Breeding and Genetics: Genomic Selection in Dairy II

538   Application of a posteriori granddaughter and modified granddaughter designs to determine Holstein haplotype effects. J. I. Weller[1,2], P. M. VanRaden[1], and G. R. Wiggans*[1], [1]*Animal Improvement Programs Laboratory, Agricultural Research Service, Beltsville, MD,* [2]*ARO, The Volcani Center, Bet Dagan, Israel.*

A posteriori and modified granddaughter designs were applied to determine haplotype effects for Holstein bulls and cows with BovineSNP50 genotypes. The a posteriori granddaughter design was applied to 52 sire families, each with > 100 genotyped sons with genetic evaluations based on progeny tests. For 33 traits (milk, fat, and protein yields; fat and protein percent; somatic cell score; productive life; daughter pregnancy rate; heifer and cow conception rates; service-sire and daughter calving ease and stillbirth; 18 conformation traits; and net merit), the analysis was applied to the autosomal segment with the single nucleotide polymorphism (SNP) with the greatest effect in the genomic evaluation of each trait. All traits except 2 had a significant ($P < 0.05$) within-family haplotype effect. The same design was applied with the genetic evaluations of sons corrected for SNP effects associated with chromosomes besides the one under analysis. Number of significant within-family contrasts was 166 without adjustment and 211 with adjustment. Of the 52 bulls analyzed, 36 had BovineHD genotypes that were used to test for concordance between sire quantitative trait loci and SNP genotypes; complete concordance was not obtained for any effects. Of the 31 traits with effects from the a posteriori granddaughter design, 21 were analyzed with the modified granddaughter design. Only sires with a significant contrast for the a posteriori granddaughter design and < 200 granddaughters with a record usable for genetic evaluation were included. Eight traits had significant within-family haplotype effects. With respect to milk and fat yields and fat percentage, the results on BTA 14 corresponded to the hypothesis that a missense mutation in DGAT1 is the main causative mutation, although other polymorphisms in that gene also modify fat yield and percentage. The positive allele for protein concentration was less frequent, which indicated that selection on that locus could be effective. DNA sequencing of the sires analyzed will be needed to determine the causative mutations.

Key Words: granddaughter design, genetic evaluation, genomic selection

539   Using 90,113 single nucleotide polymorphisms in genomic evaluation of dairy cattle. G. R. Wiggans*, T. A. Cooper, and P. M. VanRaden, *Animal Improvement Programs Laboratory, Agricultural Research Service, USDA, Beltsville, MD.*

Accuracy of genomic evaluation is expected to increase when more markers are used because of better tracking of causative genetic variants. However, Illumina BovineHD genotypes based on 777,962 single nucleotide polymorphisms (SNP) have not been used for US genomic evaluation because the small reliability gain achieved did not justify the genotyping cost. In December 2012, the GeneSeek Genomic Profiler HD (GHD) BeadChip was released with 76,867 unique nuclear SNP and 13 mitochondrial SNP. It included 28,376 (63%) of usable SNP from the Illumina BovineSNP50 v2 BeadChip as well as 48,491 BovineHD SNP selected because they had the greatest effects for Holstein net merit. Based on analysis of 1,730 animals with GHD genotypes, 3,153 SNP were not used for genomic evaluation because they were on the Y chromosome or had a low call rate, excess parent-progeny conflicts, or a minor allele frequency of < 1% for Holsteins, Jerseys, and Brown Swiss;

73,714 GHD SNP were usable for genomic evaluation, which added 44,925 to the 45,188 currently used (total of 90,113 SNP). Genotypes for those SNP and August 2009 traditional genetic evaluations for 26,200 Holstein bulls and cows were used to predict December 2012 daughter performance of 29 economically important traits for 4,024 bulls with a traditional evaluation since August 2009. Reliability gains from 90,113 SNP were greater than from 45,188 SNP by 2.2 percentage points for yield traits and 0.9 percentage points for calving traits but less by 0.8 percentage points for fitness traits and 0.5 percentage points for conformation traits. Lower gains may result from imputation errors, which will decline as more animals have GHD genotypes. Imputation from lower density chips to 90,113 SNP was about 0.5% less accurate than to 45,188 SNP. More GHD genotypes are needed to achieve adequate imputation accuracy for Brown Swiss and Jerseys, which have few high-density genotypes. The GHD chip allows additional SNP to be included in genomic evaluation without increasing genotyping cost, but higher imputation accuracy is needed before evaluation accuracy can improve for all breeds and traits.

