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

structure. Protection by NAC against cyto- and genotoxic effects of tobacco smoke in human bronchial epithelium may have clinical relevance.

EXTINCTION OF PROVIRAL EXPRESSION IN CELL HYBRIDS: APPROACHES TO THE ISOLATION OF A HUMAN SUPPRESSOR GENE

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The fusion of rat fibroblasts transformed by a single integrated copy of Rous sarcoma virus to normal mouse or human cells results in hybrids which are morphologically normal. The provirus is retained and is intact but transcriptionally inactive. Karylogical examination of normal and transformed hybrids suggests that chromosome 11 may carry the suppressor gene. In an attempt to isolate the suppressor gene we are pursuing several strategies including:

(1) the use of a retroviral vector as an insertional mutagen since the normal hybrids are often haploid with respect to their human chromosomes;

(2) DNA mediated co-transfection with an HPRT cDNA clone or pSV2neo using either back selection or fusion with the transformed parental line to distinguish spontaneous revertants from suppressed transfectants.

EXPRESSION OF FUNCTIONAL EGF RECEPTORS IN INSECT CELLS USING A BACULOVIRUS VECTOR

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To obtain large amounts of functional epidermal growth factor (EGF) receptors for biochemical and biophysical studies, we have subverted the natural life cycle of the Autographia californica Nuclear Polyhedrous Virus (AcNPV) in an insect cell line (Spodoptera Frugiperda) to express the human EGF receptor cDNA. The cDNA for the full length of EGFR was cloned into an expression vector which when cotransfected with wild type AcNPV formed recombinant AcNPV. Insect cells infected with this virus produced a membrane protein which was recognised by the monoclonal antibodies R_1 and F_4 which bind to the external and cytoplasmic domains of the human receptor respectively. EGF bound to whole cells with a kd of 10^{-8} mol showing approximately 10^6 binding sites per cell. Auto-phosphorylation of the immunoprecipitated recombinant protein showed that it possessed an active tyrosine kinase which like the natural receptor phosphorylated the three C terminal tyrosine residues designated P_1, P_2 and P_3 (1) SDS page analysis revealed that this insect cell protein was slightly smaller (160 kd) than that of EGF receptor protein found in A431 cells. Biosynthetic studies showed this size disparity was accounted for by differences in glycosylation.

It is hoped to increase the productivity of our system by using suspension-perfusion culture systems and also to compare the structure and functions of this protein with other similarly produced mutant/trancated EGF receptors.

(1)Nature, 311: 483-485, 1984.

rRNA MATURATION AS AN INDICATOR OF CYTOTOXICITY OF THE ANTINEOPLASTIC DRUG 5-FLUOROURACIL

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Subclones of the human rDNA transcriptional unit were prepared and used as probes for blot hybridisation of fractionated RNA species isolated from human colonic tumour cells growing in vitro. The results established that 5-Fluorouracil (5-FU) affected rRNA maturation and led to the accumulation of rRNA precursors. The effects correlated with cytotoxicity of 5-FU. The implications of these findings for the mode of action of 5-FU and the development of novel chemotherapeutic strategies have been evaluated.

IN VIVO AND IN VITRO BINDING OF PERCHLOROETHYLENE (PCE) TO NUCLEIC ACIDS

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PCE is hepatocarcinogenic in mice, but the evidence of its genotoxicity in short-term assays is as yet limited. Therefore, we attempted to measure covalent binding of PCE to DNA both in vivo, by