DIFFERENTIAL ALLELIC EXPRESSION AND CO-EXPRESSION REVEALED OXIDATIVE STRESS-DEPENDENT PROTEOLYSIS AS A KEY REGULATOR OF NELORE BEEF TENDERNESS

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Abstract:

The Nelore *(Bos indicus)* cattle is the most important breed in the Brazilian bovine herd. Despite being more thermotolerant and resistant to parasites, Nelore animals produce less tender beef than other cattle breeds. In the search for variants with applicability for meat quality improvement approaches, it is possible to use transcribed heterozygous single nucleotide polymorphisms (SNPs) to detect allele-specific expression (ASE), a pattern resulting from *cis*-regulation. Recently ASE was reported in bovine muscle, but the knowledge about its relationship with economically important phenotypes for livestock is limited. In this study, we associated the ASE pattern to the phenotypes by using previously reported Genomic Estimated Breeding Values (GEBVs) for 55 muscle-related traits, RNA-seq, and genotype imputation data from a Nelore population (N=190). For each trait, the animals were grouped in two contrasting unrelated sample sets (N=20) with the most divergent GEBV, classified as *Low* and *High*. To identify differential ASE SNPs regarding the phenotype, we used a beta-binomial model to compare the allelic ratio of an SNP between the two contrasting groups. We carried out a co-expression analysis from all genes containing significant SNPs using the CEMITool software. Further, we performed a gene enrichment analysis to identify the underlying biological processes. Considering all the traits, we identified 1,479 differential ASE SNPs. The corresponding genes showed a co-expression module enriched for the protein ubiquitination process, required for proteasome degradation and beef tenderness. The *UQCR11* and *NDUFA5* genes, coding to proteins belonging to the electron transport chain, were hub genes of the co-expression analysis and showed differential ASE SNPs related to fatty acid composition traits. Fatty acids are known to affect mitochondrial membrane permeability and cytochrome complexes. *UQCR11* encodes to the subunit 10 of the mitochondrial cytochrome b-c1 complex and has a role in a proteolytic process related to meat tenderization under oxidative stress, highlighting the potential relationship between mitochondrial energy metabolism, fatty acids, and tenderness. Shear force measured 24h after slaughter (WBSF0) was the trait with more significant results, with 73 differential ASE SNPs. We performed a gene set enrichment analysis for this trait, observing if the co-expression modules were induced or repressed in the contrasting groups for the WBSF0 trait. Two modules showed opposite effects, being the genes of the "M1" module showing upregulation in the *Low* WBSF0 group (tender samples) and the genes of the "M2" module showing upregulation in the *High* WBSF0 group (tougher samples). *UQCR11* is a hub gene of "M1" related to oxidative stress-dependent proteolysis. Hub genes of "M2" were related to myogenesis and growth traits. Integration with previously described epigenetics and predicted regulatory data of this population indicated that differential ASE SNPs were located in functional regions and close to variants associated with gene expression. These findings suggest the impact of *cis*-regulatory variants on both the gene expression and phenotypic variation of Nelore muscle. These results can guide the investigation of regulatory variants affecting the expression of candidate genes for animal breeding, focusing on the genomic regions that affect the phenotypes of interest.

Palavras-chave: beef; genomics; epigenetics; ;

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