Research Center for Medical Sciences
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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

Increased itching sensation depends on an increase in dorsal root ganglia interleukin 31 receptor A expression in mice with atopic-like dermatitis

Although itching and scratching are important factors in the development of atopic dermatitis, the mechanisms that underlie these phenomena are poorly understood. Cohousing with skin-lesioned NC/Nga mice, an animal model of atopic dermatitis, gradually increased itch-associated scratching behavior (long-lasting scratching, LLS) counts in several strains of mice. On the other hand, a repeated dose of interleukin (IL) 31 gradually increased LLS counts by increasing the expression of IL-31 receptor A (IL-31RA) from the dorsal root ganglia (DRG) of mice. We investigated the relationship between the LLS counts and the expression of IL-31 and IL-31RA messenger (m) RNA in the skin and DRG of mice. The LLS counts were significantly increased in NC/Nga and BALB/c mice after 3, 7, and 14 days cohoused with skin-lesioned NC/Nga mice, in a duration-dependent manner. Cohousing with skin-lesioned NC/Nga mice significantly increased the expression of mRNA for cutaneous IL-31 and DRG IL-31RA compared with these levels in noncohoused NC/Nga and BALB/c mice, while DRG IL-31 mRNA was not observed. Increased LLS counts were closely correlated with increased DRG IL-31RA mRNA expression, but not with cutaneous IL-31 mRNA expression, in NC/Nga and BALB/c mice.

Moreover, these phenomena were also observed in W/Wv and Scid mice after 2 weeks of cohousing with skin-lesioned NC/Nga mice. The expression of DRG IL-31RA was significantly higher in cohoused NC/Nga mice than in noncohoused NC/Nga mice. A single dose of IL-31 significantly increased LLS counts more clearly in cohoused NS/Nga mice than in noncohoused NC/Nga mice. These results suggest that IL-31–induced LLS is enhanced by DRG IL-31RA expression in mice and that cohousing-induced itching is regulated by DRG IL-31RA expression, as in the case of itching induced by repeated administration of IL-31.

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 the present study was to investigate whether oral immunotherapy with a 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 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 or 20 g of transgenic rice or normal rice.

No major adverse effects were observed in either group during treatment. Allergen-specific T cells 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 the subjects had eaten transgenic rice. Taken together, oral immunotherapy and a small dose of the transgenic rice are expected to be an effective treatment for cedar pollinosis.

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 cytotoxic T lymphocytes (CTLs) 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 CTLs by cross-priming were observed. Then antitumor activities were measured with vaccinations with this adjuvant and an 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 kinds of tumor by vaccination.

Publications

Arai I, Tsuji M, Miyagawa K, Takeda H, Akiyama N, Saito S. Prostaglandin D2 improves IL-31-induced alloknesis: itch-stimulation becomes pain-stimulation in mouse skin. *Itch & Pain.* 2016; **3:** e1138. Epub 2016 Jan 12.

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