

[*Jpn. J. Pharmacol.*, **85**, 250-259 (2001)]

[Lab. of Pharmacology]

Role of mast cells in antigen-induced airway inflammation and bronchial hyperresponsiveness in rats.

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The participation of mast cells in the induction of antigen-induced airway inflammation (AIAI) and bronchial hyperresponsiveness (BHR) to acetylcholine (ACh) was investigated using pharmaceutical agents and mast cell-deficient rats (Ws/Ws). Disodium cromoglycate and terfenadine did not inhibit AIAI and BHR in sensitized BN rats. In contrast, cyclosporin A (CyA), FK-506 and prednisolone significantly inhibited AIAI and BHR in sensitized BN rats. Furthermore, a significant increase in the number of leukocytes in BALF and BHR was also observed in Ws/Ws rats 24 h after inhalation of antigen; however, the magnitude of BHR in Ws/Ws rats was lower than in the congenic rats.

[*Allergol. Int.*, **50**, 89-98 (2001)]

[Lab. of Pharmacology]

Effect of repeated antigen inhalation on airway inflammation and bronchial responsiveness to acetylcholine in interleukin-5 transgenic mice.

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Three inhalations of antigen (ovalbumin) caused an increase in the number of eosinophils in bronchoalveolar lavage fluid (BALF) and a significant elevation in serum IgE in wild-type mice. In contrast with wild-type animals, systemic over-production of IL-5 resulted in massive airway eosinophilia, especially around the peribronchi and perivascular regions of the tissues, after repeated antigen provocation. In C3H/HeN background IL-5 Tg mice, repeated antigen provocation did not induce BHR similar to that of wild-type mice. In contrast, antigen-induced BHR was observed in BALB/c-background mice, but there were no significant differences between the magnitude of BHR in wild-type and IL-5 Tg mice. These findings suggest that systemic overproduction of IL-5 or airway eosinophilia is not, by itself, important in the development or aggravation of antigen-induced BHR in mice.

[*Exp. Anim.*, **50**, 187-190 (2001)]

[Lab. of Pharmacology]

High rate of IgE-mediated histamine release from rat mesenteric mast cells.

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IgE dependent histamine release from rat mesenteric mast cells was investigated. Excised mesenterium was cut into pieces and incubated with IgE overnight at 4 °C for sensitization. Over 10 pieces of mesenterium specimen could be prepared from a rat. Antigen-induced histamine release from mesenterium specimen was initiated rapidly and reached a plateau in 5 min. In an optimal condition, over 50% of total histamine was released. In contrast, unpurified and purified peritoneal mast cells release only 22.5% and 5.3% total histamine, respectively, upon IgE stimulation. Tranilast, a mast cell stabilizer, inhibited the histamine release from mesenteric mast cells significantly. The mesenterium might be a useful material from studying tissue-associated mast cell activation.

[*Skin. Pharmacol. Appl. Skin. Physiol.*, **14**, 87-96 (2001)]

[Lab. of Pharmacology]

Scratching behavior in various strains of mice.

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Scratching behavior was induced in 12 strains of mice and the frequency was compared. An injection of histamine at a dose of 50 nmol induced frequent scratching behavior only in ICR mice, although the same dose of serotonin induced frequent scratching behavior in all strains of mice except for A/J. Histamine (10 nmol), serotonin (1 nmol), substance P (50 nmol) and passive cutaneous anaphylaxis induced significant vascular permeability increase in BALB/c, ICR, ddY and Nc/Nga mice. These four stimuli also induced frequent scratching behavior in ICR mice. However, they failed to induce substantial increase in the incidence of scratching in the other three strains, except for ddY, which exhibited a slight but significant increase against substance P injection. These results suggest that the ICR mouse is a good responder for scratching behavior against various stimuli, especially against histamine. Thus ICR mice may be suitable for studying mediators and/or mechanisms for itching.