International Agency for Research on Cancer, Lyon, France.

N-nitrosamine acids (e.g. nitrosoproline) excreted per 24 hr urine, represent an index for endogenous nitrosation. Formation of endogenous N-nitroso compounds was assessed by this method in the following subjects: subjects living in high/low incidence areas (a) for stomach cancer in northern Japan and (b) for oesophageal cancer in China; (c) subjects from 26 provinces in China with different mortality for cancer of the oesophagus, stomach and liver; (d) subjects from India with different chewing habits of betel quid; and (e) patients with urinary bladder infection.

In general, higher exposures in endogenous N-nitroso compounds were found in high risk subjects, but individual exposure was greatly affected by dietary components, modifying chemicals or disease state. Vitamin C lowered the body burden of intragastrically formed N-nitroso compounds. Mechanisms by which these nitrosamines are formed in vivo have been evaluated.

ANTIMETASTATIC EFFECT OF IL-2 AND DIFFERENT LYMPHOID CELLS

I.Bašić, M.Šamija and M.Gerenčer

Department of Animal Physiology, Central Institute for Tumors and Allied Diseases and Tissue Typing Center, University of Zagreb, Zagreb, Yugoslavia

We have studied the effect of systematically administered lymphoid cells given in conjunction with IL-2 on established lung metastases. Tumours were an anaplastic carcinoma (ACA) of Y59 rat and a mammary carcinoma (MCA) of CBA mouse. IL-2 was prepared by allosensitation of rat spleen cells with mitomycin C treated mouse splenocytes. Metastases in the lung were generated by i.v. injection of tumour cells. Five days after inoculation of tumour cells, animals were injected i.v. with 10^7 spleen cells from normal or specifically immunized donors or with those cells which were expanded in vitro with IL-2. Following this and every 24 hr thereafter during the 3 consecutive days recipients were given an i.p. injection of 0.5 ml of IL-2. Results indicate that in vivo administration of IL-2 in conjunction with immune lymphocytes in adoptive immunotherapy is effective in controlling metastatic growth in the lungs. In vitro expanded lymphocyte cultures however were less effective than entire splenocyte population.

DEMONSTRATION OF THE POTENTIATION OF ENDOCYTOSIS OF AN ANTI-CEA ANTIBODY BY A COLON CARCINOMA CELL LINE USING ANTI-CEA/NCA ANTIBODIES

N.Berry, I.Z.A.Pawluczyk, R.A.Robins, M.C.Garnett, V.S.Byers and R.W.Baldwin

Cancer Research Campaign Laboratories, University of Nottingham, Nottingham NG7 2RD, U.K.

Carcinoembryonic antigen (CEA) may be a suitable target for immunotherapy of carcinoma of the G.I. tract, and factors which influence the cytotoxic effect of toxin-conjugated anti-CEA antibodies are important. In this study, factors influencing the endocytosis of an anti-CEA antibody by a gastric carcinoma cell line, MKN-45, have been investigated.

MKN cells were incubated on ice for 30 min with an anti-CEA antibody labelled with TRITC whose fluorescence was quenched by conjugation to HSA. After washing, the cells were incubated at 37° C for 2 to 6 hr. As endocytosis of the antibody occurred, the TRITC-HSA was degraded and the increase in fluorescence was quantitated by flow cytometry.

Endocytosis of anti-CEA-TRITC by MKN-45 cells was demonstrated after 2 hr and increased up to 6 hr. This was potentiated, in a dose-dependent manner, by the addition of certain antibodies defining epitopes common to CEA and normal cross reacting antigen (NCA), to the initial incubation mixture. After 6 hr, the value of fluorescence after potentiation was 1.8 times that of unpotentiated endocytosis.

PREVENTION OF EXPERIMENTAL LIVER METASTASES BY LECTIN BLOCKAGE

J.Beuth, H.L.Ko, J.Solter, G.Pulverer and G.Uhlenbruck

University Clinics of Cologne, D-5000 Cologne 41, F.R.G.

