would require ~300,000 markers.

Key Words: Linkage Disequilibrium, Genetic Markers, Cattle

410 Estimated linkage disequilibrium in a multi-breed beef herd based on the Illumina BovineSNP50 BeadChip. M. J. Kelly^{*1}, M. Sargolzaei¹, Z. Wang², D. Kolbehdari², P. Stothard², F. Schenkel¹, S. S. Moore², and S. P. Miller¹, ¹University of Guelph, Guelph, ON, Canada, ²University of Alberta, Edmonton, AB, Canada.

Genomic breeding values may enable the beef industry to select genetically superior cattle for traits that are expensive or impossible to measure in conventional breeding programs. However, to estimate genomic breeding values with sufficient accuracy or fine mapping QTLs, a high degree of linkage disequilibrium (LD) between markers and the QTL is required. The average amount of LD between markers (SNPs) and QTLs across the bovine genome was assessed using the Illumina BovineSNP50 BeadChip within a multi-breed beef herd. A preliminary experiment comprised 374 multi-breed beef cattle (predominantly progeny of cross-bred cows mated to purebred terminal sires). Breeds represented included mostly Angus, Simmental, Limousin, Charolais and Piedmontese. Animals were genotyped for 56,947 SNPs. After exclusion of SNPs from the analysis when minor allele frequency was below 10% which included monomorphic SNPs (21%), due to a high proportion of uncalled genotypes (~0.1%), deviation from Hardy-Weinberg equilibrium (0.2%), located on chromosome X (1.6%), or unlocated (15%), 35,317 SNPs remained. The average distance between adjacent SNPs, once these edits were made, was 58 kb. Therefore, on average, the maximum distance between SNPs and QTLs should be half this (29 kb). The average r^2 based on 3428 marker pairs between markers 30 to 35 kb apart was calculated to be 0.21 (SD=0.26), this is somewhat lower

than that found in purebred populations. An approximation of the power to detect QTLs with this level of LD was examined (at $p < 0.01$). A QTL had to explain at least 8.5% of the phenotypic variance in order to be detected with a statistical power greater than 90% with a sample size of 1000. To detect smaller effects (2.5% of phenotypic variance) would require larger sample sizes (~3500) or higher levels of LD ($r^2 \sim 0.7$). Thus subsequent work will focus on genotyping a larger population and fine mapping regions of interest.

Key Words: Beef, Genomics, Linkage Disequilibrium

411 Linkage disequilibria of the SLA region loci with malignant melanoma in Sinclair swine. L. Gomez-Raya^{*1}, M. Miller¹, C. S. Ho², V. Kirchoff¹, D. M. Smith², W. M. Rauw¹, D. Thain¹, A. Rink¹, and C. W. Beattie³, ¹University of Nevada, Reno, ²University of Michigan, Ann Arbor, ³University of Illinois, Chicago.

The experimental design consisted of a boar mated to 11 sows to produce 70 offspring. A total of 20 DNA-markers within the Swine Leukocyte Antigen (SLA) region were typed (SW1856, SLAM62, SLA-1, SLA-3, SLA-2, SLAM037, SLAM055, SLAMA14, SLAMA13, SLAM046, SLAMS045, SLAMS044, SLAM043, SLAMA18, SLAM095, DRB, DQB, SLAMS092, SLAM047, SW0102). Linkage disequilibrium at each pair of loci was estimated by inferring the haplotypes contributed by the dams for all informative offspring. Linkage disequilibrium between each pair of loci was estimated using the normalized D' of Lewontin but allowing for more than two alleles. Strong linkage disequilibria were estimated for each pair of DNA-markers between SW1856 and DQB (ranging from 0.95 to 1). Testing of linkage disequilibrium within the boar family was performed while searching for 1) susceptibility to SSCM (at least one tumor during the first six weeks of life), and 2) number of tumors at birth (TB), at 6 weeks post-partum (T6), and the difference in tumor number between birth and six weeks (T6-B). Loci affecting melanoma susceptibility were not detected. However, we detected a QTL affecting T6-B in this region (P-value of 0.0028 in the permutation test). We tested for population-wide linkage disequilibrium for the number of tumors using the allele inherited from the dam. Our results showed that alleles are statistically associated with T6 and T6-B (up to 2.1 tumors at $P < 0.05$). However, the strong linkage disequilibria of loci in this region may limit finer mapping of a QTL.

