

CHARACTERIZATION OF HUMAN UROTHELIAL CELL LINES OF NON-MALIGNANT AND MALIGNANT ORIGIN B.Christensen, J.Kieler, P.Don, M.Vilien and H.Wolf. Division of Environmental Carcinogenesis, The Fibiger Laboratory and Department of Urology, Hvidovre Hospital, Copenhagen, Denmark

18 cell lines derived from non-malignant and malignant human urothelium were characterized in order to define reliable and early applicable criteria of malignant alterations. Tumour production in nude mice served as criteria of malignancy. Comparison between tumourigenic and non-tumourigenic cell lines revealed that invasiveness in vitro and cytologic characteristics correlated with tumourigenicity. Numerical chromosome aberrations, growth in soft agar and growth in medium with reduced calcium or serum concentration were not correlated with tumourigenicity.

Among the non-tumourigenic cell lines 6 lines have ceased growing after 4-6 years in tissue culture, whereas 3 lines have developed into permanent or infinitely growing cell lines with distinct morphological as well as growth characteristics.

THE REACTION OF 3,4-EPOXY-1-BUTENE WITH DEOXYGUANOSINE AND DNA IN VITRO

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The reactivity of 3,4-epoxy-1-butene, a mutagenic and weakly carcinogenic compound formed as an intermediate of the metabolism of the industrially employed 1,3-butadiene, toward nucleophilic sites of DNA has been assayed in vitro. Two main covalent adducts of purine alkylation have been observed after DNA hydrolysis in a 56:44 ratio and identified as 7-(3-buten-2-ol-1-yl)guanine (I) and 7-(3-buten-1-ol-2-yl)guanine (II) by comparison with the products of the reaction of the epoxide with both deoxyguanosine and guanosine followed by acid catalyzed hydrolysis. The structures of these products have been assigned by UV, NMR and mass spectrometry.

The stability of the N-9 aminoglycosyl bonds of N-7 alkylated deoxyguanosines in DNA was fairly high, the half life for the spontaneous depurination of adducts I and II under physiological conditions being of about 45 hr.

The possible implications of the present reaction on the biological effects of 3,4-epoxy-1-butene has been evaluated.

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COMPARISON BETWEEN MICROSOME- AND CYTOSOL-MEDIATED BINDING OF 1,2-DICHLOROETHANE (DCE) AND 1,2-DIBROMOETHANE (DBE) TO DNA IN VITRO. A.Colacci, G.Arfeellini, G.Prodi, M.Mazzullo, S.Grilli and P.Rocchi. Istituto di Cancerologia, Università di Bologna, V. le Filopanti 22, 40126-Bologna, Italy.

Induced microsomal and/or cytosolic fractions, extracted from liver, lung, kidney and stomach of adult male phenobarbital pretreated-Wistar rats and Balb/c mice, were incubated with ¹⁴C-compounds (14.6 mCi/mmol, 57 μ M), coenzymes (2 mg NADPH and/or 9.2 mg GSH) under the same conditions described in IRCS Med. Sci. 11, 81, 1983 (which reports data on interaction by liver enzymes alone), with the exception of cytosolic protein amount (2 mg instead of 6 mg). Both compounds bind to DNA, being DBE equivalents binding (26-641 pmol/mg DNA) higher than DNA interaction by DCE equivalents (10-263 pmol/mg DNA). The relative effectiveness of two metabolic pathways is variable in relation to species, organ and compound tested. With microsomal + cytosolic fractions, DNA binding is mainly performed by liver enzymes in the case of DCE and by kidney fractions in the case of DBE. However, lung microsomes are very efficient (binding values equal to or higher than those seen with liver microsomes), chiefly when obtained from mouse organ. The overall data are in agreement with the relative genotoxicity of chemicals (Mut. Res. 76, 269, 1980).

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