NON-DISJUNCTIONAL ACTIVITY OF CHEMICAL CARCINOGENS IN ASPERGILLUS NIDULANS

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40 known or suspected carcinogens were tested for the induction of mitotic non-disjunction(n-d), crossing-over and gene mutations in A.nidulans by using test methods previously described (Morpurgo et al., Env. Health Perspect. 31, 81, 1979; Bignami et al., Mutation Res. 97, 293, 1982). About two thirds of the chemicals tested were able to induce at least one genetic event and among these only a few (captan, diallate, sulfallate) were unable to induce n-d. Non disjunctional agents could be classified in: a) those able to induce all three genetic events analyzed, then suggesting that the target involved is DNA (e.g. MMS, MNNG, 4-NQO, actinomycin D, mitomycin C, HCHO, dichlorvos); b) those able to induce only or mainly n-d: in some cases (e.g. benomyl, MBC, griseofulvin, trichloroethylene) the spindle apparatus seems to be the main target, while in others (e.g. CCl_4, aminotriazole, benzene, ethanol, linoleic acid lipoperoxide) there is evidence of an aspecific action on nucleophilic structures, e.g. by free radical formation.

Work partially granted by the E.E.C. (contract no. 530 ENV I (s)).

DOES THE MUTAGENICITY OF n- AND i-PROPYLNITROSOUREA DEPEND ON THE STRUCTURE OF THE ALKYLATING AGENT?

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The decomposition products of n-propylnitrosourea in aqueous solution are n-propanol (60%) and i-propanol (40%), which indicates that the free propyl cation rearranges partly to the i-form, and reacts with water to yield the corresponding alcohol. In S.typhimurium TA 1535, n-propylnitrosourea and i-propylnitrosourea are of equal mutagenic potency. It is not clear whether the propyl cation or the propyldiazohydroxide is the species which reacts with the nucleophile.

Recently we showed that diethyldithiocarbamate, formed from disulfiram in rat liver S-9 supernatant fraction scavenges electrophilic alkylating metabolites of N-nitroso compounds. We therefore performed studies to analyse the reaction products formed from n-propylnitrosourea and i-propylnitrosourea with diethyldithiocarbamate and disulfiram in in vitro experiments.

HUMAN MALIGNANT MELANOMA IN VIVO AND IN VITRO: FRESH TUMOUR AND CELL LINE KARYOTYPES

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Little is known yet of the specific chromosome changes in human melanoma. Cytogenetic studies of melanoma cell lines showed that structural abnormalities of chromosomes 1, 2, 3, 6, 7, 9, 11, 12 and 22 were the most frequent, each cell line having abnormal and/or polysomic chromosome 7, but abnormalities of this chromosome being only observed in cell lines derived from metastases. Cytogenetic studies were performed on a primary cutaneous tumour, an ocular tumour, 10 metastatic lymph nodes, a cutaneous metastatic nodule and an ascitic fluid. Numerical and structural abnormalities were observed in 11/14 tumours (modal number: 43 to 97). Numerous PCC were observed in tumour cells from the ascitic fluid. All tumours could be identified by marker chromosomes. Chromosomes 1, 3, 6, 7, 17 appeared to be more frequently involved in structural aberrations. In the primary tumour, some mitoses showed only numerical abnormalities, while others showed either structural abnormalities of chromosome 7 or numerous structural abnormalities. Multiple copies of 7q were observed in all tumours.

Thus cytogenetic analysis of fresh tumours confirms that of cell lines, and it can be hypothesized that the constant polysomy or abnormality of chromosome 7 may play a central role in the expression of malignancy in human melanoma.