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Gene Variants in Bola-Dmb, DECR1, Fasn and SREBF1 Associated with Conceptus Death on Day 16 of Pregnancy in Holstein Cows [Abstract]

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135 Gene Variants in Bola-Dmb, DECR1, Fasn and SREBF1 Associated with Conceptus Death on Day 16 of Pregnancy in Holstein Cows.

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Abstract: Investigating the influences of single nucleotide polymorphisms (SNP) associated with conceptus death (CD) on day 16 of pregnancy could distinguish cows who have inferior value for fertility traits. We hypothesized that CD is associated with SNP genotypes that disrupt maternal recognition and lead to early pregnancy loss. RNA sequences from Holstein cow pregnancies (n = 15) with normal conceptuses (Norm) or CD were subjected to SNP discovery via Qiagen CLC Genomics Workbench. Selected SNP were based on previous fertility studies, differentially expressed genes within pregnancy development analyses and proximity to SNP associated with fertility traits in the Cattle QTL Database. A second cohort of Holstein cows (n = 500) was used to conduct a validation and genotype to phenotype analysis of candidate SNP (cSNP) via DNA from blood samples and farm records. PLINK software was used to remove cows (n = 34) missing more than $\geq 20\%$ cSNP and remove cSNP with monomorphic alleles, minor allele frequency (MAF) $< 10\%$ and not in Hardy-Weinberg Equilibrium ($> 1e-15$). The GLM-one way ANOVA was used for all statistical models in SAS. Statistically significant models ($P < 0.05$) were further analyzed for LSMEANS, Bonferroni adjustment of P -values, additive allele effect and predicted effect of amino acid (aa) change on protein function via SIFT analyses tool in the Ensembl variant table (scoring 0-1.0; ≤ 0.05 being significant). Previously, we identified 69 cSNP on the RNA sequences of Norm or CD pregnancies from the initial group of Holstein cows and in proximity to ≥ 1 SNP associated with fertility traits from the Cattle QTL database. Quality control measures in PLINK reduced the number of Holstein cows in the second cohort to 466 and identified 4 cSNP associated with non-binary reproductive traits. Herein, we report an additional 4 cSNP discovered and validated with binary reproductive traits. The cSNP within

genes were associated with the following roles: BOLA-DMB (antigen loading in the immune system), DECR1 (lipid metabolism), FASN (reconstitution of body reserves during pregnancy) and SREBF1 (synthesis of fatty acids). Cows with T allele, in BOLA-DMB and SREBF1, were less likely ($P < 0.05$) to become pregnant ≤ 150 days in milk (DIM). For DECR1 and FASN, cows were less likely ($P < 0.05$) to become pregnant at 1st artificial insemination with C or A allele, respectively. Only the cSNP in SREBF1 had both an additive allele effect and a predicted effect of aa change on protein function. When cows had C allele, in the SREBF1 cSNP, there was 6% greater ($P < 0.01$) probability of becoming pregnant ≤ 150 DIM. While SIFT revealed the cSNP in SREBF1 have a predicted significant effect with a score of 0.03 for the aa change of proline/leucine. The reported cSNP, specifically those influenced by CD, add valuable information for the development of improved genetic tools for the dairy industry. USDA-NIFA#2019-07133.

Keywords: conceptus death, dairy cows, maternal recognition