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# BIODIVERSITY AND HUMAN MICROBIOTA IN HEALTH AND DISEASE

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## Abstract

Biodiversity is defined as the variety and variability of biological organisms in a defined habitat. Human microbiota, the living microorganisms found in the human body, and microbiome, the collection of genomes from all the microorganisms in the human body, are closely relevant to human health and diseases. A healthy microbiota is characterized by a high biodiversity and holds a high taxonomic diversity and microbial gene richness. The microbial communities are in symbiosis with the host, contributing to homeostasis and regulating immune function. The composition of microbiota is affected by different factors such as the type of delivery, the type of breast-feeding, the environment, the diet and the utilization of antibiotics. Therefore, microbiota dysbiosis is associated with many diseases such as cardio-vascular disease, inflammatory bowel disease, liver disease, chronic kidney disease, brain disorder, respiratory disease, cancer and obesity. Nowadays, microbial medicine represents an important field of medicine, since the modulation of the host microbiome has been proposed as a potential treatment for many human diseases.

## Keywords

Biodiversity, Microbiota, Microbiome.

## 1. *Milestones in human Microbiota research*

The importance of the gut in human health has long been studied in medicine. In 400 B.C. Hippocrates warned that "bad digestion is the root of all evil" and "death sits in the bowels." Despite being often considered as a modern field of research, the first descriptions of human microbiota date back to the 1683, when Antonie van Leeuwenhoek, the father of microscopy, described different kinds of bacteria (animalcules) present in the mouth and faecal samples in a letter written to the Royal Society of London. Further research on the meaning of these animalcules did not take place until 1900s, when a new field of research was born: Pasteur developed the germ theory of disease, Metchnikoff revealed that microbiota composition and its host interactions were essential for health, Escherich stated that the endogenous flora plays a key role for understanding the physiology of digestion and the pathology and therapy of intestinal diseases, Hungate developed the anaerobic culture techniques, which allowed to characterize the complexity of the human microbiota. Until the early 1990s studies of the human microbiota were based on culture-dependent methods, later new methods were developed such as the sequence-based identification of human associated microbiota, the shotgun library-sequencing method for the analysis of the human viroma, the software pipeline QIIME (quantitative insights into microbial ecology) which enabled the analysis and interpretation of the increasingly large datasets generated by microbiome sequencing, the metagenomic datasets which allowed the reconstruction of bacterial genomes (Pariente, 2019).

## 2. *Microbiota and Microbiome*

Microbiota represents the living microorganisms found in a defined environment, a large number of microorganisms (bacteria, yeasts, viruses, archea and unicellular eukaryotes) coexist in different sites of the human body and the composition of microbiota varies from site to site. Approximately a hundred trillion microbes, carrying about 150 times more genes compared to the entire human genome, live on and inside the human body having a pivotal role in various biological processes including health and disease (Afzaal, 2024). The digestive tract constitutes the largest interface between the sterile part of the human body and environmental factors and pathogens. It is the most important site for colonization, as a consequence gut microbiota is considered the most significant one, possesses more than one thousand microbial species belonging from six phyla including Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, Fusobacteria and Verrucomicrobia, among which Firmicutes and Bacteroidetes are the major types. Microbiota is also localized in other regions of the body including the oral cavity, skin, lung and vagina, while less well established compared with gut. Oral microbiota is considered the second largest microbial community in human (How, 2022).

Microbiome represents the collection of genomes from all the microorganisms in the environment, which includes not only the community of the microorganisms, but also the microbial structural elements, metabolites and the environmental conditions (Berg, 2020). In this regard, microbiome encompasses a broader spectrum than that of microbiota.

## 3. *Biodiversity and human microbiota*

Biodiversity is defined as the variety and variability of biological organisms in a defined habitat. Microorganisms, the oldest living organisms in the biosphere, are an essential part of life on the earth and exist in association with virtually any living thing. Conservation, stability, and maintenance of global genetic resources and ecosystems require maintaining microbial diversity. Microbial diversity is higher in the outdoor environment (different species associated with animals, plants, livestock, soil and air) compared to the indoor environment. The human microbiota is in a constant and dynamic interaction with the surrounding environment, therefore, environmental biodiversity affects the composition of human microbiota. The biodiversity hypothesis postulates that the frequent contact of people with the natural environment increases the diversity in the human microbiome, promote the immune balance and protect the individual from allergy and inflammation (Panthee 2022). A human healthy microbiota is indeed characterized by a high biodiversity and demonstrates high taxonomic diversity, high microbial gene richness and stable core microbiota (Fan, 2021). An interesting study investigated how environmental factors affect human microbiome through the characterization of gut bacterial species in faecal samples from people living in different geographical regions (the Amazonas of Venezuela, rural Malawi and US metropolitan areas), pronounced differences were found in the composition and functions in the gut microbiomes between these geographically distinct populations (Yatsunenko, 2012). Therefore, the interaction between the human and environmental microbiome affect the composition of the human microbiome diversity, which in turn affects the overall human health, both physical and mental.

