polychlorinated ethanes using different biological systems in collaboration with other Institutes.

In this report, five chlorinated ethanes such as 1,1-Dichloroethane (1,1-DCE), 1,2-Dichloroethane (1,2-DEC), 1,1,1-Trichloroethane (1,1,1-TCE), 1,1,1-Trichloroethane (1,1,2 TCE) and 1,1,2,2-Tetrachloroethane (1,1,2,2 TCE) were tested using D7 yeast strain of Saccharomyces cerevisiae with and without metabolic activation. Chemicals were tested on yeast cells from stationary and logarithmic growth phase where the level of cytochrome P-450 is high.

The results confirmed the relevance of metabolic activation and the use of yeast cells rich in cytochrome P-450 capable of metabolic activity. From this methodology 1,2-DCE, 1,1,2-TCE and 1,1,2,2-TCE show a genetic activity.

SAPINTOXIN A, A NON-PROMOTING PHORBOL ESTER ACTIVATES PROTEIN KINASE C

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In this communication we report the activity of a naturally occurring, highly fluorescent phorbol ester which activates protein kinase C (Ka 76nM) but which is neither a complete nor second stage tumour-promoter in traditional Berenblum tests. This compound, Sapintoxin-A, 12-0-[2-methylaminobenzoyl]-4-deoxyphorbol-13-acetate was isolated from the unripe fruits of Sapium indicum L., and forms one of a family of fluorescent phorbols, including Sapintoxin-D, and the protein kinase C receptor antagonist α-sapinine. Sapintoxin-A has properties in common with promoters such as TPA in that it will induce erythema in vivo, liberate PG's in vitro, induce lymphocyte mitogenesis and aggregation of human and rabbit platelets. Sapintoxin-A is therefore a suitable negative control compound for further biochemical studies concerning the involvement of protein kinase C in tumour-promotion and cell proliferation.

ANTITUMOUR EFFICACY OF HUMAN RECOMBINANT INTERLEUKIN 2

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Repeated peritumoural injections of human recombinant interleukin 2 (RIL-2) inhibited the growth of 80% of methylcholanthrene (MC)-induced murine sarcomas in syngeneic mice. Twenty percent of the MC-induced murine sarcomas were resistant to the RIL-2 immunotherapy. A direct correlation was observed between the susceptibility of the MC-induced murine sarcomas to RIL-2 immunotherapy in vivo and the sensitivity of these sarcomas to the cytolytic effect of RIL-2-activated spleen (LAK) cells in vitro. These results suggest that LAK cells represent the effector cell mechanism responsible for the anti-tumour efficacy of local RIL-2 immunotheapy, and that in vitro testing of sensitivity to LAK cell-mediated cytolysis may be used to detect tumours that will respond to IL-2 immunotherapy in vivo.

PURIFICATION OF A PHOSPHOTYROSINE PROTEIN PHOSPHATASE (PTP)

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It is now generally accepted that phosphorylation of proteins on tyrosine residues plays a fundamental role in growth regulation and oncogenesis. Many of the known oncogene products and growth factor receptors are associated with tyrosine protein kinase activity. To be of physiological significance, phosphorylation of tyrosine residues has to be reversible. A PTP activity capable of removing phosphate from tyrosine residues has been demonstrated by us and others. Of all the phosphatases known to dephosphorylate tyrosine residues, we concentrate on a membrane associated activity insensitive to EDTA/Fluoride which can be inhibited by micromolar amounts of Zn^{2+} or vanadate. The epidermal carcinoma cell line A431 was found to have high amounts of PTP activity and is being used as a source for purifying the enzyme. We are in the process of optimizing purification and recovery.

