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HAL Id: hal-02792675
https://hal.inrae.fr/hal-02792675

PLANT & ANIMAL GENOME CONFERENCE XXIV

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Identification of Candidate Causal Variants Underlying QTL in Dairy Cattle through GWAS and Bayesian Approach at the Sequence Level

Date: Saturday, January 9, 2016
Time: 4:05 PM
Room: Golden West

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Combining large genotyped and phenotyped resource populations with whole genome sequence information opens new avenues to unravel candidate mutations underlying the genetic variability of the phenotypic traits. Reference populations for genomic selection are very large (more than 100,000 dairy animals with phenotypes and genotypes in France) and increase rapidly. As shown by the 1000 bull genomes project (1682 sequenced bulls in 2015), the number of sequenced bovine genomes also increases very fast and already makes it possible to impute the reference populations up to the sequence level, although rare alleles still have limited imputation accuracy. These populations sequenced in silico are unique resources for GWAS studies. Several strategies can be applied: first, each population can be analyzed by simple GWAS one marker at a time; results for the same trait but from multiple breeds can be combined in meta-analyses; multi-markers approaches can be implemented on targeted regions (1-3 Mb) in order to reduce the effect of long range linkage disequilibrium; haplotype analyses can be used to filter out genetic variants with inconsistent effects; finally, functional annotations help selecting the best candidates and interpreting their likely effects. Examples from the PhenoFinLait project are given, showing that QTL involved in milk protein or fatty acids composition can be characterized with a high confidence up to the gene and, frequently, up to a very limited number of candidate mutations. The authors acknowledge the financial support from ANR and APIS-GENE, and the contribution of the 1000 bull genomes consortium.

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