“Nutritional strategies in the prevention and treatment of nonalcoholic fatty liver disease (NAFDL) related to visceral obesity.”

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Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in western world (20-30% of general population). Non alcoholic steatohepatitis development is a complex process not completely understood. Its etiology is believed to be multi-factorial with a genetic, dietetic and environment component. NAFLD is associated with visceral obesity, cardiovascular risk factors, and other components of metabolic syndrome (hypertension, dyslipidemia, diabetes, insulin resistance (IR)). In primary NAFLD, IR plays a key role in its pathogenesis. IR leads to hyperglycemia and consequent hyperinsulinemia, which stimulates lipid-accumulation in different tissues including the liver. Indeed, IR increases plasma non-esterified fatty acids (NEFAs) released from adipose tissue and their uptake by the liver. These changes result in abnormal hepatic fat accumulation, which may sustain the hepatic IR.

Dietary fatty acids may greatly influence positively both IR and hepatic lipid metabolism, by increasing their beta-oxidation in peroxisomes and mitochondria and interfering with formation of oxygenated eicosanoids and endocannabinoids. As a general effect, they may result in improved insulin sensitivity, adiposity repartition and hence reduction of ectopic fat in the liver.

Among different dietary fatty acids conjugated linoleic acid (CLA) and highly polyunsaturated fatty acids omega-3 (HPUFA omega-3) are good candidates. It has been shown that CLA and HPUFA omega-3 modulate peroxisomal and mitochondria beta-oxidation via PPARs and interfere with formation and incorporation into phospholipids of arachidonic acid, the substrate of pro-inflammatory eicosanoids and endocannabinoids, heavily implicated in both IR and NAFLD.
The aim of my project is to evaluate the impact of these dietary fatty acids on lipid metabolism in different tissues in relation to NAFLD as a consequence of visceral obesity, in both experimental models and humans. To quantify the impact on lipid metabolism we will employ a global approach with lipidomics, which consist of measurements of virtually all lipid molecules in that given tissue. These measurements will be carried out using different platforms: Gas chromatography, HPLC in normal and reverse phase with different detectors such as diode array and mass spectrometer. Data will be collected and analyzed by using several biostatistical methods, in order to make more evident the changes induced by the nutritional treatment on lipid metabolism.