

±PHA or ConA stimulation showed only slight inhibition of viability or growth and of macromolecule synthesis when cultured with 10 to 40 nM NA. Such NA levels inactivated S-adenosylhomocysteine hydrolase and drastically increased S-adenosylhomocysteine in the lymphoma cells resulting in transmethylation block. NA is thus a promising antilymphoma agent and its action mechanism is related to inhibition of cellular transmethylation reactions, a new route for attacking cancer cells.

PROGNOSTIC IMPACT OF DNA-PLOIDY AND S-PHASE FRACTION

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To evaluate the prognostic significance of nuclear DNA content and S-phase fraction (SPF) in human tumours, 600 archival paraffin-embedded specimens from breast, ovarian and lung cancer were analysed with DNA flow cytometry.

DNA-aneuploidy was observed in 60% of breast, 58% of ovarian and 63% of lung cancer specimens and the mean SPF was 11.1, 14.5 and 17.6%, respectively. DNA-aneuploidy and high SPF were most common in advanced stage or poorly differentiated tumours as well as in steroid receptor negative breast tumours. In breast cancer, high SPF but not DNA-aneuploidy was related to poor prognosis. In ovarian cancer both parameters were independent indicators of poor prognosis according to a Cox regression model. DNA-aneuploidy in the tetraploid mode was related to better prognosis than non-tetraploid or multiclonal DNA abnormality. We conclude that DNA flow cytometry can be used to measure new prognostic parameters on a cellular level in human cancer.

THE DIAGNOSTIC APPLICATION OF URINARY POLYAMINE MEASUREMENT IN WOMEN WITH GYNAECOLOGICAL CANCERS

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In 56 women (in the age range of 28 to 55) with gynaecological cancers, urinary polyamines were measured using an enzymatic assay method. After performing surgery and

chemotherapy, a decrease in the level of urinary polyamines was found in almost all cases. This was taken to be indicative that the measurement of urinary polyamines can be used to monitor the effectiveness of therapy.

A COMPARATIVE STUDY OF VARIOUS TUMOUR MARKERS IN CANCERS OF GASTROINTESTINAL SYSTEM

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A comparative study of eight tumour markers, including five enzymes (5'-nucleotidase, sialyltransferase, γ -glutamyltransferase, alkaline phosphatase and a Zn++ dependent nucleoside diphosphatase), two antigens (carcinoembryonic antigen and immunosuppressive acidic proteins) and sialic acid, was performed in nearly 100 patients with primary and metastatic cancer of the gastrointestinal system.

Liver scanning for liver involvement was performed in all patients and the disease in all cases was histologically confirmed.

The results showed that none of the markers used is specific for primary, stomach and colorectal carcinoma. On the other hand, 5'-nucleotidase, nucleoside diphosphatase and γ -GT, were proved very good markers for the early detection of primary or metastatic liver carcinoma. In fact, the feasibility of detecting liver involvement using these markers, is very close to that achieved by liver scanning.

MAMMARY EPITHELIAL CELL POPULATIONS ANALYSED BY MEANS OF MONOCLONAL ANTIBODIES (MAbs)

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MAbs, some of which were produced in our laboratories, have been evaluated for their potential use in (1) analysing normal mammary epithelial cells cultured *in vitro*, and (2) detecting metastases of mammary carcinomas in regional lymph nodes. A characteristic pattern of marker expression (cytokeratins, blood group

antigens, actin) was observed when comparing fresh and cultured cells. Lumenal epithelia and myoepithelia were clearly distinguishable by MAbs. The broad range anticytokeratin MAb A45-B/B3 has been used to detect metastases in regional lymph nodes from 22 breast carcinoma patients. Conventional histology and immunohistochemistry using A45-B/B3 showed a good agreement, but significantly more lymph nodes with metastases were detected by immunohistochemistry. This method seems to be superior in terms of sensitivity and reliability, and it may provide more confidence in diagnosing disease-free lymph nodes.

DOES THE EXPOSURE TO ENVIRONMENTAL FACTORS INFLUENCE THE DISTRIBUTION OF DIGESTIVE TRACT MALIGNANCIES?

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We have compared the incidence of gastrointestinal (GI) malignancies with selected environmental risk factors in a total of 109,000 people living in a defined selected region. The age distribution of the population is slightly progressive with prevailing industrial social structure.

Tumours of gastrointestinal system represent 25 to 36% of all malignancies. Their geographic distribution was modelled with the aid of a computer. The localities with high and low incidence of tumours were compared with the mean confidence interval and correlated with various environmental pollution factors.

The results of our study clearly demonstrate that some of environmental factors (water pollution, etc.) participate in the increased incidence of GI tumours.

THE FATE OF RSV SEQUENCES IN THE TRANSFORMED DUCK CELLS

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The long-term RSV passage in duck cells does not raise virus production in spite of viral genome integration even at the first passage. However, after six transfers the titre of virus sharply increased, the period of transformation was shortened and the transfecting activity of proviral DNA appeared. These alterations of RSV

properties correlate with the changes in the nucleotide sequences of the viral genome. The td mutant deleted in v-src has been isolated from the pool of duck-adapted RSV. The transforming activity of the mutant recovered after inoculation in chickens. The new isolate of rASV is replication defective. The genome has only one unusual 4 kb EcoRI fragment. The provirus contains src-specific sequences and RSV-specific LTR but lacks of all replicative genes.

ONCOGENIC POTENTIAL OF A NOVEL HUMAN src-RELATED GENE, fyn

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We have isolated cDNAs representing the complete coding sequence of a new human gene which is a member of the src family of oncogenes. Nucleotide sequence analysis revealed that this gene, termed fyn, encoded a 537-residue protein which was 74% identical to the chicken oncogene product, p60c-src, over a stretch of 191 amino acids at its carboxy terminus. In contrast, only 6% amino acid homology was observed within the amino-terminal 82 amino acid residues of these two proteins. It was possible to activate fyn as a transforming gene by substituting about two-thirds of the fyn coding sequence for an analogous region of the v-fgr onc gene present in Gardner-Rasheed feline sarcoma virus. The resulting hybrid protein molecule expressed in transformed cells demonstrated protein tyrosine kinase activity.

POLYADENYLATE POLYMERASE ACTIVITY IN SEVERAL CELL LINES

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The soluble poly(A)-polymerase content of growing and stationary cell populations from several (6) cell lines was determined. Cell populations from stationary cultures presented enzyme values with a mean of 31±12 units/mg of protein. The mean of values for growing cell populations was 62±18 units per mg of protein. A statistically significant difference was found between stationary and growing cell populations from the variety of cell lines examined. The observed differences in poly(A) polymerase levels