cells to 10^{-1} M sCT produced a marked proliferation. However, continuous treatment with 10^{-1} M sCT resulted in a 50% inhibition of the cell growth.

ADAPTIVE RESPONSE TO THE MUTAGENIC ACTION OF ALKYLATING AGENTS

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The adaptive response is an inducible form of DNA repair acting on alkylation damage, and was first studied in E.coli cells and later in mammalian cell cultures and in root tip meristems of plants. In this work, the possibility of inducing an adpative response system to the mutagenic action of alkylating agents was studied in the haploid strain meth G1 bi A1 of the fungus Aspergillus nidulans, scoring methionine revertants. A population of conidia (12.67×10^6/ml) was exposed to a low concentration (1 ppm) of the alkylating agent N-methyl-N'-nitro-N-nitrosoguanidine and then, to a high cncentration (20 ppm). The numbers of survivors (83%) and methionine revertants (45.0×10^{-6} overall frequency) were compared with those of a second population (survivors 76%, revertants frequency 67.3×10^{-6}) which was directly treated with the high concentration.

The results obtained so far indicate that the number of survivors increases (7%) and the number of revertants decreases (33.19%), when conidia are pre-treated with a low concentration of MNNG which is taken to indicate that induction of a DNA repair enzyme takes place in the fungus.

COLLATERAL SENSITIVITY TO VERAPAMIL IN VINCRISTINE RESISTANT CHO CELL LINES

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Two vincristine resistant CHO cell lines, obtained by prolonged selection in semi-inhibitory concentrations of vincristine, show considerable hypersensitivity to the calcium channel blocker verapamil in the absence of vincristine. Their D10 values are around 0.2 µg/ml compared to 23 µg/ml for unselected controls. Reversion to vincristine resistance is correlated with reversal of verapamil hypersensitivity, indicating that the two aspects of the cells' phenotype have a common cause. The cell lines are also unusually sensitive to other membrane acting agents which are not calcium channel blockers and the rate of calcium accumulation in the absence of and in the presence of verapamil is similar in the vincristine resistant cell lines and controls. These two observations suggest that the membrane change underlying the vincristine resistant/verapamil hypersensitive phenotype does not involve calcium channels. The cell lines show partial cross-resistance to adriamycin and reduced vincristine accumulation. They have characteristic protein and cytogenetic changes and are semi-dominant. This novel form of membrane change which confers vincristine resistance may be of clinical interest.

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DISTINCT PHENOTYPIC ALTERATIONS INDUCED BY CHEMICAL INDUCERS OF DIFFERENTIATION: ENZYMATIC AND HISTOCHEMICAL STUDIES

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The effects of two known chemical inducers of cell differentiation, dimethylsulphoxide (DMSO) and sodium butyrate (SB) were studied on MCF-7 breast cancer cells. Both agents inhibit MCF-7 cell growth and clonogenicity in soft agar. The anti-proliferative effects of both agents are accompanied by different phenotypic alterations. SB enhances the activities of the plasma membrane-bound enzymes γ-glutamyltranspeptidase and alkaline phosphatase. An increase in the activity of acid phosphatase was also found. Determination of estrogen-binding sites revealed a statistically not significant increase. DMSO induced a consistent increase of 73% in estradiol binding sites, but failed to induce any change in enzyme activities. DMSO and SB were also found to induce selective phenotypic alterations in melanoma cells. These data suggest that various differentiating agents induce different changes in solid tumour cell lines, rather than an ordered pattern of cell differentiation. These distinct activities may however be used in designing protocols for combined treatment of solid tumour cell lines.

THE LYMPHATIC LEUKAEMIA CELL LINE 3447 OF DOG-1-A KARYOTYPIC ANALYSIS

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A continuous cell lines has been established from a dog with leukaemia. The cells are regarded as members of the T-lymphocyte line in origin, because they did not produce immunoglobulins, did not phagocytize but did agglutinate with concanavalin A, phytohaemagglutinin and pokeweed mitogen and showed reactivity only in the lymphocyte acid phosphatase test. Their ability to grow on semi-solid agar as well as the clinical findings confirm that they are malignant.

The cells showed variability in chromosome number and extensive formation of centric fusions. Every cell was unique in chromosomal constitution and in addition, the prevalence of a nullisomy applying to many chromosomes in each cell was detected.

AFFINITY LABELLING OF THE MOUSE LIVER PROLACTIN RECEPTOR

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To detrmine the molecular weight of the prolactin receptor in the liver of lactating mice we covalently bound [125]I-iodinated human prolactin to its receptor in liver membranes using dimethyl suberimidate as a bifunctional cross-linker. SDS-PAGE and autoradiography reveals a single hormone rceptor complex at a MW of 60 kD that is competed wth an excess of cold ovine prolactin (oPRL) or human growth hormone (hGH). This suggests that the prolactin receptor has a binding subunit of about 36 kD (MW of prolactin: 24 kD). A cross-linked complex of the same molecular weight can be detected using [125]I-hGH and is competed wth cold hGH or oPRL, suggesting the use of the same binding subunit by both hormones. Immunoaffinity purification of the cross-linked ligand receptor complexes with anti-prolactin antibody is under investigation.

REGRESSION ANALYSIS OF EXPRESSION PATTERNS OF ANTIGENS IN COLORECTAL CANCER

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In addition to conventional pathological parameters in colon cancer, such as shape and size of the primary tumour, central node involvement, venous invasion, grade and stage, new variables, such as the immunoreactivity patterns at a cellular level of CEA, Ca 19-9, mucin, serotonin, secretory component and the DNA-index were tested for their potential prognostic values. A regrssion analysis was performed of the pathology data of 350 patients with primary colorectal cancer. These data were prospectively collected in a multicentre study with a follow-up of five years. All specimens were centrally reviewed.

In the multivariate analysis, stage was the predictive factor with the highest hazard ratios, but absence of central node involvement, tumours with diameters between 3,5 and 6 cm, exophytic growth, well differentiated tumours, tumours with CEA immunoreactivity, absence for staining with serotonin and diploid tumours had a favourable prognosis.

The aforementioned variables may be included in a prognostic index. Routine application of some variables is hampered by small numbers in the subgroups of hazard ratios.

MAPPING OF PAI-1 TO A REGION OF ABNORMALITIES OF CHROMOSOME 7 IN CANCER

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Alterations of chromosome 7 are frequently found in metaphases of patients with myelodysplasia or leukaemia. Dysfunction of one or more genes located in 7q21-q35 could be involved in these malignancies. Recently, several genes have been localized to this region of chromosome 7. In haematological cancers possible malfunctions of COL1A2, OI4, EPO, KIT, MET and TCRB are particularly interesting.

We have mapped the gene for plasminogen activator inhibitor, type 1 (PAI-1) by chromosomal in situ hybridization analysis to 7q21.3-q22. Interestingly, studies of genetic recombination between PAI-1 and other genes previously mapped to this region showed that it was closely linked to both