Symposium no. 8: Cancer Risk Assessment

8.007

Simultaneous induction of transformed, invasive and metastatic phenotype in BALB/c 3T3 cells by 1,1,2,2-tetrachloroethane

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1,1,2,2-Tetrachloroethane (1,1,2,2-TTCE) is a widely produced and used compound. It is toxic, mutagenic in S. typhimurium and can induce tumors in mice. It can also bind to DNA both in in vivo and in vitro system. The in vivo binding extent is typical of moderate initiators, but probably 1,1,2,2-TTCE exerts also a promoting activity. We have tested 1,1,2,2-TTCE in BALB/c 3T3 cell transformation test and have found that this compound induces a large number of transformed foci as compared to negative controls (untreated cells and solvent vehicle-treated cells). Transformed cells were capable of growing in soft agar and were tumorigenic when injected in nude mice (all injected animals developed tumor within 4 months). Untreated cells were low tumorigenic (3/9 animals developed tumors in a longer latency time). Metastasis from the subcutaneous site was rare whereas pulmonary metastases were detected in a high percentage (80%) of athymic mice injected i.v. with 1,1,2,2-TTCE transformed cells. In the control group rare pulmonary nodules were found in a low percentage of animals. Transformed cells were also able to invade a thin coating of Matrigel (MG) in the chemoinvasion assay. They also grew in a MG gel. Untreated cells did not invade or grow. These results show that 1,1,2,2-TTCE may play a role also in the late steps of carcinogenesis process. (Supported by Associazione Italiana Ricerca sul Cancro (AIRC), Milan, Italy)

8.008

An integrated approach for short-term detection of potential carcinogens.

by M. Danz

Short-term detection of tumorigenic xenobiotics became more complicated by the existence of nongenotoxic carcinogens. These, like their genotoxic counterparts, produce an additive mitotic response selectively in the adrenal zona fasciculata of rats. This effect is maximal 48 h after a single oral dose of primary mitogens and is topically different from that accompanying restorative liver growth (after partial hepatectomy) and cytotoxic agents (carbon tetrachloride, trichloromethane) which stimulate both the zona fasciculata and glomerulosa as well as from that by certain drugs (reserpine, indomethacin) stimulating exclusively the zona glomerulosa. Obviously, the 'extra-target' action of carcinogens is mediated by mechanisms acting on the systemic level. Studies concerning structure-activity-relationship and dose-dependency were performed in fluorene-derivatives.

8.009

EVALUATION OF DIFFERENT ENZYME ACTIVITIES INVOLVED IN THE SENSITIVITY TO XENOBIOTICS IN HTC AND HEPG2 HEPATOMA CELL LINES

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We have analyzed arylhydrocarbon hydroxylase (AHH), 7-ethoxyresorufin O-deethylase (EROD), 7-ethoxycoumarin O-deethylase (ECOD) and glutathione-S-transferase (GST) activities in the HTC (rat) and HepG2 (human) hepatoma cell lines. The cytotoxicity of different classes of compounds was assessed by different end-points. All determinations were performed both in basal conditions and after treatment of the cultures with inducers of monooxygenases. The results showed opposite metabolic patterns in the two cell lines, one being devoid of GST and the other of monooxygenases. The sensitivity to the toxic effects of xenobiotics revealed that these cell lines could be used in cancer risk assessment due to their expression of selected biotransformation pathways.

8.010

Medicalgenetic cancer risk assessment.

Garjkavtseva R.F., Kazoubskaja T.F.

Clinical-genetic ivestigations incluided assessment of the contribution of hereditary factors into development of embryonic tumors in children and such tumors in adults as gastric cancer, breast cancer, malignant melanoma, multiple primary malignant neoplasms. Basing on these data the development of genetic aspect of their prevention has been conducted. It was shown that the main problems of genetic counselling are organization of registry of families whith cancer on the basis of family history and identification of high-risk subjects of development malignant neoplasms in relatives of patients with these cancers. The genetics approaches to selection of "risk groups" were shown on an example of the ivestigated form tomors.

8.011

LINKAGE ANALYSIS OF SIX POLYMORPHIC MARKERS MAPPING CLOSE TO FAMILIAL ADENOMATOUS POLYPOSIS GENE

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Familial adenomatous polyposis is an autosomal dominant syndrome characterized by hundred to thousands of colorectal adenomatous polyps that can progress to carcinoma in early age. The defect responsible for FAP was mapped to the long arm of chromosome 5 (q21-22 region). The characterization of markers in the near vicinity of the FAP locus provides the opportunity for preclinical diagnosis of risk status for colon cancer among individuals in families that are segregating the genetic defect. For this purpose we have performed linkage analysis in 16 Italian families by means of six polymorphic DNA markers: pi 227; C11p11 and C11p11 DEL 1; YN5.64; EC827; CB83 and CB83-CA repeats; YN5.48. Lod score calculation was performed with LINKAGE group of programs. A positive lod score (>3) was obtained for pi 227, C11p11 and YN5.48 markers. S.A. is recipient of an AIRC fellowship.

8.012

CLINICAL-BIOLOGICAL CHARACTERIZATION OF SECOND NEOPLASM PATIENTS. Guida M, Casamassima A, Latorre A, Addabbo L, Mastria A, Lorusso V, De Lena M
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We evaluated 22 pts (median age:65) with second neoplasms (18 pts) and synchronous malignancies (4 pts). Primary cancers were mostly Hodgkin's disease, gastrointestinal, and ovarian; most frequent second neoplasms were lung, breast and transitional cell cancers. Only 7 pts received chemo-radiotherapy for primary tumor; all others were treated with surgery alone. Mean disease-free interval was 89 mo. CONCLUSIONS: 1)second tumor seems due to intrinsic or external pt risk rather than previous chemo-radiotherapy; 2)synchronous tumors seems to confirm this hypothesis; 3)ovarian and breast cancer was the most frequent association; 4)CD4 decrease was found by flow cytometry evaluation of lymphocyte subsets when compared to pts with single tumor.