The severity of nonalcoholic fatty liver disease is associated with gut dysbiosis and shift in the metabolic function of the gut microbiota

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Résumé en anglais	Several animal studies have emphasized the role of gut microbiota in nonalcoholic fatty liver disease (NAFLD). However, data about gut dysbiosis in human NAFLD remain scarce in the literature, especially studies including the whole spectrum of NAFLD lesions. We aimed to evaluate the association between gut dysbiosis and severe NAFLD lesions, that is, nonalcoholic steatohepatitis (NASH) and fibrosis, in a well-characterized population of adult NAFLD. Fifty-seven patients with biopsy-proven NAFLD were enrolled. Taxonomic composition of gut microbiota was determined using 16S ribosomal RNA gene sequencing of stool samples. Thirty patients had F0/F1 fibrosis stage at liver biopsy (10 with NASH), and 27 patients had significant F≥2 fibrosis (25 with NASH). Bacteroides abundance was significantly increased in NASH and F≥2 patients, whereas Prevotella abundance was decreased. Ruminococcus abundance was significantly higher in F≥2 patients. By multivariate analysis, Bacteroides abundance was independently associated with NASH and Ruminococcus with F≥2 fibrosis. Stratification according to the abundance of these two bacteria generated three patient subgroups with increasing severity of NAFLD lesions. Based on imputed metagenomic profiles, Kyoto Encyclopedia of Genes and Genomes pathways significantly related to NASH and fibrosis F≥2 were mostly related to carbohydrate, lipid, and amino acid metabolism. CONCLUSION: NAFLD severity associates with gut dysbiosis and a shift in metabolic function of the gut microbiota. We identified Bacteroides as independently associated with NASH and Ruminococcus with significant fibrosis. Thus, gut microbiota analysis adds information to classical predictors of NAFLD severity and suggests novel metabolic targets for pre-/probiotics therapies.
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Liens

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