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Academic Journal of Microbiology & Immunology

Iris Publishers

Mini Review

Gut Microbiota and Modulating Immune Response

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Received Date: October 12, 2020

Published Date: October 21, 2020

Abstract

A healthy body has healthy gut microbiota. Unusual interactions between the microbiome and the host's immune system in genetically susceptible individuals may contribute to the development of immune-mediated diseases. It is nearly 2kg of the host weight of the microbiome. Alteration of the microbiome, directly and indirectly, can significantly affect immune system regulation. The commensal gut microbiome plays a critical role to protect mucosal-immunity hemostasis. The intestinal tract has more resident immune cells such as the macrophages, dendritic cells, various subsets of T cells, B cells. In dysbiosis, disrupted epithelial barrier and leaky gut lead to inappropriate immune cell and gut microbiota interaction induce severe inflammation.

Introduction

The healthy gastrointestinal (GI) tract depends on healthy gut microbiota [1]. Gut microbiota educated the immune system the means, equilibrium of bacteria in our gut influences the hemostasis of our immune system, dysbiosis in the gut leads to the growth of many opportunistic pathogens, then they can shift the immune system to an inflammatory state [2]. It is well established that the failure of the immune system to maintain a balance between response and tolerance play a critical role in most autoimmune diseases such as; Inflammatory Bowel Disease (IBD), Type II Diabetes, rheumatic arthritis, and multiple sclerosis (MS) [3]. The four main human gut microbiota phyla: Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria [4]. Disorder of the gut microbiome affected by environmental factors like; antibiotic use, diet, air pollution, stress, and changes in geography can result in the systemic spreading of four main microbiota phyla, susceptibility to pathogenic invasion, and aberrant immune responses [5]. Since the microbiota is 10 fold more than the host's genome every variation on gut microbiota can regulate innate and finally adaptive immune response [6]. Maintenance of immune response homeostasis is imperative to host survival [7]. Therefore, the immune tolerance mechanism associated with gut microbiota is most critical. Foxp3 regulatory T (Treg) cells have a central role to maintain both peripheral and mucosal homeostasis [8]. Although the thymus is an important place for raising Treg cells, the gastrointestinal tract is another critical

place to specialized properties to induce Treg cells [9,10]. In the gut for inducing tolerance and Treg needs to define populations of antigen-presenting cells (dendritic cell and macrophage) and also, produce specific factors involved in the such as the cytokines TGF-β, IL-10, the vitamin A metabolite retinoic acid (RA), and microbial metabolites butyrate and acetate [7,11,12]. This review aims to investigate the regulatory pathway by antigens derived from the commensal microbiota for the control of mucosal homeostasis.

Induce regulatory response by the microbiota

Gut microbiota is a crucial and active inducer of regulatory responses. This interaction between host-gut microbiota initiates by the recognition of conserved microbial associated molecular patterns (MAMPs) to present PRRs on professional immune cells in the lamina propria (dendritic cells (DC) and macrophages). The microbiota antigen and its metabolite play an essential role in the regulatory pathway. Endotoxin in gram- negative bacterial (LPS) stimulate TLRs (TLR4) overexpression on gut epithelial cells and induce inflammation response. On the other hand, the polysaccharide A (PSA) from Bacteroides fragilis could promote regulatory response with TLR2/TLR1 expressed by T cells and IL-10 secretion [13,14]. Mazmanian et al., have shown that B.fragilis in mice can protect it from colitis induced by Helicobacter hepaticus, because of B.fragilis can promote Treg cell function and limit Th17 responses [13]. Th17 cells produce IL-17 and particularly IL-22 has a homeostatic role against the pathogens in the gut [15]. However, the induction and maintenance of Th17 depended on antigen derived from the gut microbiota. The protection of Th17 and Treg hemostasis have an important effect on producing antimicrobial peptides (α-defensins, RegIIIγ) [16], induce mucus production, increases epithelial regeneration, and regulate of ulcer repair [17]. Segmented Filamentous Bacteria (SFB) has significantly increase residents of Th17 and Th1 in the terminal ileum and also induce secretion of IgA [18,19]. However, SFB can regulate the mucosal immune system [20]. Secreted IgA (sIgA) plays a critical role in dysbiosis because of regulating adhesion of commensal bacteria to the epithelial barrier and intestinal dendritic cells. The secretion of sIgA regulates by microbiota [21]. ZPSs is a molecule that code by the genome of various bacterial phyla with anti-inflammatory properties. It has shown that Bacteroides cellulosilyticus by genetically ZPS operons can induce Treg and IL-10in in vitro [22,23]. Finally, led to the protection of a mouse model of

inflammatory disease. Invariant natural killer T cells (iNKT) are also present in the intestines to recognize glycolipid antigens. Gut microbiota can regulate the development and activation of iNKT and vis versa [24]. iNKTcells on the protection of the intestinal microbiota hemostasis. It has demonstrated, transfer of iNKT cells to knockout (KO) mice were able to restore the gut microbiota and ameliorated gut inflammation after colitis [25,26].

The metabolite of the microbiota like short-chain fatty acids (SCFAs) recognizes by PRRs leads to the control of various mechanisms of the intestinal mucosal immune system [27]. Butyrate enhanced regulatory T cell development and induce anti-inflammatory activities [28]. The microbiota can convert tryptophan into indoles that improve epithelial cell barrier function [29]. Also, the microbiota metabolites can prevent the production of pro-inflammatory cytokines by macrophages and dendritic cells [7].

An interesting point about the gut microbiome is not only regulated mucosal immunity in the intestine but also interactions with extra-intestinal organ immunity [3]. Microbiome-associated metabolites translocate from the intestinal lumen to various organs (e.g., liver, brain, or lung) which is called gut-brain-axis [30], gut-lung-axis [31], gut-Liver-axis [32]. This crosstalk led to modulation of organ-specific immune responses [3]. The gut- resident pathobiont Klebsiella pneumoniae can translocate and induce Th17 cell responses in the liver. Microbiome-derived SCFAs can regulate lung immune response in viral infections and defense against airway inflammation [3].

In conclusion, gut microbiota plays a fundamental role in promoting and regulate both innate and adaptive immunity. It has been shown to limit GI inflammation both by the induction of immunoregulation and the direct inhibition of APC activation. However, commensal dysbiosis and variation in metabolites have a critical role in most autoimmune diseases and severe inflammation immune response not only in the gut but in other organs.

Acknowledgment

The authors would like to express their gratitude to Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Perelman School of Medicine, University of Pennsylvania, Philadelphia and Harvard Medical School, Boston for their support throughout the course of this work.

Acknowledgement

None

Conflict of Interest

No conflict of interest.

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