porcine adrenal chromaffin cells. The molar ratios of dopamine to ATP (dopamine/ATP) in the effluent was 10±1.

PC 12 cells were cultured with NGF-7 S (50 ng/mℓ), dexamethasone (1 μM), reserpine (0.1 μM), bafilomycin A 1 (0.1 μM) or without drugs (control) for 2 days and the effects of these drugs on relation of stimulus-secretion coupling and on activity of enzymes which degradate released ATP were examined. The treatment with these drugs did not affect the increase of intracellular Ca^{2+} and release of relative amounts of adenine nucleotides and adenosine in response to high K^+. In NGF-treated cells, although neurite production was observed at 2 days treatment, high K^+ caused release of dopamine and ATP with similar amount to those in control cells. Dexamethasone doubled the amount of dopamine release induced by high K^+ without changing the amount of ATP release. High K^+ failed to cause dopamine release in reserpine-treated cells but evoked ATP release with similar time course and amount to those in control cells. Bafilomycin A 1 decreased both high K^+-induced dopamine and ATP release.

Based on these results, it is revealed that the molar ratios of CA to ATP released from cultured porcine adrenal chromaffin cells and PC 12 cells are almost constant regardless of the kind of secretagogues. These results suggest that releasable vesicles in both cells contain dopamine and ATP at a constant molar ratio. It is also suggested that released ATP in the effluent from cultured porcine adrenal chromaffin cells is constantly degradated regardless of the kind of secretagogues.

The results obtained from on-line measurement of dopamine and ATP from PC 12 cells which was cultured with various drugs, suggest that dopamine and ATP are stored through different pathways. The H^+-gradient across the vesicular membrane developed by vacuolar ATPase may play an important role in the vesicular uptake of ATP, like dopamine.

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Studies on experimental asthmatic model using NC/Nga mice

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The NC/Nga mice have been originally studied as a model for human atopic dermatitis, since they show spontaneous dermatitis accompanied with hyperproduction of IgE. This inherent characters of the NC/Nga mice implied the possibility that they also have propensity for allergic asthma because etiological relationship among allergic diseases is likely to exist. For these reasons, in this study, the author has established an animal model for allergic asthma using the NC/Nga mice, and investigated the characteristics of

the disease.

The NC/Nga mice were sensitized twice at one week interval, followed by a single intranasal challenge with ovalbumin (OVA). Then, some criteria, like production of OVA-specific IgE, airway responsiveness, and eosinophilic inflammation in the airway, were measured and compared with control BALB/c mice. In the NC/Nga mice, the single intranasal challenge resulted in an increase in the plasma level of OVA-specific IgE, and the appearance of typical pathological aspects of allergic asthma characterized by infiltration of numerous eosinophils, hyperproduction of mucus in bronchial epithelial cells. Moreover, both airway hyperresponsiveness to inhaled acetylcholine and marked enhancement of airway resistance after the challenge were observed in the NC/Nga mice. Massive blood eosinophilia in concert with delayed expression of mRNA of chemokines, eotaxin, regurated on activation, normal T-cell expressed and secreted, and macrophage inflammatory protein-1 a which activate eosinophils in the lung were observed in NC/Nga mice, thus showing the features very similar to clinical characteristics of patients of asthma.

To determine the cause for the eosinophilic inflammation observed in the NC/Nga mice, the author examined the profiles of representative Th 2 cytokines, interleukins (IL)-4 and-5, whose productions are known to correlate well with allergic inflammation, and a Th 1 cytokine interferon (IFN)-γ, whose effects often compete with Th 2 cytokines, in bronchoalveolar lavage fluid. The profiles of IL-4 and-5 in the NC/Nga mice were very similar to those in control BALB/c mice, while the level of IFN-γ was lower in the NC/Nga than BALB/c mice. This low production of IFN-γ was one of the characteristics observed in patients of asthma, suggesting its involvement in the induction of the severe symptoms observed in the NC/Nga mice.

To further investigate the mechanism behind the development of the blood eosinophilia, which seems to support topical eosinophilic inflammation, the differentiation of eosinophils from bone marrow cells in vitro was examined in the presence of eosinopoietic cytokines. The bone marrow cells were cultured in the presence of IL-3, granulocyte/macrophage-colony stimulating factor (GM-CSF), and IL-5, which induce the differentiation of progenitor cells into mature eosinophils. A larger number of eosinophils differentiated from the bone marrow cells derived from the NC/Nga mice than those from control BALB/c mice, suggesting that the higher production of eosinophils in bone marrow is responsible for blood eosinophilia observed in the NC/Nga mice.

Thus, the characteristic features of experimentally induced allergy observed in the NC/Nga mice shown in this study were consistent with clinical features of asthma, and it has been suggested that the NC/Nga mice is a suitable animal model to study the pathogenesis of asthma.

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