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Genomics for Animal Health: Outlook for the Future

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Gene expression profiling in divergent lines of sheep for enhanced insight into genetic resistance to mastitis

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Amongst infectious diseases, mastitis is of major importance in dairy ruminants because of its high frequency and related costs. Accumulating literature data over the last decades gives strong evidence that dairy ruminant's ability to control udder health is under genetic control. Numerous studies have reported polygenic variation for phenotypic measurements of health status such as milk somatic cell counts (SCC) and clinical mastitis. Accordingly, in addition to prophylactic management, many countries have implemented SCC (or clinical mastitis) based selection programmes to improve resistance to mastitis. However genes and mechanisms involved in genetic control of the disease are still unknown. In the context of the EADGENE mastitis working group, the INRA team of Toulouse investigated the pathogen specific response to infection using gene expression profiling. We took advantage of an INRA dairy sheep model to address the genetic basis of the response. Indeed, using dams and progeny-tested rams selected for extreme breeding values for SCC, we previously managed to create two groups of ewes with a strong divergence in SCC of about 3σ . High and Low SCC lines of sheep exhibited decreased and enhanced resistance to intra-mammary infections, respectively. Gene expression profiling was applied to two major cell types, dendritic cells, neutrophils, using the 15K ovine Agilent oligonucleotide microarray. Neutrophils were collected in two groups of 6 resistant and 6 susceptible ewes, 12 hours after experimental challenge with *Staphylococcus* bacteria. Dendritic cells (DC) progenitors were collected from bone marrow and differentiated *in vitro* from 4 resistant and 4 susceptible sheep. DC were stimulated by heat-killed *Staphylococcus aureus* which promotes DC activation/maturation. Hybridisation with the Agilent chip was carried out at the Genopole of Toulouse, and gene by gene ANOVA based on linear models was applied to find differentially expressed gene between resistant and susceptible sheep. Fifteen genes were differentially expressed in neutrophils of resistant and susceptible sheep. Most of those genes were grouped in a unique network according to the Ingenuity Pathway Analysis. Among those genes, three were involved in neutrophil extravasation. Differential gene expression profiling in dendritic cells is in progress. A comparable study is planned on epithelial cells collected in resistant and susceptible sheep in collaboration with the INRA team of Pascal Rainard (IASP, Tours). Altogether, gene expression profiling in cells of High and Low SCC sheep shall contribute to enhanced insight into the genetic basis of the hosts' resistance to mastitis.

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QTL detection for chicken production and resistance to disease traits

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Recently, approaches targeting the whole genome (genome wide selection, GWS) have expanded. However, using an additive model without possible interaction (epistasis) between loci, in particular between the few QTLs which explain a large part of the genetic variance of the traits, would be likely to reduce the efficiency of this strategy. In chickens, coccidiosis susceptibility is an economically important trait which could make the most of GWS. Therefore, we proposed to search for QTLs affecting coccidiosis susceptibility, to test if the selection of this trait could have an impact on production traits and to estimate the extent of the epistasis for all these traits. QTL detection and epistasis estimation are performed on two INRA experimental crosses (900 and 1200 F2 animals phenotyped for coccidiosis susceptibility and composition traits, respectively) genotyped by 1536 SNPs covering most part of the genome. Our aim is to implement these results for MAS or GWS in commercial lines. These lines represent 10 families totalling 1,000 animals which will be genotyped for 384 SNPs targeting the regions identified in the experimental designs. The first results will be presented.

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