Incidence of ketosis, metritis, mastitis, and retained placenta were studied on Israeli Holstein cows calving between 2008 and 2017. These diseases were selected based on their economic impact. Ketosis, metritis, and retained placenta were scored dichotomously. Mastitis was scored as absent, a single occurrence during the lactation or more than once. Ketosis and metritis were recorded during the first 21 d after calving, retained placenta during the first 5 d after calving, and mastitis up to 305 d in milk. The effects of herd-year-season, calving age, month of calving, gestation length and occurrence of dystocia were included in the first parity analysis models. All effects were significant (P < 0.001) for metritis and retained placenta. For ketosis all effects were significant, except for gestation length. For mastitis, only the effects of herd-year-season and calving age were significant. First-parity heritabilities and genetic and environmental correlations among these diseases and the traits included in the Israeli breeding index were computed by the MTC REML individual animal model program. Heritabilities and genetic and environmental correlations among the disease traits are in Table 1. All correlations were positive, but the highest correlation, between ketosis and metritis, was only 0.26. Genetic correlations between the disease traits and milk production traits were all “positive,” but all correlations were <0.25. Since mastitis is farmer recorded, a truncated data set was analyzed including only herd-year with >50 cows and >4% mastitis. Genetic correlations between mastitis and lactation somatic cell score were higher in second and third parities, and heritabilities for mastitis were slightly higher.

Table 1 (Abstr. 56). Heritabilities and genetic (above the diagonal) and environmental (below the diagonal) correlations among the disease traits in 229,571 first-parity cows1

<table>
<thead>
<tr>
<th>Trait</th>
<th>Ketosis</th>
<th>Metritis</th>
<th>Mastitis</th>
<th>Retained placenta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketosis</td>
<td>0.07</td>
<td>0.27</td>
<td>0.00</td>
<td>0.05</td>
</tr>
<tr>
<td>Metritis</td>
<td>0.16</td>
<td>0.08</td>
<td>0.03</td>
<td>0.10</td>
</tr>
<tr>
<td>Mastitis</td>
<td>0.00</td>
<td>0.01</td>
<td>0.05</td>
<td>0.01</td>
</tr>
<tr>
<td>Retained placenta</td>
<td>0.06</td>
<td>0.14</td>
<td>0.01</td>
<td>0.06</td>
</tr>
</tbody>
</table>

1All standard errors were < 0.01.

Key Words: ketosis, metritis, mastitis

58 Identification of genomic regions associated with clinical mastitis in US Holstein cattle. J. B. Cole1,1, K. L. P. Gaddis2, C. Willard1, D. J. Null1, C. Maltecca3, and J. S. Clay4, 1Animal Genomics and Improvement Laboratory, ARS, USDA, Beltsville, MD, 2Council on Dairy Cattle Breeding, Bowie, MD, 3Department of Animal Science, College of Agriculture and Life Sciences, North Carolina State University, Raleigh, NC, 4Dairy Records Management Systems, Raleigh, NC.

The objective of this research was to identify genomic regions associated with clinical mastitis (MAST) in US Holsteins using producer-reported data. Genome-wide association studies (GWAS) were performed on deregressed PTA using GEMMA v. 0.94. Genotypes included 60,671 SNP for all predictor bulls (n = 35,724) and 35,000 cows sampled from the predictor population of 112,895 females. Autosomal SNP with Wald P-values ≤ 5 × 10−8 were assigned to the closest annotated gene within 25 kbp using BEDTools v. 2.21.0 and the UMD3.1.1 assembly of the Bos taurus genome, and gene functions were determined by a review of the literature. Genes associated with MAST included CARD14 (80.16 Mbp on BTA17) and RPTOR (52.30 Mbp on BTA19), both of which were previously reported to have significant associations with clinical mastitis in Holsteins. Other genes of interest included MGAT5 (63.11 Mbp on BTA2), which regulates the biosynthesis of glycoprotein oligosaccharides; CGNL1 (52.83 Mbp on BTA10), which is involved in the formation and maintenance of tight cell-cell junctions and mediates junction assembly and maintenance; EPAS1 (28.57 Mbp on BTA11), a transcription factor associated with blood vessel development and the expression of endothelial growth factor; and ANGPTI (59.13 Mbp on BTA14), which is associated with vascular development and angiogenesis. These genes are of interest because they may be involved in the development and defense of the mammary gland, and possibly associated with changes in milk composition in response to infections of the udder. However, these results represent only statistical associations, and functional validation is needed to determine if these effects are causal, or simply represent correlations with other processes that may represent true causal mechanisms.