According to recent results, our hypothesis that organ-specific lectins (e.g. the D-galactose specific Hepatic-Binding Protein) play an important role in the organ location of metastatic malignant cells, has been evaluated. In Balb/c mice, pre-injection (1 hr) and regular application (for 3 days after tumour cell inoculation) of the lectin blocking agents D-galactose (2 mg/g body weight) or arabinogalactan (0.5 mg/g body weight) completely prevented the establishment of sarcoma L-1 tumour in the liver but did not influence the localization into other organs. Non-specific, galactose-free polysaccharides showed no

lectin blocking effect. In summary, when organ-specific lectins are blocked with competitive glycoconjugates, tumour cell colonization of the liver can be prevented. The same holds for the settling of bacteria with D-galactose residues (for instance, asialo-B-streptococci).

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CHROMOSOME ABNORMALITIES IN KAHLERS DISEASE

G.C.Beverstock(1), H.L.Haak(2), C.H.W.Leeksma(2), H.Kerkhofs(2), Els Augustinus(2) and Jose den Nijs van Weert(2)

(1)Department of Clinical Genetics, University Hospital, Leiden and (2)Municipal Hospital, The Hague, The Netherlands

Kahlers disease, otherwise known as multiple myeloma or plasma cell myeloma was first described in 1846. Cytogenetic studies have been performed on relatively few patients with this disease to date. The majority had normal karyotypes probably because malignant plasma cells undergo cell division infrequently and thus were not readily detected.

We report here our findings on 49 patients with Kahlers disease collected over a period from 1975 to the present time. Application of cytogenetic banding techniques has identified 15 patients from this group with chromosome abnormalities. Detailed karyotype analyses were performed and whilst the majority of them were complex it would appear that chromosomes 1, 11 and 14 were the most frequently involved.

EXPRESSION OF c-fos, c-myc AND hsp70 GENES IN REGENERATING RAT LIVER

E.Biesiada, J.Wiśniewski, Z.Krawczyk and M.Chorąży

Department of Tumor Biology, Institute of Oncology, Gliwice, Poland

Partial removal of rat liver induces synchronous entry of Go hepatocytes into G1 and S phases (at 22 to 28 hr) followed by the wave of mitosis (at 30 to 32 hr). Transient, but significant expression of the c-fos gene at 15 to 60 min after surgery, followed by a second peak at 4 hr was observed in regenerating liver. The c-myc gene was slightly induced within first hour and induction reached maximum at 4 to 8 hr. The second peak of c-myc induction was followed by an increase in the level of one of the hsp70 gene-like transcripts. A comparison of the hsp70 gene expression pattern in control, partially hepatectomized and heat-shocked rats revealed that hepatectomy brought about the increase in the level of this hsp70-like RNA species which was constitutively expressed in various organs of non-treated rats. Induction of this transcript started at 6 hr and remained elevated through the pre- and replication phase with a slight maximum at 8 to 10 hr of the regeneration.

CO-EXPRESSION OF ALPHA-2-MACROGLOBULIN AND GROWTH PROMOTING ACTIVITY IN HIGHLY AND POORLY TUMOURIGENIC MELANOMA CELL LINES

J.Bízik, J.F.Doré(1), A.Lizaňová and M.Grófová

Cancer Research Institute, Bratislava, Czechoslovakia, and (1)Centre Léon Bérard, INSERM U218, Lyon, France

A panel of highly and poorly tumourigenic melanoma cell lines was analyzed with respect to their expression of alpha-2-macroglobulin and growth factors. For the highly tumourigenic cell lines, shorter population doubling time was characteristic and exhibited slightly higher levels of growth promoting activity in conditioned media than the poorly tumourigenic melanoma cell lines. Heterotransplantation experiments showed that the expression of the alpha-2-macroglobulin was not crucial in the ability of the melanoma cells to form tumours in nude mice. Present results suggest the possibility that alpha-2-macroglobulin secreted by human melanoma cell lines can influence the growth promoting activity expressed by these cell lines.

METABOLISM OF DIETHYLSTILBESTROL IN HAMSTER HEPATOCYTES

G.Blaich and M.Metzler

Institute of Toxicology, University of Würzburg, Versbacher Strasse 9, D-8700 Würzburg, F.R.G.

The combined treatment of male Syrian golden hamsters with the synthetic estrogen diethylstilbestrol (DES) and 7,8-benzoflavone (7,8-FB), but not with DES alone nor 7,8-BF alone, gives rise to a near 100% incidence of liver tumours. We hypothesize that 7,8-BF modulates the hepatic metabolism of DES or vice versa, thereby leading to tumour induction. To test this hypothesis we are investigating the biotransformation of DES in freshly