Whole genome association analysis of resistance / susceptibility to paratuberculosis in French Holstein and Normande cattle

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The purpose of this study was to identify genomic regions associated with resistance / susceptibility to *Mycobacterium avium ssp. paratuberculosis* (*MAP*) infection in French Holstein and Normande cattle. A case-control genome-wide association study (GWAS) was performed. Cases were infected shedder cows (confirmed with both positive blood ELISA and positive PCR on feces) or clinical cases. The control population included only animals with three repeated negative blood ELISA, negative fecal PCR test and at least 72 months old. To limit exposure biases, the control animals were required to be born in the same herd and at the same time period as confirmed *MAP* positive cows (shedder or clinical). A total of 405 Normande (210 cases and 195 controls) and 989 Holstein (437 cases and 552 controls) cows were thus genotyped with the Illumina BovineSNP50 BeadChip (39,055 informative markers). GWAS was conducted within breed with GCTA software, accounting for the population structure through a 50K-based genomic relationship matrix.

The most significant region associated with infectious status was found on chromosome (BTA) 12 at 69.8 Mb (pvalue=2E-8) in Holstein cows. Another association was identified on BTA23 in the region of the major histocompatibility complex (MHC) in both Normande (27.8 Mb; pvalue=4E-5) and Holstein cows (25.6 Mb; pvalue=4E-6). Other chromosomal regions (pvalue < 7E-5) were found on BTA1 (55 Mb), BTA10 (91 Mb) and BTA13 (56.6 Mb) in Holstein and on BTA1 (92.6 Mb), BTA9 (39.3 Mb), BTA15 (58.4 Mb) and BTA17 (8 Mb) in Normande cows. Several additional regions were found with more moderate significance level (pvalue < 1E-4) in Normande (BTA13 and 25) and Holstein (BTA3, 9, 11, 25, 26 and 28) cows.

This on-going study presents encouraging results. Additional cases and controls will be collected and genotyped in 2016. In order to directly pinpoint candidate causal mutations, whole genome sequences of the cows will then be imputed using the 1000 bull genome reference population and GWAS will be carried out directly on whole genome sequence data.

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