cytoskeletal proteins. These modifications again mimic those seen in the embryo during comparable stages of differentiation.

REMODELLING OF INTESTINAL WALL CELLS - POSSIBLE CAUSE OF INTESTINAL FIBROSIS AFTER RADIOTHERAPY

F.Lukič, V.Simčič, R.Zorc, P.Fras, M.Pšeničnik, M.Vozelj and E.Kansky

The Institute of Oncology, Ljubljana, Yugoslavia

Ten beagle dogs (female and male), weight 10 to 12 kg, 1 to 2 years old were irradiated with 25 Gy (Cobalt-Phillips) onto the whole pelvis and tail for 20 days. Platinol was given in a 2 hour infusion every 5 days for 20 days during the radiation treatment. Ten dogs represented a control group. Ten days later the thoracic duct lymphocytes, peripheral blood and the large intestine were examined with the following parameters: laboratory, biochemical, histological, EM, SEM, densitometric, immunological, and LAMMA 500 examinations. Damage and remodelling of peripheral blood lymphocytes, thoracic duct lymphocytes, entero-endocrine cells, mast cells and lymphocytes in the intestinal smears of the lamina propria were found in all treated dogs. Of special interest was enhanced volume density of mast- and entero-endorcine cells, that could also reflect enhanced serotonin excretion, with hypoxia of the intestinal tissue. LAMMA 500 measurements established significant changes in the organic composition of the lamina propria cells. Immunological studies revealed significantly diminished transformation of lymphocytes with PHA and Con-A stimulation in the treated group. It is considered that the changes described represent a stimulus for fibrogen hyperproduction and collagen excretion in the treated group of dogs.

TRANSFORMING GROWTH FACTOR-BETA INDUCES INCRESED LEVEL OF PLASMINOGEN ACTIVATOR INHIBITOR mRNA IN HUMAN LUNG FIBROBLASTS

L.R.Lund(1), A.Riccio(2), P.A.Andreasen(1), L.S.Nielsen(1), P.Kristensen(1), M.Laiho(3), O.Saksela(3), F.Blasi(2) and K.Danø(1)

(1)Finsen Laboratory, Rigshospitalet, Copenhagen, Denmark; (2)International Institute of Genetics and Biophysics, Naples, Italy; and (3)Department of Virology, University of Helsinki, Finland

The mechanisms behind a transforming growth factor-beta (TGF-beta) induced stimulation of production of type-1 plasminogen activator inhibitor (PAI-1) in WI-38 human lung fibroblasts have been studied using a full-length cDNA probe for PAI-1, as well as monoclonal antibodies against the inhibitor. Northern and dot blot analyses showed that TGF-beta causes an early increase in the PAI-1 mRNA level, reaching a 50-fold enhancement after 8 hr. Blocking of protein synthesis with cycloheximide caused an equally strong increase in the level of PAI-1 mRNA. Quantitative immunochenical studies of the effect of TGF-beta on PAI-1 protein levels in cell extracts and culture media were consistent with the effect on PAI-1 mRNA. The results suggest a primary effect of TGF-beta on PAI-1 gene transcription.

LOSS OF HETEROZYGOSITY IN HUMAN DUCTAL BREAST TUMOURS INDICATES A RECESSIVE MUTATION ON CHROMOSOME 13

Catharina Lundberg(1), Lambert Skoog(2) and Magnus Nordenskjöld(1)

(1)Departments of Clinical Genetics and (2)Tumour Pathology, Karolinska Hospital, 2-10401 Stockholm, Sweden

The genotypes at chromosomal loci defined by recombinant DNA probes revealing restriction fragment length polymorphisms were determined in constitutional and tumour tissue from 10 cases of ductal breast cancer: eight premenopausal females and two males. Somatic loss of constitutional heterozygosity was observed at loci on chromosome 13 in primary tumour tissue from three females and one male. In two cases, specific loss of heterozygosity at three distinct genetic loci along the length of the chromosome was observed. In another case, concurrent loss of alleles at loci on chromosomes 2, 13, 14 and 20 was detected, while a fourth case showed loss of heterozygosity for chromosomes 5 and 13. In each instance, the data were consistent with loss of one of the homologous chromosomes by mitotic nondisjunction. Analysis of loci on several other chromosomes showed retention of constitutional heterozygosity suggesting the relative specificity of the events. These data indicate that the pathogenesis of ductal breast cancer may, in a substantial proportion of cases, involve unmasking of a recessive locus on chromosome 13.

TWO DIFFERENT MECHANISMS BY WHICH 5-FLUOROPYRIMIDINES INDUCE DNA LESIONS

Ulf Lönn and Sigrid Lönn