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Gut Microbiota, Dysbiosis and Immune System; A Brief Review

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Abstract

The gut Microbiota is the large population of microorganisms residing in the human gastrointestinal tract. The gut Microbiota constantly interacts with the various host organs and systems. While there are many protective functions due to the gut Microbiota, changes in the composition and function of the Microbiota, which is defined as dysbiosis, has been shown in several diseased conditions. The gut Microbiota affect the immune system. While normal gut Microbiota are essential for existence of a normal immune system, dysbiosis can result in deviation of immune responses. In this article, we will talked the effects of the gut Microbiota on different elements of immune system.

***Keywords*:** Gut Microbiota, Dysbiosis, Immune System, Inflammation

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Introduction

The gut Microbiota is the large population of microorganisms residing in the human gastrointestinal (GI) tract. The gut Microbiota is composed of more than 10^{13}–10^{14} individual microbes (1, 2). The dynamic and symbiotic ecosystem that is provided by the gut Microbiota constantly interacts with the various host organs and metabolism (3). The number of genes of the gut Microbiota is at least 150-fold more than the human genome (4, 5). The host of the gut Microbiota definitely is affected by these huge amounts of genetic resources. Such an effect is mainly related to the production of vitamins and short-chain fatty acids (SCFAs) and the novel metabolic pathways for energy harvesting (4). Therefore, the gut Microbiota may be considered as an additional organ of the body (2). The most common member of the gut Microbiota is bacteria. *Actinobacteria* (*Bifidobacterium* and *Atopobium*), *Bacteroidete* (*Bacteroides* and *Prevotella*), *Proteobacteria* (*Proteobacteria*, *Burkholderia*, *Desulfovibrio)* and *Firmicutes* (*Clostridium*, *Eubacterium*, *Roseburia* and *Ruminococcus*) are the major bacterial phylae present in the gut microbiota of healthy humans (1, 2, 4, 6, 7).

The following factors play important roles in the diversity of the human gut Microbiota: ethnicity, gender, geographic locales, lifespan, host genetics and immune status, smoking and consumption of alcohol

and drugs (8). Environmental factors, like dietary habits and rapid lifestyle changes, are important (9, 10). An increase in *Prevotella* species has been shown in carbohydrate diets, whereas protein and fat diets increase the *Bacteroides* species (11). Many studies have shown the alternation in the Microbiota composition, for example increase of Proteobacteria, in diseased conditions (11).

The gut Microbiota as our friends:

There are many protective functions due to the gut Microbiota (3). The gut Microbiota produce short chain fatty acids (SCFAs), vitamins and amino acids and facilitates the absorption of complex carbohydrates (3) (12). They produce bacteriocins and antibiotics and inhibit the colonization of pathogens (13, 14). Gut Microbiota are important players in role in element cycling (15). Furthermore, they are involved in the homeostasis and integrity of the intestinal barrier (14, 16).

Different gases, enzymes and metabolites that are produced by the gut Microbiota play beneficial roles in their host. Sixty to seventy percent of the energy supply of colonocytes and enterocytes are provided by SCFAs oxidation (17, 18). Furthermore, SCFAs that are produced by the gut Microbiota, exist in hepatic, portal, and peripheral blood. Carbohydrate and lipid metabolism are influenced by these SCFAs (18). Moreover SCFAs play important role in regulation of the blood pressure (19).

Dysbiosis

Dysbiosis is defined as changes in the composition and function of the Microbiota. Dysbiosis has been shown in several diseased conditions such as asthma (20), inflammatory bowel disease (21), obesity (22), Parkinson's disease (23), heart failure (20), diabetes mellitus (20, 24), non-alcoholic fatty liver disease (25), allergic disorders (26), cardiovascular disease (27), cancer (28, 29), chronic kidney disease (17) and psychiatric and mood disorders (30).

Dysbiosis is associated with decrease of the number, activity, metabolites or enzymes of the useful commensal bacteria; or because of a rise in the number, activity, metabolites or enzymes of the potentially harmful microorganisms.

The gut Microbiota and the immune system:

The effects of the gut Microbiota on the immune system has been shown by several studies. While a normal gut Microbiota is essential for existence of a normal immune system, dysbiosis can result in deviation of immune responses.

T-cells differentiation in the intestine and gut-associated lymphoid tissues is affected by SCFAs. Because SCFAs are transported into the blood, they affect T cell activity in other tissues, as well. Other immune cell types like antigen presenting cells and neutrophils are affected by SCFAs too. Furthermore, the innate immunity and the generation of effector T cells are promoted by SCFAs too. (31). Regulatory T cells (Tregs) play key roles in limiting the inflammatory responses and preserving the immunological self-tolerance SCFAs are the required nutrients for growth of Tregs. (20, 32). Peripherally-derived Tregs (pTregs) mainly develop in colon and SCFAs augment the expansion and function of these cells (33).

In addition to the abovementioned effects, there are other Microbiota-induced beneficial effects on immune system. For example, the gut Microbiota plays an important role in regulating the cytokine production (34). Peripheral and mucosal immune systems need the gut Microbiota for priming. Furthermore, the gut Microbiota interact with different elements of specific immune system in or out of the Peyer's patches. Such an interaction plays a key role in structural shaping and functional priming of lymphoid tissues (16, 35). The abovementioned findings are just a few examples of the beneficial and critical effects of the gut Microbiota on immune system. In brief, we can say the gut Microbiota maintain the homeostasis of innate and adaptive immune systems (36). The effect of the gut Microbiota on immune system is so deep that, no surprisingly, has resulted in the "microflora hypothesis". According this hypothesis, development of a normal immune system and homeostasis needs the commensal Microbiota that

protect their host immune system from dysregulation (37). If the gut is healthy and has an intact epithelial cell barrier, mucus, secretory IgA, defensins and pattern recognition receptors, there would be a tolerance in the intestinal immune system against the resident commensals. Such a tolerogenic environment is in favor of production of transforming growth factor β (TGF-β) and Tregs. The production of Microbiota-specific IgAs is promoted by TGF-β and interleukin 10 (IL-10) that are produced by Tregs (33).

As abovementioned, the gut Microbiota keeps homeostasis of the host immune system (36). So, it means that not all the effects of the gut Microbiota on immune system is tolerogenic. It means that in some instances a normal gut Microbiota activate immune system to accomplish a good job against the pathogens.

Dysbiosis and immune system

Unlike a normal gut Microbiota, dysbiosis is associated with deviation of immune response and abnormal cytokine production. It has been shown that production of some Proinflammatory cytokines, such as tumor necrosis factor (TNF)α and interferon (IFN)γ, is affected by specific microbial metabolic pathways. This effect may be due to microbial metabolites, such as metabolism of tryptophan. This pathway can modulate the production of cytokines. (38, 39). Specific microbial metabolic pathways produce tryptophol, a tryptophan metabolite, and palmitoleic acid, a palmitic acid metabolite (34). It has been shown that TNFα response is strongly suppressed by tryptophol and IL-1β and IFNγ-induced apoptosis is inhibited by palmitoleic acid (40). Different patterns of cytokines are associated with different differential abundance of specific species of the gut Microbiota, so it could be deduced that changes in the composition of gut Microbiota result in alteration of immune responses (41, 42). The above-mentioned findings can be considered as more evidences to explain the relationship between dysbiosis and increased disease susceptibility.

Conclusion

The pattern of the gut Microbiota can affect the immune system. Whereas a normal gut Microbiota play a crucial in maintenance of the homeostasis of the immune system, dysbiosis can lead to deviation of immune responses. Different elements of innate and adaptive immune systems can be affected by the gut Microbiota.

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