

Short-chain Fatty Acids as Main Metabolites of Intestinal Microbiota

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Abstract— The human intestine is inhabited by a complex and highly variable system of mutualistic microorganisms, composed of bacteria, fungi, viruses, archaea and protozoa. This ecosystem plays an important role in keeping the host physiology and homeostasis. Intestinal microbial species produce an extremely diverse reservoir of metabolites. In this review there is summarized research data about intestinal microbiota derived metabolites.

Keywords— Intestinal microbiota, butyrate, dietary fibers, short-chain fatty acids, microbial metabolites.

The intestinal microbiota is a key constituent that interact with the host by producing a variety of metabolite reservoirs from exogenous food substrates or endogenous host substances [1]. This abundant ecosystem facilitates a large number of physiological functions: fermentation of indigestible nutrients and synthesis of vitamins, protection against pathogens, maturation of the host immune system, and support of the intestinal barrier function [2].

In the process of evolution there was specialization and integration between separate groups of microbiota, so they act as a whole, working in concert in the interests of the entire system and the host [3].

metabolites are small molecules formed as intermediates or end products of microbial metabolism. They can result from bacterial metabolism of food substrates, modified host molecules such as bile acids, or directly from the bacteria. Signals from microbial metabolites impact immune maturation, immune homeostasis, host energy metabolism, and support of mucosal integrity [3].

The metabolites produced by the intestinal microbiota influence physiological processes both locally and systemically. They contribute to the metabolic phenotype of the host and hence may influence the risk of disease. Metabolic disorders are related to changes in the composition and function of the intestinal microbiota. Certain classes of microbiota metabolites, especially bile acids, short-chain fatty acids, branched-chain amino acids, N-oxide trimethylamine, tryptophan and indole derivatives, are involved in the pathogenesis of metabolic disorders.

short-chain fatty acids are carboxylic acids produced by dietary fiber fermentation, having 1-6 carbon aliphatic tails, with acetate, propionate and butyrate being the most abundant.

Short-chain fatty acids - acetate, propionate and, butyrate are end-products of microbial fermentation is involved in a variety of physiological functions. Short-chain fatty acids are involved in maintaining the integrity of the intestinal mucosa,

enhance glucose and lipid metabolism, and regulate the immune system and inflammatory responses.

Bacteroides thetaiotaomicron is a glutamate-fermenting commensal. Decrease of this bacterium in obese subjects is proportional to serum glutamate levels. There are suggestions that Prevotella copri and Bacteroides vulgatus directly impact host metabolism [1].

Study results indicate that low concentrations of butyrate are beneficial, while excessive luminal concentration can cause mucosal barrier disruption [5]. It has been demonstrated that high concentrations of Short-chain fatty acids induces intestinal mucosa injury in newborn rats [6]. They suppress IL-8 secretion and expression [7], although, high butyrate doses has the opposite effect [8]. Among the many microbial metabolites, short-chain fatty acids (butyric acid, acetic acid, propionic acid) are the major metabolites of the intestinal microbiota. They participate in systemic immune and inflammatory responses [9]. They lower pH and increase mucin production in the intestine. This cause reduced pathogen growth, adhesion and improved epithelial integrity. In result, these processes enhance systemic host immunity [10]. Disturbances in the composition of the microbiota are associated to the chronic diseases. The list of these diseases increased and involve inflammatory bowel disease, obesity and type 2 diabetes, autoimmune diseases such as type 1 diabetes, coeliac disease or allergic asthma [11,12]. Short-chain fatty acids molecules are found in the lungs, indicating that the lung microbiome does not produce them in large amounts and that circulating short-chain fatty acids do not accumulate in lung tissue [13,14]. Intestinal microbiota is the one of the mediators of the abnormal immune responses in hosts caused by SARS-CoV-2 [15]. Intestinal bacteria-derived molecules enter in the peripheral circulation and bone marrow and participate in the activation of the immune system, which than contributes to homeostasis and immunity in the lungs [16]. Short-chain fatty acids can also generate macrophages and dendritic cell precursors in the bone marrow [17].

Awareness of the role of microbial metabolites may provide a new approach to the treatment and prevention of inflammatory diseases.

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