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mQTL PROFILING IN PROGENY CALVES DERIVED FROM BULLS SUBJECTED TO GENETIC SELECTION FOR MEAT TENDERNESS

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I. INTRODUCTION

Beef tenderness is essential for consumer loyalty and repurchase decisions, being influenced by genetic and non-genetic factors. Despite advancements, there are still gaps in understanding the mechanisms that determine this trait throughout the animal's life. Expected Progeny Difference (EPD) has been used in genetic selection programs to identify bulls with favorable EPDs for tenderness, contributing to meat quality.

Genomics has enhanced the estimation of genetic values and enabled the identification of biomarkers associated with tenderness. However, prediction equations still show low accuracy and applicability. In this context, metabolomics emerges as a promising tool to deepen the understanding of phenotypes and, when integrated with genomics, can improve our comprehension of variability in meat tenderness.

Metabolic quantitative trait loci (mQTL) have already shown potential for studying complex diseases [3,4], but their application in animal production remains in its early stages, with no studies conducted on beef cattle or meat tenderness. This study is based on the hypothesis that selecting bulls based on EPD for tenderness influences the progeny's genome and metabolic profile. Thus, the objective is to integrate genomic and metabolomic data from Nelore calves, progeny of bulls selected for tenderness, using mQTL analysis to identify genomic regions associated with metabolic variations linked to meat tenderness.

II. MATERIALS AND METHODS

The experimental procedures followed the guidelines of the Institutional Animal Care Committee of FZEA/USP (9249180123). A total of 95 Nelore male calves, obtained through artificial insemination with semen from bulls of the same breed with EPDs for tenderness, were used. The animals were divided into two groups: Favorable for Tenderness (FT – 0,0997) and Unfavorable for Tenderness (UT – 0,0685). Blood samples were collected from the jugular vein at birth for metabolomic analyses, as previously described [1]. Nuclear magnetic resonance (1H-NMR) spectra were acquired following the methodology of [2] and processed using the Chenomx NMR Suite Professional software for metabolite identification and quantification.

Tail hair bulbs were used for genotyping with the Geneseek GGP Bos indicus 50K chip, imputed to the Illumina BovineHD® panel (777K) via Fimpute. Genotypes were established in GenomeStudio v2011.1, excluding SNPs with unknown genomic position, monomorphic markers, MAF < 0.05, located on sex chromosomes, call rate ≤ 95%, and $p \leq 10^{-6}$ for Hardy-Weinberg disequilibrium. Initially there were 51976 SNPs, after all the filtering steps 41609 in the FT group and 41614 in the UT group. The metabolome data was normalized using “scale” function in R v4.4.0. The mQTL analysis was conducted in R (v4.4.0) using the Matrix eQTL package v2.3.

III. RESULTS AND DISCUSSION

The Manhattan plots represent the mQTL analysis, indicating associations between genetic variants (SNPs) and specific metabolites. After the mQTL analysis, the SNPs and metabolites associated in the favorable EPD group were mannose (FDR = 2.986×10^{-13}), succinate (FDR = 5.447×10^{-10}), 2-Hydroxybutyrate (FDR = 4.435×10^{-9}), tyrosine (FDR = 3.092×10^{-8}), threonine (FDR = 1.261×10^{-7}), and phenylalanine (FDR = 6.240×10^{-7}). In the unfavorable EPD group, the associated metabolites were pyruvate (FDR = 4.635×10^{-8}), 2-Hydroxybutyrate (FDR = 7.531×10^{-8}), glutamine (FDR = 1.212×10^{-7}), and creatinine (FDR = 1.661×10^{-7}).

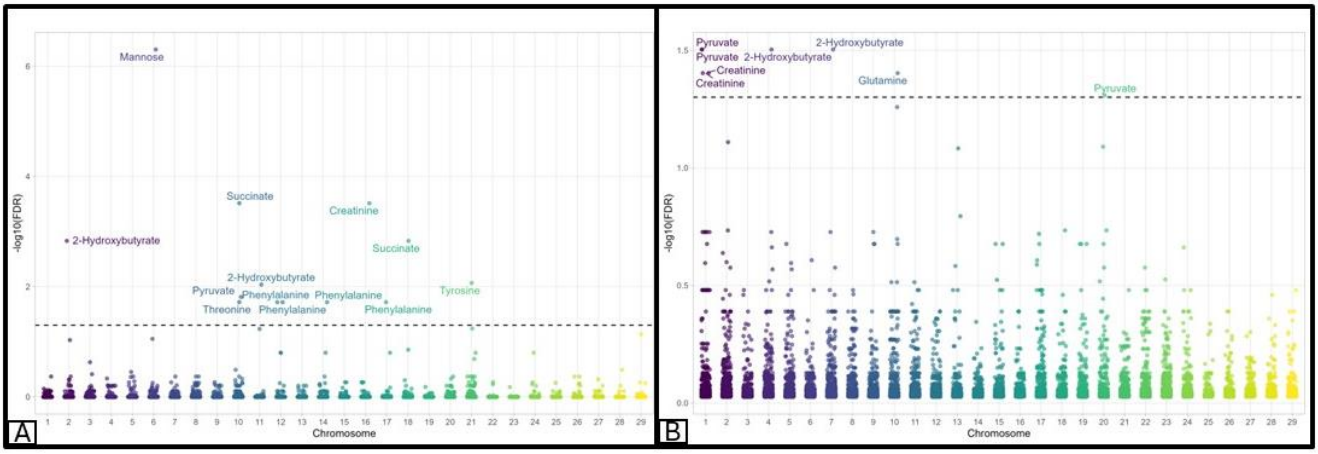


Figure 1. Manhattan plot showing the associations between metabolites and SNPs across treatments. A) FT. B) UT.

In the FT group, the metabolites are distributed across different chromosomes, suggesting that multiple genomic regions may be involved in their metabolism. The most significant SNP is located on chromosome 6, associated with Mannose, indicating a potentially relevant genomic region for carbohydrate metabolism. In the UT group, significance values are lower than in Graph A, suggesting weaker associations. Mannose showed the most significant association on chromosome 6 in the FT, reinforcing the genetic influence on its metabolism. 2-hydroxybutyrate was found in both groups, but on different chromosomes, which may indicate sire selection. Succinate (chromosomes 10 and 15 in FT) and creatinine (chromosomes 16 in FT, and chromosomes 1 in UT) suggest genetic influence on energy and muscle metabolism. Meanwhile, phenylalanine, tyrosine, and threonine showed associations across multiple chromosomes in FT, indicating an impact on protein synthesis and muscle metabolism.

CONCLUSION

The mQTL analysis revealed clear differences in SNP-metabolite associations between the favorable and unfavorable tenderness EPD groups, suggesting a potential genotype-environment interaction. Metabolites such as mannose and succinate were associated only in the favorable group, while pyruvate and glutamine appeared in the unfavorable group, indicating that genetic regulation of metabolism may differ according to genetic background. The presence of 2-hydroxybutyrate in both groups, but linked to different chromosomes, further supports the influence of sire selection. These findings suggest that specific genomic regions affect metabolism differently depending on the genetic potential for tenderness, which could help improve selection strategies.

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