Key Words: genomic evaluation, reliability, single nucleotide polymorphism

540   Methods for genomic evaluation in a small dairy population and the effect of inclusion of genotyped cows' information in multiple-parity analyses. D. A. L. Lourenco*[1], I. Misztal[1], J. I. Weller[2], S. Tsuruta[1], I. Aguilar[3], and E. Ezra[4], [1]*University of Georgia, Athens,* [2]*Institute of Animal Sciences, ARO, Bet Dagan, Israel,* [3]*Instituto Nacional de Investigacion Agropecuaria, Las Brujas, Canelones, Uruguay,* [4]*Israel Cattle Breeders Association, Caesaria, Israel.*

Methods for genomic prediction were evaluated for a dairy population in which less than 1000 progeny-tested bulls were genotyped. The inclusion of elite cows' genotypes in a single-step method was also evaluated. Two data sets were used: a complete data set with production records of 713,686 cows from 1985 through 2011, and a reduced data set with production of 563,870 cows up to 2006. For each production trait (milk, fat, protein, fat %, and protein %), a multitrait animal model was used to compute genetic evaluation for parities 1 through 3 as separate traits. Evaluations were performed for the 2006 and 2011 data sets. Genomic predictions for bulls in 2006 were obtained using genomic BLUP (GBLUP), a Bayesian linear regression method (BayesC), single-step GBLUP (ssGBLUP), and ssGBLUP considering weights for SNP (WssGBLUP). Predictions with BayesC and GBLUP were either direct or included PA in an index (IND). Genomic predictions when including elite cows' genotypes were obtained using ssGBLUP and WssGBLUP. Predictive ability was assessed by coefficients of determination (R^2) and regressions of predictions of 135 validation bulls with no daughters in 2006 on daughter deviations of those bulls in 2011. The average R^2 (%) among parities for PA, GBLUP, BayesC, GBLUP (IND), BayesC (IND), ssGBLUP, and WssGBLUP, respectively, were 14, 9, 10, 15, 15, 19 and 19 for milk; 7, 12, 14, 10, 10, 13, and 12 for fat; 3, 10, 10, 9, 8, 12, and 12 for protein; 35, 22, 29, 34, 37, 37 and 40 for fat %; 31, 24, 30, 32, 36, 39 and 44 for protein %. The average inflation (%) of GEBV among parities and traits was 24, 17, 25, 22, 7, and 15 for GBLUP, BayesC, GBLUP (IND), BayesC (IND), ssGBLUP, and WssGBLUP, respectively. Adding weights in ssGBLUP helped to improve accuracy of genomic predictions, but further modifications are needed to reduce bias observed in some traits. Adding elite cows' genotypes in single-step

methods removed bias in protein % when weights for SNP were added, and improved the overall R^2 by up to 2% in ssGBLUP and WssGBLUP.

Key Words: genomic evaluation, small populations, single-step method

541   Dissection of genomic correlation matrices using multivariate factor analysis in dairy and dual-purpose cattle breeds. N. P. P. Macciotta*[1], C. Dimauro[1], S. Sorbolini[1], D. Vicario[2], D. J. Null[3], and J. B. Cole[3], [1]*Dipartimento di Agraria, Università di Sassari, Sassari, Italia,* [2]*ANAPRI, Udine, Italia,* [3]*Animal Improvement Programs Laboratory, USDA, Beltsville, MD.*

SNP effects estimated in genomic selection programs allow for the prediction of direct genomic values (DGV) both at genome-wide and chromosomal level. As a consequence, genome-wide (G_GW) or chromosomal (G_CHR) correlation matrices between genomic predictions for different traits can be calculated. Comparison between G_GEN and G_CHR or between different G_CHR may indicate differences in the genetic control of groups of traits. In this work, a method for comparing genomic correlation matrices based on multivariate factor analysis (MFA) is presented. Two breeds were considered: 3,096 US Holstein and 460 Italian Simmental bulls, with DGV for 31 and 12 productive and functional traits, respectively. Factor analysis was carried out on G_GEN and G_CHR within each breed. In Holstein, between 7 and 9 factors were able to explain 70 to 80% of the original variance, whereas in Simmental on average 3 to 4 latent variables explained about 80% of the variance. In US Holstein, latent factors correlated (r > 0.60) with milk yield traits, milk composition, udder morphology, strength, and functional traits (productive life, SCS, daughter pregnancy rate) were obtained from G_GEN. Differences were observed at the chromosome level. For BTA14, a single factor correlated with both milk yield and composition traits was observed. For BTA18, sire calving traits and some conformation traits were correlated with the same common factor. In the G_GEN of Italian Simmental, the first latent factor was correlated positively with milk yield and milking traits, and negatively with muscularity; the second with daily gain and size; the third to feet and legs and SCS; and the fourth to milk composition traits. On BTA17, one factor is positively correlated with daily gain and negatively with milk composition. The MFA was able to detect differences in genetic correlation patterns across the genome, as well as on individual chromosomes, and may be used for preliminary identification of genome regions affecting multiple traits.