Key Words: Swine, Malignant Melanoma, Swine Leukocyte Antigen

412 QTL with dominance effect affecting residual feed intake on BTA6. G. C. Márquez^{*1}, R. M. Enns¹, M. D. Grosz², and M. D. MacNeil³, ¹Colorado State University, Fort Collins, ²Monsanto Co., St. Louis, MO, ³USDA, Agricultural Research Service, Miles City, MT.

Residual feed intake (RFI) is a measure of feed efficiency and therefore an economically relevant trait. A genome-wide scan for quantitative trait loci (QTL) affecting RFI in beef cattle was conducted. Approximately equally spaced microsatellite markers ($n = 229$) spanned the 29 bovine autosomes. Two half-sib families of backcross progeny were produced by mating two F1 Line 1 Hereford (L1) \times composite gene combination (CGC) bulls to L1 and CGC cows. Progeny of the first sire were born in 1996 ($n=155$) and of the second sire were born in 1997 ($n=120$). Phenotypic data on feed intake and weight gain was collected in 1997

and 1998 for the two calf crops. Due to serial harvest for collection of carcass data, time on feed varied from 82 to 167 days. RFI was calculated as the residual after fitting the regression of daily feed intake on average daily gain, average weight, sex, and year of birth. Genotypes and phenotypes were collected from 218 animals. The backcross progenies from L1 and CGC females were analyzed separately using composite interval mapping. In the backcross to L1 cows, evidence for a QTL affecting RFI was found on BTA6 with a LOD score of 3.2 at 58 cM. Substitution of the L1 allele for the CGC allele reduced RFI by 0.9 kg/d. This QTL was absent in the backcross to CGC cows. Presence of an allele substitution effect in one backcross, but not the other, is consistent with the dominance model of inheritance. Thus, these results indicate a putative QTL with dominance effect on RFI located at approximately 58 cM on BTA6.

Key Words: Beef Cattle, Quantitative Trait Loci, Residual Feed Intake

413 Confirmation of quantitative trait loci for carcass and meat quality traits on pig chromosome 6 in a Duroc x Pietrain resource population. I. S. Choi*, R. O. Bates, N. E. Raney, D. B. Edwards, M. E. Doumit, and C. W. Ernst, *Michigan State University, East Lansing.*

We have previously reported quantitative trait loci (QTL) affecting carcass composition and pork quality on pig chromosome 6 (SSC6) in the Michigan State University Duroc x Pietrain F₂ resource population. The objective of the present study was to confirm these QTL by

incorporation of marker genotype data for an additional 452 F₂ pigs into the QTL analysis, thus improving the QTL detection power by nearly doubling the number of informative meioses. A total of 962 F₂ pigs were genotyped for the SSC6 markers S0087, SW122, SW1881 and SW322. Other SSC6 markers genotyped for the original genome scan (510 F₂ pigs) included S0099, SW2406, SW2525, S0220 and SW2419. Data were analyzed with line cross least squares regression interval mapping methods using sex and litter as fixed effects and carcass weight or harvest age as covariates. Carcass composition phenotypes included primal cut weights, skeletal characteristics, backfat thickness, muscle pH and carcass temperature. Meat quality data collected on boneless *longissimus* muscle chops included marbling, firmness, drip loss, and objective and subjective color. QTL significant at the 1% chromosome-wise level were found for first rib, tenth rib, last rib and last lumbar vertebra backfat, and for hot carcass weight, carcass length, loin muscle area, ham weight, loin weight and belly weight. QTL significant at the 5% chromosome-wise level were found for 24 h carcass temperature, Boston shoulder weight and marbling score. These results confirmed previously identified QTL and included four new QTL (carcass weight, first rib backfat, Boston shoulder weight and belly weight). In addition, F-ratios and LOD scores were increased for all traits except marbling score. However, three previously identified QTL failed to reach the 5% chromosome-wise level of significance (subjective color score, CIE a* and spareribs weight). The incorporation of additional F₂ animal genotypes into the QTL analysis helped to improve the power and precision of QTL detection and our results confirm QTL for carcass composition and pork quality on SSC6 in the MSU resource population.

Key Words: Pig, QTL, Carcass Composition