those most likely to survive. Five human cancer cell lines (HT29, EC, GER, GYL, MDA-MB-157) were cultured individually and as a mixture for sixteen weeks without subculture. Conditioned media from these cultures were tested at intervals for their effect on the growth of freshly subcultured aliquots of the same cell lines by Neutral Red assay (Fiennes et al, 1984). Although HT29 and EC (colonic adenocarcinoma) were the slowest growing, they came to dominate the mixed culture. Over time, conditioned medium from this culture inhibited the growth of the remaining three cell types. Conditioned medium from mono-cultures of HT29 and EC had the same effect. These findings are compatible with the activity of a cell-line-specific growth inhibitory factor in the HT29 and EC conditioned media.

ALTERED CELL SURFACE CARBOHYDRATES AND METASTATIC POTENTIAL IN VARIANTS OF B16 MOUSE MELANOMA

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Variants of B16 mouse melanoma selected for wheat germ agglutinin (WGA) resistance show reduced metastatic potential as compared to the wild type F1 cells. The variant cells express a 60 to 70x increase in a specific fucosyltransferase activity, increased fucosylation of cell surface glycoproteins including expression of the SSEA-1 antigen, and (secondarily) decreased sialylation and WGA-binding of the glycoproteins. Variants selected from two WGA-resistant clones by two different lectins show reversion of the fucosyltransferase activity, the glycosylation changes and wheat germ agglutinin resistance to the original F1 phenotype. In order to assess the relationship of the glycosylation change to the metastatic potential, the cell lines were injected intramuscularly into syngeneic mice. Of the seven revertant lines isolated and tested, seven showed an increase in metastatic potential as compared to the WGA-resistant lines. The results suggest a possible relationship between the properties of cell surface carbohydrates and metastatic potential.

EXPERIMENTAL TUMOUR MODELS FOR AN ASSESSMENT OF THE THERAPEUTIC POTENTIAL OF BIOLOGICAL RESPONSE MODIFIERS (BRM)

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Various attempts for the non-cytotoxic treatment of neoplastic disease are based on the concept of stimulation of host biological responses against its own neoplasm. However, there are distinct differences between therapeutic results achieved in animal tumour systems and in clinical trials. These disappointments are suggested to be the result of the disparity between experimental models and clinical neoplasms. To study the role of immunogenicity of a tumour model in respect to "its sensitivity" to BRM, several new transplantable lines have been established from mouse tumours of spontaneous origin suggested to be non-immunogenic: rhabdomyosarcoma and mammary carcinoma of Balb/c mice, mammary adenocarcinoma of DBA/2 mice and two adenocarcinomas of CBA mice. Characterization of these tumours include the following: growth curve in vivo, TD50, immunogenicity and the ability to metastasize. The immunotherapeutic potential of BRM has been studied against primary tumours and when applicable against metastases. In general, these tumours do not respond to pustulan (glucan with immunomodulating activity). In some models an inhibition of the primary tumour has been observed but at the same time the number of spontaneous metastases have increased.

MODULATION OF SARCOMA Sa1828 GROWTH IN RATS BY HISTAMINE AND ITS H2 AGONIST AND ANTAGONIST

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This study was conducted in transplantable methylcholanthrene induced sarcoma-bearing rats to determine if tumour growth is affected after the administration of histamine (1mg/kg), dimaprit (H2 agonist, 2mg/kg) or ranitidine (H2 antagonist, 3mg/kg). Sa1828 was induced by s.c. inoculation of 2 million tumour cells/animal. All compounds and 0.9% saline (control) were given by i.p. injection 5 times weekly for 3 weeks. Body weight was monitored regularly. Of the drugs studied, ranitidine prevented the body weight loss associated with tumour growth. Likewise the tumour incidence and mean tumour mass tended to be much lower in the ranitidine treated group. Histaminics and antihistaminic normalized body histamine level and

intestinal diamine oxidase activity, both being associated with the tumour growth.

THE EPIDEMIOLOGY OF ENDOGENOUS NITROSATION IN MAN

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Epidemiological investigations designed to study the role of endogenous N-nitroso compounds in human cancer have produced inconclusive results. The development of the N-nitrosoproline (NPRO) test (1) has made possible the quantitative estimation of endogenous nitrosation. We have used this test to study nitrosating ability in relation to the risk of gastric cancer.

Healthy males aged 20 to 35 years, resident in two regions of Italy with contrasting mortality from gastric cancer have been compared using the test. NPRO is measured in 12-hour urine samples following a dose of 500 mg proline. In a separate study, patient groups with precursor lesions for gastric cancer were compared with those having normal gastric epithelia. In this case 24-hour urine samples were analysed following proline and nitrate doses.

The results of these studies have been evaluated in relation to dietary characteristics of the groups.

(1) Ohshima H. and Bartsch H. Cancer Res. 41: 3658-3662, 1981.

THERAPEUTIC EFFECT OF CHEMOIMMUNOTHERAPY ON LYMPHOMA BEARING MICE

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The therapeutic effect of a combination therapy employing anti-tumour immune lymphocytes and either doxorubicin (DX) or cis-diamminedichloroplatinum II (DDP) was tested on BALB/c mice bearing YC-8, a weakly immunogenic lymphoma. Mice inoculated with 10^4 YC-8 tumour cells given i.v. all died with liver metastasis. Therapy with immune lymphocytes alone ($30x10^6$ i.v. every 2 days x 3) gave an 80% cure rate when started 3 days after tumour inoculation; when treatment was delayed (5 days) only 20% of the mice were cured. Given at 7 days, immune lymphocytes were ineffective. DX (10 mg/kg) and DDP (6 mg/kg) i.p. gave a significant increase in survival time at all days tested but no cures were obtained. DDP was slightly more active than DX. The association of DDP (day 5) with immunotherapy (day 7) was more effective (54% cures) than DDP alone and day 5 or 7 immunotherapy alone. Only a slight increase in life span was found by combining immunotherapy with DX. The results suggest that combination of chemotherapy and immunotherapy may improve the effects of each treatment alone.

BINDING FOR cis-DIAMMINEDICHLOROPLATINUM (II) TO DINUCLEOTIDES

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Cis-diamminedichloroplatinum (II) (cis-Pt) is a widely used anticancer agent, whose main target is thought to be DNA. In this study, we have incubated cis-Pt with four homodinucleotides (GpG, ApA, CpC, and UpU) and six heterodinucleotides (GpC, CpG, GpU, UpG, GpA, and ApG) at pH 6 at 37 °C. The reaction products were purified by HPLC. Cis-Pt reacted equally well with all guanosine-containing dinucleotides, while the reaction with ApA was much slower. With CpC and UpU no reaction products were formed. The most important products were characterised by ^{1}H NMR spectra. In all the heterodinucleotides except the ones containing uridine, the main Pt-adduct was an intramolecular cross-link, in which the other binding site of cis-Pt was the N-7 atom of guanosine. The other products were intermolecular cross-links and monofunctional Pt-adducts. In the case of homodinucleotides GpG gave almost entirely intramolecular cross-links, and ApA gave both monofunctional and bifunctional Pt-adducts. These results suggest that in DNA cis-Pt is first bound to the N-7 atom of guanine, and then to another base, which may be either guanine or adenine, or even cytosine or thymine.

ISOLATION OF LYMPHOCYTE CLONES REACTING AGAINST AUTOLOGOUS HUMAN MELANOMA

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Peripheral blood lymphocytes (PBL) of a melanoma patient were cultivated with autologous melanoma cells (Auto-Me) and recombinant interleukin 2 (RIL-2, Biogen)