Abstract for Paper to be presented at WHFF 2023, Puy du Fou, France

November 21/22, 2023

Session **3. New trends and traits for the future**

    Paratubercolosis

    by **Marie-Pierre Sanchez**

Selection for resistance to paratuberculosis in Holstein cattle

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Abstract

Bovine paratuberculosis, also referred as Johne's disease (JD), is a contagious and incurable disease, caused by *Mycobacterium avium* subsp. *paratuberculosis* (MAP). After being contaminated *in utero* or more frequently via the intake of MAP-infected feces as a young calf, animals undergo a long latency phase that can last several years. Subclinical symptoms of JD are weight loss and reduced milk production together with an inconsistent humoral immune response and fecal shedding. Subclinical cases can therefore contaminate their environment. Clinical cases finally develop chronic diarrhea and severe emaciation, ending in death. JD, which has adverse effects on animal welfare and serious economic consequences, has no effective treatment and access to vaccines is restricted, it is therefore very difficult to control. Enhancing the genetic resistance of cattle could offer a viable strategy to combat this disease.

To address this issue, we conducted an extensive analysis to investigate the genetic determinism of resistance to JD in Holstein cattle and explore avenues to genetically improve the resistance of animals to MAP.

Leveraging serological data from cows in JD-affected herds in conjunction with genotyping data for genomic selection, we conducted different analyses. First, we performed genome-wide association studies (GWAS) on imputed whole genome sequences for a cohort of 4677 Holstein cows with known JD statuses. Subsequently, to estimate the accuracy of genomic

predictions, we applied a single step GBLUP, including candidate SNPs associated with JD resistance, to a pedigree of 161,253 Holstein animals, comprising 56,766 with serological phenotypic data and 12,431 with genotypic information.

Our findings revealed a moderate heritability value of 0.14 for JD resistance, while GWAS highlighted specific genomic regions on chromosomes 12, 13, 18, and 23 that exerted significant influence on resistance to paratuberculosis. Notably, we observed a slight favorable genetic trend indicating increased resistance to JD over the past two decades. Furthermore, our study yielded relatively reliable genomic predictions (reliability = 0.55) in a validation population, enabling the identification of high-risk cows susceptible to infection. In the same validation population, cows whose genomic predictions deviated by one genetic standard deviation from the mean displayed relative infection risks of 0.5 for those with lower predictions and 3 for those with higher predictions, when contrasted with the infection risk in average cows. These promising results suggest that genomic predictions hold the potential to be an effective tool for JD control in French Holstein cow farms.