## 4. *Microbiota in health*

Human microbiota has different beneficial roles in maintaining the human homeostasis such as nutrient absorption from food due to the metabolic genes which provide unique enzymes and biochemical pathways, biosynthesis of bioactive molecules such as vitamins, amino acids and lipids, metabolization of drugs and xenobiotics, modulation of hormonal pathways via microbial-derived metabolites such as modulation of the gut-brain axis, development and regulation of host immune system, protection from external pathogenic pathogens (colonization resistance) by producing antimicrobial substances (How, 2022).

## 5. *Microbiota and early life*

The exact timing of microbiota acquisition during life remains an open question, likely the foetus develops in a sterile environment and the infant acquires the initial microbiota during and immediately after birth. The composition of the microbiota of neonates varies according to the type of delivery (vaginal vs cesarean section) and the type of breast feeding (maternal vs artificial). The infant gut microbiota undergoes a period of massive change in the first years of life and by 2–3 years of age, a stable microbiota develops that resembles that of the adults in the infant's community. Postnatal factors configure the microbiota in early life (breastmilk, diet, environment and people that surround an infant, use of antimicrobials) (York, 2019).

## 6. *Microbiota and food*

Diet is one of the most important external factor modulating the composition and metabolic activities of the gut microbiome. Dietary patterns constitute the quantity and the variety of foods in a diet, as well as the frequency with which these foods are ingested.

Mixed balanced diet (Mediterranean diet) consists mainly of important sources of fiber (cereals, nuts, legumes, vegetables, and fruits), unsaturated fatty acids, and antioxidant compounds (vitamins, flavonoids, phytosterols, minerals, terpenes, and polyphenols), with moderate consumption of eggs, white meat and fish or seafood, and low consumption of red meat and sweets (Varlamov, 2017). This diet leads to a reshaped gut microbiota composition and provokes a higher microbial diversity with an increased population of the bacterial families Clostridiaceae and Lactobacillaceae and also with a decrease in members of the phyla Pseudomonadota and Bacillota and has beneficial effects on human health and longevity, reducing the risk of cardiovascular disease, cancer, obesity and other related metabolic disorders (Borrego-Ruiz, 2024).

Plant-based diet (Vegetarian diet) consists of a diet free of animal meat, characterized by low-fat and high-fiber components. This diet reduces β-diversity (the amount of differentiation between species communities) of the gut microbiome, but not the individual diversity at the local scale (α-diversity) and is a healthy and therapeutic dietary pattern for several metabolic and chronic diseases, since it induces a reduction of pathobionts in the intestinal tract (Borrego-Ruiz, 2024).

On the contrary, high-calories diet (Western diet) is characterized by a high content of refined sugars, salt, saturated fats, and proteins of animal origin. This diet leads to a decrease in Bacteroidota levels and increase in members of both Pseudomonadota and Bacillota phyla in the gut microbiota and is associated with chronic inflammation, metabolic syndrome (diabetes, hypertension and cardiovascular disease) and obesity (Borrego-Ruiz, 2024).

## *7. Microbiota and antibiotics*

Antibiotics not only act on bacteria that cause infections but also affect the resident microbiota. Antibiotic treatment reduces the overall diversity of gut microbiota species, although most bacterial groups recover after the end of treatment, several taxa did not (even after months) and the level of reconstitution varies between the individuals. Moreover, antibiotics increase gut susceptibility to colonization from pathogenic bacteria and stimulates the development of bacterial antibiotic resistance. The clinical consequences of antibiotic use can be divided in: 1) short- and medium-term consequences such as antibiotic-associated diarrhea and Clostridium difficile-associated diarrhea and 2) long-term consequences since antibiotic use in childhood has been associated with several negative outcomes later in life, including the development of obesity, asthma, allergy, and inflammatory bowel disease (Lathakumari, 2024).

