

Breeding and Genetics: Genomic Selection in Beef

314 Genomic divergence of indicine and taurine cattle identified through high-density SNP genotyping. L. R. Porto-Neto², T. S. Sonstegard*¹, G. Liu¹, D. Bickhart³, C. Gondro⁶, M. V. da Silva⁴, Y. T. Utsunomiya⁵, J. F. Garcia⁵, and C. P. Van Tassell¹, ¹USDA, ARS, Bovine Functional Genomics Laboratory, Beltsville, MD, ²University of Queensland, Gatton, Queensland, Australia, ³USDA, ARS, Animal Improvement Programs Laboratory, Beltsville, MD, ⁴Embrapa Gado da Leite, Juiz da Fora, MG, Brazil, ⁵UNESP, Aracatuba, SP, Brazil, ⁶University of New England, Armidale, NSW, Australia.

Our hypothesis is that there are genomic regions of difference between cattle breeds, and some are derived from natural selection and adaptation while others are from artificial selection to form breeds. To better detect genomic regions of difference, animals from the International Bovine HapMap were genotyped for over 750,000 SNP and compared using smoothed FST. The taurine sample was represented by 10 breeds and the contrasting zebu cohort by 3 breeds. Each cattle group had similar numbers of informative markers well distributed across the genome. Principal component analyses and unsupervised hierarchical clustering confirmed the well characterized main division between the subspecies of domestic cattle. The top 1% smoothed FST, associated to positive selection contained 48 genomic regions across 17 chromosomes. The strongest signals were on Chr7: ~50Mb and Chr14: ~25Mb; and each had very different patterns of linkage disequilibrium that potentially represent intrinsic differences between cattle types. The latter region encompassed a region of the genome affecting stature, fertility and sub-cutaneous fat. The bottom 1% of the smoothed FST values included 24 regions across 13 chromosomes, which are potentially associated to balancing selection. These regions overlapped with copy number variants, including the highly variable region at BTA23:~24Mb that harbors a large number of MHC genes. Under these regions, 318 unique Ensembl genes are annotated; many of which are linked to immune response resulting in a significant overrepresentation of immune related pathways. These regions are of particular interest to understand selective pressures to which these subspecies were exposed to and how the genetic background of these populations evolved in response to environmental challenges and human manipulation.

Key Words: SNP, cattle, selection

315 Accuracies of genomic predictions in Hereford using actual 50K, a 28K subset, or 28K imputed to 50K genotypes. M. Saatchi* and D. J. Garrick, Iowa State University, Ames.

Routine genomic predictions have been implemented in Hereford beef cattle using the Illumina BovineSNP50 BeadChip (50K). GeneSeek recently released a higher density chip known as GeneSeek Genomic Profiler HD (GGP-HD) including 77,000 SNP markers (77K) with 28,375 GGP-HD (28K) in common. The objective of this study was to compare the accuracies of genomic predictions for 10 traits in Hereford cattle using actual 50K, actual 28K, or 28K genotypes imputed to 50K. A total of 1,081 animals were genotyped with the 50K chip. Genotyped individuals were clustered into 4 groups using K-means clustering with the aim of increasing the within-group and decreasing the between-group pedigree relationships. For each clustered group, those genotypes for 28K markers common to both panels were extracted from 50K genotypes. Those genotypes were imputed to 50K genotypes using phased marker information from the other 3 groups, based on the USDA-AIPL linkage map and BEAGLE phasing software. 4-fold cross-validation was

performed using 3 groups for training (those with actual 50K or 28K genotypes) and the fourth group for validation (using either actual, actual 28K genotypes, or imputed 50K genotypes). Deregressed estimated breeding values were used as observations in a weighted analysis that estimated marker effects to derive molecular breeding values (MBV). Bivariate animal models were used for each trait to estimate the genetic correlation between trait and MBV as a measurement of the accuracy of genomic prediction. The accuracies of MBV ranged from 0.20 to 0.44 (on average 0.32) for actual 50K, from 0.06 to 0.23 (on average 0.13) for actual 28K, and from 0.20 to 0.41 (on average 0.31) for imputed 50K genotypes. With the relatively small reductions in the accuracies of genomic predictions, it is safe to recommend the GGP-HD chip for imputing genotypes in Hereford cattle. Using the 28K subset (only those markers common to both GGP-HD and 50K) is not recommended for genomic prediction in Hereford cattle.

