investigated.

PYRUVATE KINASE (PK) ISOENZYMES IN CHARACTERISTICS OF MULTISTAGE CARCINOGENESIS IN HUMAN UROTHELIAL CELL LINES

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Among 12 urothelial cell lines of normal and tumour (TCC) origin, representing different transformation grades (TGr) in vitro (I-III), a nuclear PK variant inhibited by L-cysteine has been found in the tumourigenic TGr III cell lines only. Chromatin extracts of all cell lines contained three PK isoenzymes which showed the greatest electrophoretic mobility in TGr I cells. It diminished in immortalized TGr II and III cells, and in TGr III cells the slow migrating isoenzyme acquired sensitivity to L-cysteine inhibition. From the T-24 TCC derived TGr III cell line a subline (T-24a) with reduced tumourigenic properties was isolated. This subline showed a simultaneous reduction of the sensitivity of PK to L-cysteine inhibition.

It is concluded that changes in PK isoenzymes might express multistage genotypic alterations during in vitro carcinogenesis.

DIFFERENCE IN 5'-NUCLEOTIDASE ACTIVITY AND PROTEIN PATTERN BETWEEN SEVERAL TUMOUR CELL LINES WITH LOW- AND HIGH-MALIGNANT PROPERTIES

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Data on the plasma membrane structure of several experimental tumour cell lines with different tumourigenic and metastatic properties has been obtained. These cell lines include the low-malignant mouse ascites HD33, the mouse lymphoma Eb and the rat adenocarcinoma BSp73 AS cells, and their high-malignant variants, mouse ascites HD34 and mouse lymphoma Esb, and the rat adenocarcinoma BSp73 ASML. The purified plasma membranes were investigated with respect to their protein and lipid composition, and their enzyme activity. The most prominent differences were found for the specific, concanavalin A-inhibitable, 5'-nucleotidase activity, and for the protein pattern exhibiting two to seven times higher enzyme acrivities and a greater amount of slightly acidic (basic) proteins preferentially in the lower molecular weight range (25 to 60 kD) of the low-malignant cells. The sialic acid content was found to be significantly higher in the low-metastasizing variants, and also their membrane lipid fluidity was higher compared to the high-metastasizing cell lines. The data has been evaluated in relation to the malignant properties of these tumour cells.

OVER-EXPRSSION OF CERTAIN ONCOGENES IN PRENEOPLASTIC AND NEOPLASTIC STAGES DURING RAT HEPATOCARCINOGENESIS

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Oncogenes such as ras and myc have been found over-expressed during hepatocarcinogenesis in rats. However, an interpretation of the sequential analysis of these changes in relation to other genetical and enzymatical alterations, represents a new approach. We analysed these changes in an experimental model of rat hepatocarcinogenesis where male Wistar rats were submitted to a triphasic induction protocol (initiation, selection, promotion). Isolation of messenger-RNA from rat liver, Northern blotting and hybridisation with radioactively labelled onc-probes, were carried out. A distinction was made between nodular/non-nodular tissue m-RNA and tumourigenic/non-tumourigenic tissue m-RNA. A first series of results is in accordance with published data: there is an elevated level of ras oncogene transcripts found in regenerative liver 30 hours after partial hepatectomy, in the nodules and surrounding parenchyma and in both the tumourigenic and non-tumourigenic tissue. The quantitative analysis, by densitometry of the autoradiographics, is under investigation.

LECTIN-BINDING AND AFFFINITY CHROMATOGRAPHY SEPARATION OF TUMOUR CELLS

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Tumour cell surface characteristics have been implicated in several aspects of cancer metastasis. We have made quantitative estimations of sugar groups

exposed on the surfaces of syngeneic murine tumour cells of known malignancy and with well defined metastasis characteristics.

We used 5 lectins conjugated to either ^{125}IUDR or fluoresceinisothiocyanate: Con A, WGA, PNA, SBA and UEA. The binding pattern was characteristically changed by treatment with the proteolytic enzyme (pronase) and with neuraminidase. The data were used as basis for attempts to separate cells in subfractions on Pharmacia Sepharose 6 MB columns. PNA (peanut agglutinin) was found to be the only suitable ligand in terms of cell yield and specificity.

SERUM TOCOPHEROL AND INCIDENCE OF CANCER IN FINLAND

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The 35,000 persons belonging to the Finnish Social Insurance Institution Mobile Clinic Survey were linked to the Finnish Cancer Registry. During a follow-up of 6 to 10 years 766 cancer patients were identified. Stored serum samples were available for the patients and 1:2 matched controls. The alpha-tocopherol levels were higher for controls. The association was strongest for smoking unrelated cancers. It persisted after exclusion of cases diagnosed shortly (<2 years) after the serum sample was drawn as well as after adjusting for the confounding effects of smoking, cholesterol and socioeconomic status.

17 BETA-ESTRADIOL MEDIATES GLYCOSYLATION OF HUMAN BREAST CARCINOMA GROWTH FACTOR RECEPTOR (BCGF-R)

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Malignant cells produce growth factors to which they respond because of specific receptors at their surface, thus conferring a growth advantage to these cells (Hakim, Expt. Cell Biol. 54: 193-211, 1986). Estradiol mediated the release of a serine protease (Hakim, Cancer Biochem. Biophys., 4: 173-185, 1980) from breast carcinoma, and of an immunosuppressive agent from malignant melanoma (Hakim, Annales d'Immunol., 131C: 155-170, 1980). The present investigation reveals that estradiol modulates glycosylation of the growth factor receptor on human breast carcinoma cell membrane. Short term cultures were developed from biopsies of human breast carcinomas confirmed as ductal (BDC), lobular (BLC) and colloidal (BCC). These cell lines were grown in estrogen-free (EFM) medium and in EFM supplemented with 10^{-7}M estradiol and/or tunicamycin (Tn). The cells were examined for mitogenicity, clonogenicity, ^{125}I-EGF binding ability and ^{3}H-galactosamine uptake capacity. The cells were also grown in athymic mice. Extraction of the BCGF-R followed by alkaline borohydride treatment and chromatography on Sepharose-4B showed that CBGF-R from in vitro cultured cells in presence of estradiol, or grown in nude mice treated with estradiol contained significantly higher fucosyl- and sialyl BCGF-R.

TATI, CEA AND CA 125 IN HUMAN OVARIAN CYSTS

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Tumour-associated trypsin inhibitor (TATI) is a 6kD peptide isolated from the urine of an ovarian cancer patient. Highly increased excretion of this inhibitor has been found in the urine and serum of cancer patients. We have now examined the concentration of TATI in human ovarian cysts. Very high cyst fluid concentrations of TATI were found in all mucinous cystadenomas, both benign and malignant. The mean concentration was about 100-fold compared to serum levels. This strongly suggests that this tumour-associated peptide was actually produced by the tumour. In serous cyst fluids low levels of TATI were found, similar to concentrations in serum. By immunohistochemistry TATI was demonstrated in most benign mucinous cystadenomas and in some semi-malignant and malignant tumours. Positive staining was predominantly seen in the apical parts of the cells. All serous tumours were negative in TATI staining. Very high cyst fluid levels of CEA and CA 125 were also detected, CEA exclusively in the mucinous type, CA 125 in both mucinous and serous cysts.

TUMOUR PROMOTING ACTIVITY OF TGFβ

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