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Microbiota: a relationship for life

Microbiota: una relación para toda la vida

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The microbiota is the group of microorganisms that reside in a particular niche. This article will talk address about the microorganisms that reside in the human body. The microbiota is one of the most densely populated and diverse communities on the planet. The human body harbors a significant diversity of microorganisms in the intestinal tract and genitourinary tracts, the oral cavity, nasopharynx, respiratory tract, and the skin.[1]

In the past, the scientific community believed that microbiota consisted only of commensal microorganisms (residing inside us but providing no benefit at all). However, recently multiple functions related to human physiology in which the microbiota is involved have been described. The intense research efforts to explore its role in normal and pathological processes allow scientists to define and named the microbiota as a «metabolic organ».

Some of the functions associated with the microbiota relate to nutrition, immunity, and inflammation, will be described below.

GUT MICROBIOTA (ERRONEOUSLY CALLED INTESTINAL FLORA IN THE PAST)

The intestinal tract is a reservoir of commensal/symbiotic microorganisms (their numbers can be near 1,013-1,014 trillion) of various species, among which there are more than 500 bacterial species and more than 1,100 archaea species (unicellular prokaryotes that belong to a different phylum than bacteria). They can be Gram-negative (Bacteroidetes and Proteobacteria) or Gram-positive (*Actinobacteria* and *Firmicutes*).[2]

The stablished relationship between microorganisms and intestinal epithelial cells is very complex: some of their interactions allow the formation of a mucosal barrier, it can be the site where immunological mediators are secreted, and, where bacterial antigens interact with the body. Other kind of bacteria help to metabolize the ingested food.

The composition of the human microbiota largely depends on environmental factors, such as diet and drug use. Beyond the already documented effects of diet on human health, nutrients such as carbohydrates, proteins, fats, and other compounds as polyphenols and natural and artificial sweeteners, can act on intestinal microbiota, changing the balance between the microorganisms that compose it. Preclinical studies in animals, as well as clinical studies, have shown that the consumption of a high-fat diet promotes a decrease in the number of Bacteroidetes, and an increase in *Firmicutes* and *Proteobacteria*, which could increase the ability to collect and store energy, and increase the intestinal barrier permeability promoting an inflammation condition.[3]

Something similar occurs with high-sucrose, sucralose, and stevia diets, where the number of *Firmicutes* increases causing a deleterious condition that can be synergistically incremented when high-fat diet and sucralose are combined.[4]

Changes in the normal balance among the microbiota components is known as dysbiosis, state that is responsible for the

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metabolic alterations in the body that can lead to obesity, type 2 diabetes mellitus, and cardiovascular diseases.[5]

Some examples of the roles of the gut microbiota in cardiovascular disease and health are:

Short chain fatty acid (SCFA)

The intestinal microbiota participates in the digestion of food through two main catabolic pathways, categorized as saccharolytic or proteolytic. The first one, in which the microbiota breaks down polysaccharides, is responsible for most of the SCFA production. In the second pathway, ingested fiber is fermented, also inducing the formation of SCFA along with other potentially toxic metabolites, such as amines, thiols and phenols.

SCFAs directly modulate human health through different tissue-specific mechanisms related to the function of the intestinal barrier, glucose homeostasis, immunomodulation and regulation of appetite and obesity. The digestion of fermentable dietary fiber to SCFA gives us additional energy, so it would be logical to think that this would increase obesity, however, epidemiological studies indicate that a diet rich in fiber prevents the development of obesity, probably because SCFA work as free fatty acid receptors (FFAR) ligands, that increase the expression of glucagon-like-peptide 1 or Peptide YY, (slowing intestinal transit, increasing nutrient absorption, and increasing concentrations of leptin, an anorectic hormone).[6]

In summary, SCFAs, a product of intestinal microbial action, provide great health benefits.

Trimethylamine-N-oxide

Naturally, foods such as red meat, soy, and eggs contain essential compounds for the normal functioning of human cells. Phosphatidylcholine, also called lecithin, is a molecule that participates in the stability of cell membranes and is the main phospholipid of circulating very low-density and low-density lipoproteins (VLDL/LDL). Lecithin can be oxidized to betaine and this molecule is metabolized by intestinal bacteria producing trimethylamine (TMA).

L-carnitine is another example of compounds associated with the production of TMA. It is obtained from the essential amino acids methionine and lysine, and it is essential for energy metabolism, in particular, the catabolism of fatty acids that must be esterified with carnitine to form acyl-carnitine to be transported into the mitochondria for their oxidation (degradation), and be used in the production of ATP.[7,8] Carnitine is also used in the transport of carbons (-CH3CO) in the form of acetyl-carnitine outside the mitochondrial, through the activity of the enzyme carnitine acyltransferase, promoting glucose oxidation.[9,10]

Both phosphatidyl choline and L-carnitine from food are metabolized by the intestinal microbiota to trimethylamine (TMA) which, upon reaching the liver, is oxidized by the enzyme flavin monooxygenase (FMO), producing trimethylamine-N-oxide (TMAO). This molecule has been proposed as a cause of lipid accumulation in the arterial wall, facilitating the influx of lipids, increasing in situ synthesis, and suppressing their elimination, facilitating the formation of lipid-laden macrophages (known as foam cells) within the arterial wall, which is considered to be a pathological condition associated with the development of atherosclerosis.

