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

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 cows[1]

Trait	Ketosis	Metritis	Mastitis	Retained placenta
Ketosis	**0.07**	0.27	0.00	0.05
Metritis	0.16	**0.08**	0.03	0.10
Mastitis	0.00	0.01	**0.05**	0.01
Retained placenta	0.06	0.14	0.01	**0.06**

[1]All standard errors were < 0.01.

Key Words: ketosis, metritis, mastitis

57 Gene mapping and gene-set analysis for milk fever in Holstein dairy cattle. H. A. Pacheco[1,2], A. Sigdel[1], C. K. Mak[1], K. N. Galvão[1], L. T. Dias[2], and F. Peñagaricano*[1], [1]*University of Florida, Gainesville, FL,* [2]*Federal 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 *NCS1*. 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 resistance to clinical mastitis in US Holstein cattle. J. B. Cole*[1], K. L. P. Gaddis[2], C. Willard[1], D. J. Null[1], C. Maltecca[3], and J. S. Clay[4], [1]*Animal Genomics and Improvement Laboratory, ARS, USDA, Beltsville, MD,* [2]*Council on Dairy Cattle Breeding, Bowie, MD,* [3]*Department of Animal Science, College of Agriculture and Life Sciences, North Carolina State University, Raleigh, NC,* [4]*Dairy 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 $\leq 5 \times 10^{-8}$ 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 *ANGPT1* (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