RESEARCH REPORT - No. 1505 FY 2015–2016

Title of research project	Mechanisms and pathogenesis of food allergy in infants, and risk factors of its crisis
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【Abstract】

We developed methods to determine high and low affinity of allergen-specific IgE, allergen levels in mother's milk, blood and environments, and studied the mechanisms of food allergy in infants in the project of FY 2016 – 2017. These studies were conducted by using the highly sensitive densely carboxylated protein (DCP) microarray which requires only a small volume of serum or plasma for analyses.

We selected antigen-competitive inhibition method and its IC_{50} value for measurement of antigen-affinity. The other assay method of binding inhibition by a chaotropic agent, diethylamine, was not suitable because of its conformational modification of both antibodies and antigens by the reagent. Quantitative assaymethods of allergen levels in mother's milk and environments by ELISA by using the DCP microarray had been established, but further studies are required for measurement of allergen levels in serum because of difficulty of allergen dissociation from IgGs in serum. Studies on the mechanisms of food allergy was conducted in infants during lactation period. Eighty four pairs of mothers and infants born in 2013 and 2014 at Tokushima Prefecture Naruto Hospital joined this study. To monitor development of food allergy during lactation period, a trajectory studies on egg white (EW)- and cow's milk (CM)-allergen specific immunoglobulin production associated with immunoglobulin class-switching recombination from birth to 6 months of age were conducted. Feeding of formula containing high dose CM allergens induced high allergen-specific IgG1 and IgA at 2 months of age, and subsequently simultaneous production of IgG2 and IgE at 4 months of age. Breast feeding, which provides trace amounts of EW allergens, showed slow and mild immunoglobulin subclass formation, but eczema in the 6-month-old infants induced EW-specific high IgE without induction of IgG2 and other immunoglobulins, with resultant high IgE/IgG1 ratios. In addition, allergen-specific low-affinity IgE was found in the early immunoglobulin maturation, suggesting the development of oral tolerance and high-affinity IgE in eczema infants, suggesting the development of food allergy.

In conclusion, we established the DCP microarray method for assay of allergen-specific affinity of IgE and a method to detect allergen levels in mother's milk and environments, but not in serum, by ELISA. By using these methods, the pathogenesis of food allergy was analyzed in infants from birth to 6 months of age, and possible biomarkers of food allergy and oral tolerance

were proposed. Rapid development of immunoglobulin subclass maturation with low allergen-specific IgE/IgG1 ratios and low allergen-specific affinity of IgE with significant induction of IgG2 will be biomarkers of the development of oral tolerance. Slow development of immunoglobulin subclass formation with eczema induced high allergen-specific IgE/IgG1 ratios and high allergen-specific affinity of IgE without formation of IgG2 will be biomarkers of food allergy.