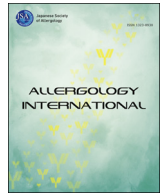




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Editorial

Genetic or epigenetic regulations in immune responses and allergic diseases



In *Allergy International* (AI) Vol. 65 Issue 2, we offer a set of review articles entitled “Genetic or epigenetic regulations in immune responses and allergic diseases” as well as original articles and letters to the editor. We believe that this review series will provide you with new understandings of immune responses and allergic diseases controlled in a transcriptional or an epigenetic manner.

Both basophils and mast cells are important players at immune responses and allergic diseases.^{1,2} In spite of some similarities, such as expression of high-affinity IgE receptor on cell surfaces, they have different characteristics—distribution in bodies and life span—so their functions are non-redundant. Basophils and mast cells develop from their common progenitors via their own progenitors. Several critical transcriptional factors are involved in their development, and these transcriptional factors organize hierarchical cascades. Prof. Tamura's group introduces the developmental pathways of basophils and mast cells as well as the transcriptional factors regulating their development.³ They show the importance of the IRF8-GATA2 pathway in generating the basophil/mast cell-common progenitors called pre-basophil and mast cell progenitors (pre-BMPs), whereas the STAT5-GATA2 pathways, followed by C/EBP α or MITF, determine the fate of pre-BMPs into basophils or mast cells, respectively. Moreover, C/EBP α or MITF expressed in mature basophils or mast cells, respectively, inhibits each other's expression, stabilizing differentiation. Thus, a sophisticated network of transcriptional factors orchestrates the development of basophils and mast cells.

Prof. Vercelli presents the concept of epigenetics as well as the status of epigenetics studies in allergic diseases.⁴ Epigenetics is defined as heritable changes in gene activity that are independent of alterations in the underlying DNA sequence.^{5–7} The potential role of epigenetics in allergic diseases is drawing more attention. One reason is that since epigenetic mechanisms transduce environmental signals and regulate developmental programs, it is possible that epigenetic regulation is involved in allergic diseases. Another is that genome-wide association studies (GWAS) cannot fully account for phenotypic variance in asthma in spite of the strong genetic component in asthma. Prof. Vercelli introduces some results of epigenetics studies in allergic diseases in this review article; however, she says that research into asthma and allergy epigenetics is still in its infancy and that several hurdles must be overcome for the field to bloom.

Among the contributors to this issue, Yoshida *et al.* report the factors associated with the severity of rhinoconjunctivitis using a nation-wide, web-based survey.⁸ Allergic rhinitis—characterized by rhinorrhea, sneezing, nasal obstruction, and nasal itching—that is accompanied by ocular symptoms is referred to as allergic rhinoconjunctivitis.⁹ The symptoms start mostly before the age of twenty, becoming evident in 40% of patients by the age of six.¹⁰ The authors enrolled 26,725 children from six to twelve years old, among whom 5175 (19.4%) presented current rhinoconjunctivitis. Living in areas with a high cedar and cypress pollen count; having concurrent eczema; and a maternal, but not paternal, history of asthma and allergic rhinitis were risk factors for severe rhinoconjunctivitis, whereas living with fur-bearing animals (pets) before the age of one was a protective factor against it. This study shows that environmental factors such as pets, pollen, comorbidities, and a maternal history of allergic diseases could be important in determining the severity of rhinoconjunctivitis.

Tsuji *et al.* show the therapeutic efficacy of immunomodulator FTY720 (fingolimod) on mite extract-treated NC/Nga mice.¹¹ FTY720 is a compound modified from myriocin (ISP-1) derived from *Isaria sinclairii*, a fungus used in traditional Chinese medicine.^{12,13} FTY720 was discovered by Prof. Fujita in collaboration with Japanese pharmacological companies. FTY720 has immunosuppressive activities different from other immunosuppressive agents such as tacrolimus hydrate or cyclosporine, and it has been approved for treatment of multiple sclerosis in many countries. On the other hand, mite extract-treated NC/Nga mice manifest steroid-resistant atopic dermatitis-like skin inflammation. In these mice, FTY720 improved skin inflammation, including epidermal barrier dysfunction. This study shows promising usefulness of FTY720 in treating intractable atopic dermatitis.

It is widely accepted that the prevalence of allergic diseases has risen worldwide; however, some reports show stable or even decreasing rates of childhood allergic diseases in Western developed countries.^{14,15} Kim *et al.* examined the prevalence of allergic diseases in Korea from 2009 to 2014 based on the Korean National Health Insurance database.¹⁶ Because a single mandatory nationwide insurance system was established by the government in 1989, Korea has a nationwide disease database that includes virtually everyone in the country. The prevalence of atopic dermatitis, allergic rhinitis, and asthma in 2014 was 19.0, 133.1, and 36.3 per 1000 people, respectively. The prevalence of allergic rhinitis continuously increased (by 3.2% per year on average), especially in the age group under ten, whereas that of atopic dermatitis and asthma

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slightly decreased in the past six years (by –2.6% and –5.8% per year on average). This is the first report using a nationwide database to suggest that the prevalence of chronic allergic diseases might have reached a plateau or have already begun to decline in some Asian country.

We offer our appreciation to all the authors for their contributions to the present issue of *Allergology International*.

Conflict of interest

The author has no conflict of interest to declare.

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