The observation that the gut microbiome can be permanently perturbed even by short-term or low-dose antibiotic treatment, and that this change can have long-term effects on health, cautions against widespread and potentially unnecessary use of antibiotics, particularly in young children and pregnant women, and illustrates that antibiotics should not be considered harmless.

## *8. Microbiota and human diseases*

The disruption of the microbiota ecosystem, referred as dysbiosis, alters the normal gut flora and leads to an overgrowth of pathogenic bacteria and a decrease in beneficial microbes, which compromises gut barrier integrity and triggers pro-inflammatory responses and dysregulated immune function. A tremendous amount of extensive research work has been done in the last decades, and has revealed that the gut microbiota dysbiosis can be associated with many pathologies within the human body, such as heart disease (hypertension and atherosclerosis), inflammatory bowel diseases (Chron's disease, ulcerative colitis, irritable bowel syndrome, celiac disease), liver diseases (hepatitis, cirrhosis), chronic kidney disease, brain disorders (depression, Alzheimer's disease, Parkinson's disease), diabetes (type I, type II and gestational), respiratory disease (asthma and bronchitis), cancer (lung cancer, colorectal cancer, pancreatic cancer and oral cancer) (Hou., 2022). In addition, several studies demonstrated a strict correlation between dysbiosis and obesity. Recent evidence from various studies of humans and mice has demonstrated that changes in gut microbiota composition may play a vital role in the development of obesity (Afzaal, 2022). Several gut microbiota species, called the obesogenic gut microbiota, can significantly contribute to obesity, such as Firmicutes, Bacteroidetes, Rhizobium, Lactococcus, and Clostridium. In particular, obesogenic gut microbiota could facilitate obesity by producing SCFAs such as butyrate, providing the host with extra energy, and inducing low-grade inflammation caused by intestinal microbiota metabolites (Cao, 2019).

## *9. Therapeutic strategies in the gut microbiota manipulation*

Microbial medicine has evolved thanks to the improvement in the understanding of genomics, metagenomics, and metabolomics in the recent years. In light of these advances, modulation of the host microbiome has been proposed as a potential treatment or prophylaxis for many health disorders. To achieve this goal, many strategies have been successful including prebiotics and/or probiotics administration and fecal microbiota transplantation (Gebrayel, 2022).

Prebiotics are a group of nutrients that are degraded by gut microbiota and defined as "a selectively fermented ingredient that results in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health" (Gibson, 2010). They are classified into many types and the byproducts of their degradation by the gut microbiota are most of all SCFAs that can exert an anti-inflammatory effect in the regulation of many human disorders, mostly in inflammatory bowel diseases (Gebrayel, 2022).

Probiotics are defined as "live organisms that when administered in adequate doses confer a health benefit to the host" (Reid, 2016) and they are administered in food (yogurt, kefir, cottage cheese, miso soup, kombucha, sauerkraut or kimchi, pickles and pickle juice), pills or powders. Some of the most frequently studied and recommended probiotics include the Lactobacillus genus (*L. acidophilus, L. rhamnosus, L. casei and L. plantarum*) and the *Bifidobacterium genus* (*Bifidobacterium longum* and *Bifidobacterium breve*). Probiotics have been successfully used in the prevention and treatment of obesity in infants and adults and irritable bowel syndrome (Gebrayel, 2022).

The fecal microbiota transplantation (FMT) consists in the introduction of liquefied or encapsulated preprocessed stool from a healthy donor into a recipient's colon. FMT is now recognized as an efficient therapeutic for the management of recurrent *Clostridioides* difficile-induced colitis, which is a major cause of nosocomial disease with increasing occurrence and mortality (Yadegar, 2024). Another emerging indication to perform FMT is the gastrointestinal tract colonization by antibiotic-resistant bacteria (Huttner, 2019). Finally, FMT may be an efficient therapeutic strategy for treatment of obesity, diabetes and metabolic syndrome (Napolitano, 2020).

## *10.Conclusions*

Human microbiota plays a critical role in host health (eubiosis) and disease (dysbiosis). Diet is the most important environmental factor influencing the composition and shape of the gut microbiome, in addition to drugs (antibiotics), physical exercise and environment (particularly in early life). Large body of evidence demonstrates that the gut microbial alteration is a key factor in the pathogenesis of systemic disorders (obesity, cardiovascular diseases, neurological and psychiatric diseases, gastrointestinal and liver diseases). Understanding the specific roles of the gut microbiome in our growth and development, as well as how it functions in health and disease, holds the potential to improve the development of microbiota-based therapy such as fecal microbiota transplantation and bacteria modulation.

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