suspected despite a CEA-value that fell within the normal range. Differing conclusions in the literature as to the accuracy of the test have also been reported.

It is concluded that out of the currently available markers periodically-repeated CEA-determinations supplemented with appropriate clinical investigations may be used for controlling patients who have undergone surgery for CC.

PROSTAGLANDIN H SYNTHASE CATALYZED METABOLISM OF HETEROCYCLIC AROMATIC AMINES OF THE IQ-TYPE AND THEIR ACTIVATION TO MUTAGENS

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IQ (2-amino-3-methylimidazo[4,5-f]quinoline) and related compounds occurring in heat-processed, protein-rich food are known to be mutagenic upon activation by mixed function oxidases and cause hepatic and extrahepatic tumours in rodents. IQ and 3 analogs (Kaiser et al, Chem.-Biol. Interact. 57: 97, 1986) were recently studied in a modified Ames-test and displayed prostaglandin H synthase (PHS)-dependent activation to mutagens in the order: iso IQ > IQ > NI>> demethyl-IQ (Wild and Degen, Carcinogenesis, 1987, in press). Metabolism of IQ and analogs incubated in vitro with PHS from ram seminal vesicle microsomes supplemented with arachidonic acid or hydrogen peroxide has now been studied by HPLC and TLC: NI, demethyl-IQ, IQ and iso-IQ were oxidized by PHS-peroxidase (80, 68, 54 and 18% respectively) and yield coloured products with different efficiency. Co-oxidation and/or co-oxygenation of IQ-type compounds may be responsible for their PHS-dependent activation to mutagens. Horseradish peroxidase under comparable conditions scarcely metabolized IQ, and interestingly, it did not activate IQ to a mutagen.

The data point to PHS as an activating system for food-borne arylamines of the IQ-type. This may be relevant for their extra-hepatic tumourigenic action.

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CHANGES IN LIVER CELL PLOIDY EMERGING DURING RAT HEPATOCARCINOGENESIS

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Nuclear DNA content of hepatocytes was quantified during the early steps of rat hepatocarcinogenesis by TV based densitometry using an image analysis device Magiscan 2A (Joyce Loebl, G.B.). Putative preneoplastic lesions as foci and nodules were induced by the triphasic "Gerlans protocol" (Initiator=DEN, Selection=2-AAF+CCl_4 or pH, Promotor=Phenobarbital). The amount of DNA in the hepatocellular nuclei was determined densitometrically on Feulgen-stained sections. The animals were sacrificed at 1 day before and 5, 8, 12, 15, 18 days after CCl_4 treatment and furthermore after 1, 2, 3, 5 months Phenobarbital (PB) treatment. Comparison is also made between the use of CCl_4 or partial hepatectomy during the selection procedure. This study reveals a shift towards a diploid hepatocellular population after the end of the selection phase and later on the emergence of preneoplastic lesions with a high frequency of diploid nuclei. The observed diploidisation might be a relevant parameter for tracing of early lesions during hepatocarcinogenesis; the analysis of the early lesions is finally improved by our TV-based image analysis system.

DETECTION OF HYALURONIDASE IN HEPATOMA CELL CULTURE MEDIUM WITH A SENSITIVE INDIRECT ENZYMO - IMMUNOLOGICAL ASSAY

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Hyaluronic acid was adsorbed onto plastic microtest plates. It was measured with an indirect enzymo-immunological technique taking advantage of its capacity to bind a proteoglycan (hyaluronectin, HN) supplemented with alkaline phosphatase conjugated rabbit anti-HN antibodies. The presence of active hyaluronidase was detected by the destruction of insolubilized hyaluronic acid in proportion to the hyaluronidase concentration of samples. Human hepatoma cell lines HepG2 and PFC/PRF/5 were cultivated with,then without foetal calf serum. Cell culture media as well as cell extracts could digest adsorbed hyaluronic acid. Soluble hyaluronic acid was degraded into smaller molecules as shown by liquid chromatography. The secretion in culture medium was estimated at 2×10^{-11} NFU/cell/min. The activity was suppressed by heating at 50° C for 5 minutes or by protease digestion. The optimum pH was 3.5.

The optimum NaCl concentration in formiate buffer was 0.25 ± 0.05 M. These features indicate that a lysosomal-like hyaluronidase is secreted by hepatoma cell lines.

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RSV-INDUCED CELL TRANSFORMATION : EFFECT OF PROTEASE INHIBITORS ON FIBRONECTIN AND PLASMINOGEN ACTIVATORS

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RSV-induced cell transformation is promoted by fibronectin fragments (FNdp), tissue-type plasminogen activator (t-PA) and by 12-0-tetradecanoylphorbol-13 acetate (TPA). It is known that high level of plasminogen activator (PA) activity is present in the conditioned medium (CM) of RSV-transformed cells which are also depleted of an organized extracellular matrix (ECM): this loss might be due to the direct catalytic action of PA on ECM proteins. In this study we report that: 1) RSV-transformed chicken embryo fibroblasts (CEF) release in the CM, in the absence of serum, FN peptides with MW between 230 and 110 kD and different molecular forms of PAs (MW ranging between 180 and 43 kD); 2) TPA induces an increased secretion of PAs and FN fragments: PAs and FN fragment release is suppressed by 2mM benzamidine but not by 100 IU/ml trasylol; 3) benzamidine is able to inhibit the transformed phenotype; some protease inhibitors exert a differential effect on the quantitative release of FN in RSV-transformed CEF and in uninfected CEF.

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MODULATION OF P53 EXPRESSION DURING CELLULAR TRANSFORMATION WITH SV40

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We recently demonstrated that SV40 transformed cells harbour non-complexed p53 (free p53) which is metabolically stable in addition to p53 complexed with the large T antigen. These findings suggested that a mechanism for p53 stabilization independent from large T/p53 complex formation also operates in cellular transformation by SV40. To explore this hypothesis further, we have analyzed p53 epression in mouse BALB/c 3T3 cells abortively infected with SV40. These cells transiently express SV40 large T, but are not stably transformed. We have shown that in these cells neither p53 complexed to large T nor free p53 is metabolically stable. However, if stably transformed cells are selected from abortively infected cells by a focus assay and analyzed for p53 expression, both complexed and free p53 are metabolically stable. Our experiments demonstate (1) that complex formation of p53 with large T *per se* does not stabilize p53 and (2) that p53 stabilization is a transformation specific event which seems to be a second step in cellular transformation by SV40.

CHOLESTEROL ESTERS AND CELLULAR PROLIFERATION IN THE LIVER

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Several investigators have attempted to correlate the induction of cholesterol synthesis with cellular proliferation. This has been repeatedly evaluated *in vitro* through the inhibition of HMGCoA reductase. *In vivo*, the inhibition of cholesterol synthesis is not easily achieved. We have studied cellular proliferation induced by an hepatic mitogen, lead nitrate, during fasting, a condition associated with very low levels of cholesterol synthesis. The accumulation and synthesis of cholesterol esters under such conditions has been investigated in relation to DNA synthesis.

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PROTEINS PHOSPHORYLATED ON TYROSINE AS MARKERS OF HUMAN MALIGNANCIES

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Previous work has shown that proteins phosphorylated on tyrosine are selectively detectable by antibodies against phosphotyrosine (P-Tyr) in cells transformed by retroviral class 1 oncogene-encoded kinases endowed with non regulated activity (Di Renzo *et al*, Eur. J. Biochem., 1986).