Summary
The intestinal environment, formed from dietary components and intestinal bacteria, plays a pivotal role in maintaining our health. Most studies have focused on the functions of dietary components and intestinal bacteria, separately. However, with the new concept of postbiotics, bacterial metabolites produced from food components as substrates, research including the perspective of the interaction between dietary components and intestinal bacteria has become important. In this paper, the importance of food is presented, including the viewpoint of postbiotics, in relation to the interaction between the intestinal environment and health.

Key Words
postbiotics, intestinal bacteria, dietary components, fermented food, immunity, personalized and stratified nutrition

As many people become more health-conscious, the function of the intestine is attracting attention. The intestine not only acts as a digestive organ, but also plays an important role as the largest immune organ in the body, where many immune cells exist and control host immunity. Immunity is a system for eliminating pathogens generally, but also contributes to the maintenance of homeostasis, and thus disrupted immunity would lead to the development of allergies and inflammatory diseases. In addition, accumulating evidence has revealed that disorders of the immune system are involved in diseases such as diabetes and dementia, which were previously thought to be unrelated to the immune system. These findings underscore the growing importance of the intestine in health.

As recognized in the antibody responses to vaccines, there are great individual differences in immunity. It is generally known that one factor that determines the strength of immunity is intestinal environment factors such as dietary components and commensal bacteria. Although gut commensal bacteria exhibit individual differences, recently probiotics (bacteria that are useful to the body) and prebiotics (food for useful bacteria) have been used in yogurt and other products to supplement the bacteria that are often lacking, so they are getting familiar to many people.

More recently, “postbiotics” has attracted attention as a new keyword to understand the effects of diet and commensal bacteria to our health. Postbiotics are metabolites produced by microorganisms in the gut and fermented foods generated from dietary components, which have useful effects on biological functions such as immunity and health conditions after being absorbed into the body. Upon the introduction of the concept of postbiotics, it is expected that the conventional ideas of “eat XX grams of food A” and “bacteria X seems be good for our health” will be replaced with the idea that “it is important that bacteria X use food A to produce a specific metabolite (=postbiotics)”.

The health benefits of short-chain fatty acids have been the focus of much attention recently. Short-chain fatty acids are metabolites derived from dietary fiber and oligosaccharides and produced by gut commensal bacteria, and thus these are one of the postbiotics. Furthermore, recent studies, including ours, have shown that postbiotics also include lipid metabolites produced from fatty acids in dietary oils.

Among the fatty acids contained in dietary oils, omega-3 and omega-6 fatty acids are called essential fatty acids since they cannot be synthesized by the body of mammals including humans, and thus they are strongly influenced by food. They have long been known to be associated with immune regulation and immune diseases (i.e., inflammation and allergies) and have attracted widespread public attention. Our group found the beneficial effects of omega-3 fatty acids to control various disease such as food allergy, allergic rhinitis, allergic dermatitis, and atherosclerosis in a mouse model (1–8). Recent advancements in metabolome analysis have made it possible to analyze in detail the effective metabolites produced from each fatty acid and the responsible receptors. Our group revealed that 17,18-ep-
oxyeicosatetraenoic acid (17,18-EpETE), 15-hydroxyeicosapentaenoic acid (15-HEPE), 12-hydroxyeicosapentaenoic acid (12-HEPE), 14-hydroxydocosapentaenoic acid (14-HDPA) and others were effective metabolites in the body, each targeting different receptors and cells for the control of inflammation and allergies (1–8). More recently, we have shown that metabolites are generated not only by metabolism in the body, but also by microorganisms in intestinal bacteria and fermented foods, some of which are absorbed into the body and affect immune functions and diseases. For example, αKetoA is produced by gut commensal bacteria, but not in the body, using α-linolenic acid as a substrate, and it exerts anti-inflammatory effects by acting on macrophages, improving allergic dermatitis and diabetes upon absorbed in the intestine (9). In addition, we are doing the analysis using human samples and data. For example, we have found that αKetoA is generally increased in those who consume high amounts of α-linolenic acid. We simultaneously found that the efficacy of αKetoA production varies among individuals even if they consume the same amount of α-linolenic acid. Gut commensal bacteria is known to show large individual differences, presumably explaining the different efficacy of αKetoA production.

Another example includes individual differences in the production of 17,18-EpETE, an anti-inflammatory metabolite produced from the omega-3 fatty acid EPA. 17,18-EpETE has been identified as a metabolite produced in the intestinal tissue, but it is also known to be produced by bacteria. In our research, we are using Bacillus to make 17,18-EpETE and apply this system to the development of drug discovery and functional foods (10).

Under the social and academic situation, we believe that it is important to investigate what kind of bacteria are present in the gut, what kinds of diets used, what metabolites produced, and how they affect our health. In our ongoing analysis, healthy individuals as well as patients participate to provide blood, feces, and saliva for the analysis of intestinal bacteria, metabolites, and health parameters and a vast amount of data on lifestyle habits such as diet and exercise, health-related information such as health checkups, medications, and medical history. These big data are analyzed by using AI and other bioinformatics methods to develop a personalized and stratified nutritional guidance system (11–13). Furthermore, we extract targeting factors related to health from human data analysis and elucidate the mechanisms of action of useful bacteria and postbiotics by linking with basic research such as animal models and biochemical methods, leading to the development of highly functional foods, drug discovery, and diagnostic systems.

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REFERENCES


