Preface

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Allergic inflammation, as in bronchial asthma, is characterized by preferential recruitment of eosinophils into tissues. Increase in eosinophil numbers and/or their mediator concentrations in peripheral blood and tissues often correlate with disease activity, clinical severity, airway hyperresponsiveness, and airflow obstruction. A decrease in these concentrations with effective treatment is accompanied with improvement in symptoms and various physiological parameters such as lung function and airway responsiveness. Furthermore, studies on eosinophil biology over the last two decades have provided significant evidence that eosinophils are capable of causing inflammatory changes in allergic diseases. Thus, the 'eosinophil hypothesis' stating that eosinophils are the major effector cells in allergy has been proposed. However, a recent clinical trial in asthma with an anti-IL-5 monoclonal antibody has questioned the importance of eosinophils in allergic diseases including asthma [1], and has initiated a debate that has shaken the hypothesis and even societies of eosinophil research.

Leckie et al. [1] treated asthmatic patients with a humanized anti-IL-5 monoclonal antibody (SB-240563) to target eosinophils and found that allergen-induced late asthmatic responses (LAR) and nonspecific airway responsiveness did not change although the numbers of eosinophils in peripheral blood and sputum dramatically decreased. These findings argued against a central role of eosinophils in the pathogenesis of asthma. Logical criticism of the view that discounts the role of eosinophils based on initial clinical experience, however, has also emerged. First, LAR is not the right endpoint to evaluate eosinophil effector functions in asthma since basophils,

not eosinophils, are directly involved in LAR [2]. Second, it was not clarified whether the antibody eliminated tissue eosinophils. If eosinophils remained in the tissue, they could still cause asthma. Actually, a subsequent study by Kay et al. [abstract presented at the 58th Annual Meeting of the American Academy of Allergy, Asthma, and Immunology, 2002] has found that SB240563 caused merely a 55% reduction of eosinophils in the lung although it caused an 88% reduction in peripheral blood. Furthermore, there is a report indicating that targeting IL-5 alone was not sufficient to block eosinophil infiltration in the lung and airway hyperresponsiveness [3]. Downregulation of IL-5 receptors and upregulation of GM-CSF receptors on tissue eosinophils in allergen-challenged asthmatics have also been suggested [Kelly, Busse, et al., pers. commun.]. Collectively, failure of the anti-IL-5 treatment does not necessarily minimize the pathogenic role of eosinophils. More studies will clarify whether targeting eosinophils will be useful in the treatment of asthma and whether IL-5 will be the effective target to treat eosinophilic inflammation.

In the midst of the heated debate on the role of eosinophils in asthma, the 14th Annual Workshop on 'Eosinophils in Allergy and Related Diseases 2001' was held in Tokyo on June 16, 2001, with 25 research presentations in the fields of basic and clinical sciences on eosinophil biology and its clinical correlations. Forefront researchers in this field in Japan presented and discussed their cutting-edge data including gene expression of eosinophils, the role of lipid mediators, cytokines, chemokines and adhesion molecules in eosinophil activation and mobilization, and the role of eosinophils in diseases with eosino-

philia. The effect of viral infection on eosinophilic inflammation was also discussed.

The present proceedings include two original papers and two reviews. Ten abstracts, some of which have been published elsewhere, are also included. The remaining eleven titles presented at the workshop are listed in the back of this issue. We hope that these studies will contribute to a better understanding and repositioning of eosinophils in allergy and eosinophil-related diseases.

Finally, we would like to express our sincere appreciation to Novartis Pharma K.K. (Tokyo) for supporting this workshop and to the International Medical Publisher (Tokyo) for excellent assistance in publishing these proceedings.

References

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- 2 Gauvreau GM, Watson RM, O'Byrne PM: Kinetics of allergen-induced airway eosinophilic cytokine production and airway inflammation. *Am J Respir Crit Care Med* 1999;160:640–647.
- 3 Webb DC, McKenzie AN, Mattheai KI, Rothenberg ME, Foster PS: Distinct spatial requirement for eosinophil-induced airways hyperreactivity. *Immunol Cell Biol* 2001;79:165–169.