Sequence-based GWAS, network and pathway analyses reveal genes co-associated with milk cheese-making properties and milk composition in Montbéliarde cows
Marie-Pierre Sanchez, Yuliasix Ramayo Caldas, Valérie Wolf, Cécile Laithier Cécile, Mohammed El Jabri, Alexis Michelet, Mekki Boussaha, Sébastien Taussat, Sebastien Fritz, Agnès Delacroix-Buchet, et al.

To cite this version:
Marie-Pierre Sanchez, Yuliasix Ramayo Caldas, Valérie Wolf, Cécile Laithier Cécile, Mohammed El Jabri, et al.. Sequence-based GWAS, network and pathway analyses reveal genes co-associated with milk cheese-making properties and milk composition in Montbéliarde cows. International Milk Genomics Consortium IMGC, Nov 2019, Aarhus, Denmark. hal-02737048

HAL Id: hal-02737048
https://hal.inrae.fr/hal-02737048
Submitted on 2 Jun 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L’archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.
Sequence-based GWAS, network and pathway analyses reveal genes co-associated with milk cheese-making properties and milk composition in Montbéliarde cows

Marie-Pierre Sanchez1*, Yuliaxis Ramayo-Caldas1, Valérie Wolf2, Cécile Laithier3, Mohammed El Jabri3, Alexis Michenet1,4, Mekki Boussaha5, Sébastien Taussat1,4, Sébastien Fritz1,4, Agnès Delacroix-Buchet1, Mickaël Brochard5, Didier Boichard1

1 GABI, INRA, AgroParisTech, Université Paris Saclay, F-78350 Jouy-en-Josas, France
2 Conseil Elevage 25-90, F-25640 Roulans, France
3 Institut de l’Elevage, F-75012 Paris, France
4 Allice, F-75012 Paris, France
5 Umotest, F-01250 Ceyzériat, France

Milk quality in dairy cattle is routinely assessed via analysis of mid-infrared (MIR) spectra; this approach can also be used to predict the milk’s cheese-making properties (CMPs) and composition. When this method of high-throughput phenotyping is combined with efficient imputations of whole genome sequence data from cows genotyping, it provides a unique and powerful framework with which to carry out genomic analyses. The goal of this study was to use this approach to identify genes and gene networks associated with milk CMPs and milk composition in the Montbéliarde breed.

Nine CMP traits (three measures of cheese yield, five coagulation traits, and milk pH) and contents of proteins, fatty acids, minerals, citrate, and lactose were predicted from MIR spectra in the From’MIR project. Phenotypes from primiparous Montbéliarde cows with at least three test-day records (1,506,037 test-day records from 194,934 cows) were adjusted for non-genetic effects and averaged per cow. 50K genotypes, available for a subset of 19,586 cows, were imputed in two steps: at the high density (HD) level using genotypes of 522 Montbéliard bulls and then, at the sequence level using Run6 of the 1000 Bull Genomes Project (comprising 2,333 animals including 54 Montbéliard bulls). The individual effects of more than 8.5 million variants, imputed with high accuracy, were evaluated in a genome-wide association study (GWAS) in a mixed model including a random polygenic effect estimated using a genomic relationship matrix calculated from HD genotypes. The results of the GWAS were then subjected to further analysis via an Association Weight Matrix and the Partial Correlation and Information Theory (AWM-PCIT) approach. This strategy led to the detection of 59 QTL regions, most of which had highly significant effects on CMPs and milk composition. From the GWAS results, we then identified a set of 736 co-associated genes. Among these, the well-known caseins, PAEP and DGAT1, together with dozens of other genes such as SLC37A1, ALPL, MGST1, SEL1L3, GPT, BRI3BP, SCD, GPAT4, FASN, and ANKH, explained from 12–30% of the phenotypic variance of CMP traits. We were further able to identify metabolic pathways (e.g., phosphate and phospholipid metabolism and inorganic anion transport) and key regulators, such as PPARA, ASXL3, and bta-mir-200c, that are functionally linked to milk composition.

By utilizing an approach that integrated GWAS with network and pathway analyses at the whole-genome sequence level, we were able to highlight co-associated candidate genes that are functionally linked to milk CMPs and composition. Here, we propose candidate variants that explain a substantial proportion of the phenotypic variance of CMP traits and which therefore could be included in genomic evaluation models to improve milk CMPs in Montbéliarde cows.

This study was funded by the French Ministry of Agriculture, Agro-food and Forest (CASDAR), the French Dairy Interbranch Organization (CNIEL), the Regional Union of Protected Designation cheeses of Franche-Comté (URFAC) and the Regional Council of Bourgogne- Franche-Comté, under the project From’MIR.