isolated hamster hepatocytes of high viability, as measured by the efflux of lactate dehydrogenase, the intracellular and extracellular distribution of Na+ and K+, and the plasma membrane potential. DES was metabolized by these cells to several oxidative metabolites and also to glucoronides and sulphates. The oxidative compounds comprise Z,Z-dienestrol, 1-hydroxy-DES and 3'-hydroxy-DES. Interestingly no isomerization of Z-isomers could be detected.

This study demonstrates the ability of isolated hamster hepatocytes to metabolize DES via conjugative and oxidative pathways. Liver cells should therefore be useful in studying the effect of 7,8-BF pretreatment on DES metabolism, thereby helping to clarify the role of metabolic activation in DES-mediated tumourigenesis.

Supported by the Deutsche Forschungsgemeinschaft (SFB 172).

EXPRESSION OF THE TRANSFORMATION-ASSOCIATED PROTEIN p53 IN RODENT CELLS TRANSFORMED BY HUMAN ADENOVIRUSES WHICH DIFFER IN THEIR ONCOGENIC POTENTIAL

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The steady-state levels of p53 protein and mRNA were analyzed in a range of rodent cells transformed by highly oncogenic Adenovirus (Ad) type 12 or non-oncogenic Ad2 or Ad5. Analysis of the steady-state level of p53 protein by Western blotting showed a reduction in the level of p53 protein in Ad12 transformed cells when compared to Ad2 or Ad5 transformed cells. The half-life of p53 was similar (approximately 10 to 15 hr) in cells transformed by either Adenovirus serotype.

In order to analyze further the level of control of p53 expression, the steady-state concentration of p53 mRNA in each transformed cell line was analyzed by Northern blotting. This showed a marked reduction in the steady-state level of p53 mRNA in Ad12 transformed cells compared to Ad2 transformed cells. There appears therefore to be no strict correlation between the steady-state level of p53 protein and mRNA and the oncogenicity of Ad-transformed cells examined in this study.

MOLECULAR AND BIOLOGICAL CHARACTERIZATION OF FIBROBLAST GROWTH FACTOR FGF, A POTENT INDUCER OF ANGIOGENESIS

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Two proteins (16 to 17 kD), acidic and basic FGF, have been isolated and structurally characterized by protein sequencing and cDNA cloning. The FGFs are related by structure, possess similar biological activities and are present in many tissues. In vitro, they are strongly mitogenic for vascular endothelial and other mesodermal cells, and also modulate non-mitogenic cellular activities (endocrine, differentiated functions). In vivo, FGFs induce the formation of new capillary blood vessels and promote wound healing. These data suggest that FGFs may have a physiological role as local regulators of normal tissue growth, repair and maintenance. FGFs may also be implicated in various pathological conditions involving altered neovascularization, e.g. in solid tumour growth. Certain tumour cells synthesize basic FGF and the growth of tumours can be inhibited by antibodies that neutralize the mitogenic activity of basic FGF.

EARLY CHANGES IN GENE EXPRESSION INDUCED BY TUMOUR PROMOTERS IN MOUSE SKIN KERATINOCYTES

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The potent tumour promotor 12-0-tetradecanoylphorbol-13-acetate (TPA) causes alterations of both epidermal differentiation and proliferation patterns in vivo as well as in cultured keratinocytes. To characterize early changes (within 4 hr) in gene expression, a cDNA library representative for mRNAs expressed in mouse epidermis in vivo after TPA treatment was constructed and screened with a cDNA probe enriched in sequences preferentially expressed after TPA treatment. Here we describe the characteristics of two cDNA clones λB3 (430 bp) and λ B10 (850 bp) consistently showing differential hybridization. The clones recognize unique TPA inducible transcripts of 0.6 and 5.0 kb, respectively. In primary mouse keratinocytes a low basal level of expression is observed, which is markedly reduced when cells are induced to differentiate. Similar to that observed for ornithine decarboxylase mRNA, new protein

synthesis is not required for the TPA induced increase in mRNAs recognized by λB3 and λB10. Addition of a protein synthesis inhibitor alone leads to marked accumulation of mRNA recognized by λB3. Analysis of genomic organization indicates that λB10 contains sequences belonging to a repeated gene family or a family of closely related genes whereas sequences present in λB3 may correspond to a unique gene. The expression patterns of mRNAs recognized by λB3 and λB10 suggest that they may be associated with early phases of the genetic programme for growth, although a specific function in this programme remains to be shown.

TUMOUR PROMOTER PMA REVRSES THE ORDER IN WHICH CELLS ENTER MITOSIS

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Tumour promoting phorbol ester derivatives are known to stimulate as well as inhibit the cell cycle traverse of many kinds of cells, but it is not known whether or how these effects are related to tumour promotion. It is shown here that the potency of the phorbol diester PMA to cause a delay of cell division in human fibroblasts depends on the cycle status at the beginning of exposure to the PMA. Cells which become exposed while they are in an early stage of the cycle are less effectively delayed and reach mitosis earlier than those for which exposure begins at a later stage of the cycle. Thus PMA actually reverses the cycle-age distribution and the order of cell division within a normally growing population. Since growth regulation in self-renewing tissues is dependent on intercellular communication which is likely to be effected by the relative cell cycle positions of neighbouring cells, this reversal of cell cycle age may cause a disturbance of growth regulation, leading to hyperplasia and tumourigenesis.

FUCOSE AND SIALIC ACID AS PROGNOSTIC INDEXES IN PATIENTS WITH BREAST CANCER

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Fucose and sialic acid were determined in sera of 700 patients with breast cancer in various stages of evolution and compared with 150 patients with benign lesions of the breast and 80 healthy women, respectively. Both parameters levels increased together with tumour volume enhancement. The most relevant results were found for fucose which was found significantly increased starting with stage I, its values being more frequently elevated and with higher magnitude in cases when homolateral lymph nodes were invaded. In patients with recurrences and/or metastases higher levels of fucose were found in 96% of cases and the modifications occurred at about 2 to 3 months before any clinical or radiological evidence of recurrences or metastases. Our results revealed that fucose is a better marker than sialic acid both in tumour volume estimation and disease expansion as well as in prognosis of breast cancer.

TRISOMY 13 - A RARE ACQUIRED CHROMOSOMAL ABERRATION

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Trisomy 13 occurring as the sole aberration in an acquired clone was seen in three patients, two males and one female, aged 77, 44 and 53 respectively, in over 15,000 patients studied because of malignant disorders. All three patients had acute non-lymphocytic leukaemia (ANLL). One patient had had RAEB-T diagnosed previously, two others had findings suggesting that their leukaemia had evolved through a myelodysplastic phase. ANLL types were M2, M2 and M2/M4 respectively. Haematologically, the patients were rather different (Hb range : 92 to 165 g/l; WBC : 3.1 to 250 x 10^9; platelets : 31 to 255 x 10^9/l.

Cells with trisomy 13 as well as normal cells were found in the bone marrow of all patients. Peripheral blood lymphocytes had a normal karyotype. One patient had two additional clones in the bone marrow : 47,XX,+13,7q- and 48,XX,+13,+21.

Trisomy 13 thus is a rare acquired aberration which, based on these three patients, occurs in ANLL with a preceding myelodysplastic phase.

GENETIC ACTIVITY OF CHLORINATED ETHANES

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This work, sponsored by Associazione Italiana Ricerca sul Cancro (AIRC), is a part of an interdisciplinary program on