

## Department of Allergology

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### General Summary

The Department of Allergology was established this year by donation. Our research concerned the biological significance of allergic immune reactions by immunoglobulin (Ig) E, mast cells, eosinophils, and basophils.

### Research Activities

#### *Mechanisms of atopic dermatitis*

We reported on the NC/Nga mouse as a model of spontaneous development of atopic dermatitis with hyper-IgE. Genetic analysis identified that dermatitis was controlled by 1 recessive gene and that hyper-IgE was controlled by 2 recessive genes. No linkage was found among these genes. Infection of mites was frequently found in NC/Nga mice raised under conventional conditions. Mite infection induced infiltration of mast cells and eosinophils in the skin. Numbers of mast cells and eosinophils in the skin of NC/Nga mice with dermatitis were significantly higher than those in mice without dermatitis. An inhibitor of mast cell-specific chymase developed by us suppressed the development of dermatitis and infiltration of mast cells and eosinophils in the skin of NC/Nga mice. One mechanism of these phenomena is the activation of stem cell factor by chymase. Activated stem cell factor is a major molecule for the differentiation of mast cells and for the chemotaxis of eosinophils. In addition, injection of chymase to the skin elicited eosinophil infiltration in mice. These results suggest that mast cells and chymase play roles in the development of atopic dermatitis.

#### *Dengue virus infection and mast cells*

Dengue virus infection is associated with several diseases, including Dengue fever (DF), Dengue hemorrhagic fever (DHF), and Dengue shock syndrome (DSS), by the criteria of the World Health Organization. Both DHF and DSS are severe forms of Dengue infection and are characterized by increased vascular permeability and hemorrhagic manifestations. To clarify the involvement of mast cells in severe Dengue diseases, levels of mast cell-derived mediators were measured in patients and control subjects in Vietnam. Levels of mast cell-specific chymase and tryptase were significantly higher in patients with DHF or DSS than in patients with DF or in control subjects. Serum levels of vascular endothelial cell growth factor derived from mast cells were significantly elevated in patients with DHF or DSS. When the patients had recovered, the levels of these mediators had returned to levels similar to those of control subjects. Levels of the mast-cell activators interleukin 9 and 17 were also increased in patients with DHF or DSS. These findings suggest that mast cells participate in the pathogenesis of DHF and DSS.

## Publications

**Ogata A<sup>1</sup>, Fujieda Y<sup>1</sup>, Terakawa M<sup>1</sup>, Muto T<sup>1</sup>, Maruoka H<sup>1</sup>, Nagahira K<sup>1</sup>, Fukuda Y<sup>1</sup>, Tomimori Y<sup>1</sup>, Watanabe N<sup>1</sup> (Asubio Pharma).** Pharmacokinetic/pharmacodynamic analyses of chymase inhibitor SUN138334 in NC/Nga mice and prediction of effective dosage for atopic dermatitis patients. *Int Immunopharmacol.* 2011; **11**: 1628-

32.

## Reviews and Books

**Watanabe N.** Search after new concepts on IgE (in Japanese). *Tokyo Jikeikai Ika Daigaku Zasshi.* 2011; **126**: 149-62.