Fatty Liver and Therapy

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Metabolic Phenotype Transfer Through Gut Microbiota Transplantation from HFD-Fed and Quercetin Treated Donors Modulates Obesity-Related NAFLD in Germ-Free Mice

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Background and Aims: Gut microbiota is involved in obesity, metabolic syndrome and nonalcoholic fatty liver disease (NAFLD). Strategies to modulate it, including faecal transplantation and administration of prebiotics as quercetin, are actively being examined. The present study aims to investigate benefits of experimental gut microbiota transfer from donors to germ-free mice (GFm) in a high-fat diet (HFD)-based NAFLD model.

Methods: GFm were colonised with gut microbiota from donors and fed with control or HFD for 16 weeks. Gut bacterial communities were identified pyrosequencing the 16S-rRNA from caecal samples of donors and GFm.

Results: Caecal microbiota donors were selected from control (C), HFD-fed (HFD- and HFD+, as non-responder and responder to the HFD, respectively) and control and HFD supplemented with quercetin (CQ and HFDQ) groups, according to obesity, metabolic syndrome, hepatic steatosis, endotoxemia, gut-liver axis alteration, inflammation and lipid metabolism deregulation. HFD- and HFDQ-receiver groups fed with HFD showed reduced body weight gain, NAFLD activity score, HOMA-IR and endotoxemia, with respect to other receivers, exhibiting similar results to C-receiver fed with control diet. HFD+ phenotype transfer was associated with increased NAS index and hepatic markers alteration in control diet-fed mice. The microbial composition at phylum level in donor mice was similar to their corresponding group, except HFD- and HFDQ, which showed an increase in *Firmicutes* and *Verrucomicrobia*, respectively. At the genus level, a higher detection of *Helicobacter* was observed in HFD+ *vs.* HFD- donor, while *Oscillospira*, *Lactobacillus* and *Alkaliphilus* exhibited an opposite pattern. Interestingly, a dramatically increase of *Akkermansia* was detected in HFDQ donor with respect the others. In C, CQ, HFD- and HFDQ-receivers when GFm were fed with HFD a notable increase in *Verrucomicrobia* was observed, which was undetectable in HFD+-receiver diet-independently. *Akkermansia* genus was increased in HFD- and HFDQ-receivers and undetected in HFD+-receiver. This different microbiota composition could be associated with the transfer of a complex metabolic phenotype with specific functionality in the receivers.

Conclusions: Our data support the role of phenotype transfer by intestinal microbiota transplantation on NAFLD development, sustaining its suitability as a therapeutic approach for obesity-associated NAFLD. Supported by BFU2013-48141-R, LE063U16 (JCyL and FEDER) and GRS 1428/A/16. CIBERehd is funded by ISCIII.

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Fatty Liver and Nutrition

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The Effect of Betaine on Hepatic Steatosis and Oxidative Stress Induced by High Fructose Containing Diet in Rats

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Background and Aims: High fructose (HFr) diet affects both glucose and lipid metabolism and results in several metabolic abnormalities such as insulin resistance, impaired glucose tolerance, hypertriglyceridemia and fatty liver. Although the pathogenesis of HFr-induced changes are not clearly known, oxidative stress is considered to be one of the key underlying mechanisms. Thus, the effect of several antioxidant compounds in HFr-fed animals has been of interest to many researchers. Betaine (BET; *trimethylglycine*) is a choline metabolite, which functions as an osmolite. It has antioxidant and hepatoprotective potency. Several investigators have reported that BET treatment is effective in alleviating hepatic lesions such as fatty liver, necrosis and fibrosis in animal models. Therefore, in this study, we investigated whether or not BET has any regressive effect on existing HFr-induced metabolic changes, including fatty liver.

Methods: Rats were treated with/without BET (10 g/L in drinking water) for 4 weeks after the cessation of HFr (60% fructose containing) diet-treatment for 8-week period and insulin resistance, lipids, oxidative stress and hepatic histopathology were investigated. Serum glucose, insulin, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) values were measured and homeostasis model assessment (HOMA) index was calculated. Total cholesterol and trygliceride (TG) levels were also assayed in both serum and hepatic tissue. To evaluate oxidative stress, malondialdehyde (MDA), diene con-