Research Center for Medical Sciences
Division of Molecular Immunology

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General Summary

Our research interests have focused on the analysis of the basic immune system, which protects us from a number of diseases, and of immune disorders, such as hypersensitivity diseases and autoimmune diseases.

Research Activities

Regulation of Th2 responses by different cell types expressing the interleukin-31 receptor
Interleukin-31 (IL-31) is a recently identified cytokine produced by Th2 cells that is involved in the development of atopic dermatitis-induced skin inflammation and pruritus. Its receptor, IL-31RA, is expressed by a number of cell types, including epithelial cells, eosinophils, and activated monocytes and macrophages. To date, however, the regulation of Th2 responses by distinct cell types and tissues expressing IL-31RA has not been well studied.
In this study, Cry j 2, one of the major allergens of Japanese cedar pollen, was administered to IL-31RA-deficient or wild-type (WT) mice via nasal or intraperitoneal injection for induction of specific Th2 responses.
After nasal administration of Cry j 2, IL-31RA-deficient mice showed lower Cry j 2-specific CD4+ T cell proliferation, Th2 cytokine (IL-5 and IL-13) production, and Th2-mediated (IgE, IgG1, and IgG2b) antibody responses than WT mice. In contrast, IL-31RA-deficient mice administered Cry j 2 intraperitoneally showed stronger Th2 immune responses than WT mice.
These results indicate that IL-31R signaling positively regulates Th2 responses induced by nasal administration of Cry j 2, but negatively regulates these responses when Cry j 2 is administered intraperitoneally. Collectively, these data indicate that the induction of antigen-specific Th2 immune responses might depend on tissue-specific cell types expressing IL-31RA.

Evaluation of allergen-specific immune responses induced by oral immunotherapy with transgenic rice containing major T-cell epitopes of Japanese cedar pollen allergens in patients with cedar pollinosis
Oral immunotherapy with dominant T-cell epitopes is safer and more effective than conventional immunotherapy for the treatment of immunoglobulin E-mediated allergic diseases. In the previous study, a blinded, randomized, placebo-controlled trial employing oral immunotherapy with 80 g of steamed pack rice for cedar pollinosis was performed for 20 weeks. Thus, oral administration of the rice was found to be a safe therapy without

side effects. The aim of this study was to investigate whether oral immunotherapy with small dose of the transgenic rice seed is effective to induce oral tolerance in patients with Japanese cedar pollinosis. Double blinded, randomized, placebo-controlled trial employing oral immunotherapy with 5 g or 20 g of steamed pack rice for cedar pollinosis was performed for 8 weeks. Twenty-one subjects were enrolled and divided into 3 groups that ate 5 g or 20 g of transgenic rice or normal rice.
No major adverse effects were observed in either group during treatment. Allergen-specific T-cell responses were evaluated. The ratio of allergen-specific T cells proliferative responses to 7Crp peptide, Cry j 1, and Cry j 2 were significantly lower in subjects who ate transgenic rice than in subjects who ate normal rice. Furthermore, allergen-driven IL-5 and IL-13 were also significantly reduced in culture supernatants of peripheral blood mononuclear cells after subjects had eaten transgenic rice. Taken together, oral immunotherapy with small dose of the transgenic rice was expected to be an effective treatment for cedar pollinosis.
Current clinical studies are being conducted to evaluate the clinical efficacy of oral immunotherapy with small dose of the transgenic rice.

Adjuvant for inducing antigen-specific cytotoxic T lymphocytes via cross-presentation of cationic lipids
Vaccine that raises specific cytotoxic T cells against tumors or pathogens is the convincing approach to overwhelm these diseases. By the past study, we have developed a new liposome based adjuvant to induce CTL by just mixing protein antigens and adjuvant before the administration. After administration with antigens having some kind of protein structure and adjuvant, inductions of antigen specific CTL by cross priming were observed. Then anti-tumor activities were measured by vacctinations with this adjuvant and melanoma cell extract. As a result, the growth and metastasis of melanomas were significantly inhibited. At present, we are developing the methods to induce specific CTLs against other kind of tumors by vaccination.

Publications

Ito H, ***Noda K***, ***Yoshida K***, ***Otani K***, ***Yoshiga M***, ***Oto Y***, ***(Saito S)***, ***Kurosaka D.*** Prokineticin 2 antagonist, PKRA7 suppresses arthritis in mice with collagen-induced arthritis. *BMC Musculoskelet Disord.* 2016; **17:** 387.