Gene co-expression networks from RNA sequencing of dairy cattle identifies genes and pathways affecting feed efficiency - DTU Orbit (14/03/2019)

**Gene co-expression networks from RNA sequencing of dairy cattle identifies genes and pathways affecting feed efficiency**

**Background:** Selection for feed efficiency is crucial for overall profitability and sustainability in dairy cattle production. Key regulator genes and genetic markers derived from co-expression networks underlying feed efficiency could be included in the genomic selection of the best cows. The present study identified co-expression networks associated with high and low feed efficiency and their regulator genes in Danish Holstein and Jersey cows. RNA-sequencing data from Holstein and Jersey cows with high and low residual feed intake (RFI) and treated with two diets (low and high concentrate) were used. Approximately 26 million and 25 million pair reads were mapped to bovine reference genome for Jersey and Holstein breed, respectively. Subsequently, the gene count expressions data were analysed using a Weighted Gene Co-expression Network Analysis (WGCNA) approach. Functional enrichment analysis from Ingenuity® Pathway Analysis (IPA®), ClueGO application and STRING of these modules was performed to identify relevant biological pathways and regulatory genes. Results: WGCNA identified two groups of co-expressed genes (modules) significantly associated with RFI and one module significantly associated with diet. In Holstein cows, the salmon module with module trait relationship (MTR) = 0.7 and the top upstream regulators ATP7B were involved in cholesterol biosynthesis, steroid biosynthesis, lipid biosynthesis and fatty acid metabolism. The magenta module has been significantly associated (MTR = 0.51) with the treatment diet involved in the triglyceride homeostasis. In Jersey cows, the lightsteelblue1 (MTR = − 0.57) module controlled by IFNG and IL10RA was involved in the positive regulation of interferon-gamma production, lymphocyte differentiation, natural killer cell-mediated cytotoxicity and primary immunodeficiency. Conclusion: The present study provides new information on the biological functions in liver that are potentially involved in controlling feed efficiency. The hub genes and upstream regulators (ATP7b, IFNG and IL10RA) involved in these functions are potential candidate genes for the development of new biomarkers. However, the hub genes, upstream regulators and pathways involved in the co-expressed networks were different in both breeds. Hence, additional studies are required to investigate and confirm these findings prior to their use as candidate genes.

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