Key Words: genomic prediction, chromosome, genomic correlation

542   International genomic evaluation of young Holstein bulls. J. H. Jakobsen*[1] and P. G. Sullivan[2], [1]*Interbull Centre, Swedish University of Agricultural Sciences, Uppsala, Sweden,* [2]*Canadian Dairy Network, Guelph, ON, Canada.*

Genomic tested young bulls with no daughter proofs yet are of interest for international trade. A genomic multitrait across country evaluation (GMACE) procedure was applied to Mendelian sampling (MS) deviations of young bulls: national GEBV minus parent average from classical MACE. Fifteen Holstein populations provided GEBV data for as many as 38 traits while classical EBVs for the same traits were included from 31 populations. Only GEBV data passing GEBV validation tests; for minimal bias, and for improvement in accuracy compared with national parent averages, were included in the study. Further, national GEBVs were required to be from the same model and on the same base and scale as the national EBVs of progeny-tested bulls provided for classical MACE. GEBVs of bulls less than 7 years of age and with no classical MACE proof were included for the breeding value prediction while bulls 2–5 years of age were included for genomic variance estimation. Numbers of GEBV included in GMACE were 1.96 for 80,765 bulls for protein, while numbers of EBV for classical MACE was 1.23 for 130,349 bulls. Multiple GEBV of a young bull occur due to sharing of data and genotypes among countries for national GEBV predictions. Such genomic data sharing at the national level was accounted for in GMACE by fitting residual correlations among the national GEBV input data. The residual correlations were based on proportions of common reference (i.e., phenotyped) bulls and cows used for genomic predictions by each country. International GEBV had equal or higher reliability than corresponding national GEBV. For example, protein yield national GEBV reliabilities were generally between 65 and 75, while the international reliabilities ranged between 75- 80. Reliability increases were highest if bulls had multiple national GEBV, and if the GEBV were from countries with less genomic data sharing. Each young bull with one or more national GEBV received international GEBV on all 31 population scales, including the populations with no national GEBV. A first official release of MACE GEBV and MACE GREL of young Holstein bulls is planned for August 2013.

Key Words: GMACE, dairy

543   Whole genome analysis for SNP variation in indigenous cattle population in Pakistan. H. Mustafa*[1], H. Heather[2], K. Javed[1], T. Pasha[1], M. Abdullah[1], I. Mohsin[1], K. Euisoo[2], A. Ali[1], A. Ajmal[1], and T. Sonstegard[2], [1]*University of Veterinary and Animal Sciences, Lahore, Pakistan,* [2]*Bovine Functional Genomics Laboratory, ARS/ USDA, Beltsville, MD.*

Although a large number of single nucleotide polymorphisms (SNPs) have been identified from the bovine genome- sequencing project, few of these have been validated at large in Bos indicus breeds. We have genotyped 96 animals, representing 10 cattle populations of Pakistan, with the Illumina Bovine 777K SNP BeadChip. These include 8 Achi, 4 Bhagnari, 13 Cholistani, 10 Dhanni, 10 Dajal, 2 Kankaraj, 13 Lohani, 9 RedSindhi, 14 Sahiwal and 13 Tharparkar breeds. Frequency of minor allele frequency (MAF), distribution, and deviation from Hardy-Weinberg equilibrium (HWE) were estimated. Analysis of 500,393 SNP markers revealed that the mean minor allele frequency (MAF) was 0.23, 0.20, 0.22, 0.22, 0.20, 0.18, 0.20, 0.22, 0.21 and 0.18 for Achi, Bhagnari, Cholistani, Dhanni, Dajal, Kankaraj, Lohani, Red sindhi, Sahiwal and Tharparkar cattle, respectively. Significant differences of MAF were observed in the indigenous Pakistani cattle populations ($P <$ 0.001). Across the Pakistani cattle populations, common variant MAFs ($\geq$0.10 and $\leq$ 0.5) accounted for 79% of 500, 939 SNPs. The level of SNP variation identified in this particular study highlights that these markers can be potentially used for genetic studies in indigenous cattle breeds in Pakistan.

