Thesis project: "Nutritional modulation of intestinal microbiota by probiotics: impact in the development of obesity"

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Context of the Proposal:

The World Health Organization (WHO) has listed that 35 % of adult aged upper than 20 overweight and 400 million were obese in 2008 (1). In 2015, 2.3 billion and 700 million of adult were respectively overweight and obese. Eating habits have dramatically changed since the mid-20th century with an abundance of food and a progressive decrease in expenditure energy. These developments have led to diet high in fat, sugars and too low fiber playing a key role in the increased prevalence of chronic disease of nutritional origin, such as metabolic syndrome (obesity, diabetes,…), cardiovascular diseases, cancers and osteoporose. Besides, the eating disorders are often involved in the excess of feeding. These diseases are no longer limited to "rich countries", and now a growing public health problem in developing countries. The increase in the prevalence of metabolic disorders and associated diseases such as diabetes, obesity, is currently talking about an "epidemic", has resulted in a public awareness and strengthening of the fundamental research effort.
We know now that the microbial population in the gut is different between obese and lean people and that when the obese people lost weight their microflora reverted back to that observed in a lean people (2). This finding supports the concept of an involvement of bacteria in the gut in the management of energy metabolism. Indeed, the microbiota is able to regulate the storage of fatty acids and affect the recovery of energy from food. Indeed, some published data suggest that diet and/or probiotics can modulate markers of metabolic stress associated with overweight in mice (3). Moreover, experimental data have shown that administration of probiotics, indigestible food ingredients could target certain bacteria in the intestinal microbiota and decrease adiposity, fatty liver and glucose levels in different mice model of obesity (4) (5). So, the manipulation of the composition of the microbial ecosystem in the gut might be a novel approach in the treatment of obesity. The mainly aim of our work is to develop a potential effect of probiotic strains on the reduction of weight and body fat.

Hypothesis:

The idea of modulating the composition and/or activity of the intestinal microbiota in order to influence positively the health of the host, is emerging as a new way of therapeutic development.
Does the probiotic treatment is able to counteract the deleterious effect of obesity development by the regulation of gut microbiota

Aims of the proposal:

To test the effect of oral administration of several probiotics strain on the dysregulation of the energetic metabolism in mice submitted to high fat diet. Once the probiotic selected for these properties to maintain weight, I will investigated the involvement of probiotics in the dialogue between the brain and the gut in order to develop probiotic ingredients acting in long-term on the satiety and weight management for subjects have difficulty to regulate their eating behavior.

Program of thesis:

Year 1: Evaluate the effect of several probiotics on the lipid metabolism and microbiota alteration induced by high fat diet.

Year 2: According to the result obtained in year 1, we will select the potential probiotic to maintain the body weight in obese mice and we will investigate the mechanism of action of probiotic on the energetic metabolism in the regulation of the eating behavior.

Year 3: articles and thesis redaction.

Knowledge and skills:
The candidate will have an initial training in physiology. Knowledge in nutrition and metabolism will appreciate. An essential skill is handing rodents with samples collected and optionally surgery. Training in animal experimentation will be provides by the university of Toulouse.

References:
1. WHO source: *http://www.who.int/en/*

2. Microbial ecology: human gut microbes associated with obesity Ley et al. Nature 2006; 444(7122): 1022-1023.

3. Antiobesity and lipid-lowering effects of Bifidobacterium spp. in high fat diet-induced obese rats. An et al. Lipids Lipids Health Dis 2011; **10:**116.

4. Gut microbiota fermentation of prebiotics increases satietogenic and incretin gut peptide production with consequences for appetite sensation and glucose response after a meal. Cani et al. Am J Clin Nutr (2009); **90**(5): 1236-1243

5. The nonfermentable dietary fiber hydroxypropyl methylcellulose modulates intestinal microbiota. Cox et al. FASEB J (2013); **27**(2): 692-702.