tumourigenic and relatively normal counterparts. The immortal but non-tumourigenic human bladder urothelial cell lines HCV29 and Hu609 were compared with the immortal, tumourigenic line T24, and the mortal, non-tumourigenic line Hu1752. Slot Blot analysis of basal levels of oncogene mRNAs demonstrated that the immortal, non-tumourigenic lines overexpressed 20-fold either c-myc or c-sis, while T24 overexpressed both of these oncogenes 20-fold. TPA induced c-fos but not c-myc RNA in HCV29, Hu609 and T24 while both these oncogenes were induced in Hu1752 (Skouv et al, J. Cell. Biochem., in press). Southern blotting revealed no rearrangement or amplification of the c-myc gene which might account for its overexpression or lack of TPA inducibility. Several other oncogenes also appeared structurally intact and unamplified. Only T24 demonstrated a mutation at codon 12 of the H-ras gene. The mechanisms of the c-myc and c-sis overexpression are under further investigation.

HEPARAN SULPHATE ISOLATED FROM BASEMENT MEMBRANE SOURCES PROMOTES TUMOUR CELL INVASION OF 3-DIMENTIONAL MATRICES

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In order to evaluate the roles of individual matrix components during tumour cell invasion, we examined the behaviour of several different metastatic murine tumour cells seeded onto collagen I gels containing a second defined matrix component. After 10 days of culture, the numbers of cells which had invaded the complex gels and total cell numbers were determined. Heparan sulphates isolated from basement membrane sources gave a singular promotion of invasion of the complex gels for all tumour types tested, with more highly metstatic variants exhibiting further enhanced invasion. Depending on the cell type, hyaluronic acid gave either a marginal promotion or a slight suppression of invasion. Laminin and chondroitin sulphate gave no effect or a slight decrease, while addition of collagen IV led to a decrease in all cases. Comparison of the effects of dextran and dextran sulphate suggested tha negative charge per se was not important. Heparan sulphate appears to have a particular importance in tumour cell matrix invasion.

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CHEMOTHERAPY AND COLLAGEN MATRIX IN TUMOUR TRANSPLANTS

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Chemotherapeutic drugs affect not only the tumour cell itself but also the collagen matrix and its components. The subrenal capsule assay method offers a new model for studying the effect of different drugs on matrix structure, distribution and synthesis and their mode of action.

In this study, mammary tumours were transplanted into the renal capsule of immunocompetent mice and rats and subjected to chemotherapy. The results showed a high transplant success rate with primary tumour structure being retained. Drugs having limited effects, showed preserved tumour basement membranes, moderate drug effects were reflected in thinning or thickening of the collagen I and III positive fibres. As shown in this study chemotherapeutic drugs cause alterations in amount and structure of collagen matrix depending upon the efficacy of the drug affecting the survival and growth of the transplanted tumour.

CHARACTERIZATION OF A TUMOUR-ASSOCIATED SERINE PROTEASE

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Cancer patients have elevated serum and urine levels of a 6 kD trypsin inhibitor called tumour associated trypsin inhibitor, TATI (Stenman et al, Int. J. Cancer, 30: 53, 1982; Huhtala et al, J. Biol. Chem. 257: 13713, 1982). Expression of protease inhibitors in cancer is associated with increased protease activity. Of earlier known proteases only trypsin and acrosin are readily inhibited by TATI, but these proteases are not known to be expressed by tumours. We have therefore searched for other proteases reacting with TATI and now identified and characterized such a protease in fluid from mucinous ovarian cysts. The substate specificity of this protease is similar to that of trypsin. In contrast to trypsin it has a pH optimum of 10 and an isoelectric point of 4. These characteristics suggest that we have identified a new tumour-associated protease, which could play a role in the elevation of TATI in cancer patients.