and lymph node status. The percentage of positive tumours slightly increased with patients' age. It seems that elastosis has a limited value as a single prognostic factor.

ANTIGENS EXPRESSED IN VIVO FROM THE BamH1 W FRAGMENT OF EPSTEIN BARR VIRUS

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A gene bank was prepared in a plasmid expression vector from small fragments of Epstein Barr Virus (EBV) DNA. When screened with serum from patients known to be immunopositive for EBV, a number of colonies which expressed EBV antigens were identified. Subsequent screening of these colonies with a probe for the repeated BamH1 W fragment showed that 4 of them originated from that region of the EBV genome.

The exact locations of the antigen coding sequences were established by DNA sequencing. All correspond to parts of potential open reading frames which had previously been identified by sequence analysis. These are in three different reading frames and two of the sequences, which are in different reading frames, contain overlapping sequences. The DNA fragments identified in this study do not correspond to exons shown previously to be part of EBNA2 or EBNA5.

DEREGULATION OF THE TYROSINE KINASE ASSOCIATED WITH THE BOMBESIN RECEPTOR IN SMALL CELL LUNG CARCINOMAS

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It has been hypothesized that bombesin-like peptides produced by small cell lung carcinomas (SCLC) may sustain deregulated proliferation through an autocrine mechanism. We have recently identified, using phosphotyrosine antibodies, a 115 kD tyrosine kinase (p115) which is part of the bombesin receptor complex in mouse Swiss 3T3 fibroblasts (Cirillo D., Gaudino G., Naldini L. and Comoglio P.M., Mol. Cell. Biol. 6: 4641-4649). We now report that phosphotyrosine antibodies recognize a protein of 115 kD, phosphorylated at tyrosine, in four human SCLC lines producing bombesin, but not in a non-producer "variant" line. P115 from detergent treated SCLC does bind to bombesin-Sepharose and becomes phosphorylated at tyrosine in the presence of radiolabeled ATP and MN++ ions. As in the case of p115 kinase immunoprecipitated from mouse fibroblast, the SCLC p115 is phosphorylated in an immunocomplex kinase assay. However, the latter does not require the presence of exogenous bombesin activity. Binding data, obtained using radiolabelled ligand, indicate receptor occupancy in the cell lines producing bombesin. These observations fulfill the hypothesis of autocrine control of human small cell lung carcinoma cell proliferation, via constitutive activation of bombesin receptors.

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GROWTH FACTOR PRODUCTION BY NORMAL HUMAN MESOTHELIAL CELLS AND MESOTHELIOMA CELL LINES

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It has been shown that normal human mesothelial cells (NHM) blocked in G1 by serum starvation can be induced to undergo a round of DNA synthesis either by TGF-beta or by PDGF. Seven human mesothelioma cell lines were compared to NHM primary cultures by northern analysis for their level of expression of mRNA hybridizing with cDNA for PDGF A chain, PDGF B chain (c-sis) or TGF-beta. NHM cells produced no detectable B-chain mRNA and low levels of A chain message. Mesothelioma cell lines produced high levels of either A or B chain message or both. Both normal and tumour cells produced TGF-beta mRNA. NHM cells transformed by transfection with an SV40 T antigen construct produced levels of message for all three growth factor genes which fell within the normal range of hybridization analysis. Mesothelioma lines but not NHM cells are positive for PDGF by immunoprecipitation or bioassay of conditioned medium. Thus, mesothelioma cell lines produce a growth factor which is mitogenic for NHM cells. An autocrine role of PDGF in tumourigenesis is being investigated.

ROLE OF HOST RESPONSES IN THE DRUG TREATMENT OF METASTASES

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When total tumour eradication cannot be achieved by conventional treatment, the prevention of tumour metastasis by drugs selectively inhibiting the process of tumour spread may be of interest. Remarkable and approximately equal antimetastatic effects are caused in mice bearing Lewis lung carcinoma (3LL) by N-diazoacetylglycinamide (DGA) and by potassium p-(3,3-dimethyl-1-triazeno) benzoate (DM-COOK). When drug treatment is followed by surgical removal of primary tumour, DM-COOK produces about 40% long term survivors whereas DGA causes none in spite of its pronounced antimetastatic action, suggesting that host responses, contributing to the cures caused by DM-COOK which is weakly immunodepressive, are not available after treatment with DGA which strongly depresses cell mediated immune responses. A further investigation on host responses has been made by comparison of tumour growth, spread and response to cyclophosphamide (CY) in mice bearing 3LL kept in conventional housing (CH), or in a protected environment (PE) and subjected to emotional stress (anxiety for spatial disorientation, SD). Tumour growth, and particularly metastasis weight, are remarkably small in mice kept in PE, while they have usual values in mice in CH or in PE plus SD. When the mice are treated with CY, cure rates vary from about 70% in CH to 100% in PE, dropping to 0 in PE plus SD. These findings indicate the importance of host responses and stress in drug treatment, with implications of interest for experimental and clinical situations.

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HYALURONECTIN: DETECTION WITH MONOCLONAL ANTIBODIES IN HUMAN TUMOURS

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Hyaluronectin (HN), a proteoglycan which exhibits a high affinity to hyaluronic acid has been characterized in the nervous system. It was also found to be associated with embryonic mesenchyme and with tumour connective tissue. Two MAbs were obtained against human brain HN. The ELISA additivity test demonstrated they bound to two different epitopes. This finding was confirmed with immuno-histological techniques performed on human and rat tissues: the first MAb recognized only human HN while the second MAb recognized both human and rat HN. The staining on tumour sections was superimposable with that obtained with rabbit polyclonal anti-HN antibodies. Both MAbs stained desmoplasia of carcinomas and sarcomas, the extracellular matrix of fibrosarcomas and gliomas and also the benign proliferation of fibromas. Since HN is a marker of all types of tumours anti-HN MAbs could be of great interest in the medical imaging of tumours.

REGULATED EXPRESSION OF A TRANSFECTED DIPHTHERIA TOXIN GENE AS A NOVEL MECHANISM FOR KILLING TUMOUR CELLS

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We have shown that transfection of a diphtheria toxin A (TDA) chain gene linked to appropriate transcriptional regulatory elements can achieve selective cell killing (Maxwell *et al.*, Cancer Res., 46: 4660, 1986). In experiments now in progress we have constructed vectors which include the regulatory elements of the heat shock response gene (hsp 70) (Morgan *et al.*, Mol. Cell Biol., 7: 1129, 1987) as well as elements from Epstein Barr Virus (EBNA-1 and Ori-P) which should allow such vectors to replicate as episomes (Sugden *et al.*, Mol. Cell Biol., 5: 410, 1985). We will attempt to derive permanent cell lines which may be induced to express a mutant toxin gene, Tox 176 (Maxwell *et al.*, Mol. Cell Biol., in press, 1987) and thus commit suicide by transient exposure to 42° C. Controlled toxin gene expression may prove useful in eliminating malignant cells which express marker proteins or other characteristics via *trans*-activators not found in normal cells.

IMMUNOGENICITY OF HYBRID TUMOUR CELLS AND MHC ANTIGEN EXPRESSION

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In a model of murine fibrosarcoma of H-2b haplotype, we isolated from a somatic hybrid cell (H-2b x H-2k) several variants differing in their ability to induce