Modulation of Specific mRNAs by Serum n-3 and n-6 Fatty Acids

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Nutritional status, particularly fat and energy intake, can affect serum composition and both are linked to incidence of diseases such as obesity, diabetes and cardiovascular diseases. To identify some possible mechanism underlying the molecular basis of these associations, we previously investigated the effect of the direct addition to cultured human hepatoma cells (HepG2) of serum samples from hypercholesterolemic and normocolesterolemic male individuals. Since nutrition is the commonest cause of hypercholesterolemia, we assumed it as the original cause differentiating patients. HepG2 gene expression profiles were evaluated by DNA microarray analysis. We considered the most regulated genes comparing cells treated with hypercholesterolemic sera versus cells treated with normocolesterolemic sera and their involvement in metabolic pathways. To correlate observed modulations to specific serum components, we analyzed the effect of polyunsaturated fatty acids docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA) and arachidonic acid (AA), and of saturated fatty acid stearic acid (SA), since polyunsaturated fatty acids resulted in higher concentrations in serum samples of hypercholesterolemic subjects. These nutrient molecules are important components of serum lipids, associated with dietary behavior and incidence of dyslipidemic diseases. Results show significant regulations of HMGCS2, GSTA1, LEAP2, ApoM (NLM codes) mRNAs after DHA, EPA and AA treatment while SA did not affect these genes. 22(R)-hydroxycholesterol, as cholesterol analogue, did not show any effect, indicating that observed differences were not due to cholesterolemia. Data indicate that several differential gene expression modulations due to serum samples from patient with different nutritional and lipemic status, could be also produced by polyunsaturated fatty acids.