[*Biochem. J.*, **336**, 429-436 (1998)] [Lab. of Biochemistry]

Roles of the C-Terminal Domains of Human Dihydrodiol Dehydrogenase Isoforms in the Binding of Substrates and Modulators : Probing with Chimaeric Enzymes.

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Human liver dihydrodiol dehydrogenase exists in isoforms (DD1, DD2 and DD4) composed of 323 amino acids. DD1 and DD2 share 98 % amino acids identity, but lower identities (approx. 83 %) with DD4, in which a marked difference is seen in the C-terminal ten amino acids. In this study, we have prepared chimeric enzymes, in which we exchanged the C-terminal 39 residues between the two enzymes. Using this chimeric proteins, we carried out to clarify the roles of the C-terminal loops in the differential catalytic properties of DD1 and DD4. The kinetic comparison among the wild-type and chimeric enzymes indicates that the binding of substrates, inhibitors and activators to the two enzymes is controlled by residues in their C-terminal domains; multiple residues coordinately act as determinants for substrate specificity and inhibitor sensitivity.

[*NIHON HINYOUKIKAGAKUKAI ZASSHI*, **89**, 434-440 (1998)] [Lab. of Biochemistry]

Changes in Blood Polyamine Levels Following Chemotherapy in Patients with Invasive Urinary Bladder Carcinoma.

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Polyamines are recognized as cell growth factors. We attempted to determine whether blood polyamines are useful biochemical markers for monitoring the efficacy of the chemotherapy on bladder tumors. The blood concentration of three polyamines, diamine, spermidine and spermine, were determined in 31 patients with invasive urinary bladder carcinoma, following chemotherapy. One week after chemotherapy, the levels of spermine and total polyamine in the patients with CR and PR were significantly lower than those in the patients with NC. Similarly, one week after chemotherapy, the levels of spermine and total polyamine in the patients with grade 3 and 2 were significantly lower than those in the patients with grade 1b, 1a, 0. The study suggested that the levels of blood polyamines could be used as markers for monitoring the efficacy of chemotherapy in patients with bladder carcinoma.

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Citrus Auraptene Exerts Dose-dependent Chemopreventive Activity in Rat Large Bowel Tumorigenesis: The Inhibition Correlates with Suppression of Cell Proliferation and Lipid Peroxidation and with Induction of Phase II Drug-metabolizing Enzymes.

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The inhibitory effect of *Citrus* auraptene was investigated using an animal colon carcinogenesis model with a colon carcinogen, azoxymethane (AOM, s.c. injection to male F344 rats). The dietary administration of auraptene caused significant inhibition in AOM-induced large bowel carcinogenesis during both initiation and postinitiation phases. The feeding of auraptene suppressed the levels of ornithine decarboxylase, polyamines and products of lipid peroxidation in the colonic mucosa, and increased the activities of phase II drug metabolizing enzymes in the liver and colon.

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Possible Role of Nitric Oxide in IgE-Mediated Allergic Cutaneous Reaction in Mice.

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The role of nitric oxide (NO) in the development of allergic cutaneous reactions in mice was investigated. NO synthase inhibitors, L-N^G-nitroarginine methyl ester (L-NAMA) and N^G-monomethyl-L-arginine, significantly inhibited both immediate and late phases of the IgE-mediated biphasic cutaneous reaction. Simultaneous treatment with L-arginine attenuated the inhibitory effect of L-NAMA. An NO donor, 3-morpholinosydononimine-N-ethylcarbamide, caused a potent edematous reaction in the mouse ear. Furthermore, L-NAME inhibited cutaneous reactions caused by both interleukin-1β and tumor necrosis factor-α. These results indicate that NO participates, at least in part, in the development of ear edema in the IgE-mediated biphasic cutaneous reaction in mice.