[*Science*, **285**, 739-743 (1999)] [Lab. of Biochemistry]

Genetic Mechanisms of Age Regulation of Human Blood Coagulation Factor IX.

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Blood coagulation capacity increases with age in healthy individuals. Through extensive longitudinal analyses of human factor IX gene expression in transgenic mice, two essential age-regulatory elements, AE5' and AE3', have been identified. These elements are required and together are sufficient for normal age regulation of factor IX expression. AE5', a PEA-3 related element present in the 5' upstream region of the gene encoding factor IX, is responsible for age-stable expression of the gene. AE3', in the middle of the 3' untranslated region, is responsible for age-associated elevation in messenger RNA levels. In a concerted manner, AE5' and AE3' recapitulate natural patterns of the advancing age-associated increase in factor IX gene expression.

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Effect of Am-80, a Synthetic Derivative of Retinoid, on Experimental Arthritis in Mice.

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Am-80 is a newly synthesized retinoid with the structure of one aromatic amide among retinobenzoic acids. We investigated the effect of Am-80 on collagen-induced arthritis (CIA) in mice and the immunopharmacological action on the production of several cytokines in the in vitro and in vivo models. Am-80 significantly inhibited the severity and development of the arthritis index, progression of footpad swelling, bone damage and histopathological alterations. Am-80 selectively inhibited bacterial lipopolysaccharide-induced IL-6, but not TNF-α and IL-1β production in mice. These findings suggest that the inhibitory effect of Am-80 on CIA is partially mediated by modulating the production of the proinflammatory cytokine, IL-6.

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Effect of Overproduction of Interleukin 5 on Dinitrofluorobenzene-induced Allergic Cutaneous Response in Mice.

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The effect of overproduction of interleukin (IL) 5 on the allergic cutaneous response was investigated in IL-5 transgenic (Tg) mice. In IL-5 Tg mice, significant accumulation of eosinophils in skin lesions was observed after five paintings of 2,4-dinitrofluorobenzene (DNFB), and the magnitudes of eosinophilia and IL-5 messenger RNA expression were significantly higher than in wild-type mice. The dinitrophenol-specific and total IgE in the serum were higher in IL-5 Tg mice. The late phase reaction of IgE antibody-mediated biphasic cutaneous response was potentiated in IL-5 Tg mice. These results indicate that overproduction of IL-5 resulted in the potentiation of DNFB-induced dermatitis by elevation of IgE production, cutaneous response and eosinophilia.

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Inhibitory Mechanisims of Glycoprotein Fraction Derived from *Miscanthus Sinensis* for the Immediate Phase Response of an IgE-mediated Cutaneous Reaction.

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We investigated the inhibitory effect of the glycoprotein fraction extracted from *Miscanthus sinensis* Andersson on biphasic cutaneous reactions in mice passively sensitized with IgE. Results obtained here suggest that the inhibitory effect of this fraction on an IgE-mediated allergic inflammatory reactions is due to the protection of mediator vascular permeability and that in addition to the inhibition of an inflammatory reactions, a sedative action is responsible for the inhibition of allergy-induced scratching responses.