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Genome-wide association study of residual feed intake in Hereford cattle

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Introduction

Residual Feed Intake (RFI) is a commonly used measure of feed efficiency in cattle, which is independent from body weight and growth (Koch et al., 1963). The availably of phenotypic, pedigree and whole-genome genotyping data provides a unique framework for genomic studies, such as genome-wide association studies (GWAS) which have revealed many putative functional genes and pathways for relevant traits in cattle (Taussat et al., 2020, Brunes et al., 2021). The aim of this study was to detect genomic regions and putative candidate genes associated with RFI in Hereford cattle by single-step GWAS (ssGWAS).

Materials and methods

Feed intake data of 1623 Canadian and 1108 Uruguayan Hereford bulls and steers were included in this study. They were recorded in post-weaning tests of 70 days, after 28 days of acclimatization to diet and feeding system, using an automated feeding system. The estimation of RFI, measured as the difference between actual and expected feed intake based on the average daily gain, fat depth and metabolic weight, is described by Ravagnolo et al. (2018). The binational pedigree file included 7068 animals and 2603 genotypes, which were imputed to an Illumina 50k array from four different panels, keeping 52.890 single nucleotide polymorphism (SNP) after quality controls. Methodology and model used for the prediction of Genomic Estimated Breeding Values (GEBV) are also detailed by Ravagnolo et al. (2018).
The SNPs effects were calculated from GEBV and used for the calculation of percentage of variance explained by them based on ssGWAS proposed by Wang et al. (2012), using the BLUPF90 software adapted for genomic analysis (Misztal, 2017), combining pedigree and genomic information (Aguilar et al., 2010). Candidate genomic regions were identified using the genetic variance explained by 2.0 Mb windows of adjacent SNPs, and those explaining more than 0.5% of the genetic variance were analyzed. Relevant SNPs in the top 5% with the most significant effects were mapped with the latest bovine reference genome ARS-UCD 1.2 in a 15 kb (up- and downstream), to capture genes or regulatory regions for the functional genetics' analysis (Sigdel et al., 2021), using Bioconductor package biomaRT (Durink et al., 2005).

Results and Discussion

A significant pathway identified by the gene-set enrichment analysis was the *Thyroid hormone signaling pathway* (bta04919) with significant enriched terms involved in *thyroid hormone generation* (GO:0006590) and *thyroid hormone mediated signaling pathway* (GO:0002154), in agreement with GWAS results in French beef cattle for residual gain (Taussat et al., 2020) and maybe related to lipogenesis and lipolysis (Reyer et al., 2017). Another enriched pathway was the *vascular smooth muscle contraction* (bta04270) and *cardiac muscle contraction* (bta04260). Related GO terms enriched with these pathways were associated with cardiovascular structure and function (actomyosin, GO:0042641), actomyosin structure organization (GO:0031032), muscle cell differentiation (GO:0042692), cardiac muscle cell differentiation (GO:0055007), cardiac muscle hypertrophy in response to stress (GO:0014898). It has been reported that inefficient animals visit feed bunks more times than efficient animals (Guimaraes et al., 2017) leading to increasing cardiovascular overwork (Munro et al., 2019). Genomic regions explaining the highest proportions of RFI genetic variance were on BTA1, BTA4, BTA9, BTA17, BTA19 BTA23 and BTA27, which harbor putative genes (Figure 1). The complete list was analyzed for enriched GO terms for biological processes and the most significant were regulation of appetite (GO:0032098), feeding behavior (GO:0007631) and digestion (GO:0007586). Associated genes with these terms were PYY, PYY2 and PPY, where secretion of PYY regulates feeding behavior and satiety (Arora, 2006) as an important satiation-signaling peptide in the communication between gut microbiome and the central nervous system (Wang and Kasper, 2014). Thyroid hormone signaling pathway was related to the MED13L gene and Thyroid hormone receptor beta gene (THRB), both from BTA 27 identified in the top 5% SNPs list.

Conclusions

Significantly enriched signaling pathways associated with RFI were identified, as well as SNP variations and putative genes, that contribute to a better understanding of the genetic background of feed efficiency with potential benefits for genomic selection programs.

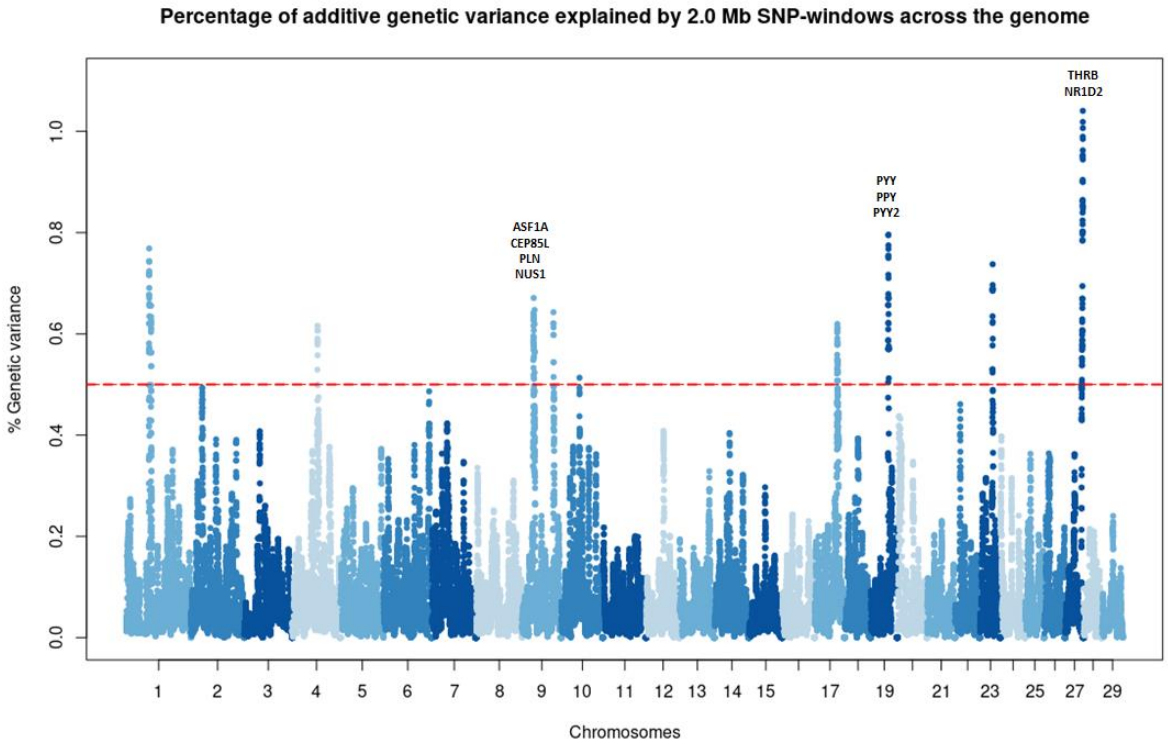

Figure 1: Manhattan plot for RFI in Hereford cattle. Each point represents the percentage of additive genetic variance explained by 2.0 Mb SNPs windows across the bovine genome.

Keywords: ssGWAS, feed efficiency, residual feed intake

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