differences were seen in structure of c-Ha-ras proto-oncogene in the tumour and in the lymphocyte DNA isolated from the same person. However, some differences in several loci were detected when DNA containing multilocus repeated sequences (minisatellite DNA) was used as a probe. These results indicate that loss or redistribution of some DNA sequences occurs in neoplastic tissue.

THE SENSITIVITY TO CYTOSTATICS OF THE HUMAN MELANOMA XENOGRAFTS IN IMMUNE-DEPRIVED MICE

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We established two human malignant melanoma xenografts, MEL-1 and MEL-2, subcutaneously into immune-deprived mice by melanoma cells derived from the primary monolayer culture. The xenografts grew progressively till the animals death. Mel-1 was the faster growing tumour. Both xenografts spontaneously metastasized to the lung. The histological appearance of the xenografts and their metastases were similar to that of original tumours. Both melanoma xenografts were sensitive to DTIC and Cis-platinum in all parameters tested. It is concluded that the lung colony assay provides the best possibility to assess the antitumour activity of the cytostatics used.

ADDUCT FORMATION OF DIETHELSTILBESTROL AND STEROIDAL ESTROGENS WITH AMINO ACIDS IN VITRO

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Recent evidence suggests that the induction of changes in chromosome number, i.e. aneuploidy, is a critical event in the process of neoplastic cell transformation induced by stilbene estrogens such as diethylstilbestrol (DES) and also by natural estrogens and their metabolites. We postulate that the biochemical mechanism underlying aneuploidy induction by estrogens involves covalent binding of metabolically activated estrogens to proteins of the spindle apparatus. In support of this proposition, we have recently demonstrated that DES and 2-hydroxy estradiol (2-HO-E2), the major metabolite of estradiol-17β, are able to bind covalently to a specific binding site in the C-terminal region of tubulin upon activation with peroxidase/hydrogen peroxide. In order to identify the binding amino acid(s), we have now studied the reactivity of perioxidative metabolites of DES and 2-HO-E_2 towards various amino acids in vitro. Using [14]C-labelled estrogens and high performance liquid chromatography, we found the greatest extent of adduct formation with cysteine and tyrosine, while other amino acids gave only small amounts of adducts or did not react at all. This preferential binding of reactive estrogen metabolites to certain amino acids may help to explain the observed specificity in the covalent binding to tubulin.

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MORPHOLOGICAL TRANSFORMATION OF SYRIAN HAMSTER EMBRYO CELLS AND THE EFFECT ON SOME MARKER ENZYMES BY PEROXISOME PROLIFERATORS

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Many hypolipidemic drugs and industrial plasticizers cause peroxisome proliferation in rat liver, and induce hepatic neoplasms in rats and mice. The peroxisome proliferators (PPs) show little or no evidence of direct interaction with DNA. The effects of the PPs clofibrate (CLO) and diethylhexyl phthalate (DEHP) on different marker enzymes and of morphological transformation are studied in Syrian hamster embryo (SHE) cells. Preliminary results indicate that both chemicals induce morphological transformation of SHE cells. They induced an increase in catalase activity (peroxisomes), while no increase was found for glucose-6-phosphatase (endoplasmic reticulum) and acid phosphatase (lysosomes). Malate dehydrogenase (mitochondria) showed more inconsistent results. We were not able to detect peroxisomal beta-oxidation in either PP-exposed or control cells. Electron microscopical studies of SHE cell peroxisomes are in progress.

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COMPARISON OF THE ABILITY OF GLASS FIBERS AND ASBESTOS TO INDUCE MORPHOLOGICAL TRANSFORMATION OF SYRIAN HAMSTER EMBRYO CELLS

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