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When total tumour eradication cannot be achieved by conventional treatment, the prevention of tumour metastasis by drugs selectively inhibiting the process of tumour spread may be of interest. Remarkable and approximately equal antimetastatic effects are caused in mice bearing Lewis lung carcinoma (3LL) by N-diazoacetylglycinamide (DGA) and by potassium p-(3,3-dimethyl-1-triazeno) benzoate (DM-COOK). When drug treatment is followed by surgical removal of primary tumour, DM-COOK produces about 40% long term survivors whereas DGA causes none in spite of its pronounced antimetastatic action, suggesting that host responses, contributing to the cures caused by DM-COOK which is weakly immunodepressive, are not available after treatment with DGA which strongly depresses cell mediated immune responses. A further investigation on host responses has been made by comparison of tumour growth, spread and response to cyclophosphamide (CY) in mice bearing 3LL kept in conventional housing (CH), or in a protected environment (PE) and subjected to emotional stress (anxiety for spatial disorientation, SD). Tumour growth, and particularly metastasis weight, are remarkably small in mice kept in PE, while they have usual values in mice in CH or in PE plus SD. When the mice are treated with CY, cure rates vary from about 70% in CH to 100% in PE, dropping to 0 in PE plus SD. These findings indicate the importance of host responses and stress in drug treatment, with implications of interest for experimental and clinical situations.

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HYALURONECTIN: DETECTION WITH MONOCLONAL ANTIBODIES IN HUMAN TUMOURS

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Hyaluronectin (HN), a proteoglycan which exhibits a high affinity to hyaluronic acid has been characterized in the nervous system. It was also found to be associated with embryonic mesenchyme and with tumour connective tissue. Two MAbs were obtained against human brain HN. The ELISA additivity test demonstrated they bound to two different epitopes. This finding was confirmed with immuno-histological techniques performed on human and rat tissues: the first MAb recognized only human HN while the second MAb recognized both human and rat HN. The staining on tumour sections was superimposable with that obtained with rabbit polyclonal anti-HN antibodies. Both MAbs stained desmoplasia of carcinomas and sarcomas, the extracellular matrix of fibrosarcomas and gliomas and also the benign proliferation of fibromas. Since HN is a marker of all types of tumours anti-HN MAbs could be of great interest in the medical imaging of tumours.

REGULATED EXPRESSION OF A TRANSFECTED DIPHTHERIA TOXIN GENE AS A NOVEL MECHANISM FOR KILLING TUMOUR CELLS

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We have shown that transfection of a diphtheria toxin A (TDA) chain gene linked to appropriate transcriptional regulatory elements can achieve selective cell killing (Maxwell *et al.*, Cancer Res., 46: 4660, 1986). In experiments now in progress we have constructed vectors which include the regulatory elements of the heat shock response gene (hsp 70) (Morgan *et al.*, Mol. Cell Biol., 7: 1129, 1987) as well as elements from Epstein Barr Virus (EBNA-1 and Ori-P) which should allow such vectors to replicate as episomes (Sugden *et al.*, Mol. Cell Biol., 5: 410, 1985). We will attempt to derive permanent cell lines which may be induced to express a mutant toxin gene, Tox 176 (Maxwell *et al.*, Mol. Cell Biol., in press, 1987) and thus commit suicide by transient exposure to 42° C. Controlled toxin gene expression may prove useful in eliminating malignant cells which express marker proteins or other characteristics via *trans*-activators not found in normal cells.

IMMUNOGENICITY OF HYBRID TUMOUR CELLS AND MHC ANTIGEN EXPRESSION

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In a model of murine fibrosarcoma of H-2b haplotype, we isolated from a somatic hybrid cell (H-2b x H-2k) several variants differing in their ability to induce

immunity against the tumour parental cell. We investigated by RIA the expression of the MHC class I and class II antigens on these variants and the modulation of this expression by agents of differentiation such as DMSO and IFN. Our results suggested that enhancement of immunogenicity was not merely due to the presence of allogeneic class I antigens, since they are expressed at a low leel on all variants. For tumour syngeneic class I antigens, a threshold of expression seems to be necessary but not sufficient to induce enhancement of immunogenicity. Class II molecules were not expressed even after treatment with DMSO and IFN. Rather, it seems that differential modulation of H-2D and H-2K, induced by some agents of differentiation, could be occurring during the development of the immune response.

INHIBITORY EFFECTS OF ELLAGIC ACID ON GENOTOXICITY INDUCED BY N-NITROSO COMPOUNDS

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It has been reported that ellagic acid - a naturally occurring plant phenol - inhibits the mutagenicity and carcinogenicity of benzo(a)pyrene. We tried to study the inhibitory influence of ellagic acid on genotoxicity induced by N-nitrosodimethylamine (NDMA) and N-methyl-N-nitro-N- nitrosoguanidine (MNNG). The methods were: in vivo - in vitro DNA alkaline assay (DNA Damage), Ames test on S.typhimurium strains (TA 1538 and Ta 100) and sister chromatid exchange (SCE) method. Dimethyl sulphoxide was used for compound dissolution and as a negative control. Data from all experiments demonstrate that ellagic acid distinctly inhibits the genotoxicity induced by N-nitroso compounds especially before the giving of the genotoxicants.

The following results showing the inhibitory effects of ellagic acid were obtained:

DNA-Damage	- from 59% to 39%
SCE	- from 0.040 to 0.024
Ames revertants/plate	- from 2500 to 36

PATTERNS OF ADA, 5'NT, POLY(A)POLYMERASE AND SURFACE LIGHT CHAIN EXPRESSION IN CLL

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Investigation of enzymes and immunological markers contribute to the definition of subsets of lymphoid malignancies and the prognosis of the disease. The pattern of distribution of the activity levels of adenosine deaminase (ADA), ecto-5'-nucleotidase (5'NT) and poly(A)-polymerase as well as that of the expression of surface light Ig chains was studied in 47 CLL cases. ADA activity was found to have a positive correlation with poly(A)-polymerse activity ($r=0.345$). Increased values of the latter enzyme, which is responsible for the polyadenylation of mRNA, are associated with aggressive disease. Correlation of enzymatic activities with the surface light chain phenotype revealed the association of "λ type" leukaemias - considered to be more aggressive compared to those of "κ type" - with low 5'NT activities ($p<0.01$). We conclude that the analysis of surface markers and enzymatic patterns of malignant cells may contribute to more accurate classification and monitoring of neoplasias.

PROTECTION BY N-ACETYLCYSTEINE (NAC) AGAINST ADVERSE EFFECTS CAUSED BY CIGARETTE SMOKE (CS) IN CULTURED HUMAN BRONCHIAL CELLS

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The effects of CS and several cigarette smoke condensate fractions were investigated in human bronchial epithelial cells cultured in serum-free conditions. Cellular survival was decreased to 50% by 0.4 ml CS per ml of thiol-free growth medium. Supplementation with NAC up to 100 µM had a dose-dependent protective action against CS-induced loss of survival. Other effects caused by CS in bronchial cells include depletion of cellular thiols and formation of DNA single strand breaks. When cellular effects of smoke condensate, a semi-volatile and a non-volatile fraction were compared total condensate was the most cytotoxic, whereas the semi-volatile fracion was the most potent to decrease cellular thiols. Further fractionation of the semi-volatile fraction indicated that a neutral subfraction was more potent than the basic, acidic or phenolic subfractions in causing cytopathic effects. Concomitant exposure to NAC significantly protected against condensate-induced effects on survival, growth rate, thiol content and DNA