Key Words: clinical mastitis, disease resistance, genomic evaluation

56 Genetic and environmental analysis of diseases with major economic impact in Israeli Holsteins. J. I. Weller1,1, E. Ezra1, and M. van Straten1, 1ARO, The Volcani Center, Rishon LeZion, Israel, 2Israel Cattle Breeders Association, Caesarea Industrial Park, Israel, 3Hachaklait, Mutual Society for Veterinary Services, Caesarea Industrial Park, Israel.

Ketosis, metritis, mastitis, and retained placenta were previously reported to have significant associations with clinical mastitis (MAST) in US Holsteins using producer-reported data. Genome-wide association studies (GWAS) were performed on deregressed PTA using GEMMA v. 0.94. Genotypes included 60,671 SNP for all predictor bulls (n = 35,724) and 35,000 cows sampled from the predictor population of 112,895 females. Autosomal SNP with Wald P-values ≤ 5 × 10−8 were assigned to the closest annotated gene within 25 kbp using BEDTools v. 2.21.0 and the UMD3.1.1 assembly of the Bos taurus genome, and gene functions were determined by a review of the literature. Genes associated with MAST included CARD14 (80.16 Mbp on BTA17) and RPTOR (52.30 Mbp on BTA19), both of which were previously reported to have significant associations with clinical mastitis in Holsteins. Other genes of interest included MGAT5 (63.11 Mbp on BTA2), which regulates the biosynthesis of glycoprotein oligosaccharides; CGNL1 (52.83 Mbp on BTA10), which is involved in the formation and maintenance of tight cell-cell junctions and mediates junction assembly and maintenance; EPAS1 (28.57 Mbp on BTA11), a transcription factor associated with blood vessel development and the expression of endothelial growth factor; and ANGPTI (59.13 Mbp on BTA14), which is associated with vascular development and angiogenesis. These genes are of interest because they may be involved in the development and defense of the mammary gland, and possibly associated with changes in milk composition in response to infections of the udder. However, these results represent only statistical associations, and functional validation is needed to determine if these effects are causal, or simply represent correlations with other processes that may represent true causal mechanisms.

Key Words: ketosis, metritis, mastitis

57 Gene mapping and gene-set analysis for milk fever in Holstein dairy cattle. H. A. Pacheco1,2, A. Sigdel1, C. K. Mak1, K. N. Galvão1, L. T. Dias3, and F. Peñagaricano*, 1University of Florida, Gainesville, FL, 2Federal University of Paraná, Curitiba, PR, Brazil.

Milk fever (MF) is an important metabolic disorder of dairy cows around the time of calving. MF leads to important economic losses due to deaths, reduction in milk production and productive lifespan, as well as costs associated with both prevention and treatment. The objective of this study was to unravel the genomic architecture underlying MF in Holstein dairy cattle. Data consisted of 28k producer-recorded MF event records from 14k cows. The analysis included a whole-genome scan to identify genetic variants and genes regulating MF, and a subsequent gene set analysis for detecting pathways and biological mechanisms associated with MF. The association analysis identified several regions located on BTA6, BTA7, BTA14, BTA16, BTA17, and BTA23 that explained a significant amount of genetic variance for MF. These regions harbor several genes; for example, GC, CAMK2A, CAMK1G and CPNE5, that are directly involved in calcium and vitamin D metabolism. Notably, these regions also harbor microRNAs that regulate the expression of genes implicated in calcium ion transmembrane transport, such as CACNA1D and NCSI. Moreover, the gene set analyses revealed several significant functional categories, including endorphins, potassium channels, phosphatidylinositol phosphates, and NFATC transcription factors. Most of these terms are associated either with hypocalcemia or the cascade of events that occur during MF. Overall, our study contributes to a better understanding of the genetic control of this complex disease. These findings can provide opportunities for improving MF in dairy cattle through marker-assisted selection.

