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SYSTEM BIOLOGY APPROACH TO DETECT AND ASSIGN BIOLOGICAL FUNCTIONS AND REGULATOR GENES TO FEED EFFICIENCY TRAITS IN NELLORE CATTLE

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Feed efficiency (FE) is important for livestock production not only for its impact on productivity and profitability, but also for reducing the environmental impact of food production. Residual intake and body weight gain (RIG) is one of feed efficiency traits. Measuring animal's individual RIG for a determined period of time is an onerous and time consuming task for breeding programs. To overcome this issue, previous studies reported several genomic regions associated with this phenotype that could be used to select superior animals. However, genomic markers alone are not necessarily the cause of the phenotypic alteration and therefore cannot clearly elucidate the mechanisms involved in regulation of the trait. The objective of this study was to use a system biology approach to identify biological mechanisms involved on FE in Nellore (*Bos indicus*) cattle and its possible regulator genes. For this purpose, 98 Nellore bulls were tested in a 70-d feeding trial and liver biopsies were collected from the top and bottom 8 animals, ranked by RIG. RNA was extracted from samples and an average of 27.7 million paired-end 100bp reads were sequenced per sample in Illumina® platform. After quality control and alignment to bovine reference genome, reads were normalized by FPKM and used to create a weighted co-expression network using WGCNA R package. Two modules of co-expressed and highly inter-connected genes correlated to feed efficiency were identified and named Brown and Grey. A modular enrichment analysis was performed on *GeneCoDis* to assign the main biological function to each module. Brown module is composed of 155 genes and its main function is related with protein synthesis as many of the genes are structural constituents of ribosome. Protein turnover in animals is an energetically expensive process and it was already demonstrated that greater protein turnover is associated with low FE animals. Grey module is composed of 34 genes. It presented no results in modular enrichment analysis but for singular enrichment analysis of GO terms it was most significantly associated with protein transport, regulation of cell proliferation, positive regulation of apoptotic process, heme binding and extracellular matrix. Gene regulators for the two modules were assigned using Lemon-tree algorithms. *FOXS1* and *RAMP3* were identified as regulators of a 25-genes cluster belonging to Brown module and *ZNF274*, *HPCAL1* and *HTRA2* are regulators of the same number of genes in Grey module. Using a system biology approach we identified important biological functions associated with FE. Hub genes in both modules and their regulators are candidate genes for feed efficiency in Nellore cattle that could be used in animal selection.

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