

## Two-month consumption of bread enriched with a fiber mix: impact on gut microbiota and cardiometabolic profile in at cardiometabolic-risk subjects.

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### Abstract

#### Introduction

Increased adiposity, dyslipidemia and insulin resistance are associated with increased risk of developing cardiometabolic diseases (CM). Such deleterious phenotypes have been shown to be associated with a low gene-richness microbiota that can partly be restored by a short-term dietary intervention (energy-restricted high-protein diet, low glycemic index, enrichment with fibers) in parallel to an improvement of CM profile. In this study, we aimed at increasing fiber intake in quantity and diversity through a two-month consumption of bread enriched with a mix of selected fibers and evaluated the impact of this dietary intervention on gut microbiota gene richness and CM risk profile in subjects at risk of developing CM.

#### Materials and methods

In a randomized double blind cross-over design, thirty-nine subjects with CM risk profile (18–70 years old, BMI: 25–35 kg/m<sup>2</sup>, waist circumference > 80 cm for women and > 96 cm for men, fiber intake < 20g/day, low fiber diversity) consumed daily for 8 weeks 150 g of standard bread vs. 150 g of bread enriched with a 7-selected fibers mix (5.55 g vs. 16.35 g of fiber respectively; 4-week washout). Gut microbiota and CM risk factors' analyzes were conducted before and after intervention. Stool samples were analyzed by shotgun metagenomics; microbial genes and metagenomics species (MSP) profiles were generated by mapping reads on a reference genes catalog (1529 MSP).

#### Results

The included dyslipidemic subjects with CM risk profile presented a lower microbiota gene richness compared to reference healthy cohorts. The two-month consumption of fiber-rich bread did not alter microbiota gene richness but modified microbiota composition with a significant decrease of *Bacteroides vulgatus* ( $q = 1.7e-4$ ) and a significant increase of *Parabacteroides distasonis* ( $q = 2.8e-6$ ), *Fusicatenibacter saccharivorans* ( $q = 5e-5$ ) and *Clostridiales* ( $q = 3.8e-2$ ). We observed in parallel a significant decrease in total cholesterol (- 0.26 mmol/L; - 5%;  $p = 0.021$ ), LDL-cholesterol (- 0.2 mmol/L; - 6%,  $p = 0.0061$ ) and an improvement of insulin sensibility estimated by HOMA index (3.23–2.54 mUI/L; - 21%;  $p = 0.0079$ ). These effects were even significantly more pronounced for subjects presenting the higher waist circumference. Anthropometric parameters were not altered.

#### Discussion

The enrichment of the diet with a mix of selected fibers for 2 months altered microbiota composition by modifying the relative abundance of specific gut bacterial species, in parallel to a significant improvement of cholesterol and insulin sensitivity parameters. Increasing the quantity and diversity of dietary fiber intake could be used as an efficient tool to favorably impact CM profile.

#### Conflict of Interest

This study was funded by Bridor. I.Dussous and L.Roger work for Bridor as an employee and consultant respectively. The remaining authors declare no conflict of interest.