PEROXISOMAL ALTERATIONS DURING HEPATOCARCINOGENESIS IN RATS. H.Tsukada, Y.Mochizuki and N.Sawada. Department of Pathology, Cancer Research Institute, Sapporo Medical College, Sapporo, Japan.

The response of peroxisomes of preneoplastic rat hepatocytes to CPIB was examined to analyze preneoplastic phases of the cells. Rats were fed 2-AAF or 3'-Me-DAB, and then 1% CPIB for the last 4 weeks of carcinogen feeding. A marked proliferation of peroxisomes was induced by CPIB in normal hepatocytes,as assessed histochemically and electron microscopically. Sequential preneoplastic processes relating to alterations of peroxisomes were characterized by (1) a remarkable induction of peroxisomal proliferation without or with seldom formation of matrical plates, (2) a moderate induction of peroxisomes with a marked formation of matrical plates, (3) a moderate induction of peroxisomes with formation of matrical tubules in addition to the plates, and (4) ultimately, almost no induction with no more formation of these matrical inclusions, as the cells appeared to be in more advanced preneoplastic phases. Decreases in sensitivity of the cells to cytotoxicity of dimethylnitrosamine or phalloidin were in parallel with the progression of the preneoplastic phases which was recognized using the peroxisomal alterations as parameter.

INHIBITION OF TUMOUR PROMOTION BY A LECANORIC ACID ANALOGUE. K.Umezawa[1], T.Matsushima[1] and T.Takeuchi[2]. [1]Institute of Medical Science, University of Tokyo, and [2]Institute of Microbial Chemistry, Tokyo, Japan.

Lecanoric acid has been isolated from culture filtrates of Streptomyces as an inhibitor of histidine decarboxylase. Because lecanoric acid was easily metabolized in animals, its stable analogues were synthesized, and were shown to inhibit histidine decarboxylase. Since 12-O-tetradecanoylphorbol-13-acetate (TPA), a tumour promoter in mouse skin, is known to enhance an activity of histidine decarboxylase, we studied the inhibitory effects of lecanoric acid analogues on tumour promotion. Among them 3', 5'-dichloro-2,4'-dihydroxybenzanilide inhibited skin tumour promotion induced by TPA in female CD-1 mice, when it was applied at the same time with the tumour promoter. This lecanoric acid analogue is a new inhibitor of tumour promotion with low toxicity.

CHARACTERIZATION OF NUCLEAR ACIDIC PHOSPHOPROTEINS IN CELL LINES FROM HUMAN MENINGIOMAS, NORMAL FIBROBLASTS AND THE HUMAN FIBROSARCOMA CELL LINE HT 1080. G.Unteregger, K.D.Zang and O.G.Issinger. Department of Human Genetics, D-6650 Hamburg/Saar, F.R.G.

Much work has been focused on the role of the nuclear non-histone proteins during gene regulation, mainly due to their species and tissue specifity and the importance of post-translational modifications associated with some of them. In order to disclose the function of some of these proteins during the onset of tumourgenesis, we analysed the nuclear protein fraction from meningioma cells, fibroblasts from the same patients and from the fibrosarcoma cell line HT 1080 by high resolution two dimensional PAGE according to O'Farrell and modified by our group. Beside a characteristic pattern for each cell type, some polypeptides are common to all cell lines so far characterised, including a set of proteins with a Mr near 23 kD and an appearent pI from 4.2-4.8. These polypeptides were detected after radioactive labelling of the cell cultures with ^{35}S-methionine. *In vivo* labelling with ^{32}p-orthophosphate also led to the phosphorylation of these acidic proteins. When the nuclear fraction was labelled *in vitro* with the catalytic subunit of the cAMP dependent protein kinase (R2C2) more than 50 proteins became labelled including the acidic polypeptides which had been shown to become phosphorylated *in vivo*. These results indicate that despite differences in morphology and proliferation behaviour of the different cells, some acidic proteins behave strictly conservatively with respect to phosphorylation and rate of synthesis. There is evidence that combining high resolution separating systems with specific labelling procedures may contribute to a more detailed elucidiation of the role of nuclear proteins during gene regulation at the onset of tumourgenesis.