higher trend to develop secondary changes.

RELATIONSHIP BETWEEN AUTOPHOSPHORYLATION AND KINASE ACTIVITY OF P56LCK

R.Fagard, I.Boulet and S.Fischer

INSERM U 15, Institut de Pathologie Molécularie, 24 rue du Fg St. Jacques, 75014-Paris, France

A novel putative oncogene has been described: lck is a member of the Tyrosine Kinase (TPK) family, it shares 70% homology with src. We have described the TPK (P56) coded for by lck in LSTRA, a murine lymphoma induced by MoMuLV. P56 is highly expressed in LSTRA, in several human lymphomas, in one case of acute myeloblastic leukaemia, it has been detected in normal and mitogen stimulated T lymphocytes. It is expressed at a very low level in B lymphocytes and is thought to be lymphatic specific. We have studied P56 both in crude membrane preparations and with immunopurified P56 using a specific antibody prepared by immunizing rabbits against a peptide from the N-terminal region of P56, a region sharing no homology with other known TPKs (in particular P60src). In the two systems, we observed that P56 autophosphorylation leads to an increased TPK activity towards exogenous substrates. Chemicals that change the autophosphorylation of P56 have identical effects on the TPK activity. From these data, it appears that autophosphorylation is an important step of the activation of P56lck.

THE THERAPEUTIC USE OF RADIOACTIVE C215 IN MURINE TRANSPLANTED TUMOURS

B.Fermer(1), N.A.Habib(1), L.Lindholm(2), F.C.McCrae(3), B.Larsson(2), M.Palmer(4), C.B.Wood(5) and R.C.N.Williamson(1)

Departments of (1)Surgery and (3)Medicine, Bristol Royal Infirmary, Bristol, U.K.; (2)Department of Microbiology, Gothenberg University, Gothenberg, Sweden; Department of (4)Radiology and (5)Surgery, Royal Postgraduate Medical School, London, U.K.

The therapeutic role of monoclonal antibody C215 labelled with ^{131}I was investigated in transplantd murine mammary carcinomas. Fragments (approximately 10mg of mammary tumour from (P x Pc) F1 hybrid mice) were implanted subcutaneously in 15 mice of the same strain. Eight mice were injected with ^{131}I-C215 starting from day 12 following tumour implantation and these survived subsequently. In contrast, all 7 control mice died within 35 days. Therefore this study has shown a beneficial anti-cancer effect of radiolabelled C215 in improving survival in the treated mice.

STEARIC ACID AND CARCINOGENESIS

B.Fermor(1), N.A.Habib(1), C.B.Wood(2), K.Apostolov(3), W.Barber(3), M.J.Hershman(2) M.Aslam(3), D.Heinemann(2), W.E.Jenkins(4), J.R.W.Masters(4) and M.J.Embleton(5)

(1)Department of Surgery, Bristol Royal Infirmay, Bristol, U.K.; Departments of (2)Surgery and (3)Virology, Royal Postgraduate Medical School, London, U.K.; (4)Department of Pathology, Institute of Urology, London, U.K.; (5)Cancer Research Campaign Laboratories, University of Nottingham, Nottingham, U.K.

Decreased membrane rigidity is one of the characteristics of malignant cells, resulting in part from the desaturation of stearic acid into oleic acid. In this study, we investigated the influences of stearic acid in tumour cell inhibition in vitro and tumour development in vivo. Stearic acid inhibited the colony-forming ability of four out of five rat and two human tumour continuous cell lines in vitro. In contrast, the colony-forming ability of rat fibroblasts was not inhibited. Using a model of rat mammary carcinoma induced by nitrosomethyl urea (MNU), the subcutaneous injection of stearic acid at weekly intervals prevented tumour development in 5 of 10 rats. Using iodostearic acid twice weekly, 11 of 19 rats were alive and tumour free at week 22 whilst all of 14 animals injected with NMU alone had died of tumour by the sixteeenth week. The ratio of stearic to oleic acids in erythrocyte membranes was significantly reduced in the tumour-bearing rats, but was normal in tumour-free animals treated with stearic or iodostearic acid. These preliminary data indicate that stearic acid kills human tumour cells in vitro and inhibits tumour development in rats.

GROWTH INHIBITORY ACTIVITY OF HUMAN COLONIC ADENOCARCINOMA CELL LINES IN VITRO

A.G.T.W.Fiennes, A.G.Grant, D.A.Winterbourne, and J.Hermon-Taylor

Department of Surgery, St. George's Hospital Medical School, Cranmer Terrace, London SW17 0RE, U.K.

Under competitive culture conditions cells with growth-inhibitory activity should, if themselves refractory, be among

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

J.Finne(1,2), H.Haidvogl(2), S.Castori(2), T.Feizi(3) and M.M.Burger(2)

(1)Department of Biochemistry, University of Kupoio, Finland; (2)Department of Biochemistry, Biocenter, University of Basel, Switzerland; (3)Clinical Research Centre, Harrow, U.K.

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)

Ł.Fiszer-Maliszewska, M.Mordarski and Z.Zawadzka

Institute of Immunology and Experimental Therapy, Wrocław, Poland

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

W.A.Fogel, D.Kierska and C.Maslinski

Department of Biogenic Amines, Polish Academy of Science, P-225 Lodz 1, Poland

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