

[Biol. Pharm. Bull., **18**, 9-12 (1995)]

[Lab. of Biochemistry]

**Kinetic Studies of the Inhibition of a Human Liver 3 α -Hydroxysteroid/
Dihydrodiol Dehydrogenase Isozyme by Bile Acids and Anti-inflammatory Drugs.**

YOSHIYUKI MIYABE, TETSUYA AMANO, YOSHIHIRO DEYASHIKI,
AKIRA HARA*, FUMITAKE TSUKADA

We have investigated the steady-state kinetics for a cytosolic 3 α -hydroxysteroid/dihydrodiol dehydrogenase isozyme and its inhibition by several bile acids and anti-inflammatory drugs. The bile acids and drugs, competitive inhibitors with respect to the alcohol substrate, exhibited uncompetitive inhibition with respect to the coenzyme, whereas indomethacin exhibited noncompetitive inhibition. The kinetics of the inhibition by a mixture of the two inhibitors suggests that bile acids and drugs bind to overlapping sites at the active center of the enzyme-coenzyme binary complex.

[Cancer Res., **55**, 1277-1282 (1995)]

[Lab. of Biochemistry]

**Modifying Effects of Naturally Occurring Products on the Development
of Colonic Aberrant Crypt Foci Induced by Azoxymethane in F344 Rats.**

TOSHIHIKO KAWAMORI, TAKUJI TANAKA, AKIRA HARA*,
JOHJI YAMAHARA, HIDEKI MORI

Modifying effects of dietary exposure of seven naturally occurring products on the development of colonic aberrant crypt foci (ACF) induced by azoxymethane (AOM) were investigated in male F344 rats. The effects of these compounds on proliferation biomarkers such as number of silver-stained nucleolar organizer region protein, ornithine decarboxylase activity, and polyamine concentration in the colon were also estimated. Among the test chemicals, costunolide decreased four AOM-induced biomarkers. These results indicate that costunolide has blocking effects against rat colon carcinogenesis and is a possible chemopreventive agent against colon tumorigenesis.

[Eur. J. Biochem., **228**, 381-387 (1995)]

[Lab. of Biochemistry]

**Cloning, Expression and Tissue Distribution of Mouse Tetrameric
Carbonyl Reductase. Identity with an Adipocyte 27-kDa Protein.**

MASAYUKI NAKANISHI, YOSHIHIRO DEYASHIKI, KIYOSHI OHSHIMA, AKIRA HARA*

In this investigation, we isolated and sequenced a full-length cDNA for tetrameric carbonyl reductase from a mouse lung cDNA library. The expression of the cDNA in *E. coli* resulted in synthesis of a protein structurally and functionally similar to the enzyme purified from mouse lung. Although Northern-blot analysis of mouse tissues showed the enzyme mRNA to be 1.1 kb only in lung, low expression of the mRNA in all the extrapulmonary tissues, including adipose tissue, was demonstrated by a RT-PCR method. This is the first report on an identification of the putative gene product of adipocytes as tetrameric carbonyl reductase, the expression of which is tissue-specifically regulated.