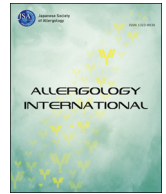




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Editorial

Old friends, microbes, and allergic diseases



In *Allergology International* (AI) Vol. 66, Issue 4, we offer a set of review articles entitled “Old friends, microbes, and allergic diseases” as well as original articles and letters to the editor. We believe that this issue will be of great help in understanding how microbes are associated with the onset of allergy.

Although genetic factors are undoubtedly involved in the pathogenesis of allergic diseases, environmental factors are thought to be responsible for the recent rapid increase in the number of cases. In 1989, Strachan proposed the so-called “hygiene hypothesis” to explain the recent rise in allergic diseases in the modern world.¹ This theory holds that exposure to pathogens early in life encourages the development of the human immune system and that consequently, the highly sanitary conditions found in “westernized” countries hamper the development of beneficial immunities. Since commensals but not pathogens are microbes we encounter daily, the hygiene hypothesis has been replaced by the “old friend hypothesis” proposed by Rook in 2010.² In this hypothesis, “old friend” refers to non-harmful microbes that co-evolve with humans, including some parasites that humans have lived with for a long time. The enormously diverse “old friend” microbes interact with the human immune system and induce balanced regulatory immunity to prevent hyper-reaction.³ It is postulated that the use of antibiotics and/or changes in diet may have led to a loss of diversity and thus to an uncontrolled immune system.

At two to three years of age, the human gut microbiome varies in composition and metabolic functions. After this period, the gut microbiota includes adult-like, more stable microbial species. The importance of the infant gut microbiome in preventing long-lasting type 2 immune response is elegantly demonstrated by a pioneering study by Japanese researchers using a mouse model.⁴ Perinatal factors such as mode of delivery, diet, genetics, etc. contribute to microbial colonization in the gut of neonates. In this issue, Prof. Nakayama and his colleague summarize recent findings regarding the establishment of gut microbiota, including the importance of various factors related to the development of the immune system and allergic diseases later in life.⁵ It is of note that while it has long been thought that infants are sterile and encounter microbes only after birth, several recent studies have revealed that human intestinal microbiotas are seeded before birth.⁶

Recent studies indicate that nutrients and their metabolites have a profound effect on the shaping of the immune system.⁷ Gut microbiomes produce both useful and harmful metabolites from dietary materials. Prof. Kunisawa and his colleague contribute

an excellent review of the role of gut microbiomes in regulating the immune system through their metabolites.⁸ Since diet can modulate the composition of gut microbiomes, we need to feed ourselves appropriately.

The internationally endorsed definition of probiotics is “live microorganisms that, when administered in adequate amounts, confer a health benefit on the host.” Prebiotics is defined by FAO/WHO as “a non-viable food component that confers health benefit(s) on the host associated with modulation of the microbiota.” Synbiotics is a combination of probiotics and prebiotics, originally developed to overcome possible survival difficulties for probiotics. Very recently, although there is not yet a great deal of evidence, the World Allergy Organization (WAO) has recommended probiotics and prebiotics for the primary prevention of allergic diseases in high-risk infants. Prof. West and his colleagues give a comprehensive review of probiotics, prebiotics, and synbiotics for prevention of allergic diseases.⁹ As shown above, the definition of probiotics is “live microorganisms”; thus, dead microbes are not probiotics. However, recent studies have shown that inactivated microorganisms strongly affect the modulation of the immune system.¹⁰ Further studies are warranted to better understand the function of gut microbiota in shaping the immune system and overall human health.

Although much fewer compared with those in the gut, a substantial number of microbiota species live on the skin.¹¹ Using a molecular method, Kong, *et al.* have shown that the skin microbiome changes in association with disease flares and treatment in children with atopic dermatitis.¹² Prof. Núñez and his colleagues contribute an excellent update on the skin microbiome and atopic dermatitis, especially focusing on the role of *Staphylococcus aureus*.¹³ We expect that in the coming years, studies on microbiota in the nose and bronchus will shed light on the role of microbiomes in allergic airway diseases.

Honda *et al.* report cutting-edge findings regarding hereditary angioedema (HAE).¹⁴ Besides having a deficiency of the C1 esterase inhibitor, two-thirds of HAE patients showed immunological abnormalities, including lower opsonization, lower rates of immune complex solubilization, and/or the presence of serum anti-C1q antibody plus elevated levels of immune complex. Decreased phagocytosis of serum-treated apoptotic cells and delayed clearance of the immune complex might be followed by dysregulation of C1q-related immunological response, inducing the production of anti-C1q antibody. Long-term immunological monitoring of patients with HAE would be beneficial in understanding the pathogenesis and progression of these abnormalities.

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Chronic rhinosinusitis is a common nasal disease. Eosinophilic chronic rhinosinusitis (ECRS) is characterized by eosinophilic infiltration; the number of such cases has been increasing in Japan. The molecular biological mechanism underlying the refractoriness of ECRS is unclear. Tokunaga *et al.* performed whole-transcriptome analysis with next-generation sequencing (RNA-seq) to investigate the molecular biological mechanism of ECRS.¹⁵ They found for the first time that TRPV3 (transient receptor potential cation channel, subfamily V, member 3) is highly expressed in ECRS nasal polyps. This novel discovery may give a clue to clarifying the molecular biological mechanism responsible for the refractoriness of this disease.

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Conflict of interest

The authors have no conflict of interest to declare.

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