

Intestinal Microbiota: A New Actor in the Fight Against Obesity?

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The human intestine contains over a thousand species of diverse microorganisms, collectively known as "intestinal microbiota", essential to the integrity of the mucosal barrier function. Alterations such as quantitative of microbiota (composed mainly of bacteria, viruses and fungi), which are able to alter this delicate balance, are involved in neurological and systemic diseases (among others, Ulcerative Colitis and Crohn's disease, irritable bowel syndrome, stomach and colon cancers, allergies and intolerances, diabetes, atherosclerosis, etc.). Laboratory and human studies also showed an interesting relationship between gut microbiota and obesity [1,2]. Obesity is a medical condition which affects a growing number of people, especially in Western countries. In the United States more than 50% of the population is overweight and about 1/3 is frankly obese. It is also a predisposing condition for a number of diseases that can seriously compromise the health of the individual. No doubt a high-calorie diet and lack of physical activity are the leading causes of obesity, but certainly fascinating is the study of the complex mechanisms involved in the regulation of energy balance and their alterations. In this regard, recent studies suggest that the gut microbiota can play an important role in the pathogenesis of obesity and metabolic syndrome as able to influence nutrient absorption and distribution of energy. Mice bred in sterile conditions (the so-called "germ free", scilicet without microbiota) need a significantly higher amount of calories compared to the counter part grown under conventional conditions to maintain the same body weight and, in equal diet, have a considerably lower amount of fat mass. Very interesting is that the subsequent colonization of germ-free mice with a normal colonic microbiota determines a rapid and significant increase in body weight and body fat of these animals. Underlying these evidences there are a variety of mechanisms. Bacteria of the microbiota, in fact, appear likely to reduce intestinal expression of a factor, the fasting-induced adipose factor (Fiaf), which is itself an inhibitor of lipoprotein lipase. It follows an abnormal activation of this enzyme, which favors the release of fatty acids from circulating lipoproteins VLDL and chylomicrons with subsequent accumulation of triglycerides in the adipose tissue. Intestinal bacteria are also able to reduce expression, whether in the liver that muscular, of an enzyme, AMPK (adenosine monophosphate-activated protein kinase), which is critical in stimulating β -oxidation of fatty acids. Another recently described mechanism involves rather short-chain fatty acids produced by bacterial fermentation of carbohydrates, which are able to regulate the expression of intestinal hormones, such as Peptide YY, which regulate the production and digestive enzyme release. Finally, monosaccharides produced by fermenting bacteria action of the microbiota, once absorbed and transported to the liver by the portal circle, are able to bind and activate a cytoplasmic factor (the carbohydrate responsive element binding -ChREBP), which, migrating from the cytoplasm to the nucleus, activates enzymes involved in lipogenesis. Finally, another highlight on the possible role of intestinal flora in obesity comes from the evaluation of the role of lipopolysaccharide (LPS) of the wall of gram negative bacteria in chronic systemic inflammation and therefore insulin resistance and obesity. High-fat diets in particular alter composition of the microbiota (increase Gram negative bacteria/Gram positive) leading to increased levels of circulating LPS; this, in turn, is able to induce the production of pro-inflammatory cytokines (TNF- α , IL-1, IL-6, plasminogen activator inhibitor) [3,4] which in turn regulate the glucose tolerance, encouraging the development of insulin resistance [5]. It follows then a possible role of LPS in chronic inflammation associated with diets [6,7] high in fat, with a predisposition to the development of insulin resistance and thus of diabetes. It is easy to understand, therefore, that both experimental animals and humans there are significant differences in the composition of the microbiota [8-15] between qualitative and quantitative obese and lean. In particular, recent studies have clearly demonstrated a significant reduction of bacteria belonging to the family of Bacteroidetes and a proportional increase of bacteria belonging to the family

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of Firmicutes and Archea. This results in an increase in the intestinal lumen, of non-digestible polysaccharides capable of breaking down hydrolases, including the β -fructosidases and increased transport proteins needed in absorption of products of fermentation, including the Phospho transferases. Always in obese, the preponderance of methane-producing bacteria, which use hydrogen to produce methane, maintains a constant low hydrogen partial pressure, thus optimizing the processes of bacterial fermentation [16-18]. Ultimately, these quantitative and qualitative changes in metabolic way of bacterial flora guarantee guests to extract maximum energy value from the diet, taking calories also in even potentially low foods, like fibers. The surprising is that these alterations of gut microbiota are absolutely reversible: a low-calorie diet, in fact, is able to balance Bacteroidetes/Firmicutes, reformulate the metabolic structure of the intestinal flora and induce a weight loss that goes along with the balance of the intestinal ecosystem. At present, antibiotics, probiotics, prebiotics and synbiotics are tools used to modulate the bacterial flora in terms of quality and quantity [19-21]. It is clear that an ever deeper knowledge in this field and new data on bacteria able to influence the metabolism, such as *Akkermansiamuciniphila*, or inflammation, such as *Fecalibacteriumprausnitzii* may in the future to suggest therapeutic actions on complex microbial intestinal balance which is the basis of obesity and its complications.