Key Words: genomic breeding values, Hereford, GGP

316 Factors associated with recombination in beef cattle. Z.-Q. Weng*¹, M. Saatchi¹, R. Schnabel², J. Taylor², and D. Garrick¹, ¹Iowa State University, Ames, ²University of Missouri, Columbia.

The objective of this study was to locate recombination hotspots on autosomes, map quantitative trait loci (QTL) influencing genome-wide recombination events, and associate number of haplotypes with 1-Mb window-wide recombination rate in beef cattle. A total of 2,778 Angus and 1,485 Limousin parent-verified sire/offspring pairs with BovineSNP50 genotypes were used in this study. SNPs were removed with call rate < 0.95, minor allele frequency < 0.01, or p value for a Hardy Weinberg Equilibrium test < 0.001. BEAGLE (Browning and Browning, 2007) was adopted to impute missing genotypes. Then, phasing was performed using pedigree-based DAGPHASE (Druet and Georges, 2010) with UMD3.1 assembly. Recombination events were identified by pairwise comparison of all combinations of parental and offspring haplotypes. Double crossovers occurring in intervals <2 cM were attributed to phasing errors and ignored. The expected numbers of recombination events were estimated using Karlin's method that assumes recombination events follow a binomial distribution. Recombination hotspots were detected near 23, 24, 31, 73 and 79Mb on *Bos taurus* autosome (BTA) 15 in Angus, and near 23, 31, 73, 75, and 79Mb in Limousin. BayesC approach in GenSel software was used to map QTL influencing genome-wide recombination events. Top 20 1Mb windows which could explain more than 4% (cumulative) genetic variance were considered to be promising QTL. Based on the information from OMIM and Human-Bovine comparative map, 2 candidate genes were identified in such windows. Specifically, RAD51 located at 37 Mb on BTA10, and MRE11A located at 1 Mb on BTA29. The average number of haplotypes within 1-Mb windows was 43.1 on BTA15. Sixty-eight haplotypes were observed in hotspot windows whose recombination rates > 0.02. The average number of haplotypes observed in coldspot windows whose recombination rate < 0.005 was 22.4. Number of haplotypes declined with window-wide recombination rate, because new haplotypes are formed by recombination. 23, 31, and 79Mb on BTA15 are common recombination hotspots across 2 breeds. Genetic variation in RAD51 and MRE11A influence genome-wide recombination number. Further analyses are needed to validate these results.

Key Words: beef cattle, recombination

317 Genetic effects of GDF8 and CAPN1 for carcass and meat traits. G. L. Bennett^{*1}, R. G. Tait Jr.¹, S. D. Shackelford¹, T. L. Wheeler¹, D. A. King¹, E. Casas^{1,2}, and T. P. L. Smith¹, ¹USDA, ARS, Roman L. Hruska U.S. Meat Animal Research Center, Clay Center, NE, ²USDA, ARS, National Animal Disease Center, Ames, IA.

The objective was to improve genetic marker effect estimates of SNP previously associated with muscle traits in beef cattle (F94L marker in GDF8 and 316 marker of CAPN1). Multiyear selection in a composite population segregating both SNP increased minor allele frequency (MAF) to intermediate levels that are more optimal for estimating additive and nonadditive genetic effects. Final MAF of the lysine-encoding allele of GDF8 (allele L), and the C allele of CAPN1 316 were 0.43 and 0.44. During 3 consecutive years following selection, 176 steers were evaluated for carcass, meat quality, tenderness, and meat color traits. Analyses adjusted traits for age at harvest. The 9 genotypes (3 CAPN1 316 × 3 F94L) affected marbling score, ribeye area, adjusted fat thickness, Vision Yield grade (all $P < 0.001$) and L* reflectance ($P = 0.02$). Contrasting the estimates for the 9 genotypes for additive, recessive, and epistatic effects associated with the 2 SNP showed significant ($P < 0.001$) additive effects of F94L allele L for decreased marbling score, adjusted fat thickness, and Vision Yield grade and increased ribeye area and L* reflectance. Differences between FF and LL genotypes were 1.9 to 2.4 RSD for these traits except L* reflectance (1.0 RSD difference). These differences did not reflect the small, nonsignificant difference in carcass weight of 4 kg (0.16 RSD). The F94L L allele tended to be recessive to F for marbling score ($P = 0.08$) and ribeye area ($P = 0.05$). Contrasting CAPN1 316 estimates did not detect significant or suggestive additive, recessive, or epistatic effects for any trait, including tenderness measurements. The F94L L allele, prevalent in Limousin but almost absent in other US breeds, had 1/2 to 2/3 of the effects found for GDF8 mutations in Belgian Blue and Piedmontese, and has strong additive effects for fat and muscle traits that may obscure any relationship of CAPN1 with tenderness. Intermediate frequencies following selection contributed to accuracy of genetic effect estimates.

