

[*J. Allergy Clin. Immunol.*, **106**, S91-98 (2000)]

[Lab. of Pharmacology]

**Role of Mast Cells in the Onset of IgE-mediated Late-phase Cutaneous Response in Mice.**

Hiroichi NAGAI\*, Toru ABE, Itaru YAMAGUCHI, Kanako MITO, Masako TSUNEMATSU,  
Masahiro KIMATA and Naoki INAGAKI

The role of mast cells in IgE-mediated late phase cutaneous reaction in mice was investigated. Degranulation of mast cells was observed between 4-24 hours after challenge. The number of IL-6-positive mast cells was increased after 4 hours and peaked at 8 hours after challenge. Mast cells were confirmed to be positive for IL-6 mRNA at 6 hours after challenge. Therefore, mast cells are important for the onset of late phase allergic cutaneous reaction in mice.

[*Biochem. Pharmacol.*, **60**, 589-594 (2000)]

[Lab. of Pharmacology]

**Roles of Mitogen-activated Protein Kinase Pathways for Mediator Release  
from Human Cultured Mast Cells.**

Masahiro KIMATA, Naoki INAGAKI, Toshinobu KATO, Toru MIURA,  
Isao SERIZAWA and Hiroichi NAGAI\*

Roles of MAPKs for mediator release from human cultured mast cells were investigated. U0126, an ERK pathway inhibitor, inhibited ERK activation, LT, PGD<sub>2</sub> and GM-CSF release. SB203580, a p38 MAPK pathway inhibitor, potentiated JNK activation and GM-CSF release. These results suggest that MAPK pathways play important roles in mediator release from human mast cells.

[*Pharmacology*, **61**, 70-77 (2000)]

[Lab. of Pharmacology]

**Effect of a Novel Anti-allergic Agent, HSR-609, on Antigen-induced Airway  
Hyperresponsiveness in Mice.**

Keiichi MUSOH, Yoshizou MAEDA, Hiroyuki TANAKA,  
Naoki INAGAKI and Hiroichi NAGAI\*

Effects of HSR-609 on allergic airway hyperresponsiveness and airway inflammation were investigated in mice. HSR-609 inhibited the antigen-induced airway hyperresponsiveness, whereas cetirizine and terfenadine did not. HSR-609 also inhibited the eosinophilia and IL-5 production in BALF. HSR-609 suppressed the accumulation of eosinophils elicited by stimulated Th2 cells in the peritoneal cavity of AKR mice.

[*J. Exp. Med.*, **192**, 405-412 (2000)]

[Lab. of Pharmacology]

**Human Monocyte-derived Dendritic Cells Induce Naive T Cell Differentiation  
into T Helper Cell Type 2 (Th2) or Th1/Th2 Effectors.  
Role of Stimulator/Responder Ratio.**

Hiroyuki TANAKA\*, Christian E DEMEURE, Manuel RUBIO,  
Guy DELESPESE and Marika SARFATI

The subset of dendritic cells (DCs) and the nature of the signal inducing DC maturation determine the capacity of DCs to generate polarized immune responses. In this study, we show that the ability of human monocyte-derived DCs (myeloid DC(1)) to promote T helper type 1 (Th1) or Th2 differentiation was also found to be critically dependent on stimulator/responder ratio. At a low ratio (1:300), mature DCs that have been differentiated after inflammatory or T cell-dependent stimulation induced naive T cells to become Th2 effectors. Th2 differentiation was dependent on B7-CD28 costimulation and enhanced by OX40-OX40 ligand interactions. However, high DC/T cells ratio (1:4) favored a mixed Th1/Th2 cell development.