COVALENT DNA BINDING, MUTAGENESIS AND LETHALITY OF AFLATOXIN B_1: COMPARISON BETWEEN MICROSOMAL AND PHOTO-ACTIVATION SYSTEMS. Avishay A.Stark, Hagar K.Israel, Lilly M.Mor, Department of Biochemistry, Tel-Aviv University, Tel Aviv, Israel.

Non-specific nuclease(s) in metabolic activation systems prevent the study of AFB_1 interactions in vitro with homogenous DNA molecules of known sequence and topology. Activation of aflatoxins with near U.V. (365 nm) light circumvents this problem. Photoactivated ^{3}H-aflatoxin-DNA interactions were studied by (i) in vitro covalent binding to calf-thymus DNA, (ii) photomutagenesis in S. typhimurium TA100, and (iii) determination of in situ ^{3}H-AFB_1 binding to DNA and RNA in TA100 cells mutagenized with metabolically activated or photo-activated ^{3}H-AFB_1. Levels of AFB_1, AFB_2, AFG_1 and AFG_2 photobinding to calf thymus DNA correlated with aflatoxin photomutagenesis. Levels of AFB_1 binding to DNA mutagenized cells were proportional to mutation induction and lethality in strain TA100. AFB_1-DNA lesions produced by photo- or microsomal-activation were of comparable lethality and mutagenicity. Covalent binding of AFB_1 to RNA did not correlate with lethality or mutagenesis. Increased cytotoxicity of photoactivated AFB_1 compared with AFB_2 at comparable mutagenesis levels indicates that, in analogy to psoralens, photoactivated AFB_1 produces DNA cross-links whereas AFB_2 does not. Photoactivation of aflatoxins can be used to study in vitro aflatoxin-DNA interactions with minimal non-specific damage to the DNA substrate.

PROPERTIES OF METHYLBENZYLNITROSAMINE-TRANSFORMED RAT ESOPHAGEAL EPITHELIAL CELLS. Gary D.Stoner, Dominick A.Scaramuzzino and Alvin Malkinson. Department of Pathology, Medical College of Ohio, Toledo, OH. and School of Pharmacy, University of Colorado, Boulder, CO, USA.

The purpose of this study was to compare the in vitro properties of N-nitrosobenzylmethylamine (BMNA)-treated rat esophageal epithelial cell lines with their tumorigenic potential in vivo. Nine cell lines derived from BMNA-treated explants of esophagus and four cell lines from untreated explants were propagated for 1/2-2 years. All cell lines are polygonal in shape, possess tonofilaments and junctional complexes, and react with antibodies to mouse skin keratins. Four of the 9 BMNA-treated lines and 1 of the untreated lines produced squamous cell carcinomas (SCC) 8-9 months after s.c. inoculation into 1 day-old syngeneic rats. Cell lines derived from these tumours were highly malignant when reinoculated into the host. There was no correlation between either the growth rate, soft agar growth potential, or calmodulin content of the cell lines and their ability to produce SCC. The tumourigenic cell lines differ from the non-tumourigenic lines in that they exhibit clonal growth in serum-free medium containing only 0.001 mM added calcium. In addition, in medium containing 1 mM calcium and 5-10% serum, the tumourigenic lines continue to proliferate whereas the non-tumourigenic lines undergo terminal differentiation. By one-dimensional gel electrophoresis there were differences in the profile of keratin proteins and of protein phosphorylation between tumourigenic and non-tumourigenic cell lines. These data suggest that differences in the synthesis of keratin proteins and endogenous protein phosphorylation of BMNA-treated rat esophageal epithelial cells more closely parallel their tumourigenic potential than their in vitro growth characteristics

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LEUKAEMIA RISK AFTER IRRADIATION FOR CERVICAL CANCER IN DENMARK 1943-1977. A CASE-CONTROL STUDY.
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A cohort of 27 437 patients diagnosed with cervical cancer as first cancer (non-melanoma skin cancers excluded) between 1943 and 1977 in Denmark were followed in the Danish Cancer Registry until July 1982. The population were categorised according to radiation treatment as notified to the Cancer Registry. In the irradiated group observed to expected ratios for acute and granulocytic leukaemias as well as chronic lymphatic leukaemias (CLL) were below 1, i.e. probably no radiation effect. A case control study on radiation exposure based on hospital records was performed. Among 27 leukaemia cases and 108 matched controls from the cervical cancer population 16 acute leukaemias was found. The matched analysis reveal a RR of 6.58 Chi-value 1.96 (CI 95%: 1.0-43.28) for acute leukaemia after radiation exposure whereas an excess risk was not found among patients with CLL. In spite of the results from the cohort analysis and results from other similar studies among cervical cancer patients this case control study indicates that even among cervical cancer patients irradiation is leukaemogenic.