animal model system with well-established tumour inheritance, such as the hereditary melanoma formation in small tropical fish, platyfish and swordtails. In this system, a 1:1 Mendelian segregation of benign and malignant melanomas is observed. As suggested by Vielkind (1976) and Ahuja, Schwab and Anders (1980), this is due to a single regulatory locus. Studies on the differentiated state of the pigment cells in the two melanoma types show almost completely differentiated cells in the benign and very poorly differentiated cells in the malignant type. We have now mapped this locus, and can show a recessive, perhaps deletogenic, mode of melanoma inheritance. Thus the regulatory locus, termed Diff, presumably codes for information necessary in differentiation; it does not influence the severity of the melanoma in a dominant fashion.

[99m]Tc AND [111]In LABELLING OF MONOCLONAL F(ab')$_2$-FRAGMENTS AGAINST PROSTATIC ACID PHOSPHATASE FOR RADIOIMAGING OF PROSTATIC CANCER

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Tumour detection by external imaging following administration of radiolabelled monoclonal antibodies specific for tumour-associated antigens has drawn considerable attention in the diagnosis of cancer. Although radioisotopes of iodine have been employed for labelling antibodies, these labels are not stable, and significant deiodination may take place rapidly in vivo. An alternate approach to attach [99m]Tc or [111]In to the antibody using the anhydride of DTPA as a bifunctional chelate.

Monoclonal F(ab')$_2$-fragments (1 to 10 mg/ml) against prostatic acid phosphatase were derivatized with cDTPAA (molar ratio of cDTPAA/F(ab')$_2$ = 1:1, 5:1, 10:1, 20:1). The best labelling efficiencies (90 to 95% or 70 to 80%) using [111]In or [99m]Tc were obtained with molar ratio of cDTPAA/F(ab')$_2$ of 5:1 and with protein concentrations of 10 mg/ml. Under these conditions the antibodies retained their immunoreactivity totally and had no aggregation formation when studied by SDS-PAGE. A successful purification process for [99m]Tc labelled antibodies was developed to increase specific activity of labelled antibody. The radioactive antibody derivatives synthesized revealed metastases of prostatic cancer when used in radioimaging studies.

URACIL-DNA GLYCOSYLASE IN NORMAL AND MALIGNANT HAEMATOPOIESIS

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The activity of uracil-DNA glycosylase, a repair enzyme for the excision of uracil from DNA, was studied systematically in different types of blood and bone marrow cells in normal individuals, in haematological malignancies, and in established leukaemia cell lines. The patients represented a wide range of acute and chronic leukaemias.

The highest uracil-DNA glycosylase activities were found in primitive cells of normal and malignant haematopoiesis, although considerable variation was noted in blastic leukaemias. The expression of uracil-DNA glycosylase gradually diminished towards the more mature cells. This was observed in normal bone marrow, in chronic granulocytic leukaemia, and in TPA-induced malignant histiocytes. Blood lymphocytes in healthy individuals and in chronic lymphoproliferative disorders had stronger uracil-DNA glycosylase expression than the other mature cells, such as erythrocytes, granulocytes, and platelets.

INVESTIGATION OF CALCITONIN (CT) BINDING TO ITS RECEPTORS (CTR) IN MCF-7 HUMAN BREAST CANCER CELL LINE

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The CTR content of 10 breast cancer tissues was measured by a single-point inhibition technfique using human [125]-I-CT as labelled ligand and salmon CT (sCT) as inhibitor. Six cases out of 10 proved to be CTR-positive, the CTR content (mean ± SD) was 620±298 femtomol/mg protein and all the normal samples were CTR-negative. In the CTR-positive cancer tissue the cytosol estradiol receptor (ER) level was 154±90 femtomol/mg protein. On the basis of our human study the CT binding to MCF-7 human ER-positive breast cancer cell line was investigated. The CTR content of the intact cells was 5.3 femtomol/10^6 cells and the Kd value was 0.413×10^9 M, indicating that the binding was very specific to the CTR. According to an exchange assay, the CTR binding sites were already occupied by the sCT within 10 min. A 3 hr exposure of the

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.

Financial support from the Yorkshire Cancer Research Campaign is gratefully acknowledged.

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