Identification of genes and causal mutations affecting resistance to paratuberculosis in dairy cattle

Université Paris-Saclay, INRAE, AgroParisTech, GABI, 78350 Jouy-en-Josas, France

Genetics and Genomics Bovine team (G2B)

Desired profile
- Master 2 student
- Interest in genetics and statistics
- Good level in English

Durée / Localisation
- 6 months from January -March 2023
- INRAE, Jouy-en-Josas (78)

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Context

Bovine Genetics & Genomics (G2B) team associates INRAE, Institut de l'Elevage and Eliance (eBIS Joint Technology Unit) within the UMR GABI in the field of bovine genetics. The scientific interests of GABI concern the study of the structure and the function of animal genomes, the understanding of the determinism of complex traits (immunity and health, quality of products, differentiation and growth, adaptation) and the proposing of strategies for management, evaluation, improvement and valorization of animal genetic resources contributing to the development of innovative, competitive and sustainable production systems.

Topic

Paratuberculosis, or Johne's disease (**JD**), is a mycobacterial disease affecting ruminants. This disease has important economic consequences, especially in cattle, since it leads to a decrease in milk production, digestive disorders, severe weight loss and finally death. The risk of infection of the young calve in case of exposure is important. The disease has a long incubation period, so that infected animals are only clinically affected after several years. There is no approved treatment or vaccine. Work is being conducted in the G2B team to analyze the genetic determinism of susceptibility to JD and more particularly to identify genomic regions (QTL and potentially causal mutations) that affect resistance or susceptibility to the disease in the Holstein and Normande cattle breeds. After a first study conducted with 1600 Holstein and 600 Normande* cows, we now have at our disposal several thousands of Holstein and Normande animals, with a status for JD and genotypes (EuroGMD chip used for genomic selection).

The work of the internship will consist of several steps. The first step will be to prepare and select the data in the two breeds. The student will then perform imputations of genotypes to the sequence level and sequence-based genome wide association analyses (GWAS) in each of the Holstein and Normande breeds using the available phenotypes. A GWAS analysis combining both breeds (multi-breed analysis or meta-analysis) may also be performed. In some of

the identified regions, causal mutations could be better targeted via multi-marker or haplotypic analysis. Using available functional annotations (data produced in the G2B team or data available in public databases), candidate genes and candidate mutations will then be searched in QTL regions.

Ultimately, most relevant candidate mutations identified through these statistical and bioinformatic analyses can be validated by means of cell line-based functional assays. Thus, the student will participate in the development and execution of these experiments, which will aim at assessing the effect of these mutations on gene function in a targeted manner. The implementation of these assays will require the use of basic molecular biology techniques (PCR, RT-PCR, molecular cloning, mutagenesis) and cell culture techniques (maintenance of cell lines, transfection).

To do this work, the student will benefit from the experience and skills of the team in bioinformatics, quantitative genetics and molecular genetics.

* Sanchez M.-P., Guatteo R., Davergne A., Grohs C., Taussat S., Fritz S., Boussaha M., Blanquefort P., Delafosse A., Joly A., Schibler L., Fourichon C., Boichard D. 2020. Identification of the ABCC4, IER3, and CBFA2T2 candidate genes for resistance to paratuberculosis from sequence-based GWAS in Holstein and Normande dairy cattle. Genetics Selection Evolution 52:14. https://doi.org/10.1186/s12711-020-00535-9