activated by S9 fraction from control and Aroclor-induced mice, respectively. There were also differences in the inhibitory potency between BHA and BHT. Our data suggest that type of S9 fraction (control or induced by different monooxygenase inducters) maya be critical for the evaluation of results obtained in SOS Chromotest, when the effects of chemopreventive agents on the genotoxicity of indirect acting compounds are analysed.

REVERSION OF THE NEOPLASTRIC PHENOTYPE IN Ha-ras-TRANSFORMED RAT CELLS INDUCED BY TRANSFECTION WITH DNA FROM NORMAL HUMAN CELLS

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The neoplastic phenotype of FE-8 rat cells transformed by an activated human Ha-ras gene is suppressible upon fusion with normal cells (Griegel et al, Int. J. Cancer, 38: 697, 1986). The nature of the gene(s) involved in the suppression of neoplastic transformation is unknown. We attempted to revert the transformed phenotype in FE-8 cells by introduction via tranfection of DNA from normal human cells rather than by cell fusion. Six thousand transfectants harbouring the genetic information of normal human cells and of a cotransfected selectable marker (pY3) were isolated and subsequently selected for the normal phenotype based on the relative resistance of normal cells to treatment with ouabain. Primary and secondary transfectants were isolated in which the normal phenotype (dependence of serum and anchorage) appeared to be restored. The tumourigenicity in nude mice of these clones was also reduced. The expression of the mutant ras gene was not substantially reduced in revertants, nor was the biological activity of the oncogene impaired. From the presence of human repetitive DNA fragments in secondary transfectants we conclude that transfected DNA sequences are associated with the reversal of the neoplastic phenotype.

AMPLIFICATION OF THE N-myc GENE IN PROGRESSION OF HUMAN NEUROBLASTOMA

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Neuroblastoma is a childhood tumour, whose cells frequently show cytogenetic evidence for amplified DNA - "double minutes" (DMs) or "homogeneously staining chromosome regions" (HSRs). By serendipitous screening a DNA domain derived from the short arm of chromosome 2 was identified to be amplified in all tumours and cell lines derived from neuroblastomes and carrying DMs or HSRs. The core region of this DNA domain is characterized by the presence of a cellular gene N-myc that is related to c-myc in structure, sequence and the protein it encodes. N-myc is one member of a family of genes that have in common two highly conserved nucleotide boxes and are referred to as "myc-box" genes. Amplifications of another "myc-box" gene, L-myc, is frequently found in human small cell lung cancers.

Amplification of N-myc has been detected, with few exceptions, only in advanced stages of neuroblastoma. Early stages with amplification have extremely poor prognosis. The estimated progression free survival of patients with the most advanced form of neuroblastoma (stage IV) is roughly 50% in case there is a single copy of N-myc, 20% and 0% in case there are 3 to 10, or more than 10 copies respectively. These data suggest that amplification of N-myc may contribute to malignant progression of human neuroblastoma.

THE INHIBITION OF POLYPLOIDIZATION OF CARCINOGEN-TREATED HEPATOCYTES PERSISTS IN PRIMARY CARCINOGENESIS AND AFTER TRANSPLANTATION

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During treatment of normal rats with 2-acetylaminofluorene (2-AAF) the liver normally increases in weight, protein and DNA content. However, polyploidization of hepatocytes is blocked, as indicated by the reduced percentage of bi-nuclear cells. After removal of 2-AAF polyploidization proceeds normally. In liver previously treated with the initiating agent diethylnitrosamine (DENA) and subsequently with 2-AAF, the hepatocytes never attained the degree of polyploidy of normal hepatocytes. In later appearing nodules and cancers most cells were diploid. Hepatocytes transplanted after the sequential treatment with the 2 agents appeared to be constitutively blocked in their ability to polyploidize, since nodules and cancers isolated from the host liver consisted predominantly of diploid cells. Treatment of the host with the polyploidization-promoting agent phenobarbital did not lead to more polyploid