Key Words: calpain, myostatin, selection

318 CAPN1 and GDF8 genetic marker effects on heifer performance, reproduction, and first calf performance traits in beef cattle. R. G. Tait Jr.^{*}, R. A. Cushman, T. P. L. Smith, H. C. Freetly, and G. L. Bennett, USDA-ARS, U.S. Meat Animal Research Center, Clay Center, NE.

To increase the accuracy of effect estimation and assess potential unintended correlated effects for 2 marker systems used commercially for muscling and meat tenderness, a composite beef cattle population segregating the markers was selected for multiple years to increase minor allele frequency (MAF) or frequencies of divergent haplotypes (FDH). Substantial increases in FDH and MAF were achieved, with SNP haplotypes in the μ -calpain 1 gene (CAPN1) (haplotypes C-C or G-T at markers 316 and 4751, respectively) with haplotype increases from 0.264 to 0.386 and 0.195 to 0.332, respectively, and a lysine encoding allele (L) of the F94L marker in myostatin (GDF8) increased MAF from 0.282 to 0.450. The objective of this study was to understand if these markers affect female performance and reproductive traits. Heifers born between spring of 2007 and 2009 from this population ($n = 149$) were evaluated using MIXED and GLIMMIX procedures of SAS for birth weight, weaning weight, weight at 326 d, 368 d, or 411 d, achieving puberty by 326 d, 368 d, or 393 d, first breeding season pregnancy status, success of weaning first calf. Additionally, first calf performance traits of: birth date, birth weight, weaning weight, weight of calf weaned per cow exposed, and 205-d adjusted weight of calf

weaned per cow exposed were evaluated. There were suggestive effects ($P < 0.10$) for GDF8 on own birth weight and CAPN1 on own weaning weight. GDF8 had significant effects ($P < 0.05$) on puberty, with LL homozygotes having a lower proportion of heifers pubertal than FL or FF genotypes, at all 3 time points. However, the delayed puberty effect of GDF8 did not lead to an effect on pregnancy rates ($P = 0.53$). CAPN1 haplotype of the cow did significantly affect ($P < 0.05$) first calf birth weight. Other own performance, reproduction, and first calf performance traits were not affected ($P > 0.10$) by CAPN1 or GDF8 genetic markers in this study. These marker effects for unintended traits may be important for incorporation into the breeding objective and for marker-assisted management strategies. USDA is an equal opportunity provider and employer.

Key Words: calpain, myostatin, puberty

319 Genome-wide association study of reproductive efficiency in female cattle. T. G. McDanel^{d*1}, L. A. Kuehn¹, M. G. Thomas², W. M. Snelling¹, E. J. Pollak¹, T. P. L. Smith¹, and J. W. Keele¹, ¹USDA, ARS, U.S. Meat Animal Research Center, Clay Center, NE, ²Colorado State University, Fort Collins.

Reproductive efficiency is of economic importance in commercial beef cattle production, as failure to achieve pregnancy reduces the number of calves marketed per cow exposed to breeding. Identification of genetic markers with predictive merit for reproductive success would facilitate accurate prediction of daughter pregnancy rate in sires enabling effective selection of bulls producing daughters with improved fertility. To identify regions of the genome harboring variation affecting reproductive success, we applied a genome-wide association approach based on the >700,000 SNP marker assay. To include the largest number of individuals possible under the available budget, cows from several populations were classified according to reproductive efficiency, and DNA was pooled within population and phenotype before genotyping. Populations evaluated included a research population at USMARC, 2 large commercial ranch populations, and several smaller populations (<100 head) across the US. Significant associations for reproductive efficiency ($P < 1.04 \times 10^{-7}$) were detected by this approach on BTA 5, 13, 15, 18, and 29. A genomic segment located on BTA 5, spanning the region of 25–70 Mb, contained 223 SNP having significant association with classification, representing the most robust signal in the genome. The remaining significant SNP lie on BTA 13 (4 SNP), BTA 15 (1 SNP), BTA 18 (1 SNP), and BTA 29 (1 SNP). In addition to our novel findings, we confirmed previously published associations for over 200 SNP encompassing substantial diversity including *Bos indicus* and *Bos taurus* breeds. From these data we have identified regions of the genome associated with reproductive efficiency. These regions are being evaluated further to identify specific DNA variations that are affecting reproduction in beef cattle. USDA is an equal opportunity provider and employer.

