In the present study, P-Tyr antibodies were used to investigate the existence of human tumours expressing abnormal levels of tyrosine phosphoproteins and tyrosine kinases. Among eighteen cell lines examined, the antibodies identified a number of tumours with a detectable level of proteins phosphorylated on tyrosine. Among these were a major protein with an approximate Mr of 150,000 in a gastric carcinoma; two proteins, with Mr of 130,000 and 100,000 in a colon carcinoma; a major protein with Mr of 170,000, tyrosine phosphorylated in both a urinary bladder and an epidermoid carcinoma. Among the haemopoietic malignancies screened, in two Philadelphia-positive chronic myelogeous leukaemias, P-Tyr antibodies recognized the chymeric bcr-abl 210,000 Mr protein and its substrates. These phosphoproteins were not found in samples harvested from normal gastro-intestinal or urinary bladder epithelium, nor in control fibroblasts and lymphocytes. Two of the above proteins have associated tyrosine kinase activity. These data support the idea that a number of human malignancies contain an abnormal level of proteins phosphorylated on tyrosine and that the latter is an exploitable tumour marker.

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GROWTH SUPPORT, TOXICITY AND SOME METABOLIC EFFECTS OF HOMOCYSTEINE IN NON-TRANSFORMED AND CHEMICALLY TRANSFORMED C3H/10T1/2 CELLS

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Inability to grow in a medium where methionine is replaced by homocysteine has been demonstrated for several malignant cell lines and postulated as a characteristic feature of the neoplastic phenotype as most normal cells thrive under these conditions.

To investigate this hypothesis in a well defined cell culture system we examined the effects of homocysteine on non-transformed (Cl 8) and two malignant clones (Cl 16 and Cl T422) of the C3H/10T1/2 mouse embryo fibroblasts, with regard to toxicity, ability to support growth and effects on methionine metabolism and glutathione level. Homocysteine was toxic to all cell lines and showed a drastic effect on cell morphology. These effects were not seen with homocysteine thiolactone.

Homocysteine thiolactone supported growth of the normal Cl 8 cells almost to the same extent as methionine, the malignant Cl 16 cells showed moderate growth reduction whereas Cl T422 grew slowly when methionine was replaced with homocysteine thiolactone.

The ability of homocysteine to support growth correlated well with alteration of methionine metabolism as the intracellular level of S-adenosylhomocysteine increased in all three cell lines in homocysteine thiolactone supplemented medium, while the S-adenosylhomocysteine content increased in Cl 8 cells, was constant in Cl 16 cells decreased in Cl T422 cells under the same conditions.

The glutathione content showed small variations between normal cells and Cl 16 cells during exponential growth, Cl T422 showed a distinct lower level of glutathione in methionine supplemented medium, and, in contast to Cl 8 and Cl 16 cells, showed 3-4 fold increase in glutathione when methionine was replaced by homocysteine.

EFFECTS OF BUTYLATED HYDROXYANISOLE OF THE MONOXYGENASE SYSTEM AND THE ACTIVATION OF BENZO(A)PYRENE BY 3-METHYLCHOLANTHRENE-INDUCED NUCLEAR FRACTION

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The effect of dietary administration of butylated hydroxyanisole (BHA) on the 3-methylcholanthrene (MC)-induced hepatic monooxygenase system (MFO) of nuclear fractions was investigated in male mice. The experiment has indicated similar qualitative effects of BHA on components of MC-induced and control MFO. BHA did not change the amount of cytochrome b5 and activity of NADH- and NADPH-cytochrome c reductases, but lowered the content of cytochrome P-450 and aryl hydrocarbon hydroxylase activity. These effects of BHA resulted in similar significant differences in benzo(a)pyrene (BP) metabolism after incubation of BP with both control and MC-induced nuclear fractions. BHA feeding reduced the BP metabolism and the binding of BP metabolites to DNA in control and MC groups. These experiments have indicated the greater effect of BHA on MC-induced nuclear fraction compared with the control. This effect is opposite to our previous findings with microsomal fractions.

SELECTION OF HUMAN MELANOMA METASTATIC VARIANTS

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