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[Lab. of Biochemistry]

**Reduction of Prostaglandin D<sub>2</sub> to 9 $\alpha$ , 11 $\beta$ -Prostaglandin F<sub>2</sub> by a Human Liver 3 $\alpha$ -Hydroxysteroid/Dihydrodiol Dehydrogenase Isozyme.**

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Prostaglandin (PG) specificity of two 3 $\alpha$ -hydroxysteroid/dihydrodiol dehydrogenase isozymes, DD2 and DD4, of human liver was examined. DD2 exhibited NADPH-linked reductase activity for 9-, 11- and 15-ketoprostaglandins, whereas DD4 reduced only 15-ketoprostaglandin F<sub>2</sub>. DD2 showed the highest V<sub>max</sub>/K<sub>m</sub> value for PGD<sub>2</sub>, and the reduced product of PGD<sub>2</sub> was identified to 9 $\alpha$ , 11 $\beta$ -PGDF<sub>2</sub> by GC-MS. More than 77% of the PGD<sub>2</sub> 11-ketoreductase activity in ammonium sulfate fractions of liver cytosols was immunoprecipitated by antibodies against DD2. These results suggest that DD2 is a major soluble PGD<sub>2</sub> 11-ketoreductase species in human liver.

[Cancer Res., 54, 4653-4659 (1994)]

[Lab. of Biochemistry]

**Chemoprevention of 4-Nitroquinoline 1-Oxide-Induced Oral Carcinogenesis by Dietary Curcumin and Hesperidin: Comparison with the Protective Effect of  $\beta$ -Carotene.**

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The modifying effects of two natural products, curcumin and hesperidin, given during the initiation and postinitiation phases of oral carcinogenesis initiated with 4NQO were investigated in male F344 rats and compared with that of  $\beta$ -carotene, with respect to the incidences of tongue neoplasms and preneoplastic lesions, polyamine levels in the tongue tissue, and cell proliferation activity. These results indicated that curcumin and hesperidin inhibited 4NQO-induced oral carcinogenesis as did  $\beta$ -carotene, and such inhibition might be related to suppression of cell proliferation.

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[Lab. of Pharmacology]

**The effect of anti-tumor necrosis factor (TNF)- $\alpha$  monoclonal antibody on allergic cutaneous late phase reaction in mice.**

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Biphasic cutaneous reaction with peak responses at 1 hour (early phase) and 24 to 48 hours (late phase) after epicutaneous challenge with dinitrofluorobenzene was examined in both actively and passively sensitized mice. Prednisolone at doses of 3 to 10 mg/kg clearly inhibited both early and late phase reactions in either sensitized mice. Monoclonal anti-tumor necrosis factor (TNF)- $\alpha$  antibody inhibited the late phase cutaneous reaction only in actively sensitized mice. Anti-interleukin-5 monoclonal antibody had no effect on both phase reactions in either actively and passively sensitized animals. These results indicate the possible participation of TNF- $\alpha$  in allergic cutaneous late phase reaction in actively sensitized mice.