Key Words: enrichment analysis, hypocalcemia, whole-genome scan

58 Identification of genomic regions associated with clinical mastitis in US Holstein cattle. J. B. Cole1,1, K. L. P. Gaddis2, C. Willard1, D. J. Null1, C. Maltecca3, and J. S. Clay4, 1Animal Genomics and Improvement Laboratory, ARS, USDA, Beltsville, MD, 2Council on Dairy Cattle Breeding, Bowie, MD, 3Department of Animal Science, College of Agriculture and Life Sciences, North Carolina State University, Raleigh, NC, 4Dairy Records Management Systems, Raleigh, NC.

The objective of this research was to identify genomic regions associated with clinical mastitis (MAST) in US Holsteins using producer-reported data. Genome-wide association studies (GWAS) were performed on deregressed PTA using GEMMA v. 0.94. Genotypes included 60,671 SNP for all predictor bulls (n = 35,724) and 35,000 cows sampled from the predictor population of 112,895 females. Autosomal SNP with Wald P-values ≤ 5 × 10−8 were assigned to the closest annotated gene within 25 kbp using BEDTools v. 2.21.0 and the UMD3.1.1 assembly of the Bos taurus genome, and gene functions were determined by a review of the literature. Genes associated with MAST included CARD14 (80.16 Mbp on BTA17) and RPTOR (52.30 Mbp on BTA19), both of which were previously reported to have significant associations with clinical mastitis in Holsteins. Other genes of interest included MGAT5 (63.11 Mbp on BTA2), which regulates the biosynthesis of glycoprotein oligosaccharides; CGNL1 (52.83 Mbp on BTA10), which is involved in the formation and maintenance of tight cell-cell junctions and mediates junction assembly and maintenance; EPAS1 (28.57 Mbp on BTA11), a transcription factor associated with blood vessel development and the expression of endothelial growth factor; and ANGPTI (59.13 Mbp on BTA14), which is associated with vascular development and angiogenesis. These genes are of interest because they may be involved in the development and defense of the mammary gland, and possibly associated with changes in milk composition in response to infections of the udder. However, these results represent only statistical associations, and functional validation is needed to determine if these effects are causal, or simply represent correlations with other processes that may represent true causal mechanisms.

Key Words: clinical mastitis, disease resistance, genomic evaluation
59  Single-step genome-wide association study of digital dermatitis and sole ulcer in Holstein cattle. F. Malchiodi*1, L. F. Brito1, A.-M. Christen2, A. Fleming2, D. F. Kelton3, F. S. Schenkel1, and F. Miglior1,4, 1Centre for Genetic Improvement of Livestock, Department of Animal Biosciences, University of Guelph, Guelph, ON, Canada, 2Valacta, Sainte-Anne-de-Bellevue, QC, Canada, 3Department of Population Medicine, OVC, University of Guelph, Guelph, ON, Canada, 4Canadian Dairy Network, Guelph, ON, Canada.

