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Special Issue: Interaction between gut microbiota and host immune cells

Brief Review

Interaction between gut microbiota and host immune cells

Akihiko Yoshimura

Department of Microbiology and Immunology, Keio University School of Medicine, Shinjuku-ku, Tokyo, Japan, and Japan Science and Technology Agency (JST), CREST, Chiyoda-ku, Tokyo, Japan

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Correspondence should be addressed to:
Akihiko Yoshimura, PhD., Department of Microbiology and Immunology, Keio University School of Medicine, Shinjuku-ku, Tokyo 160-8582, Japan. Phone: +81-3-5363-3767, Fax: +81-3-3360-1508, E-mail: yoshimura@a6.keio.jp

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The surface of the human body, including the respiratory and gastrointestinal (GI) tracts, is populated with complex communities of microorganisms, termed microbiota, with the highest density of colonization (>10^{12} organisms/cm^2) found in the GI tract[1]. The vast majority of these organisms have not been cultivated as they are anaerobic bacteria, which require complicated techniques for phenotypic profiling and application[2, 3]. Recent advances in culturing techniques, however, have allowed the retrieval of hundreds of bacterial species from human stool samples[4].

Over the last few years, the field of mucosal immunology has revealed that the microbiota plays important roles in the host immune system. Here, we have summarized recent studies regarding the interaction between microbiota and the mucosal immune systems in health and diseases. We specifically assess their contribution to obesity and cancer (chronic inflammatory conditions) as well as to inflammatory autoimmune diseases (e.g., inflammatory bowel disease and type 1 diabetes) and allergic syndromes. Optimization of the microbiota composition has been attempted via the intake of probiotic bacteria in various fermented foods and via fecal microbiota transplantation (FMT) from healthy donors to patients with *Clostridium difficile*-induced colitis. The presence of certain microbiota species affects the development and function of various types of immune cells, such as regulatory T (Treg) cells and interleukin-17-producing helper T (Th17) cells. Furthermore, innate lymphoid cells (ILCs) have also been shown to be regulated by microbiota. These findings indicate that manipulation of the microbiota could improve health and chronic diseases via immune regulation.

In this review, we invited specialists in this field. Dr. Nakagawa and I summarized the relationship between microbiota and diseases, especially food allergy. Dr. Hara's group has been studied relationship among intestinal microbiota, obesity and cancer.

Using mouse models, they found that dietary or genetic obesity provokes alterations of gut microbiota profile,

thereby increasing the levels of deoxycholic acid (DCA), a gut microbial metabolite product. They fond that DCA increases the levels of DCA in liver and provokes DNA damage-induced cellular senescence and hepatocellular carcinoma (HCC) development. Dr. Honda's group has first discovered specific microbes that induce Th17 or Treg cells in the intestine. Their findings suggest that various intestinal bacteria differentially regulate the development and function of different immune cell populations. Although it is clear that regulation of the hostcommensal relationship is crucial to mammalian health, the underlying mechanisms regulating gut homeostasis are yet to be elucidated. Dr. Ohno's group discusses about unique "gut ecosystem" which is generated by a complex host-gut microbiota interactions. This ecosystem is thought to play a variety of roles in host physiology and pathology, including the modification and shaping of the host immune system. By using (meta)transcriptome and metabolome, his group recently discovered the mechanism by which the gut microbiota-derived short-chain fatty acid acetate protects mice from enterohemorrhagic Escherichia coli O157-infectious death by promoting peripherally derived regulatory T cells. Dr. Hase's group focused on epigenetic modifications, including DNA methylation and histone methylation/acetylation modified by host and gut microbiota interactions. Dr. Hachimura's group and Dr. Kanai's group focused on the relationship between treatment of diseases and microbiota. Probiotics may prevent or alleviate allergy through inhibition of Th2 responses by enhancement of Th1 response, induction of apoptosis, induction of Treg cells, and other mechanisms. Recent advances in next-generation sequencing techniques revealed a correlation between alteration of composition of gastrointestinal microbiota and inflammatory bowel disease (IBD). Dr. Kanai's paper summarized trials for the treatment of IBD by restoring altered microbiota using such methods as probiotics and fecal microbiota transplantation.

Significant lifestyle and environmental changes in modern developed countries may be responsible for the altered gastrointestinal microbiota, and may have greatly contributed to the rapid rise of various diseases. Our goal is not only the understanding of the role of microbiota and diseases, but also modification of microbiota for the disease treatment. I hope this special issue of the Inflammation and Regeneration is useful for readers of a variety of fields.

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