Lipidomics and proteomics to understand the health benefits of marine fish oil enriched diets

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The consumption of ω-3 marine lipids, EPA and DHA, may potentially modulate inflammation and oxidative stress that are involved in the development of CVD and type-2 diabetes. However, despite the growing evidence of the health benefits of ω-3 supplements, there is a lack of evidence about the right amounts of EPA vs DHA and no agreement about a recommended proportion of EPA and DHA in the diet has been still achieved. In this study, novel lipidomic and proteomic approaches have been developed to determine lipid biomarkers of oxidative stress and inflammation in plasma and to evaluate liver protein carbonylation.

**Metabolomics**

These lipid metabolites (Fig.1) are involved in the progress and regulation of many inflammatory processes, metabolic conditions and oxidative stress. Our aim was to develop a robust and sensitive analytical platform based on SPE-LC-ESI-IT-MS/MS to analyze a wide range of different pro/anti-inflammatory compounds. This methodology was applied to determine these lipid biomarkers in rats from a dietary study focused on the determination of the optimal EPA:DHA ratio in diet to reduce oxidative stress and inflammation processes.

**Proteomics**

Liver protein oxidation was quantified by labeling carbonyl residues in vivo-generated with FTSC-tag (Fig. 3) and measuring fluorescence signal on gel-electrophoresis. Carbonylated proteins were identified by tandem mass spectrometry (LC-ESI-IT-MS/MS) after prefractionation by 2D-gels.

**Fig. 1: Targeted eicosanoids and docosanoids**

**METHODOLOGY OPTIMIZATION**

Results (Fig.2) suggested a down-regulation of strong pro-inflammatory eicosanoids when dietary amounts of EPA and DHA were balanced. These results, together with the protective effect of these diets against protein oxidation, shed light about the different influence of EPA and DHA promoting an anti-oxidant environment that leads to lower oxidative stress and inflammation in vivo.

**Fig. 2: Levels of lipid mediators produced by the studied diets**

The fish oil supplementations decreased protein carbonylation levels (Fig. 4), being the EPA:DHA 1:1 ratio the most effective one. Additionally, our proteomics method allowed to identify specific protein targets of the health effect of EPA and DHA supplementations (albumin, argininosuccinate synthetase, 3-α-hydroxysteroid dehydrogenase, aspartate aminotransferase, actin).

The combination of lipidomics and proteomics approaches provides complementary information, extremely useful for nutritional analysis. Results contributed to the general knowledge of marine lipid benefits and the importance of specific dietary designs to potentiate these health benefits.

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