

Genome-wide association studies on fertility and health traits in Holstein dairy cows

This study was carried out to identify genomic regions associated with reproductive traits in Holstein cows genotyped in Illumina Bovine HD SNP Chip (777,962 markers). A total of 2,505 cows were selected from 11,733 cows calving during the warm (WS: May-Aug) and cool (CS: Oct – Jan) seasons in 16 farms located in 4 regions (Northeast [4 herds], Midwest [6 herds], Southeast [1 herd], and the Southwest [5 herds]). 592,788 SNPs remained after removing those located on sex and mitochondrial chromosomes, without map position information, with call rate < 0.95, minor allele frequency < 0.01 and deviation from HWE ($p < 10^{-10}$). The following traits were analyzed: lameness, metritis, mastitis, resumption of cyclicity, pregnant on day 60 after first AI, and the reproductive index (IndexP60). GBLUP and Genome-wide association studies (GWAS) were performed using linear mixed model for IndexP60, and logistic mixed model for the others. The AI-REML algorithm was used to estimate the variance components and the marker effects were evaluated using the *score* test. Although the heritability for all these traits was low, some interesting peaks were found in the GWAS analysis (Table 1).

Table 1. Estimates of genetic variance (V_g), heritability (h^2) and number of significant SNPs using single marker regression mixed models in Holstein dairy cattle

Trait	V_g (s.e.)	h^2 (s.e.)	No. of sig. SNP (p -value<1e-5)	Genes
Lameness at 40 days in milk	0.103(0.029)	0.030(0.048)	21	RIMS2 and U6
Metritis	0.222(0.009)	0.063(0.026)	3	FHIT and OPCML
Mastitis	0.164(0.023)	0.047(0.042)	1	-
Resumption of cyclicity	0.248(0.009)	0.070(0.026)	5	STAC ABI3BP, FOXJ3, GC-201, NBEA, NPFFR2, SLC7A8 and TRIM71
Pregnant on day 60 after first AI	0.408(0.010)	0.110(0.024)	49	FOXJ3, GC, NPFFR2 and TRIM71
Reproductive index	0.002(0.000)	0.126(0.029)	38	NPFFR2 and TRIM71

Most of these significant markers have been associated to genes (ABI3BP, member 3 binding protein; FHIT, fragile histidine triad gene; FOXJ3, forkhead box J3; GC, vitamin D binding protein; NBEA, neurobeachin-like 2; NPFFR2, neuropeptide FF receptor 2; OPCML, opioid binding protein; RIMS2, regulating synaptic membrane exocytosis 2; SLC7A8, cationic amino acid transporter; STAC, SH3 and cysteine rich domain; TRIM71, tripartite motif-containing 71; and U6, spliceosomal RNA) described in *Bos taurus*. The chromosomal regions identified have confirmed several previous findings that may contribute to variation in fertility and health traits in dairy cattle.