[*Gen. Pharmacol.*, **30**, 777-782 (1998)] [Lab. of Pharmacology]

Cyclosporin A and FK-506 Inhibit Development of Superantigen-potentiated Collagen-induced Arthritis in Mice.

Yuko TAKAOKA, Hiroichi NAGAI,* Masahiko TANAHASHI and Kenji KAWADA

Staphylococcal enterotoxine B (SEB; superantigen) accelerated the onset of arthritis in mice preimmunized with type II collagen. Cyclosporin A and FK-506 inhibited the induction and development of clinical signs and histopathological changes of SEB-potentiated collagen-induced arthritis in mice. Simultaneously, both cyclosporin A and FK-506 inhibited the development of humoral and cellular immunity to type II collagen. The expression of IL-2 receptor (CD25) by SEB on splenocyte T cells from collagen-preimmunized mice was inhibited by both agents in ex vivo experimentation.

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Effect of Spikelets of Miscanthus Sinensis on IgE-Mediated Biphasic Cutaneous Reaction in Mice.

Chie WATANABE, Koji HASE, Toru OKU, Fumitomo KOIZUMI, Shigetoshi KADOTA, Hiroichi NAGAI* and Ikuo SAIKI

The effect of spikelets of M. sinensis on IgE-mediated biphasic cutaneous reactions was investigated in passively and actively sensitized BALB/c mice. Skin reactions were elicited by an epicutaneous challenge of dinitrofluorobenzene (DNFB). The administrations of a nondialysable water extract of M. sinensis significantly inhibited the biphasic cutaneous reactions. The inhibitory effect was much stronger than those of prednisolone and amlexanox. The active component(s) was predominantly located in the glycoprotein fraction. The fraction suppressed the accumulation of inflammatory cells. The biphasic ear swelling was also improved by an administration of the fraction 24 h before active sensitization. The glycoprotein fraction of M. sinensis is suggested to inhibit not only the IgE-mediated allergic inflammatory reaction but also the IgE formation.

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Pharmacological Modulation of LPS-Induced MIP-1α Production by Peripheral Blood Mononuclear Cells.

Masahiro KIMATA, Michitaka SHICHIJO, Michio DAIKOKU, Naoki INAGAKI, Hiroshi MORI and Hiroichi NAGAI*

In the present study, we investigated the effects of some anti-asthmatic drugs on the production of macrophage inflammatory protein-1α (MIP-1α), in response to LPS by peripheral blood mononuclear cells. MIP-1α production was induced by LPS concentration-dependently. Actinomycin D and cycloheximide inhibited MIP-1α production completely. Although β-agonists only showed a slight inhibitory effect on MIP-1α production, it was potentiated by the simultaneous treatment with roliplam. db-cAMP suppressed MIP-1α production dose-dependently. Present data indicate that the production of MIP-1α is regulated by cAMP and that cAMP could provide a useful target for therapeutic treatment in asthmatic diseases and other diseases where MIP-1α is involved in their etiology.

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Involvement of Bruton's Tyrosine Kinase in FcεRI-dependent Mast Cell Degranulation and Cytokine Production.

Daisuke HATA, Yuko KAWAKAMI, Naoki INAGAKI, Chiris S. LANTZ, Toshio KITAMURA, Wasif N. KHAN, Mari MAEDA-YAMAMOTO, Toru MIURA, Wei HAN, Stephen E. Hartman, Libo YAO, Hiroichi NAGAI,* Anne E. GOLDFELD, Frederic W. Alt, Stephen J. GALLI, Owen N. WITTE and Toshiaki KAWAKAMI

We investigated the role of Bruton's tyrosine kinase (Btk) in FcεRI-dependent activation of mouse mast cells, using xid and btk null mutant mice. In xid mice, IgE-mediated anaphylactic reactions were blunted. Cultured mast cells derived from the bone marrow cells of xid or btk null mice exhibited mild impairments in degranulation, and more profound defects in the production of several cytokines upon FcεRI cross-linking. Transcriptional activities of these cytokine genes were severely reduced. Present results demonstrate an important role for Btk in the full expression of FcεRI signal transduction in mast cells.