for the determination of NOR and its hydrolysis products. The method was based on derivatization by heptafluorobutyric anhydride. The structures of the derivatives were established by GCMS. The rate of disappearance of NOR at 37 degrees and pH 7.4 was about 20 min, and a similar rate was noted irrespective of whether NOR or PAM was used as starting material. N-(2-chloroethyl)-N-(2-hydroxyethyl)amine (NOR-OH) appeared with a half-life of 19 min when NOR was used, but with a half-life of 23 min when PAM was used as starting material. The main difference in product yields was the relatively higher amounts of NOR-OH and N,N-bis(2-hydroxyethyl)amine (NOR-OH-OH) formed when PAM instead of NOR was used as starting material. This suggests the formation of NOR-OH and NOR-OH-OH from NOR as well as from the hydroxylated derivatives of PAM.

REDUCTION TO HOMOZYGOSITY OF GENES ON CHROMOSOME 11 IN HUMAN BREAST NEOPLASIA

Iqbal U.Ali, Rosette Lidereau and Robert Callahan

There is increasing evidence that recessive genetic lesions might be involved in the genesis of several paediatric and adult tumours. These recessive mutations are unmasked when tumour cells attain hemi- or homozygosity for particular genes. In primary breast tumours an allelic loss of c-Ha-ras-1 locus (chromosome 11p) was detected in 27% of patients heterozygous for this proto-oncogene. Restriction fragment length polymorphism analysis of tumour DNAs provided evidence for reduction to homozygosity of not only c-Ha-ras-1 gene but also of several markers on the short arm of chromosome 11. This loss of normal cellular sequences was specific for chromosome 11 and had a significant correlation with the most aggressive form of the disease. Our analysis also suggested that the deletion of the region between the B-globin and PTH loci might be important in this subset of tumours.

A systematic study of the possible alterations in other proto-oncogenes strongly suggests that human breast neoplasia, a highly complex and genetically heterogeneous disease, might involve abnormalities of several proto-oncogenes.

GROWTH FACTOR AND ONCOGENE EXPRESSION DURING MEGAKARYOBLASTIC DIFFERENTIATION OF K562 LEUKAEMIA CELLS

R.Alitalo, T.P.Mäkelä and L.C.Andersson

Transplantation Laboratory, University of Helsinki, Helsinki, Finland

Platelets contain PDGF and TGF-beta, but their site of synthesis has not been proven since megakaryocytes are difficult to obtain for studies of this nature. Our results of studies with the chronic myeloid leukaemia (CML) cell line K562 suggest that the genes encoding the two PDGF chains and TGF-beta (1) and the synthesis of the corresponding proteins are induced during the megakaryoblastic differentiation process. The expression of the bcr-c-abl oncogene mRNA remained unaltered during the differentiation of K562 cells, but the kinase activity of the corresponding fusion protein is almost completely shut off suggesting that an active c-abl oncogene is incompatible with K562 cell differentiation.

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MONOCLONAL ANTIBODIES AGAINST NIH 3T3 CELLS TRANSFORMED BY HUMAN THYROID CARCINOMA DNA

R.Alzani, G.Della Torre(1), C.Traversari(2), M.Pierotti(1), S.Ménard, G.Della Porta(1) and M.I. Colnaghi

Experimental Oncology E, (1)Experimental Oncology A and (2)Experimental Oncology D, Istituto Nazionale Tumori, Milan, Italy.

First-cycle transfectants of NIH 3T3 transfected with human metastatic thyroid carcinoma DNA were used as an immunogen to obtain monoclonal antibodies against antigens induced by the transfected tumour DNA. The transfected cell line (M33) was shown to contain ALU sequences. Two monoclonal antibodies were selected on the basis of their differential reactivity toward NIH 3T3 or M33 cell lines. By biological and biochemical analysis, the first monoclonal antibody (MTr1) recognised an epitope on cytoskeletal filaments of proliferating murine fibroblasts. Similar filaments labelled by MTr1 were also found to accumulate into cytoplast-like structures produced by M33 cells.

Characterization by immunofluorescence of the second monoclonal antibody, MTr2 indicated that it recognizes a specific human antigen associated with normal thyroid tissues and differentiated thyroid tumours.

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