

### WHAT IS THE HUMAN MICROBIOTA AND THE MICROBIOME?

Microbes live in and on us, mostly in a mutually beneficial relationship, and it has been estimated that close to 95% of these microbes are found in our gut, especially the large intestine. Our stomach and small intestine are more sparsely colonized. There are trillions of bacteria that until this century we knew very little about. With the technological advances in microbiology and gene sequencing, we are starting to better understand the functions of these microbes and the metabolites they produce. Following these interesting discoveries, the terms microbiota and microbiome have started to be used widely.

The microbiota refers to the community of microorganisms, including bacteria, fungi, viruses and yeasts, present in a defined environment and residing on or within human tissues such as the skin, lung, oral mucosa, and the urogenital and gastrointestinal tracts.

The microbiome represents the microbiota (and its genes) living in a given environment; it can be seen as a “living ecosystem”.

### WHY IS THE MICROBIOTA SO IMPORTANT?

The impact of the microbiota on human health is far-reaching, from benefits to our digestive and immune system, to playing a key role influencing the interactions between our nervous system and the rest of the body. The microbiome represents a crucial interface between the environment we live in, the food we eat and our overall health.

### WHEN IS THE MICROBIOTA ESTABLISHED AND HOW DOES IT CHANGE THROUGHOUT LIFE?

Immediately after birth, the gut of newborns starts to be colonized by microbes from contact with Mom’s stool, vagina, skin, breast milk and environment, which initially develops into a relatively simple community or ecosystem dominated by Bifidobacteria. The complexity of this community increases and evolves during the first 2 years of life before it is considered to be an established “adult type” of microbiota which is dominated by Firmicutes and Bacteroidetes. Even then the composition might regularly change based on our life experiences (diet changes, traveling, stress, smoking...) the microbiota overall is relatively stable. This might change at older age, when the diversity of the microbes present was noticed to decrease.

### MAIN FACTORS THAT INFLUENCE OUR MICROBIOTA COMPOSITION

Many factors can affect the initial microbiota establishment as well as the composition and diversity later in life:

Factors affecting microbiota in early life:

- Full term or preterm delivery,
- Vaginal or C-section delivery,
- Breastfeeding or formula feeding,
- Having pets.

Factors affecting microbiota later in life:

- Type of diet,
- Eating fermented foods,
- Consuming probiotics and prebiotics,
- Using medications such as antibiotics and proton pump inhibitors,
- Stress,
- Smoking and alcohol consumption,
- Physical activity,
- Living in rural or urban areas,
- Time spent indoors or outdoors.

## MAIN BENEFICIAL ROLES OF THE MICROBIOTA IN HUMAN HEALTH

Our microbiota plays a myriad of key roles including:

- Digestion of food compounds that cannot be digested by our body (e.g., fibers),
- Production of essential nutrients such as vitamins,
- Synthesis of essential molecules such as short-chain fatty acids which have anti-inflammatory and gut barrier protection effects.
- Improvement in the bioavailability of non-essential nutrients such as polyphenols,
- Potential contribution to the homeostasis of host's amino acids,
- Elimination of toxic compounds,
- Protection from pathogens by producing antimicrobial molecules and competing for space and resources,
- Enhancement of the mucosal barrier in the digestive tract,
- Maintenance of normal intestinal transit time flow of food and material in the gut and overall digestive health,
- Maturation of immune system and cognitive development in early life,
- Modulation of immune responses in the gut and throughout the body.
- Production of hormones and neurotransmitters which are thought to have an impact on mood or appetite.

## HOW PROBIOTICS IMPACT THE MICROBIOME AND HUMAN HEALTH?

The mechanisms of action of probiotics are complex and very often strain specific. Probiotic benefits are often a result of the interaction of the probiotic microbes with the resident microbiota and the host. These interactions can be metabolic, microbiological, physiological, endocrinological, neurological or immunological in nature, with different combinations thereof. Although scientists find it difficult to exactly define what a healthy microbiome is, studies show that certain probiotic microbes can help promote resilience and help normalize a gut microbiota that was disturbed by antibiotics or other stressors. In doing so, these microbes can improve health.

Examples of some of the mechanisms by which probiotics can influence the gut microbiome include:

- Cross feeding interactions where metabolic products from microorganisms can serve as food for others,
- Changes in the gastrointestinal microenvironment (e.g., pH lowering), creating a more acidic ecosystem, less favorable to pathogenic (bad) microbes,
- Competition with undesired microbes for nutrients and binding sites,
- Production of strain-specific antimicrobial compounds, such as bacteriocins,
- Reintroduce specific bacteria associated with health benefits,
- Reduce harmful microbial metabolites,
- Uptake and breakdown of carbohydrates,
- Production and/or release of vitamins (e.g., Vitamin B and Vitamin K), antioxidants, polyphenols, and conjugated linoleic acids,
- Development of the immune system during early life,
- Support of normal healthy immunity during life,
- Maintenance of gut barrier function,
- Molecular signaling to other parts of our body by activation of receptors on the neurons that populate our digestive tract

### WHAT IS THE FUTURE FOR PROBIOTICS AND THE MICROBIOME?

Further understanding of the role of the human microbiome represents an opportunity to improve human health. It is plausible that in the future, we will use specific probiotics that are tailored to change specific body functions, providing specific health benefits.

The next-generation probiotics should be selected for their ability to complement microbiome deficiencies or disturbances. In the future, we can conceive that each of us will also be able to tailor the use of specific microbes or specific probiotics to improve their personal microbiome and health needs; this could help address risk factors for different disorders at the earliest possible moment and potentially reduce the risk to develop a particular disease or halt its progression. For example, the discovery of key microbes and gut microbiota-derived metabolic end products such as conjugated linoleic acids, neuro-mediators, hormones, bacteriocins, polyphenols, iron scavengers, vitamins, trimethylamine, short chain fatty acids, exopolysaccharides, lipoteichoic acids, and antioxidants will facilitate the design of this new generation of probiotics. More widespread use of gut microbiota profiling will make it easier to identify the individuals most likely to benefit from such probiotics.

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