was not produced. Thus, these compounds may possibly be toxic carcinogens. To test this hypothesis estradiol and catecholestradiols were administered to Sprague-Dawley rats. An increase in prostate mass was observed. In human hyperplasia of the prostate we found that the catecholestrogen concentration was three times higher in malignant tumours than in benign growths.

INOSITOL PHOSPHATES AND PHOSPHOINOSITIDES IN RAT LIVER NODULES

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We have investigated the inositol phosphate turnover system in liver nodules from rats. These nodules, considered to be preneoplastic lesions, have many histological and biochemical alterations, e.g. a larger growth fraction and an altered response to growth factors.

The total amounts of phosphoinositides and inositol phosphates were measured in normal and nodular liver, as well as the turnover rate of the different compounds after stimulation with vasopressin.

Consistent with earlier findings, the basal level of phosphatidyl inositol was roughly doubled in the nodules, though neither the polyphosphoinositides nor the inositol phosphates showed any marked differences.

The nodular cells responded to vasopressin with a quicker than normal elevation of the inositol trisphosphate amount, but to the same level as the normal liver. The normal cells showed a six-fold increase of inositol tetrakisphosphate, which we have not been able to show in nodular cells.

INDUCED DIFFERENTIATION IN HUMAN LEUKAEMIA/LYMPHOMA CELL LINES. A SHORT OVERVIEW

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In recent years cell lines representative of most types of human leukaemia and lymphoma have been established in vitro. Such lines have been found to be instrumental in studies aimed at understanding (1) whether the differentiation block, typical of leukaemia/lymphoma in vivo, is reversible in vitro and if so, whether the induced differentiation will be terminal, i.e. associated with a G1/G0 cell cycle block, and (2) the deranged genetic control of proliferation/differentiation in leukaemia/lymphoma. These studies clearly show that at least for non-lymphoid cell lines (HL-60, U-937, K-562, MEL, Ku 812, M 1-2, THP-1) induction of terminal differentiation is indeed possible by e.g. phorbol ester, vitamin D3, retinoic acid, interferon, and that several protooncogenes are regulated during this process.

ANTI-MELANOMA PROPERTIES OF CHEMICAL INDUCERS OF DIFFERENTIATION: IN VITRO AND IN VIVO STUDIES

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The effects of three chemical inducers of cell differentiation, sodium butyrate, dimethylthiourea (DMTU) and tetramethylurea (TMU), were studied on mouse and human melanoma cell lines and B16 melanoma tumours. Sodium butyrate, dimethylthiourea (DMTU) and tetramethylurea (TMU) were found to inhibit melanoma cell growth, clonogenicity in soft agar and tumourigenicity in syngeneic mice. Sodium butyrate, DMTU or TMU also induced morphological and biochemical changes in melanoma cell lines. These changes include cell enlargement, development of endoplasmic reticulum and golgi complexes, and enhancement of NADPH cytochrome c reductase and γ-glutamyl transpeptidase activities. These phenotypic alterations are in part compatible with a more differentiated phenotype. Systemic administration of sodium butyrate, DMTU or TMU to mice inoculated with B16 melanoma cells resulted in delayed tumour appearance and prolonged survival of the mice. These studies form a basis for further evaluation of the potential therapeutic use of chemical inducers of differentiation in solid tumours.

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DOWN REGULATION OF NK CELL ACTIVITY IN MoLV LEUKAEMOGENESIS: EVIDENCE FOR TUMOUR CELL MEDIATED SUPPRESSION

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