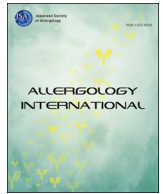




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Notes from Japanese Society of Allergology

Celebration of the 50th anniversary of IgE discovery



IgE (gamma E) was discovered by Kimishige and Teruko Ishizaka, who are honorary fellows of Japanese Society of Allergology, in 1966 as the material identity of reagin (reported in 1921 by Prausnitz and Kuestner as an internal factor that is present in serum of atopic patients and can cause skin allergic reaction by antigen challenge). In 1967, almost at the same time, Johansson and Benich discovered IgE myeloma (ND myeloma). Then, after confirmation by these investigators, it was officially recognized as the new class of immunoglobulin in 1968.

We, Japanese Society of Allergology, therefore, celebrated the discovery of IgE on 19th of June, 2016, the last day of 65th Annual Meeting of the Society, by holding lectures of internationally outstanding professors, who are closely related to Ishizakas' research activities, in addition to Prof. Kimishige Ishizaka himself, who was the first speaker (Fig. 1).

Around 1965, almost all people believed that the reagin belongs to IgA immunoglobulin class. However, Kimishige Ishizaka, though he had once reported this theory as well as other investigators, kept investigating other possibilities since there were several inconsistencies about the theory of reagin to be IgA. Then, he discovered that reaginic activity of the IgA fraction is associated with an impurity, which was not detectable by usual immunochemical methods of 1960's. Thus, they gave up purification of reagin, since it was estimated less than 1 µg per mL in serum of the patients. They switched their strategy to prepare the rabbit antibodies specific for reagin, and to identify the reagin in vitro, by using the rabbit antibodies. Although now every researcher can conceive it, such a strategy was unprecedented. It was another Columbus's egg.

After exchanging IgE-containing sera, the Swedish group did not send their myeloma protein purified from the first patient to Ishizakas anymore, since Pharmacia Company developed Radio-Allergo-Sorbant-Test and retained its patent. However, the second patient with IgE myeloma was found in Dartmouth. The patient, Mr. Peter Shackford generously agreed to give his plasma, and thus Ishizakas

were able to obtain IgE myeloma plasma of more than 30 L until he passed away.

Ishizakas could monopolize the extremely valuable plasma. However, they did not do so. In fact, Ishizakas sent the P.S. IgE over almost all researchers of this field upon request without any conditions, even to their rival researchers who once accused Ishizaka's discovery since they could not reproduce it probably due to technical immaturity. Then, basophils and mast cells were found to have receptors for IgE a few years after discovery of IgE. Thus, almost all the mechanisms involved in the IgE-mediated allergic reaction were clarified soon after.

The second speaker was Prof. Thomas A.E. Platts-Mills whose talk's title was "The relevance of IgE antibodies to the diagnosis and treatment of allergic diseases". His talk included his recent discovery of galactose-specific IgE present in the patients with the delayed anaphylaxis to red meat (Fig. 2). The third lecture was given by Prof. Stephen J. Galli and the title was "What good are mast cells and IgE? They can enhance survival during innate and acquired host responses to venoms". He has recently discovered IgE and mast cells playing a protective role in host defense by efficiently destroying venoms (Fig. 3). Then, Prof. Toshiaki Kawakami gave us a lecture about the divergent properties of IgE molecules. He showed that some IgE molecules can bind to the histamine-releasing factor and play more enhanced roles in allergic diseases such as food allergy (Fig. 4). The last speaker was Prof. Tadamitsu Kishimoto, who discovered IL-6 and is



Fig. 1. Prof. Kimishige Ishizaka, La Jolla Institute for Allergy and Immunology, USA.

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Fig. 2. Prof. Thomas A.E. Platts-Mills, University of Virginia School of Medicine, USA.



Fig. 4. Prof. Toshiaki Kawakami, La Jolla Institute for Allergy and Immunology, USA.



Fig. 3. Prof. Stephen J. Galli, Department of Pathology, Stanford University School of Medicine, USA.



Fig. 5. Prof. Tadamitsu Kishimoto, Osaka University Immunology Frontier Research Center, Japan.

known to be the most famous pupil of Prof. Kimishige Ishizaka. He succeeded to develop the monoclonal antibody against IL-6 (tocilizumab), which was found extremely safe and effective for some autoimmune diseases including rheumatoid arthritis (Fig. 5).

We have drastically decreased the number of fatal asthmatic patients in the past 50 years by mainly developing inhaled corticosteroid drugs and by providing therapeutic guidelines recommending the use of such drugs. However, compared to the effect of tocilizumab for autoimmune diseases, we seem not to have such biologics highly effective for many allergic diseases, yet. This fact suggests that allergic diseases are more complex diseases than we previously thought. Indeed, whilst IgE-mediated reactions of allergic diseases were clarified in the past 50 years, non-IgE-mediated reactions remained unidentified until recently. Several genome-wide association studies repeatedly identified IL-33 as being a key molecule for asthma and allergies, which trigger proliferation and activation of natural helper cells (group 2 innate lymphoid cells) which can produce extremely high amount of type 2 cytokines in the absence of allergen and IgE. All the molecular mechanisms of allergic diseases are expected to be elucidated

soon. Recent discovery about the important role of skin barrier dysfunction during infancy on the development of food allergy and the subsequent allergic diseases (allergic march) as well as the development of eczema brought us the paradigm shift regarding the preventative method of allergic diseases starting at infant period. Safe and inexpensive methods to prevent the development of allergic diseases, which could be a potential threat for the next generation, are also highly expected especially regarding medical economics.

Conflict of interest

The author has no conflict of interest to declare.

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