References

- Chambers ES, Viardot A, Psichas A, Morrison DJ, Murphy KG, et al. Effects of targeted delivery of propionate to the human colon on appetite regulation, body weight maintenance and adiposity in overweight adults. *Gut*. 2015 Nov;64(11):1744-1754.
- Ridaura VK, Faith JJ, Rey FE, Cheng J, Duncan AE, et al. Gut microbiota from twins discordant for obesity modulate metabolism in mice. *Science*. 2013 Sep;341(6150):1241214.
- Wang XA, Zhang R, She ZG, Zhang XF, Jiang DS, et al. Interferon regulatory factor 3 con- strains IKK β /NF- κ B signaling to alleviate hepatic steatosis and insulin resistance. *Hepatology*. 2014 Mar;59(3):870-885.
- Aguirre M, Jonkers DM, Troost FJ, Roeselers G, Venema K. *In vitro* characterization of the impact of different substrates on metabolite production, energy extraction and composition of gut microbiota from lean and obese subjects. *PLoS One*. 2014 Nov;9(11):e113864.
- Vajro P, Paoletta G, Fasano A. Microbiota and gut-liver axis: their influences on obesity and obesity-related liver disease. *J Pediatr Gastroenterol Nutr*. 2013 May;56(5):461-468.
- Gulati S, Misra A, Colles SL, Kondal D, Gupta N, et al. Dietary intakes and familial correlates of overweight/obesity: a four-cities study in India. *Ann Nutr Metab*. 2013;62(4):279-290.
- Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011-2012. *JAMA*. 2014 Feb;311(8):806-814.
- Ley RE, Turnbaugh PJ, Klein S, Gordon JI. Microbial ecology: human gut microbes associated with obesity. *Nature*. 2006 Dec; 444:1022-1023.
- Clavel T, Desmarchelier C, Haller D, Gérard P, Rohn S, et al. Intestinal microbiota in metabolic diseases: from bacterial community structure and functions to species of pathophysiological relevance. *Gut Microbes*. 2014 Jul;5(4):544-551.
- Sweeney TE, Morton JM. The human gut microbiome: a review of the effect of obesity and surgically induced weight loss. *JAMA Surg*. 2013 Jun;148(6):563-569.
- Verdam FJ, Fuentes S, de Jonge C, Zoetendal EG, Erbil R, et al. Human intestinal microbiota composition is associated with local and systemic inflammation in obesity. *Obesity (Silver Spring)*. 2013 Dec;21(12):E607-E615.
- Bervoets L, Van Hoorenbeeck K, Kortleven I, Van Noten C, Hens N, et al. Differences in gut microbiota composition between obese and lean children: a cross-sectional study. *Gut Pathog*. 2013 Apr;5:10.
- Turnbaugh PJ, Hamady M, Yatsunencko T, Cantarel BL, Duncan A, et al. A core gut microbiome in obese and lean twins. *Nature*. 2009 Jan;457(7228):480-484.
- Vijay-Kumar M, Aitken JD, Carvalho FA, Cullender TC, Mwangi S, et al. Metabolic syndrome and altered gut microbiota in mice lacking Toll-like receptor 5. *Science*. 2010 Apr;328(5975):228-231.
- Lam YY, Ha CW, Campbell CR, Mitchell AJ, Dinudom A, et al. Increased gut permeability and microbiota change associate with mesenteric fat inflammation and metabolic dysfunction in diet-induced obese mice. *PLoS One*. 2012;7(3):e34233.
- Swann JR, Want EJ, Geier FM, Spagou K, Wilson ID, et al. Systemic gut microbial modulation of bile acid metabolism in host tissue compartments. *Proc Natl Acad Sci USA*. 2011 Mar;108 Suppl 1:4523-4530.
- Ye D, Li FY, Lam KS, Li H, Jia W, et al. Toll-like receptor-4 mediates obesity-induced non- alcoholic steatohepatitis through activation of X-box binding protein-1 in mice. *Gut*. 2012 Jul;61(7):1058-1067.
- Franchi L, Muñoz-Planillo R, Núñez G. Sensing and reacting to microbes through the inflammasomes. *Nat Immunol*. 2012 Mar; 13(4):325-332.
- Henao-Mejia J, Elinav E, Jin C, Hao L, Mehal WZ, et al. Inflammasome-mediated dysbiosis regulates progression of NAFLD and obesity. *Nature*. 2012 Feb;482(7384):179-185.
- Russell WR, Hoyles L, Flint HJ, Dumas ME. Colonic bacterial metabolites and human health. *Curr Opin Microbiol*. 2013 Jun;16(3):246-254.
- Devkota S, Wang Y, Musch MW, Leone V, Fehlner-Peach H, et al. Dietary-fat-induced taurocholic acid promotes pathobiont expansion and colitis in *Il10*^{-/-} mice. *Nature* 2012 Jul;487(7405):104-108.