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Immunopharmacological Studies on Experimental Allergic Encephalomyelitis in DA Rats

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The immunopharmacological profile of experimental allergic encephalomyelitis (EAE) in DA rats was compared to that in Lewis rats. DA rats showed higher susceptibility to EAE than Lewis rats. The immunological studies indicated that DA rats showed higher humoral and cellular immune response to myelin basic protein (MBP) than Lewis rats. This is probably due to the susceptible T cells to mitogen and autoreactive T cells to MBP in DA rats. Cyclosporin A, FK-506 and prednisolone suppressed the development of EAE in both strains similarly. These results suggest the existence of two different types of T cells in DA rats, one is highly reactive to mitogen and MBP and the other is susceptible to cyclosporin A and FK-506.

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Effect of Isoenzyme Selective Phosphodiesterase Inhibitors on Bacterial Lipopolysaccharide-induced Bronchial Hyperreactivity in Guinea Pigs.

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Effects of cilostazol and vesnarinone (selective PDE III inhibitors), rolipram (selective PDE IV inhibitor) and theophylline (nonselective PDE inhibitor) on LPS-induced bronchial hyperreactivity were investigated in guinea pigs. Cilostazol, vesnarinone, rolipram and theophylline significantly inhibited bronchial hyperreactivity to acetylcholine and TNF release into bronchoalveolar lavage fluid following LPS exposure. None of these compounds influenced neutrophil influx into bronchoalveolar lavage fluid. Rolipram and theophylline antagonized acetylcholine-induced bronchoconstriction in normal guinea pigs.

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Modulation of Th1- and Th2-Like Cytokine Production from Mitogen-stimulated Human Peripheral Blood Mononuclear Cells by Phosphodiesterase Inhibitors.

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Effects of phosphodiesterase (PDE) inhibitors, dibutyryl cAMP (dbcAMP) and a β-agonist on the production of cytokines by PHA-stimulated human peripheral blood mononuclear cells were investigated. PDE inhibitors suppressed the production of IFN-γ and IL-2 dose-dependently, but IL-4 and IL-5 production was inhibited only by the highest concentration of type IV inhibitor. dbcAMP inhibited the production of IFN-γ and IL-2 more potently than that of IL-4 and IL-5. A β-agonist increased the inhibitory effect of PDE inhibitors. cAMP-elevating agents, therefore, modulate the production of Th1 cytokines more effectively than that of Th2 cytokines.

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Effect of Anti-IL-4 and Anti-IL-5 Antibodies on Allergic Airway Hyperresponsiveness in Mice.

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Effects of the combination of anti-IL-4 and anti-IL-5 monoclonal antibodies (mAbs) on IgE response, airway inflammation and airway hyperresponsiveness were studied in sensitized Balb/c mice. Three inhalations of antigen caused an increase in the number of eosinophils in bronchoalveolar lavage fluid and in airway responsiveness to acetylcholine, with a significant elevation in the serum antigen-specific IgE level. Anti-IL-4 mAb inhibited IgE production, and anti-IL-5 mAb inhibited airway eosinophilia. The combined administration of anti-IL4 and anti-IL-5 mAbs, however, inhibited IgE antibody production, airway eosinophilia and hyperresponsiveness. These results suggest that the simultaneous inhibition of IL-4 and IL-5 effectively suppress the onset of antigen-induced airway hyperresponsiveness in mice.