yet been accomplished.

Supported by grant Special Project CNR "Oncology", contract no. 85.855.44.

IDENTIFICATION OF HUMAN UROTHELIAL CELLS PROPAGATED IN CULTURE

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Cell lines derived from non-malignant and malignant human urothelium have been established. These cell lines have a human karyotype, express keratin and react with monoclonal antibodies against either normal urothelium or bladder tumour associated antigens. The human and epithelial origin of these cell lines was further confirmed by studies of species specific isozymes, by electron microscopy and by tumour histology. Based on life-span in culture, tumourigenicity in nude mice, the cell lines have been classified into three diffeent categories of transformed cells. Ongoing research aims at characterizing the cell lines with respect to isozyme phenotype and karyotype. These characteristics will be compared with the tissue-type of the cell lines in order to evaluate the value of isozyme phenotyping and chromosomal characteristics as methods for the identification of established cell lines.

ACTIVATION OF THE ras-GENE: TRUNCATION INSTEAD OF POINT MUTATION

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Identically to the transforming cellular ras genes detected by gene transfer assay in 3T3 cells, Harvey-ras in Harvey sarcoma virus and Balb sarcoma virus is thought to be activated by point mutations at codon 12 (Balb SV), or 12 and 59 (HaSV) of the transforming protein p21. To test this hypothesis, we have exchanged parts of viral ras containing codons 12, or codons 12 and 59, or the complete coding region with the corresponding regions of normal rat proto-ras 2 or proto-ras 1 respectively. Viruses generated from the proviral clones all showed efficient transforming function in vitro and in vivo. Sequence comparison between normal and viral Harvey-ras genes revealed a previously undetected 5' exon termed exon (-1) that is contained in normal proto-ras but is always truncated in transforming viral ras genes. Because of the uncertainty of the 5' ends of ras, transforming cellular ras genes are also possibly truncated. We conclude that point mutations are not necessary for the transforming function of ras and propose that truncation of the normal gene activates the Harvey-ras gene. We have reisolated a few of the recombinant viruses and have obtained sequence data. The transforming function of new recombinant viruses containing upstream sequences of proto-ras which are truncated in the wild type virus has been investigated.

INDUCTION OF THE AROMATIC HYDROCARBON (AH) RECEPTOR AND OF DRUG METABOLIZING ENZYMES BY VARIOUS AROMATIC AMINES IN RAT LIVER

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The aromatic amines 2-acetylaminofluorene (AAF), transacetylaminostilbene (AAS) and 2-acetylaminophenanthrene (AAP) have different carcinogenic properties in rat liver. Only AAF is a complete carcinogen and exerts promoting effects. These have not yet been defined on a molecular basis. We have now studied interactions with the Ah receptor which has been suggested to play a role in promotion. The amines (100 µmol/kg, AAS 20 µmol/kg) and 3-methylcholanthrene (MC) as a control were administered by intraperitoneal injection into female Wistar rats daily for 5 days, for induction of ornithine decarboxylase (ODC) for one day. In addition to ODC activity and the hepatic Ah receptor level, the activity of Ah receptor controlled drug metabolizing enzymes and of microsomal epoxide hydrolase (EHm) were determined. All amines tested induced ODC in rat liver. The time course of this induction differed. AAs increased both the hepatic Ah receptor level and EHm 2-fold. AAF and AAP stimulated ethoxyresorufin-O-deethylase activity maximally by 4.2-fold, which is a small effect in comparison to the 80-fold increase by MC. The results indicate that AAF and AAP, but not AAS, may interact with the Ah receptor in vivo. AAS, however leads to other specific biological responses.

A TUMOUR-SPECIFIC INHIBITING FACTOR: MS-TIF

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A cell line derived from a MSV-M induced sarcoma spontaneously lost tubourigenicity after approximately 40 in vitro passages. At the same time these cells began to produce a "factor" inhibiting colony growth in soft agar. This factor is not cell or species-specific because it is active on cells from different tumours, both of human (6/9 lines tested) and murine (6/8 lines) origin. The inhibiting factor is not produced by another cell line (MS-2) derived from the same tumour, which maintains its tumourigenicity. The inhibiting factor has little or no activity on normal cells. The activity is resistant to acid treatment (0.01 N HCl), to heat (4 min at 100° C) and to lyophilization. It is not due to a polyamine and it has no antiviral effect if tested for interferon activities. It inhibits thymidine incorporation, in tumour cells after a treatment of 48 to 72 hr, but it has no activity against DNA or RNA or protein synthesis if tested in cell-free systems. The inhibiting activity appears to be linked to a hydrophilic molecule of low molecular weight.

EXAMINATION OF THE STRUCTURE AND BIOSYNTHESIS OF THE HUMAN PDGF RECEPTOR

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The sequence of a 2.8 kb cDNA clone, corresponding to most of the translated part of the human platelet derived growth factor (PDGF) receptor was determined. The homology between the murine (Yarden et al., Nature 323, 266-232) and human nucleotide sequence is 80 to 85%. The information on the primary structure of the PDGF receptor, deduced from the nucleotide sequence, was correlated with an examination of the biosynthesis and processing of the receptor. It is synthesized as a 145 kD precursor, which carries about ten N-linked oligosaccharide groups, and is chased to a 165 kD molecule within 15 min in the absence of PDGF and even more rapidly in its presence. After additional modifications, for example addition of phosphate, the receptor reaches a final size of 170 to 175 kD.

EWING'S TUMOUR: PHENOTYPIC CHARACTERIZATION AND LONG RANGE MOLECULAR ANALYSIS AROUND THE CHROMOSOMAL BREAKPOINTS

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Ewing cells have been demonstrated to express antigens associated with the neuroectoderm lineage, including the neural cell adhesion molecule NCAM and the receptor for the nerve growth factor. In addition, Ewing and neuroepithelioma cells display the same cytogenetic abnormality, a chromosomal translocation t(11;22) (q23-24;q11-12) which suggests that both tumours are derived from closely related neuroectodermal cells. Several genes could be implicated in the molecular mechanism of malignant transformation. Genes located on chromosome 11 encode NCAM, the delta subunit of the T lymphocyte T3 antigenic complex and Thy-1. In addition, the proto-oncogene c-ets also maps to this chromosomal region. On chromosome 22, the bcr gene maps to band q11. None of these genes was found rearranged when DNA from a variety of Ewing cell-lines was analysed by hybridization of Southern blots obtained by conventional methods. Using recently described techniques and pulse field gel electrophoresis, we have now explored a significant portion of Ewing genomic DNA in the region of the chromosomal breakpoints.

IDENTIFICATION OF A LEUKOCYTE ANTIGEN WITH A HIGH FREQUENCY EXPRESSION IN LEUKAEMIA PATIENTS

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In this report we describe the production and characterisation of a monoclonal antibody to HL-60 cells (a human promyelocytic leukaemia cell line). The antibody, termed NC-2, did not react with any other human cell lines tested. NC-2 precipitated a 50 and 57 kD protein from ^{125}I labelled HL-60 cells. Cell distribution and molecular weight studies indicated that the protein was not an HLA antigen. When NC-2 was screened for reactivity against human peripheral blood cells, 7 individuals from a population of 130 showed a reaction. Blood and bone marrow cells from leukaemia patients (n=50) exhibited a much higher level of reactivity, with cells from 20 individuals showing a reaction with NC-2. In these patients the antigen was expressed on both leukaemic and normal cells. The association of the antigen identified by NC-2 with leukaemia has been evaluated.

ROLE OF CHROMOSOME TRANSLOCATIONS IN HUMAN NEOPLASIA

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