Transcriptomic and MicroRNA Analyses Identify Gene Networks Regulated by Eicosapentaenoic Acid in Brown Adipose Tissue from Diet-Induced Obese Mice

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Brown adipose tissue (BAT) dissipates chemical energy as heat and protects against obesity by increasing energy expenditure. In this study, we used RNA sequencing (RNA-Seq) and microRNA (miRNA) profiling, as powerful methods to identify novel regulators of BAT transcriptome. These techniques were applied on BAT from C57BL/6J mice fed either a high fat diet (HF, 45% kcal fat) or HF diet supplemented with EPA (HF-EPA containing 36g EPA/kg diet) for 11 weeks. RNA sequencing was performed using Illumina Hi-Seq and 831 genes were identified that were differentially expressed (95% confidence and $p<0.05$) in BAT from HF compared to HF-EPA fed mice. HF-EPA had significantly higher expression of genes in fatty acid oxidation and thermogenesis such as peroxisome proliferator-activated receptor-α (Ppar-α), retinoid X receptor (Rxr), phosphatase and tensin homolog (Pten) and reduced expression of inflammatory genes such as nuclear factor kappa-light-chain-enhancer of activated B cells (Nf-κb), and Tumor necrosis factor receptor 1 (Tnfr1). Moreover, miRNA profiling identified nine upregulated miRNAs and six downregulated miRNAs by EPA respectively. MiRNAs identified including miR-455-3 and miR-150-5p are key regulators of BAT thermogenic function. In summary, combining RNA-Seq and miRNA profiling help to identify novel biomarkers mediating nutritional regulation of thermogenesis.

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