Digital dermatitis and sole ulcer represent the most prevalent lesions in Canada, with almost 20% and 8% of cows affected by these lesions, respectively. This study aimed to perform a genome-wide association study (GWAS) and functional analysis to uncover genomic regions associated with digital dermatitis and sole ulcer. Hoof lesions were recorded by hoof trimmers during the routine trimming activity in 1,080 Canadian herds between 2009 and 2016. Hoof lesions were coded as binary traits (0; 1), where 1 was assigned to the presence of a lesion in any claw. The final data set contained 249,709 observations from 105,450 animals, while the pedigree file contained 351,215 animals. Of those animals, 20,188 were genotyped either with 50K SNP panel or a low-density panel and imputed to 50K. The model implemented in the weighted single-step GWAS included the fixed effects of herd-date of hoof trimming, hoof trimmer, parity at trimming, stage of lactation at trimming, and the random additive genetic animal and permanent environmental effects. Important genomic regions associated with digital dermatitis and sole ulcer were identified and a list of functional candidate genes within or next to these regions was created.

Key Words: digital dermatitis, sole ulcer, ssGWAS

62  Multitrait modeling of first versus later parities for US yield, somatic cell score, and fertility traits. P. M. VanRaden* and M. E. Tooker, USDA Animal Genomics and Improvement Laboratory, Beltsville, MD.

Genetic merits in first vs. later parity with correlations <1 were compared with official repeatability models using 88 million lactation records of 34 million cows for yield traits and fewer records for SCS and 2 cow fertility traits. Estimated genetic correlations of first with later parity ranged from 0.85 for SCS to 0.95 for fertility traits. These estimates were also applied to permanent environmental and herd-by-sire interaction effects that were constants within later parities and correlated with first-parity effects. Previous parity variance adjustments were removed. Computation took twice as many processors and required more iteration because of slightly slower convergence. All-parity merit combined first and later merit with weights of 0.33 and 0.67, respectively; genetic correlations of all-parity merit with either first or later merit ranged from 0.96 to 0.99. For all bulls progeny-tested since 1995, correlations with official evaluations were very high (0.999) for all traits. Correlations for the 2 most recent years of progeny-tested bulls were lower (0.991 for SCS to 0.997 for fat yield) because many of these bulls had only or mostly first-parity daughters. Computed reliabilities of these recent bulls averaged 3 percentage points less than official reliabilities. With the latest 5 yr of data removed, correlations of truncated and current evaluations were compared for the most recently proven US bulls. Correlations for SCS were higher for the new model than for the traditional model for Holsteins (0.875 vs. 0.867) and Brown Swiss (0.800 vs. 0.76) but not for Jerseys (0.822 vs. 0.826). Correlations for yield traits did not improve for any breed. In a separate test, modeling maturity effects using random regressions on parity gave predictions very similar to modeling first vs. later records. Modeling lactations as correlated traits can possibly reduce biases from early daughters and slightly improve stability for SCS when bulls transition from genomic predictions to observed daughter records, but did not improve correlations with future evaluations for other traits.

Key Words: maturity effect, parity, genetic correlation

63  Relationships between daughter phenotypes and sire PTA for production and fertility traits in US organic Holstein cows. L. C. Hardie*1, I. W. Haagen1, L. Han1, B. J. Heins2, D. D. Fitzsimmons3, and C. D. Dechow1, 1University of Minnesota, Minneapolis, MN, 2USDA Animal Genomics and Improvement Laboratory, University Park, PA, 3Pennsylvania State University, State University, Alfred, NY.

The objective of this study was to evaluate the relationship between daughter performance on US organic farms with sire predicted transmitting ability (PTA) estimated through national evaluations. Production and fertility data were collected from 3,002 Holstein cows housed on 9 commercial organic farms across the US. Only records from the year of organic certification through 2017 were used, and for a cow to be included in the data set, her first parturition must have occurred during or after the year of organic certification. Daughters belonged to 513 sires with the most commonly used sire having 185 daughters. We regressed 1,560 daughter records of 305-d mature equivalent (ME305) milk, fat, and protein yield on sire PTA for milk, fat, protein, respectively, and we regressed 1,624 records of average lactation SCS, on sire PTA for...
Genetic analysis of heat tolerance for conception rate in US Holstein cows. A. Sigdel1, 4, J. A. Vacía1, I. Aguilar2, R. Abdollahi-Arpanahi1, 3, and F. Peñagaricano1, 1University of Florida, Gainesville, FL, 2Instituto Nacional de Investigación Agropecuaria, Las Brujas, Canelones, Uruguay, 3University of Tehran, Tehran, Pakdasht, Iran.

