Bioinformatics analyses to characterize how proteome regulates metabolome and its impact on muscle-specific fresh beef color stability

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Introduction: Proteomic and metabolomic approaches have been utilized to examine the molecular basis for muscle-specific differences in fresh beef color stability (Joseph et al., 2012; Abraham et al., 2017). Physiologically, proteins regulate the formation of metabolites and thus govern the ultimate phenotypical changes in cells and tissues. The application of bioinformatics tools allows researchers to understand the interactive nature of metabolites and proteins. Integrative methods that discovers significantly enriched pathways across multiple omics datasets, while using statistical data fusion and heightening associated genes and compounds, are currently employed. However, limited research has utilized the combination of metabolomic and proteomic approaches to elucidate the interactive basis for muscle-specificity in color stability of beef Longissimus lumborum (LL) and Psoas major (PM) muscles. The objective of the current study was to integrate datasets of published differentially abundant metabolites and proteins in beef LL and PM muscles from our laboratories to identify any variances in the interactive molecular basis for muscle-specific color stability.

Methods: A web-based search was conducted on publicly available peer-reviewed research on color stability of LL (color stable) and PM (color labile) muscles with keywords USDA Choice/Select grade, proteomics, metabolomics, LL, and PM. A total of two previous publications that determined the molecular basis of differential color stability in LL and PM (Joseph et al., 2012; Abraham et al., 2017) met the search criteria and were utilized for interactive bioinformatics analyses. The list of differentially abundant metabolites in LL and PM identified by Abraham et al. (2017) were converted to their corresponding compound identities using the KEGG compound database, while the accession numbers of the differentially abundant proteins identified by Joseph et al. (2012) were converted to their corresponding gene identities using the g:Profiler web server gene ID conversion tool using Bos taurus as the target organism and Entrezgene as the target namespace. The integrated enrichment pathways and metabolite-protein network analysis were performed on the list of the annotated differentially abundant metabolites and proteins in LL and PM muscles using MetaboAnalyst V.5.0 joint pathway enrichment and network analysis platforms under default settings.

Results: The interactive metabolite-protein pathway enrichment analysis showed enrichment for glycolysis and gluconeogenesis (pathway impact > 0.65, $P < 0.01$), citric acid cycle (pathway impact > 0.56, $P < 0.01$), and the pentose phosphate (Pathway impact >0.54, $P < 0.01$) pathways. The metabolite-protein pathway network analysis showed that within the enriched pathways, the up-regulated proteins in LL including pyruvate dehydrogenase (PDHX), enolase (ENO3), triose phosphate isomerase 1(TPI1), and aldo-keto reductase family member A1(AKRA1) exhibited interaction with up-regulated metabolites in LL involved in glycogen metabolism such as glucose-6-phosphate, fructose-6-phosphate, and pyruvic acid. While the down-regulated protein aconitase hydratase and mitochondrial (ACO2) in LL exhibited interaction only with citric acid. This, in part, might explain the observed decrease in abundance of citric acid in LL compared with PM. However, the overabundant antioxidant and chaperon proteins (HSPB1, HSPA1B, and PDX2) associated with color stability in LL muscles did not show any interactions with the differentially abundant metabolites. Thus, these results confirm that the variation in energy metabolism pathways between LL and PM muscles could contribute to muscle-specific differences in beef color stability.

Conclusion: Bioinformatics analyses revealed the interactive role of metabolites and proteins in the up-regulation of glycolytic metabolism in beef LL. Thus, integrating multiple omics datasets can provide a better understanding of the interactive basis for muscle-specific color stability of fresh beef.

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Literature:

Abraham A. & Dillwith J. W. & Mafi G. G. & VanOverbeke D. L. & Ramanathan R., (2017) "Metabolite Profile Differences between Beef Longissimus and Psoas Muscles during Display", Meat and Muscle Biology 1(1).

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