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Gut biofilm forming bacteria in inflammatory bowel disease

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ABSTRACT

Inflammatory bowel disease (IBD) symbolizes a group of intestinal disorders in which prolonged inflammation occur in the digestive tract (esophagus, large intestine, small intestine mouth, stomach). Both genetic and environmental factors (infections, stress, diet) are involved in the development of IBD. As we know that bacteria are found in the intestinal mucosa of human and clinical observations revealed bacterial biofilms associated with patients of IBD. Various factors and microbes are found to play an essential role in biofilm formation and mucosal colonization during IBD. Biofilm formation in the digestive tract is dependent on an extracellular matrix synthesized by the bacteria and it has an adverse effect on the immune response of the host. There is no satisfactory and safe treatment option for IBD. Therefore, the current research aims to disrupt biofilm in IBD and concentrates predominantly on improving the drug. Here, we review the literature on bacterial biofilm and IBD to gather new knowledge on the current understanding of biofilm formation in IBD, host immune deregulation and dysbiosis in IBD, molecular mechanism, bacteria involved in biofilm formation, current and future regimen. It is urgently required to plan new ways to control and eradicate bacteria in biofilms that will open up novel diagnostic and therapeutic avenues for IBD. This article includes the mechanism of signaling molecules with respect to the biofilm-related genes as well as the diagnostic methods and new technologies involved in the treatment of IBD.

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1. Introduction

Bacterial biofilms are self-regulating, aggregated form of bacteria that form communities of single as well as multi species which cooperate with the environment to carry out different processes. The bacteria produce exo-polysaccharide (EPS) to form an EPS matrix for the stability of biofilm [1]. The bacteria have properties to adhere on the solid surfaces to form slimy, slippery coat on different surfaces which are most prevalent on wet surfaces [2]. The major steps involved in the biofilms formation are – formation of conditioning layers, bacterial adhesion, growth and lastly biofilms maturation. The basic composition of bacterial biofilms [3] are microbial cells (2–5%), DNA and RNA (<1–2%), polysaccharides (1–2%), proteins (<1–2%) and water (up to 97%). The basic characteristics of biofilms include the syntrophic relationships in which biofilms provide an ideal environment for the establishment of the syntrophic relationship that enables two metabolically distinct types of bacteria to depend on each other to utilize certain substrates for energy production [4]. The antibiotic resistance where biofilms are associated with an emergence of antibiotic resistant bacteria [5]. The EPS matrix prevents certain antimicrobial agents restricting diffusion of compounds from the surrounding into the biofilms. The intercellular communication where biofilms enable cells to live close to each other to facilitate the exchange of plasmids and free DNA that enable them to overcome different environmental stresses. The bacteria in biofilms use chemical communication known as quorum sensing that helps them to coordinate their metabolism and other complex processes [6].

Inflammatory bowel disease (IBD) is a chronic disease that comprises of Crohn's disease (CD) and ulcerative colitis (UC). Crohn's disease involved the gastrointestinal tract having characteristic by patchy transmural inflammation and the ulcerative colitis involved the colon only having mucosal inflammation. Ulcerative colitis (UC) is a chronic relapsing form of IBD in which the inflammatory response is located mainly within the colonic mucosa. The distal colon is always affected, and the disease generally progresses from its initiation site in the distal bowel toward the proximal large intestine. The severity condition in the UC can severely affect the quality of life and also if medical treatments are not effective then surgical removal of all or most of the colon is necessary. The role of commensal gut bacteria is significant and they help in the initiation and maintenance of UC [7]. This article includes that how bacterial biofilm enhances the severity of the disease. In addition to this, it will also explain the mechanism of pathogenesis of IBD through bacterial biofilm.

2. Biofilm, immune deregulation and dysbiosis in IBD

The biofilms represent the assemblage of microbial communities. The process of attachment to the surfaces regulates the activity of growth medium, cell surface etc. These biofilms are composed of EPS and microbial cells. The EPS are differed at chemical and physical level but composed of polysaccharides. The medium the composition will affect the biofilms formation that is nutrient rich medium form more biofilms as comparison to nutrient poor medium [8]. In the development of IBD, the immune system plays an important role and it invades the effect of microorganisms that are necessary for potentiating. The wall of intestine mainly consists of four layers that are *i*) the mucosa which is separated by a thin layer of smooth muscle from *ii)* the submucosa, *iii)* the muscularis propria, which is layers of smooth muscle and *iv)* the serosa, which is an outer layer of connective tissue. The mucosa mainly consists of a single layer of epithelial cells that involved in borders of the lumen, with the underlying loose connective tissue known as the lamina propria which contains numerous immune cells. The epithelial layer plays an essential role in the proper functioning of the gastrointestinal (GI) tract, involving secretion and absorption it also prevents unwanted solutes, microorganisms, and luminal antigens from entering the body [9,10]. Since the epithelium has to provide an effective barrier against harmful macromolecules and microorganisms; it must be permeable to nutrients as well as macromolecules during a controlled exposure of the mucosal immune system to microbial factors [11]. The impairment of this barrier function leads to the activity of increased permeability to luminal antigens that has been proposed as an initiating factor in the pathogenesis of chronic human inflammatory bowel diseases (IBD) like ulcerative colitis (UC) and Crohn's disease (CD) which are characterized by the activity of aberrant immune responses against microorganisms that are present in the intestine. Therefore these properties of increased permeability may play an important role in the inflammatory process and may be linked to the chronic mucosal damage that is observed in IBD.

A therapy for IBD involves the activity of oral administration of all three types that is probiotics, prebiotics, or synbiotics. Probiotics are live microorganisms that are beneficial to health when ingested by or administered to the human host. The prebiotics are food ingredients which stimulate the growth as well as the activity of intestinal bacteria that have properties of health-promoting [12]. In present, according to its superiority in weight, the overwhelming use of prebiotics are indigestible oligosaccharides (NDO) which include galacto-oligosaccharides (GOS), lactulose, inulins, and their fructo-oligosaccharide (FOS) derivatives that have been investigated extensively [13,14]. The term indigestible involves only to the