

[*Science*, **287**, 2013-2017 (2000)]

[Lab. of Pharmacology]

Prostaglandin D₂ as a Mediator of Allergic Asthma.

Toshiyuki MATSUOKA, Masakazu HIRATA, Hiroyuki TANAKA, Yoshimasa TAKAHASHI,
Takahiko MURATA, Kenji KABASHIMA, Yukihiro SUGIMOTO, Takuya KOBAYASHI,
Fumitaka USHIKUBI, Yoshiya AZE, Naomi EGUCHI, Yoshihiro URADE,
Nobuaki YOSHIDA, Kazushi KIMURA, Akira MIZOGUCHI, Yoshihito HONDA,
Hiroichi NAGAI* and Shuh NARUMIYA

The role of PGD₂ in allergic asthma was investigated by the generation of mice deficient in the PGD receptor (DP). Sensitization and aerosol challenge with ovalbumin induced increases in the serum concentration of IgE in DP-KO mice similar to wild type mice. However, the concentrations of Th2 cytokines and the extent of lymphocyte accumulation in the lung of DP-KO mice were greatly reduced compared with those in wild type mice. Moreover, DP-KO mice showed only marginal infiltration of eosinophils and failed to develop airway hyperreactivity.

[*J. Immunol.*, **164**, 2193-2199 (2000)]

[Lab. of Pharmacology]

CD47 Engagement Inhibits Cytokine Production and Maturation of Human Dendritic Cells.

Christian E. DEMEURE, Hiroyuki TANAKA* , Veronique MATEO, Manuel RUBIO,
Guy DELESPESE and Marika SARFATI

Upon encounter with bacterial products, immature dendritic cells (iDCs) release proinflammatory cytokines and develop into highly stimulatory mature DCs. In the present study, we show that human monocyte-derived DCs functionally express the CD47 Ag, a thrombospondin receptor. Intact or F(ab')₂ of CD47 mAb suppress bacteria-induced production of IL-12, TNF- α , GM-CSF, and IL-6 by iDCs. The inhibition of IL-12 and TNF- α is IL-10-independent inasmuch as IL-10 production is down-modulated by CD47 ligation counteracts the phenotypic and functional maturation of iDCs. We conclude that following exposure to microorganisms, CD47 ligation may limit the intensity and duration of the inflammatory response by preventing inflammatory cytokine production by iDCs and favoring their maintenance in an immature state.

[*J. Trad. Med.*, **17**, 49-58 (2000)]

[Lab. of Pharmacology]

Effects of Sho-seiryu-to (Xiao-Qing-Long-Tang) on Experimental Allergic Reactions.

Hiroichi NAGAI*, Hiroshi TAKEDA, Takeshi NISHIYORI, Takashi OCHI,
Masatsugu SAWADA, Toshinobu KATO, Naoki INAGAKI,
Masafumi MORITA and Yasuhiro KOMATSU

Effects of Sho-seiryu-to (TJ-19) on experimental allergic reactions were studied. TJ-19 inhibited IgE-dependent biphasic cutaneous reaction in mice and biphasic increase in nasal airway resistance in guinea pigs. Although TJ-19 inhibited histamine- and TNF- α -induced cutaneous reactions in mice, it did not affect allergic histamine release from cells. In contrast, TJ-19 did not affect type II, III and IV allergic reactions.

[*Clin. Exp. Allergy*, **30**, 501-508 (2000)]

[Lab. of Pharmacology]

Effects of Luteolin, Quercetin and Baicalein on Immunoglobulin E-mediated Mediator Release from Human Cultured Mast Cells.

Masahiro KIMATA, Michitaka SHICHIJO, Naoki INAGAKI, Toru MIURA,
Isao SERIZAWA and Hiroichi NAGAI*

The effects of luteolin on IgE-mediated allergic mediator release from human cultured mast cells were investigated and compared to those of baicalein and quercetin. The three compounds inhibited the release of histamine, leukotrienes, PGD₂ and GM-CSF in a concentration-dependent manner. Luteolin and quercetin inhibited Ca²⁺ influx, PKC translocation and PKC activity. Luteolin and quercetin also suppressed the activation of ERKs and JNK. Luteolin is a potent inhibitor of human mast cell activation through the inhibition of Ca²⁺ influx and PKC activation.