Fine mapping of a QTL for mastitis resistance on OAR3 in Lacaune dairy sheep

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Genome-wide association analysis of resistance to paratuberculosis and mastitis in dairy sheep

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The aim of this study was to identify genomic regions that affect resistance to paratuberculosis (PTB) and mastitis in dairy sheep by using a genome-wide association analysis. The experimental population considered included 917 backcross Sarda × Lacaune ewes sired by 10 F1 rams and two generations of their descendants (1,497 ewes) that were sired by 33 Sarda rams. All animals were genotyped with the Illumina 50K BeadChip. Daily somatic cell count (SCC) was calculated as the arithmetic mean of a.m. and p.m. milking that were recorded bimonthly. Lactation Somatic Cell Score (LSCS) was calculated as the arithmetic mean of the log-transformed daily SCC. Blood samples of ewes were collected from 1 to 2 times per year and tested by ELISA for presence of antibodies against PTB. Two phenotypes were analyzed: the ewe's status (positive or negative) at 3 years of age, and the status when her entire productive life was considered. Yield deviations were analyzed by LD, LDLA and LA approaches by multiple regression of phenotypes on the probabilities of carrying the analyzed Sarda haplotypes. For LSCS, one region on OAR 4 and further 7 regions were 1% and 5% chromosome–wise significant respectively. For PTB, significant locations at 5% genome–wise threshold were found on OAR 14 and 20. Moreover, 1% chromosome–wise significant peaks were found on OAR 1, 6, 9, 10, 12, and 24. Further 8 regions were significant at the 5% chromosome-wise threshold. The most significant regions are being further investigated by whole genome re-sequencing of trios of animals in which the QTLs were expected to be segregating. These results are obtained through the EC-funded FP7 Project 3SR-245140.

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A QTL controlling somatic cell score (SCS), as the trait pertaining to mastitis resistance, has been previously detected on OAR3 in an association study of 1013 AI rams from a Lacaune grand-daughter design using the Illumina Ovine SNP50 chip. Linkage and linkage disequilibrium analyses showed very close localization with narrow confidence intervals (<2 Mb) around 130 Mb. The QTL explained 5% of the variance of the analyzed trait (DYD for SCS). Here we report validation and fine mapping for this QTL. The QTL was confirmed in an independent population of 117 Lacaune rams. SCS EBVs of rams carrying the most favorable phases were significantly higher (+0.82 standard deviation) than for rams carrying the most unfavorable phases. For further fine mapping, full sequencing, with a coverage of 12X, was performed in one trio of individuals. The trio included a segregating sire (Qq), and two sons of extreme divergent phenotype suspected to be homozygous for alternative alleles of the QTL (QQ and qq). Among a total of 1543 SNPs found in a region of 0.5 MB, one SNP mapped to a coding region of a highly conserved functional candidate gene with a non-synonymous change in one amino acid. A KASPar™ test was implemented to genotype 614 Lacaune sheep in the discovery population for the potential causal mutation. The frequency of the mutation was 20.6% and highly significant correlation with SCS EBVs was confirmed. Altogether these results provided good evidence for the identification of a causal mutation controlling SCC in sheep milk. Further functional assays should reinforce the hypothesis and allow characterizing the effect of the mutation on the mastitis resistance trait. This work was funded through the EC-FP7 '3SR'project (no. 245140) with the support of the French 'Roquefort'in' project.

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