DIFFERENT GLYCOCONJUGATES ON HUMAN NORMAL AND TUMOURS TISSUES DEFINED BY THE MONOCLONAL ANTIBODY, MLuC1

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The monoclonal antibody (MAB) MLuC1

reacts with normal and tumour cells of several human epithelia including breast and lung. It recognizes a saccharidic epitope heterogeneously carried by different kinds of glycoconjugates, i.e. mucins, glycoproteins and a glycolipid. Soluble and glycolipid extracts from surgical specimens of normal breast and lung tissues, mammary carcinomas and lung carcinomas of different histotypes were analyzed by SDS-PAGE and immunoblotting or immunoreaction on HPTLC. Although glycoproteins of various molecular weight were present on almost all the tissues examined, the expression of the glycolipid molecule seemed to be limited to neoplastic conditions. These results suggest that, as for other MAB-defined structures, it is more likely the type of antigenic glycoconjugate rather than the presence of the defined determinant that is specific for the differentiation and/or transformation of epithelial cells.

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LATENCY, ANTIGENICITY AND ras GENE ACTIVATION OF METHYL-CHOLANTHRENE- INDUCED MURINE FIBROSARCOMAS

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To see whether the short latency period of chemically-induced, highly immunogenic murine fibrosarcomas is associated with the presence of activated ras-oncogenes, high molecular weight DNA from 6 antigenic and 4 non-antigenic methyl-cholanthrene (MCA)-induced BALB/c fibrosarcomas were used to transfect NIH/3T3 recipient cells. DNAs from 5 of 6 antigenic but only 1 of 4 non-antigenic tumours, contained transforming genes as shown by the foci observed after 14 to 21 days of culture. Multiple copies of λ-phage sequences, used as a marker, were present in DNAs isolated from the transfectants. Preliminary results of a Southern blotting analysis of the first cycle transfectants using Ha, Ki, and N-ras probes indicate the activation of ras-family genes in 6 transfectants derived from 3 different antigenic fibrosarcomas. Thus, the transforming activity of BALB/c fibrosarcomas DNAs, mediated by activated ras oncogenes in transfection assay, seems to be associated with their degree of antigenicity.

INDUCTION OF HEAT SHOCK GENE EXPRESSION IN RAT LIVER DURING GROWTH AND NEOPLASIA

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We investigated the expression of rat hepatic heat shock protein (HSP) gene expression under the influence of growth and hepatocarcinogenicity, because of the potential of heat shock as a therapeutic modality and the importance of the heat shock response induced by cellular stress. We found a 5-fold increase over baseline in both HSP 83 and HSP 70 (Mr 83,000 and 70,000) transcripts by 24 hr after partial hepatectomy which normalized by 5 days. A 42° C rat heat shock for 3 min induced a 4.5 and 20-fold increase in HSP 83 and HSP 70 mRNAs. Acute administration of diethylnitrosamine induced a time and dose (50 to 200mg/kg) dependent increase in HSP 80 mRNA; 4 weeks of dietary 2-acetylaminofluorene also did likewise. Primary hepatocellular carcinomas (HCC) had constitutively elevated HSP gene transcripts compared to age-matched controls, which increased further on rat heat shock. This elevated constitutive HSP gene expression was also found in several heptoma cell lines and 4/8 human hepatomas. HSP gene expression is thus increased transiently during normal liver growth, by acute and chronic carcinogens, and in a stable manner in rat and human primary hepatomas.

IN VITRO CHEMOSENSITIVITY TESTING OF HUMAN LUNG CARCINOMA CELLS

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In vitro evaluation of drugs against human cancers is of clinical interest because the procedure may predict the chemotherapeutic response in patients. Drug sensitivity of lung carcinoma cells from freshly explanted tumours was determined using two tests: the Clonogenic Assay and the Dye Exclusion Test. Three drugs, Cis-platinum, Adriamycin and Vincristine were tested in a group of patients with small cell carcinoma and adenocarcinoma. The data obtained from this study reveal that the clinical activity of these standard drugs is confirmed by the findings that a significant number of tumour specimens were also sensitive to these drugs in vitro. The rates of drug activity in adenocarcinoma were much lower corresponding to the clinically recognized resistance of ths tumour type. Detailed prospective in vivo-in vitro correlations have not as