Heat stress has adverse effects on the reproductive performance of dairy cows. Even with heat abatement systems, conception rates are negatively affected during heat conditions. Genetic selection is an attractive alternative for reducing the effects of heat stress on dairy cattle fertility. The first goal of this study was to estimate genetic components of conception rate across lactations considering heat stress. The second goal was to identify genomic regions, individual genes, and pathways responsible for thermotolerance. Data included 74,221 pregnancy records on 13,704 Holstein cows. Multi-trait repeatability test-day models with random regressions on THI values were used to estimate variance components. The models included herd-test-day and DIM classes as fixed effects, and generic and heat tolerance additive and generic and permanent environmental as random effects. Genetic variance for heat tolerance increased by 80% from first to second parity and 66% from second to third parity, suggesting that cows become more sensitive to heat stress as they age. Heritability estimates for conception rate at THI 78 were between 0.02 and 0.03, whereas genetic correlations between general merit and thermotolerance were always negative, ranging from −0.35 (0.21) to −0.82 (0.08). Whole-genome scans were performed using ssGBLUP. One region on BTA23 that harbors PADI6 and HCRTR2 was found to be strongly associated with general merit across all parities. Gene PADI6 influences oocyte competence whereas HCRTR2 is implicated in maternal recognition of pregnancy and implantation. Genomic regions on BTA10 and BTA11 were found to be strongly associated with thermotolerance; these genomic regions harbor RGS6 and PRKCE, genes implicated in intracellular protein trafficking and heat shock response. Gene-set analysis revealed several functional categories, such as protein refolding, lipid modification, and gap junction, that are involved in biological processes and functions closely related to conception and pregnancy maintenance. Overall, this study contributes to a better understanding of the genetics underlying heat stress and points out novel opportunities for improving thermotolerance in dairy cattle.

Key Words: heat stress, fertility, gene mapping


Fertility is arguably a very important economic trait in dairy cattle. Despite recent advances, reproductive performance remains suboptimal in most dairy herds, resulting in significant economic losses for the dairy industry. Recent studies suggest that a significant percentage of reproductive failure is attributable to bull subfertility. As such, our main objective was to dissect the genetic architecture of sire fertility in US Jersey cattle. The data set included 1.5k Jersey bulls with sire conception rate (SCR) records and 96k single nucleotide polymorphism (SNP) markers spanning the whole genome. The analysis included whole-genome scans for both additive and non-additive effects, and subsequent functional enrichment analyses using KEGG Pathway, Gene Ontology (GO) and Medical Subject Headings (MeSH) databases. The association analyses identified 10 different regions associated with Jersey bull fertility. These 10 1.5 Mb SNP windows jointly accounted for roughly 7% of the SCR additive genetic variance. Several candidate genes were annotated in these regions, such as PKDREJ, STX2, PDHB, and RhoA. These genes are directly involved in spermatogenesis, sperm differentiation, sperm capacitation and fertilization process. Moreover, the non-additive scan revealed 3 putative fertility genes, FER1L5, CNNM4 and DNAH3, with marked recessive effects. The gene-set analysis identified several significant functional terms, including gap junction, MAPK signaling pathway, regulation of cation channel activity, pyrophosphatase activity, synaptic vesicle exocytosis, GTPase activity, membrane fusion, and calcium channels. Most of these terms are known to be involved in biological processes and functions closely related to male fertility. Overall, our results contribute to the identification of genomic regions and pathways underlying sire fertility in Jersey cattle, which may point out new strategies for improving service sire fertility via marker-assisted selection.

Key Words: bull fertility, gene set analysis, whole-genome scan