Fattening Bacteria: New Insights into the Obesity Epidemics

A study of genetically obese mice reveals that their gut microbial community has a greater capacity for harvesting energy than the one of lean littermates [1]. Although the majority of mouse gut species are unique, mouse and human microbiota are similar at the division (super-kingdom) level, with *Firmicutes* and *Bacteroidetes* dominating [2]. Compared with lean mice, obese animals have a 50% reduction in the abundance of *Bacteroidetes* and a proportional increase in *Firmicutes*. These division-wide changes, indicate that, in this mouse model, obesity affects the diversity of the gut microbiota [2]. The relative abundance of the two predominant bacterial divisions (deep evolutionary lineages or super-kingdoms) in mice differs between lean and obese animals: genetically obese mice have 50% fewer *Bacteroidetes*, and correspondingly more *Firmicutes*, than their lean siblings [1]. To investigate the relation between gut microbial ecology and body fat in humans, the authors have studied 12 obese people, who were randomly assigned to either a fat-restricted or to a carbohydrate-restricted low calorie diet. Before diet therapy, obese people had fewer *Bacteroidetes* ($P<0.001$) and more *Firmicutes* ($P=0.002$) than did the lean controls. Over the time and irrespective of the diet type, the relative abundance of *Bacteroidetes* increased ($P<0.002$) [1]. The dynamic linkage between adiposity and gut microbial ecology described in both studies, among mice and humans, indicates that manipulation of gut microbial communities could be another approach in the treatment of the obesity epidemics that humanity is facing in the 21st century [1].

A team from the Washington University in St-Louis, Missouri (USA) performed microbiota transplantation experiments to test directly the notion that the obese microbiota has an increased capacity to harvest energy from the diet and to determine whether increased adiposity is a transmissible trait [3]. Adult-germ free mice were colonized (by gavage) with a microbiota harvested from the cæcum of obese or lean donors (one donor and 4-5 germ-free recipients per treatment group per experiment; two independent experiments). The obese donor microbiota had a greater relative abundance of *Firmicutes* compared with the lean donor microbiota. Furthermore the obese recipient microbiota had a significantly higher relative abundance of *Firmicutes* compared with the lean recipient microbiota [3]. Strikingly, the mice colonized with an obese microbiota exhibited a significantly greater percentage increase in body fat over two weeks than mice colonized with a lean microbiota. This finding provides support for the more general concept that the gut microbiome should be considered as a set of genetic factors that, together with host genotype and lifestyle (energy intake and expenditure), contribute to the pathophysiology of obesity [3].

Results indicate that, if the gut microbiome of obese humans is comparable to that of obese mice, then it may be a biomarker, a mediator and a new therapeutic target for people suffering from this increasingly worldwide disease [3]. One interesting possibility is that the rapidly rising incidence of insulin resistance (and related diseases) might be correlated with underlying dysbiosis [4]. More controversially, the root of this medical problem could be related to the increase in antibiotic use since World War II, as it is inconceivable that antibiotics have not exerted selection pressure on human commensal microorganisms in the same way that some microorganisms have developed antibiotic resistance [4]. The conclusion of these recent discoveries could be that the reckless and largely uncontrolled use of antibiotics might not only change human society through the increased risks associated with multiple antibiotic resistance, but also through irreversibly altering the symbiotic microbiome with which we have co-evolved [4].

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4. Nicholson, J.K., E. Holmes, and I.D. Wilson, *Gut microorganisms, mammalian metabolism and personalized health care.* Nat Rev Microbiol, 2005. **3**(5): p. 431-8.

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