Multiple clinical studies have shown a positive correlation between the presence of metabolites associated with the production of TMAO (choline, betaine, and L-carnitine) and cardiovascular diseases such as, acute myocardial infarction and stroke. Patients with high circulating TMAO concentrations have a 2.5 times higher risk of suffering a major cardiovascular event, independent of other risks such as lipid concentration. In addition, it is important to consider that dysbiosis, particularly due to the increase of non-commensal bacteria (usually harmless to our body) such as genus *Shigella*, *Vibrio* or *Aeromonas* can produce high amounts of TMA using different substrates from the diet which increases the risk. Thus, the balance of the intestinal microbiota depends mainly on the ingested diet and the adequate regulation of the concentrations of TMA absorbed in the intestine. Therefore, the concentrations of circulating TMAO can be modulated with correct habits and healthy diet.

MICROBIOTA AND OBESITY

As mentioned, a high-fat diet in and the consequent obesity, generates changes in the balance of the normal microbiota components, mainly increasing the ratio of *Firmicutes*/*Bacteroidetes*. This event can be reversed with changes in diet, from a one high in fat to another low in both, carbohydrates and fat (hypocaloric regimes).

Type 2 diabetes mellitus, strongly associated with obesity, has also been associated with low concentrations of SCFA, in particular, butyrate (produced by bacteria in the intestine). When analyzing the feces of patients with metabolic syndrome and insulin resistance, it was found that their microbiota contained minor amounts of butyrate-producing bacteria.

CONCLUSION

The human intestinal microbiota participates in the metabolism of various compounds contained in the diet, and their metabolites can be absorbed by the intestine and modulate the permeability of the intestinal barrier. The bacterial composition varies throughout life, depending on various environmental factors, mainly the type of diet; If the diet is high in fat, carbohydrates, sweeteners (natural or artificial) or low in fiber, it will create a favorable environment for the growth of *Firmicutes* and other non-commensal bacteria. More and more evidence shows that a state of dysbiosis is related to the development of multiple diseases such as atherosclerosis, arterial hypertension, heart failure, chronic kidney disease, obesity and type 2 diabetes mellitus, among many others. For these reasons, the prevention and treatment of cardiovascular diseases must pay attention to the restoration of the patient's microbiota. After all, microbiota will accompany us throughout life ... until death do us part.

REFERENCES

1. Petrosino JF, Highlander S, Luna RA, Gibbs RA, Versalovic J. Metagenomic pyrosequencing and microbial identification. Clin Chem. 2009; 55: 856-866.
2. Qin J, Li R, Raes J, Arumugam M, Burgdorf KS, Manichanh C et al. A human gut microbial gene catalogue established by metagenomic sequencing. Nature. 2010; 464: 59-65.
3. Murphy EA, Velazquez KT, Herbert KM. Influence of high-fat diet on gut microbiota: a driving force for chronic disease risk. Curr Opin Clin Nutr Metab Care. 2015; 18: 515-520.
4. Wang QP, Browman D, Herzog H, Neely GG. Non-nutritive sweeteners possess a bacteriostatic effect and alter gut microbiota in mice. PLoS One. 2018; 13: e0199080.
5. Swithers SE, Shearer J. Obesity: sweetener associated with increased adiposity in young adults. Nat Rev Endocrinol. 2017; 13: 443-444.
6. Delzene N, Cano PD. Interaction between obesity and the gut microbiota: Relevance in nutrition. Annu Rev Nutr. 2011; 31: 15-31.
7. Ussher JR, Lopaschuk GD. The malonyl CoA axis as a potential target for treating ischaemic heart disease. Cardiovasc Res.2008; 79: 259-268.
8. Lozupone CA, Stombaugh JI, Gordon JI, Jansson JK, Knight R. Diversity, stability and resilience of the human gut microbiota. Nature. 2012; 489 (7415): 220-230.
9. Muoio DM, Noland RC, Kovalik JP, Seiler SE, Davies MN, DeBalsi KL et al. Muscle-specific deletion of carnitine acetyltransferase compromises glucose tolerance and metabolic flexibility. Cell Metab. 2012; 15: 764-777.
10. Noland RC, Koves TR, Seiler SE, Lum H, Lust RM, Ilkayeva O et al. Carnitine insufficiency caused by aging and overnutrition compromises mitochondrial performance and metabolic control. J Biol Chem. 2009; 284: 22840-22852.

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