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Systematic metabolomic analysis of eicosanoids after omega-3 poly-unsaturated fatty acid supplementation by a high-specific LC-MS/MS–based method

Xu Zhang[1,2], **Nan Yang**[2], **Ding Ai**[3] and **Yi Zhu**[2,3]
[1]Tianjin Medical University, China
[2]Peking University Health Science Center, China

Omega-3 poly unsaturated fatty acids (PUFAs) have beneficial effects in many pathological processes, especially cardiovascular disease, and their protective eicosanoid metabolites are thought to play important roles. However, how omega-3 PUFAs affect the eicosanoid profile has not been elucidated comprehensively. Here, we systematically analyzed the eicosanoid metabolites induced by omega-3 PUFA supplementation. We developed an LC-MS/MS–based method covering 32 arachidonic acid (ARA) metabolites and 37 omega-3 PUFA-derived products. The limits of detection for eicosanoids were between 0.0625 and 1 pg and the detection specificity was optimized. We then quantified eicosanoids in mouse and human plasma and mouse aorta samples after omega-3 PUFA supplementation. Levels of EPA hydroxyl products, 4-HDoHE, 17,18-EEQ, 17,18-DiHETE, TXB2, and LXA4 were significantly changed in both mouse samples, and that of 2-series PGs, EDPs and DHA hydroxyl products were changed in aorta samples. Correlation network analysis of mouse plasma data revealed that some eicosanoids were more important than others after omega-3 PUFA induction. Eicosanoids in human plasma were profiled across 5-time points after omega-3 PUFA supplementation. Fuzzy c-mean clustering algorithm suggested that the time curves of eicosanoid activity could be described with 3 kinetic patterns: sustained upregulation, short-term upregulation and downregulation. This is the first systematic profiling of eicosanoids with omega-3 PUFA induction. The highly specific eicosanoid metabolomic and related data analysis methods would be powerful tools for comprehensive eicosanoid study.

zhuyi@tijmu.edu.cn