[*Pharmacology*, **59**, 127-134 (1999)] [Lab. of Pharmacology]

Effects of a New Antiallergic Agent, VUF-K-8788, on Experimental Asthmatic Reactions in Guinea Pigs.

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The effects of 7-[3-[4-]2-quinolinylmethyl]-1-piperazinyl]propoxyl]-2,3-dihydro-4*H*-1,4-benzothiadin-3-one (VUF-K-8788) on experimental asthmatic reactions in guinea pigs were investigated. VUF-K-8788 inhibited histamine-induced bronchoconstriction. VUF-K-8788 also inhibited anaphylactic broncoconstriction. In addition, VUF-K-8788 inhibited immediate- and late-phase asthmatic reactions in actively sensitized guinea pigs. Moreover, VUF-K-8788 inhibited the infiltration of eosinophils and macrophages into bronchoalveolar lavage fluid. These results indicate that VUF-K-8788 may be useful for the treatment of bronchial asthma.

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Interleukin-1β Induces Interleukin-6 Production through the Production of Prostaglandin E_2 in Human Osteoblasts, MG-63 Cells.

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This study was conducted to investigate the mechanism of interleukin (IL)-1β-induced IL-6 production in human osteoblasts (MG-63 cells). Stimulation with IL-1β resulted in the production of IL-6 and prostaglandin (PG) E_2. IL-6 production gradually increased and peaked 96h after stimulation. The pattern of PGE_2 production and the expression of cyclooxygenase-2 (COX-2) mRNA were biphasic after stimulation. Anti-PGE_2 antibody markedly reduced the production of IL-6. In addition, stimulation with 17-phenyl-PGE_2, a PGE receptor-1 (EP1) agonist, led to the expression of IL-6 mRNA after pretreatment of IL-1β. These findings indicate that IL-1β-induced IL-6 production in MG63 cells involves the following sequence of steps: IL-1β -induced COX-2 activation, PGE_2 production, and EP1 receptor signaling prior to IL-6 production.

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A Third-phase Cutaneous (Very Late Phase) Response after Elicitation with Dinitrofluorobenzene in Passively or Actively Sensitized Mice.

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Previous studies have reported that the mice passively sensitized with anti-dinitrophenyl IgE antibody exhibited IgE-mediated cutaneous reaction with an immediate phase response (IPR) at 1h and a late phase response (LPR) at 24h after the challenge with dinitrofluorobenzene (DNFB). We found that the third-phase inflammatory reaction with intense and persisting infiltration of eosinophils, named 'very late phase reaction' (vLPR), was induced following IPR and LPR in response to DNFB in actively and passively sensitized mice, and that the peak response of vLPR was at 8 days after the challenge, which may be mediated by T cells, partially by mast cells and/or IgE antibody.

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Nerve Growth Factor Release with Mast-cell-derived Mediators in a Patient with Systemic Mastocytosis after Middle-wave Ultraviolet Irradiation.

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We evaluated mast-cell-derived mediators and cytokines before and after exposure to ultraviolet light in the patients with systemic mastocytosis. Before irradiation, the levels of mast cell-derived mediators and metabolites were elevated. Among various cytokines, only the level of nerve growth factor was elevated. After irradiation, the nerve growth factor was further increased along with the levels of mast cell-derived mediators and metabolites. Middle-wave ultraviolet light may activate mast cell to release nerve growth factor and mediators in systemic mastocytosis.