suspensions have been elaborated. The investigations have given conclusive evidence that the degree of aneuploidy of the endometrial carcinomas, documented by DNA histograms, is the most significant marker for a prognostication of the outcome of the disease. An inverse relationship has been found between variations of nuclear DNA and cellular estrogen receptors of the carcinomas.

STEROID HORMONE RECEPTORS IN HUMAN BREAST AND PANCREATIC TUMOURS

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The presence of estrogen (ER) and progesterone (PR) receptors in breast cancer is now accepted as an indicator for potential hormonal therapy. The beneficial effects of antiestrogen therapy are well documented in breast cancer. During the last few years ER and estrogen-binding proteins have been discovered in the normal pancreas and in pancreatic neoplasia. Data concerning localization and the amount of ERs and estrogen binding proteins in the normal and tumourous pancreatic tissue are still controversial.

In our study 150 primary breast carcinomas and 25 benign and malignant pancreatic tissues were investigated by the same quantiative biochemical and qualitative histochemical methods. Our findings suggest that estrogen and progesterone receptors are localized in exocrine part of the pancreas.

TRANSFORMING GROWTH FACTORS AND ONCOGENES

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The two types of TGF that have been purified and cloned have very divergent biological activities. TGF-alpha is a potent mitogen for many cell types while TGF-beta is the most potent growth inhibitory polypeptide known for most cell types. TGF-alpha binds to the EGF receptor and has biological activities very similar to those of EGF. TGF-beta is very different from TGF-alpha in molecular structure and has its own specific cell surface receptors. TGF-beta and its receptor are highly ubiquitous. Stimulation of proliferation by TGF-beta in at least some fibroblastic cells appers to be indirect through induction of c-sis and autocrine stimulation by endogenous platelet-derived growth factor. TGF-beta is a growth inhibitor for most cell types including human keratinocytes which also produce TGF-beta, but in a latent form. Activation of the latent form is thought to be a major regulatory step in TGF-beta action and may occur through the action of endogenous proteases such as plasmin. It is hypothesized that autocrine stimulation by endogenous TGF-alpha (many cells) or TGF-beta (fibroblastic cells) or loss of sensitivity to the normal autocrine or paracrine inhibitory effect of TGF-beta (epithelial cells) could lead to an increased proliferative potential and thereby contribute to the transformed phenotype.

A MODEL FOR THE STUDY OF TREATMENT RESPONSE IN HUMAN NORMAL AND TUMOUR CELLS IN VITRO

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Since all chemotherapy and radiation treatments affect normal cells, the establishment of differential sensitivities is fundamental to the success of treatment with a particular agent.

Our group has developed a model for testing the response of oesophageal and bladder explants from tumour and surrounding normal tissue in the same patient to chemotherapy and radiation, both singly and in combination. Both oesophageal adeno and squamous cell carcinomas and bladder carcinomas were found to be 3 to 5 times more radioresistant than surrounding normal mucosa. Addition of appropriate concentrations of carboplatin (10 to 50 µg/ml) to irradiated (7.5Gy) bladder samples reversed this ratio and caused 9 times more cell death in tumour explants than in similarly treated normal cells. Treatment of irradiated oesophageal tissue explants with bleomycin (20 µg/ml) had a similarly dramatic effect and required only a very low dose of radiation (2.5 Gy) to reverse the ratio.

STIMULATORY EFFECTS OF TWO GROWTH FACTORS ON BONE MARROW CULTURES FROM PATIENTS WITH ACUTE MYELOID LEUKAEMIA AT DIAGNOSIS AND IN COMPLETE REMISSION

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We have compared the proliferation and differentiation capacity in agar and liquid cultures of the crude conditioned media from the human urinary bladder carcinoma cell line- 5637 (BCM) and from the human placenta (HPCM). The colony stimulating factors (CSF) were added to bone marrow (BM) cultures from patients with acute myeloid leukaemia (AML) at diagnosis or in complete remission (CR) as well as to normal controls. Compared with HPCM, the BCM increased clonogenicity in 2/10 day 7 cultures from AML patients at diagnosis and in 3/15 of patients in CR. The corresponding figures for day 14 cultures were 2/6 and 1/13. When agar cultures were preceded by a liquid phase, the clonogenicity was not further increased. Observed increases were about 2-fold. The simultaneous use of both CSF had no additive effect. Cell yield was lower in 6/10 BCM stimulated liquid cultures from patients at diagnosis, and in 5/10 in CR, while the differentiation capacity was similar in BCM- or in HPCM-treated cultures. In normal controls the 2 CSF produced comparable results.

In conclusion, BCM - known as a pluripotent hemopoietic CSF - increases the clonogenicity in cultures of some AML patients when compared with HPCM.

SENSITIVE ELISA METHOD DETECTS CISPLATIN-DNA ADDUCTS

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Highly sensitive immunoanalytical methods have recently become available for detecting structural DNA modifications caused by chemical carcinogens. With these methods it is possible to detect femtomole quantities of carcinogen-DNA adducts.

We have been developing sensitive ELISA methodologies to detect cisplatin-DNA adducts. Cisplatin (Cis-diamminedichloroplatinum(II)) is an antitumour drug, the main target of which is considered to be DNA. Polyclonal and monoclonal antibodies have been produced against cisplatin-DNA, cisplatin-polyG and cisplatin-GpG. The sensitivities of these antibodies are in the range of 50 to 100 fmol of cisplatin. They do not react with control DNA or cisplatin only. Cisplatin-GpG antibodies recognize enzymatically hydrolyzed cisplatin-DNA better than antibodies against cisplatin-DNA or cisplatin-polyG. Cisplatin-DNA antibodies react with DNA which has been purified from tissues of rats after intravenous injection of cisplatin. Recently, studies have been undertaken on cisplatin modifications of DNA in blood cells of cancer patients receiving cisplatin chemotherapy.

PLASMINOGEN ACTIVATOR OF CLONOGENIC CELL POPULATIONS SEPARATED FROM FIBROSARCOMA

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Fibrosarcoma cells produce plasminogen activator (PA), a protease that converts the zymogen plasminogen into plasmin. Several studies indicate that tumour invasion is accompanied by proteolysis and that plasminogen activator, generated by highly malignant cells, is by far the most ubiquitous protease associated with malignant transformation. We have fractionated the fibrosarcoma cells on renographin 60 density gradients and compared the clonogenicity of these cells with their level of plasminogen activator production. Five populations of cells were separated in continuous gradients of renographin in the density range of 1.05 to 1.18 g/cm^2. PA activity of unseparated and five separated populations were determined using [125]I-fibrin as a substrate in a reaction between cell lysate and plasminogen. Cell populations collected at densities between 1.05 and 1.09,B1B2 were the most clonogenic. PA analysis demonstrate that PA activity is restricted mostly to B1 and B2. The differences in cell cycle parameters, determined by flow microfluorometry, between density separated bands are not striking. The results suggest that PA production is a characteristic of invasive cells.

UTILIZATION OF N-ACETYL PUTRESCINE BY HUMAN MELANOMA CELLS IN VITRO FOR GROWTH IN THE PRESENCE OF DIFLUOROMETHYLORNITHINE (DFMO)

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The clinical response of human melanoma to DFMO has resulted in encouraging but limited benefit. A mechanism of resistance