L'INSTITUT SERVIER SCIENTIFIC COLLOQUIA

2018 COLLOQUIUM
Intestinal microbiota and its host: harmony or discord?

The intestinal microbiota: definitions, constitution and challenges

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INTRODUCTION

Microbes are responsible for 25% of global mortality, with 14 million deaths per year; children are particularly affected.[1] Infectious disease mortality involves mainly low-income countries, where it is the leading cause of death.[2, 3] Global epidemiological data also indicate a considerable emergence of new infectious diseases: between 1940 and 2004, 335 new infectious diseases were identified.[4]

Microbes are not a homogeneous group of organisms, as they include yeasts, fungi, viruses and bacteria. The human body contains approximately 100,000 billion bacteria of more than 500 different species. The term "microbiota" refers to all the bacteria found in humans that cohabit with them, regardless of their location. Like the human fingerprint, the microbiota is specific to each individual, made up according to the combination the host inherited at birth and all of their experience thereafter.[5] The host and all of the bacteria that constitute their microbiota share a multi-faceted, partnership-based life, animated by various correlations and interactions. Parasitism, an interaction that kills, is an example of this, as is symbiosis, an interaction that protects. The immune system learns, by the microorganisms that it tolerates, to resist those that are dangerous to it. "On one side parasites, microbes, fungi or viruses that live at the expense of the host and force him to evolve to ward off their attacks; on the other, the symbiosis, the beneficial alliance between two species seeking a good agreement, or better, a profit, as much for the parasite as for the host".[5]

The microbiota is now considered an organ. Nevertheless, even more surprising than being an organ, the microbiota reveals a phenomenon of coevolution, a phenomenon much more general than the sole fact of its bacterial content: the interaction between an estimated 1014 bacteria that make up this organ and what really constitutes the human being. Resulting from a coevolution, two living beings become one. This is probably one of the dominant factors in the evolution of species throughout the history of mankind. In fact, "man owes the multitudes of bacteria that live for him and with him, to have crossed the billions of years that separate him from their first meeting".[5]

THE INTESTINAL MICROBIOTA

The intestinal microbiota, formerly and still commonly called the "intestinal flora", is the most important microbiota of the human body. Between the mouth and the anus, which has a considerable surface area of nearly 400 m^2, several hundreds of billions of bacteria coexist. In fact, it is in the digestive tract that there is the greatest number of bacteria in the human body, and these bacteria seem to be the bacteria with the greatest influence on the physiology of the body. In addition to the considerable protective importance of these bacteria, there are correlations – of which we do not yet know the precise role – of the intestinal microbiota with some diseases. The microbial ecology and diversity of the human microbiota is immense,[6] with a distribution in the gut microbiota showing the prevalence towards firmicutes and bacteroides.[7]

The gut microbiota also contains, with more or less importance depending on the publication, other bacteria such as actinobacteria and proteobacteria, some of which may play a significant physiological or pathological role.[8-10] We can also note the existence of archaebacteria. This has led to an increasing interest in assessing the function and number of different phyla in the gut, and how these makers of health and disease may change in certain disease states.

PRESENTATION

The gut microbiota is only one of all the microbiota existing in the human body.[7] It is characterized by a preferential localization of the different bacterial populations along the digestive tract, induced by both intrinsic and extrinsic factors that regulate these populations.[11] As they pass through the digestive tract, bacteria undergo a sort of selective or attractive pressure, dependent on the local environment. The specific role of pH and stomach acidity is especially important for *Helicobacter* for example, or oxygen for the majority of bacteria that are anaerobic. The motility of the digestive tract and mucus also plays a substantial role on the location and behavior of bacteria throughout the gut, as well as other gastrointestinal secretions. Furthermore, antimicrobial peptides may also have a significant role to play, such as immunity with IgA secretions. Beside these intrinsic factors, the full range of which remain to be discovered, extrinsic factors also play a role in the composition of the microbiota. Among these, food is at the forefront: "We are what we eat". Other extrinsic factors have been identified,[8] such as antibiotics (a crucial point in the context of the current fight against antibiotic resistance and the repeated use of these agents), and laxatives that modify motility. This important ecological diversity varies, dependent on food, region and population.