Key Words: bovine, GWAS, reproductive efficiency

320 Molecular mechanism of neuropeptide Y affected by progesterone and estradiol on prepubertal Nellore heifers. J. Diniz-Magalhaes^{*1}, M. Maturana-Filho¹, J. L. M. Vasconcelos², and L. F. P. Silva¹, ¹Universidade de Sao Paulo, Pirassununga, Sao Paulo, Brazil, ²Universidade Estadual Paulista Julio de Mesquita Filho, Botucatu, Sao Paulo, Brazil.

The understanding of the molecular mechanisms by which nutrition, genetics and hormonal treatments affect the beginning of puberty is of great importance for developing strategies aiming to reduce the age at

first calving, and therefore increase the slaughter rate in Nellore cattle. The effects of progesterone device and of endogenous estradiol on the molecular mechanisms controlling the attainment of puberty in Nellore heifers have been investigated. Specifically, the molecular pathways of progesterone (P4) and estradiol on NPY signaling were studied in the hypothalamus. Thirty-five non-pubertal heifers, between 13 and 14 mo of age, were divided into 4 treatments (9 or 8 per treatment): P4 device without estradiol (P-E), P4 device with estradiol (P+E), without P4 device and without estradiol (E-), and without P4 device and with estradiol (E+). The heifers were fed after weaning until they reach approximately 280 kg, with water access. At the end of the hormonal treatments all heifers were slaughtered and the preoptic area from hypothalamus were harvested, processed for analysis and then stored at -80°C. Total RNA of hypothalamus were extracted, treated with DNase I and submitted to cDNA synthesis for gene expression quantification of neuropeptide Y (Npy) and their receptor (Npy1r) by real time PCR (qRT-PCR). The exogenous progesterone increases the Npy expression ($P < 0.05$) on heifers treated only with P4. Similar effect was observed on the E+ treatment. These results indicate that the presence of progesterone and estradiol would be become preoptic area of hypothalamus more sensitive to the inhibitory action of Npy. A comprehensive study of the effects of progesterone administration and endogenous estrogen on attainment of puberty will also be conducted through next-generation sequencing (RNA-Seq), to identify possible candidate genes in the hypothalamus.

Key Words: reproduction, hypothalamus, neuropeptide Y

321 Model comparison in genome-wide association study of fertility traits of first service conception and heifer pregnancy in Brangus cattle. S. O. Peters^{1,2}, K. Kizilkaya^{3,4}, D. J. Garrick³, R. L. Fernando³, J. M. Reecy³, I. G. Imumorin¹, G. A. Silver⁵, and M. G. Thomas^{5,6}, ¹Cornell University, Ithaca, NY, ²Berry College, Mt Berry, GA, ³Iowa State University, Ames, ⁴Adnan Menderes University, Aydin, Turkey, ⁵New Mexico State University, Las Cruces, ⁶Colorado State University, Fort Collins.

First service conception (FSC) and heifer pregnancy (HPG) binary traits from Brangus heifers (i.e., 3/8 Brahman-*Bos indicus* × 5/8 Angus-*Bos taurus*; n ≈ 800) were used to compare Bayes C Logit, Probit and Robit models for a genome-wide association study (GWAS). Marker genotypes were from 53,692 loci on the BovineSNP50 chip. Yearling heifers were estrous synchronized, bred by AI, and then exposed to natural service breeding. Reproductive ultrasound and DNA-based parentage testing were used to determine if the heifer conceived by AI or natural service and to code for the traits of FSC and HPG. Success rates for FSC and HPG were 53.3 ± 0.01% and 78.0 ± 0.01%, respectively. Analyses fitted Bayes C, Logit, Probit or Robit model that treated SNP effects as random with an assumed fraction pi = 0.9995 having no effect on phenotype. The fixed effects fitted in the model were year (i.e., 2005 to 2007), location of birth, calving season, age of dam and contemporary group. In GWAS, simultaneous association of 1-Mb SNP windows with phenotype was undertaken with Bayes C, Logit, Probit or Robit analyses using GenSel software. The 1-Mb windows contained 21.3 ± 1.1 SNP. Results showed that there was more concordance in 1-Mb SNP windows among the 3 models for FSC trait than with HPG trait. Among the top fifteen 1-Mb SNP windows across the 3 models, nine 1-Mb SNP windows were common among the models for FSC while only five 1-Mb SNP windows were common for HPG. The nine 1-Mb SNP windows common among the 3 models used for FSC were identified on chromosomes 1, 6, 8, 16, 23 and 26, and the five 1-Mb SNP

