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HUMAN BLADDER CELL-MEDIATED MUTAGENESIS AND DNA REPAIR ACTIVITY

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Unscheduled DNA synthesis (UDS) and the Ames *Salmonella*/microsome test were used as markers for metabolism of chemical carcinogens, e.g. 4-nitroquinoline-1-oxide (4NQO), benzo(a)pyrene (BP) and 2-naphthylamine (NA), by a human bladder cell line, HCV29. Exposure of bladder cells to 4NQO induced UDS in a dose-dependent manner. Addition of dicumarol, a DT-diaphorase inhibitor, inhibited this induction. When the medium from this incubation was tested in the Ames test, the mutagenic activity disappeared within 30 min, indicating that bladder cells mainly convert 4NQO into non-genotoxic substances. Using the same standard tissue culture conditions, HCV29 cells were found unable to metabolize NA and BP in quantities that could be detected by UDS or the Ames test. A study using NA, BP and HCV29 cells cultured under conditions that induce the oxidative metabolism of BP is in progress.

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IN VITRO BINDING OF ¹⁴C-NITRILOTRIACETIC ACID (NTA) WITH DNA

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NTA is considered to be one of the more efficacious substitutes for phosphates in detergents, but high doses are toxic, induce chromosome aberrations and give some indication of carcinogenicity in rodents. Therefore, we aimed at determining if this compound is activated by liver enzymatic fractions to react covalently with DNA in cell-free systems. Two mg of microsomal or 6 mg of cytosolic proteins from livers of adult male Wistar rats and BALB/c mice were incubated with 2.5 μ Ci ¹⁴C-NTA (11.5 mCi/mmol), 2 mg NADPH or 9.2 mg GSH, 1.5 mg DNA in 0.08M K-phosphate buffer, pH 7.7, at 37°C for 60 min, in the dark. Appropriate controls were always included. After incubation, DNA was reisolated, exhaustively washed with 0.2N HClO₄ or dialyzed until no radioactivity was present in the supernatants and its labelling was determined. Results show no evidence for enzyme-mediated binding of NTA with DNA, microsomal RNA and proteins, or cytosolic proteins; GSH is a good scavenger for NTA. Nevertheless, chemical reactivity *per se* of NTA with DNA (~2000 dpm/mg) is 10 fold higher than that found with other compounds, as 1,2-dichloroethane and 1,2-dibromoethane, which become mutagenic after metabolic activation (J.Cancer Res. Clin. Oncol., **108**, 204, 1984) and could explain the low mutagenicity of NTA tested on EUE cells as observed in another laboratory in this Institute.

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E-ROSETTE INHIBITION OF T-LYMPHOCYTES IN THE PRESENCE OF TUMOUR ASSOCIATED ANTIGEN (IN BREAST CANCER AND MELANOMA PATIENTS)

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The *in vitro* effects of tumour-associated antigens (TAA) on circulating lymphocytes were investigated. Lymphocytes from patients with breast cancer were incubated for 60 min with a pool of breast cancer extracts (BTAA) and lymphocytes from melanoma patients were incubated with a pool of melanoma tumour-associated antigens (MTAA). The results were compared with those obtained with lymphocytes from the following controls: healthy persons, patients with benign tumours and patients with different malignant tumours. Incubation of lymphocytes with allogeneic BTAA or MTAA produced a significant decrease in the percentage of E-rosettes (high affinity and total T-lymphocytes). The pattern of results obtained with the two types of cancer studied was different: in breast cancer, 68.2% of patients (15 of 22) showed a decrease in the percentage of total E-rosettes following incubation of lymphocytes with BTAA, while in melanoma, 100% of patients (18 of 18) showed a decrease in the percentage of high affinity E-rosettes with MTAA.