DEVELOPMENT AND COLONIZATION

At birth, the microbiota is sterile. Colonization by aerobic bacteria and bifidobacteria (blue flora) depends on various influencing factors such as the mode of delivery, food, environment, antibiotic therapy or age. The gut microbiota develops throughout life, from birth.[12] The conditions of birth, followed by the first years of life, are of considerable importance. Microbiotas differ dependent on the mode of delivery: vaginally, with the influence of the vaginal flora, or by cesarean section. They are also be influenced by the child's diet, one of the many factors that shape the microbiota. The microbiota of a breastfeeding newborn differs from a newborn receiving formula feeding. In fact, the ingestion of breast milk sows the newborn's developing microbiota with micro-organisms from the mother's milk, and influences its composition even when breastfeeding is no longer the main diet. Breastfeeding promotes bifidobacteria, has more than 130 different sugar molecules, and varies according to maternal diet and species. Subsequently, the evolution of food intake in children is a factor of primary influence on the composition of their microbiota.

In spite of the known differences in the gut microbiota of children, the reasons for this disparity have not been fully elucidated, and the possible effect of the early ages of life on the later stages of life has not yet been precisely identified. Gradually, as newborns grow and their food supply evolves between 6–24 months of age, a series of changes occurs in their microbiota and interactions are created with various factors, particularly cytokines.[12]

ROLE OF THE NORMAL MICROBIOTA

Microbiota and digestion

One of the two main functions of the microbiota is its role in the digestion of food that the host cannot digest. The microbiota degrades those resistant starches present in a large number of foods, and dietary fiber, such as those present in fruits, helping to provide energy and produce vitamins. Different bacterial populations have different families of enzymes, each of them having the ability to break down different sugars.[13]

In addition to their action on carbohydrates, bacterial enzymes also have the ability to degrade peptides. Nine essential amino acids out of 20 cannot be synthesized by humans; the microbiota provides support for this synthesis, beyond the secretion of digestive juices, trypsin and pepsin.[14]

Bacterial enzymes also have an effect on lipids and cholesterol metabolism. This activity is currently being investigated, as well as their interference with vitamins including vitamins K and B12.[15, 16]

Microbiota and immune defenses

A question related to the understanding of microbiota and its role in immunity is to determine how potentially pathogenic bacteria are eliminated. Several possibilities have been identified as being able to contribute to the inhibition of micro-pathogens: direct inhibition, competition with nutrients, and stimulation of immune defense (IgA secretion).[17]

Another question relates to the interactions of the intestinal microbiota with the immune system. The second function of the microbiota is to develop systems of recognition of the immune system, to adapt it to the recognition of danger signals by differentiating and educating the immune system against these signals. A specific equilibrium should be reached, corresponding to a balance between the capacities these commensal bacteria have to be pro- and anti-inflammatory, and the immune system itself. In an efficient and tolerant immune system, this balance (eubiosis) is associated with a robust T Reg immune system, T cells playing a key role in immunoregulation. A dysbiosis, or bacterial imbalance, consists of an excess in proinflammatory commensal bacteria inducing a decreased tolerance, or a reduction of proinflammatory commensal bacteria indicating an ineffective immune system. In either case, the immune system is impaired, causing or exacerbating local or systemic inflammation.

THREATS AND CHALLENGES RELATED TO GUT MICROBIOTA

The results of research in various diseases indicate that the intestinal microbiota is probably responsible, at least in part, for their occurrence. Obesity,[18,19] cancer,[20] neuropsychiatric and behavior disorders,[21,22] allergic,[23,24] inflammatory[25] and auto-immune[26,27] diseases, have all been shown to occur or worsen based on the commensal bacteria in the gut. The intestinal microbiota is also an interface between mucosal immunity, metabolism, energy homeostasis, physiology and health, and a series of diseases.[28]

SUMMARY AND CONCLUSION

The microbiota is one of the main examples of symbiosis, essential to the individual's life, behaving with the host cells as a superorganism. It contributes greatly to the digestion of food, providing its host with energy and vitamins. It also has a considerable role in the development of the immune system and its adaptation to recognize danger signals.

Metagenomics has made it possible to better characterize the microbiota, confirming the numerical importance of these bacterial populations, their diversity of species and their functional richness. Dysbiosis phenomena have linked microbiota abnormalities to various diseases, such as digestive cancers, metabolic disorders, obesity, autoimmune disorders and neuropsychiatric disorders. Thus, the characterization of the microbiota, its functions and defects represents an important challenge and one of the major issues for the study of human physiology and diseases.[5]

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