windows common for HPG were found on chromosome 2, 3, 20, 28 and 29. However, there were no overlapping SNP windows among those associated with these fertility traits. The SNP windows on 28 Mb and 17 Mb of chromosomes 8 and 26 were consistently ranked by the 3 models compared as the greatest contributor to the genetic variance for FSC trait while there was no consistent order for the SNP windows associated with HPG.

Key Words: GWAS, fertility, heifer

322 Discovery and validation of single nucleotide polymorphisms with phenotypic associations in beef cattle grazing endophyte-infected tall fescue. B. Bastin^{*1}, C. Bagley³, B. Campbell^{1,2}, A. Houser³, C. Kojima¹, A. Saxton¹, J. Waller¹, and L. Wojakiewicz¹, ¹University of Tennessee, Knoxville, ²Virginia Tech University, Blacksburg, ³Tennessee Tech University, Cookeville.

Development of a multi-locus marker panel will allow for genetic selection for improved production in cattle grazing endophyte-infected tall fescue. Tall fescue (*Lolium arundinaceum* Schreb.) is the most prevalent forage in the Mid-south United States due in part to the presence of the endophytic fungus *Neotyphodium coenophialum*. The fungus, while conferring hardiness to tall fescue, contributes to decreased production efficiency in cow-calf operations. A genome-wide association study was performed using the Illumina 50k bovine SNP chip. Twenty-four SNPs were found to be associated ($P < 0.05$) with adjusted birth weight and adjusted 205-d weights of calves from 48 beef cows at Ames Plantation. Taqman genotyping assays (Applied Biosystems) were subsequently designed to genotype each SNP in beef cattle located at Tennessee Tech University (n = 654), to validate associations in a large, independent herd. Genotype-phenotype associations were tested using mixed models (SAS 9.3, Cary, NC) accounting for variability in calving season in calf-related traits, and least squares means compared with Fisher's least significant difference ($P < 0.05$). Eleven of the GWAS SNPs were informative for such phenotypes as hair coat (scored 1–5), body condition (scored 1–9), weight per day of age (kg/d), adjusted 205-d weight (kg), and days to first calf (Table 1). These data indicate that genetic polymorphisms found to be informative in a small herd can be validated in a larger representative population in a cost-effective manner.

Table 1. Significant associations for GWAS-detected SNPs

Phenotypic association	SNP	P-value	Genotype means		
			A	H	B
Hair coat score	BTA9B	0.028	1.7 ^B	1.8 ^A	1.8 ^{AB}
	BTA9C	<0.001	1.9 ^A	1.6 ^B	1.7 ^B
	BTA9F	0.009	1.8 ^A	1.7 ^B	1.8 ^{AB}
	BTA9I	0.045	1.7 ^B	1.7 ^B	1.9 ^A
	BTA14J	0.001	1.8 ^B	1.6 ^C	2.0 ^A
	BTA19A	0.003	1.6 ^B	1.8 ^A	1.8 ^A
Body condition score	BTA26	0.001	1.8 ^A	1.7 ^B	1.6 ^B
	BTA11	0.037	5.0 ^A	4.8 ^B	5.1 ^A
Weight gained per day of age	BTA11	0.002	0.52 ^A	0.44 ^B	0.52 ^A
	BTA14B	0.032	128 ^A	116 ^B	
Adj. 205-d weight	BTA23	0.033	129 ^{AB}	119 ^B	134 ^A
	BTA9H	0.002	749 ^B	1185 ^A	725 ^B
Days to first calf	BTA11	0.024	715 ^B	1073 ^A	781 ^B
	BTA19A	0.001	989 ^A	723 ^B	709 ^B

Key Words: fescue toxicosis, cattle, SNP