New Approaches to Cancer Diagnosis and Management

Preparation and Preliminary Characterization of New Monoclonal Antibodies versus Estradiol Receptor.

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Using SDS-denatured estrogen receptor (ER) purified from calf uterus cytosol we immunized BALB/c female mice to prepare new monoclonal antibodies (MoAbs). Antigen were purified by DEAE-FastFlow, Heparin-agarose and MoAb Js34/32-protein A-agarose. Spleen cells were fused with Sp2/0Ag14 myeloma. Twenty well surnatantes out of 48 were positive to screening by immunoadsorbing hormone labeled partially purified ER ('antigen capture'), and/or by 'antibody capture' using purified antigen adsorbed on plastic (ELISA). 13 hybridomas were cloned by limited dilution. Western blotting revealed specific MoAbs versus bovine ER that were able to immunopurify ER and recognize the complex formed between the purified ER and Estrogen Response Element. The MoAbs bound ER, cytosolic (8S or 4S) and purified ER, with affinity between 0.3 and 2 nM. Human ER fragments (hER) translated in rabbit reticulocyte lisate mapped the epitopes recognized by the different MoAbs. We found two groups of MoAbs competing for the hER fragments containing the hormone domain (DEF regions) without reciprocal overlapping and a third MoAbs group that overlapped both. A fourth group bound a fragment containing the aminoterminal domain and the DNA binding domain (ABC regions) without interfering with the DNA binding. Western blotting analysis of cytosolic and nuclear ER from MCF-7 confirmed the ability of most MoAbs to bind human ER. Two molecoles, a 67KDa and/or a shorter molecole of about 45KDa were recognized. The 45KDa was found principally in cytosolic fraction also when MCF-7 were grown in presence of the hormone. These bands were not found in HeLa cells.

11.003

TREATMENT OF HEPATOCELLULAR CARCINOMA (HCC) BY PERCUTANEOUS ETHANOL INJECTION (PEI).

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44 patients, affected by primary HCC (51 nodes), have been treated by PEI. Tumour sizes ranged from 0.5 to 7.0 cm. Patients were injected 1 to 21 times and were followed by US, AFP, cyto/histopathology and CT to assess response. 31 patients (35 nodes) experienced complete tumour regression; in 11 patients (14 nodes) control biopsies showed the co-existence of necrosis and residual cancer cells; 2 patients (2 nodes) underwent liver transplantation after 1 and 4 alcohol injections. No lethal complications ensued. The only side effects were transient local or epigastric pain or fever. The cumulative survival rate (Kaplan-Meier method) at 12, 24 and 36 months, was 92%, 74% and 53% respectively. Our data suggest that intra-tumoral ethanol injection of small HCC is a valid therapeutic procedure, comparable with other treatments commonly used in this disease.

11.005

THE ASSAY OF THROMBIN ANTI-THROMBIN III (TAT) COMPLEXES IN LUNG CANCER: PRELIMINARY REPORT OF A PROSPECTIVE STUDY.

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Coagulation disorders are frequently detected in patients affected by different tumours even though clinical symptoms occur in a very little percentage of such subjects. Coagulation processes are probably involved in the mechanism of metastatic spread. Quantitation of even latent hypercoagulability has now become easy by means of an enzyme immuno assay detecting serum TAT complexes (TAT, Behringwerke AG, Marburg, Germany) that we used in the present study. We studied 71 patients (Pz) with lung cancer (17 small cell (SC) and 54 non small cell (NSC)) at different stages of the disease. All Pz underwent a follow up of several months (mean 175 days). After this follow up period, the Pz were divided into three groups according to their clinical condition: progression of disease (P), partial response or stationariness (PR) after chemiotherapy, no evidence of disease after surgery (NE). **SC**: 8 out of 9 Pz (79%) of the P group showed increasing serum levels of TAT complexes whereas in 5 out 7 Pz (71%) of the PR group TAT levels decreased or showed no modification. **NSC**: in 13 out of 21 Pz (62%) of the P group TAT levels increased while 14 out of 18 (77%) of the PR group showed TAT levels either decreasing or unchanged. In the NE group we observed decreased or unchanged values in 12 out of 15 Pz (80%). Our study shows that TAT complexes assay could be a useful tool in the management of patients either with SC or with NSC lung cancer.

11.002

METABOLIC ABERRATION IN PRENEOPLASTIC AND NEOPLASTIC RAT RENAL CLEAR CELL LESIONS

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Renal clear cell tubules and tumors storing glycogen in excess were induced in male Sprague-Dawley rats with N-nitrosomorpholine (stop model). The metabolic pattern of focal glycogenotic lesions was studied by means of enzyme and immunohistochemistry. The histochemical findings are consistent with the origin of the rat renal clear cell tumors from the collecting duct system. Several changes in the activity of enzymes of the alternative pathways of carbohydrate metabolism were evident. There was a strong activity of glycogen synthase and a marked elevation of the activity of glycogen phosphorylase. Glucose-6-phosphatase activity was negative like in normal collecting duct epithelium. Hexokinase, glyceraldehyde-3-phosphate dehydrogenase and glucose-6-phosphate dehydrogenase activities were reduced. The activity of pyruvate kinase usually showed a slight increase. Glucose transporter type 1 was reduced in glycogenotic cells. From various other enzymes studied, a reduction in the activity of succinate dehyrogenase and malate dehydrogenase and an increase in the content of glutathione-S-transferase-P are noteworthy. The results suggest that the excessive storage of glycogen is not due to an increased uptake of glucose from the blood, but results from alterations in the concentration of intracellular metabolites. Mitochondrial respiration may be reduced. The slightly increased activity of pyruvate kinase might provide an alternative source of energy.

11.004

EFFICACY OF INTERLEUKIN-2 (IL-2)IN THE PALLIATIVE THERAPY OF NEOPLASTIC EFFUSIONS.

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Conventional therapies are often ineffective in the neoplastic effusions.Beucause of their antitumor and fibrosis stimulating activities,some cytokines,including interferons and IL-2,may represent a new therapeutical strategy.To evaluate the efficacy of IL-2 in the palliative therapy of neoplastic effusions,10 consecutive patients(pts) (mesothelioma:4;lung cancer:3;breast cancer:2;ovarian cancer:1)received IL-2 intraserously, after complete drainage of the effusion,at a dose of 6 million IU over 15 mins,every 7 days,for at least 2 cycles.The sites of effusion were:pleura:7;peritoneum:2; pericardium:1. IL-2 was effective in preventing further drainages for at least 3 months in 7/10(70%)pts,and in particular in all pts with mesothelioma.No toxicity was seen.The study shows that IL-2 intraserously is an effective and well tolerated therapy of neoplastic effusions.

11.006

HUMAN TUMOR AND NORMAL TISSUE REACTIVITY OF THE ANTI-BREAST CANCER MONOCLONAL ANTIBODY CDI 315 B

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A mouse monoclonal antibody (CDI 315 D) raised against 3M KCl extract of the breast carcinoma was previously shown to react with a 50-80 kDa glucoproteins preferentially expressed in the cytoplasm of breast carcinoma cells. In this report, the reactivity of this mAb with a large number of normal and malignant human tissues was analyzed using immunoperoxidase technique. CDI 315 B reacted mostly in heterogenous staining patterns with 88% of 73 breast carcinoma, 15% of 14 normal breast and 24% of 33 benign breast tissue sections. No immunostaining was detected with several other tumors. Only exception was melanoma. CDI 315 B showed a significant percentage of reactivity with melanoma (63% of 8 melanoma sections.