Key Words: indigenous cattle, minor allele frequency

544   Increasing the accuracy of genomic predictions of fat yield in New Zealand Holstein Friesians using *DGAT1* genotypes. M. K. Hayr*[1], M. Saatchi[1], D. L. Johnson[2], and D. J. Garrick[1], [1]*Iowa State University, Ames,* [2]*LIC, Hamilton, NZ.*

Accurate genomic estimated breeding values (GEBV) are essential for preventing the accumulation of inaccuracies when unproven parents are selected. This study investigated the effect of including the known large effect *DGAT1* mutation in calculating GEBV. Data were provided by LIC, a New Zealand dairy cattle breeding company, and included Illumina SNP50 (50k) genotypes and deregressed estimated breeding values (DEBV) for fat yield. *DGAT1* genotypes were provided for 1,133 cows and 655 bulls and imputed for the remaining 4,528 cows

and 1,632 bulls in BEAGLE. Three models were run using Bayes C in GenSel and 5-fold cross-validation with 97.5% of SNPs assumed to have no effect on the trait: (1) a model relying on linked 50k markers to pick up the *DGAT1* effect; (2) a model with 50k markers and *DGAT1* as a random effect; and (3) a model with 50k markers and with *DGAT1* genotype as a fixed effect. These models were run separately for bulls and for cows, and repeated, once using animals where *DGAT1* had been directly genotyped and once using all animals. The GEBV accuracy was defined as the correlation between DEBV and GEBV. Regression of DEBV on GEBV was computed to quantify bias in GEBV. Accuracy was lowest when only 50k markers were included in the model and increased when *DGAT1* was included in the model, with the highest accuracy observed when *DGAT1* was a fixed effect. The regression coefficient was sufficiently close to one to assume there is little to no bias in GEBV; nevertheless it was closest to one when *DGAT1* was as a fixed effect. These results suggest that including *DGAT1* genotype as a fixed effect when calculating GEBV both increases accuracy of the GEBV and reduces bias. Differences in using direct versus direct and imputed genotypes could be due to sample size or incorrect imputation.

Table 1. Regression coefficient (b) and correlation (cor) between DEBV and GEBV

Sex	Model	Direct genotypes		Direct and imputed genotypes	
		b	cor	b	cor
M	50k	1.104	0.402	0.908	0.377
	50k + DGAT1 (Random)	1.102	0.406	0.011	0.381
	50k + DGAT1 (Fixed)	1.014	0.425	0.917	0.389
F	50k	1.189	0.559	1.022	0.695
	50k + DGAT1 (Random)	1.187	0.564	1.021	0.698
	50k + DGAT1 (Fixed)	1.090	0.574	1.017	0.702

Key Words: dairy, *DGAT1*, genomics

545   Profitability of combined use of sexed semen and genomic testing in dairy heifers. A. De Vries*[1] and J. A. Salfer[2], [1]*University of Florida, Gainesville,* [2]*University of Minnesota Extension, St. Cloud.*

The objective of this study was to evaluate the profitability of the combined use of sexed semen and genomic testing in dairy heifers. The use of sexed semen may result in more dairy heifer calves than are needed to replace culled cows, allowing increased selection intensity. Genomic testing increases the reliability of selection. Combined, the genetic progress of the selected heifers may offset the costs due to the use of sexed semen, including decreased fertility, and genomic testing. First, an algorithm was developed to determine which heifer calves should be genomically tested based on reliability of pre-ranking for net merit, cost of testing, and selection intensity. The net value of the genetic gain in the selected heifers was used in a herd budget simulation model that mimicked a closed herd including young stock and cows. Surplus dairy heifer calves were sold. Annual cull rate in the cow herd was 39% for all scenarios. Four scenarios were tested: (A) no genomic testing, no sexed semen, (B) optimal genomic testing, no sexed semen, (C) optimal genomic testing, first insemination with sexed semen in all heifers, (D) optimal genomic testing, first and second inseminations with sexed semen in all heifers. Genomic testing increased the reliability of net merit breeding values from 20% to 60%. The surplus of dairy heifer calves in scenarios A to D was 7%, 7%, 18%, and 22% of those born alive. Optimal genomic testing (in the lower pre-ranked heifer calves) in scenarios B to D added $25, $60, and $72 per heifer selected. The cost to raise heifers, including the value of genomic selection, was $627, $616, $621, and $627 per milking cow per year (scenarios A to D). The sale of bull calves and surplus dairy heifer calves resulted in revenues of $38, $38, $46, and $50 per milking cow per year. Considering all costs and benefits, herd profit per milking cow per year was $255, $265, $274, and $273 for scenarios A to D. In conclusion, strategic use of genomic testing and use of sexed semen in first inseminations in heifers was the most profitable scenario and increased profit by $20 per milking cow per year.

Key Words: sexed semen, genomics, profitability

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