THE CARCINOGEN N-ACETOXY-ACETYLAMINOFLUORENE REACTS PREFERENTIALLY WITH A CONTROL REGION OF THE INTRACELLULAR SIMIAN VIRUS 40 CHROMOSOME

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The chromosome of Simian Virus 40 (SV40) is well suited for studies of the interaction of chemical carcinogens with chromatin. Like chromatin of eukaryotic cells, it is organised into nucleosomes. We have investigated the binding of the ultimate carcinogen N-acetoxy-acetylaminofluorene (AAAF) to specific regions of the SV40 chromosome in situ in the intact infected cell. SV40-infected cells late in the lytic cycle were incubated with ^{3}H-AAAF. SV40 DNA was extracted, digested with restriction enzymes HaeIII and KpnI, and radioactivity in each DNA fragment determined. The results indicated that a stretch of DNA near the origin of replication of the intracellular SV40 chromosome was more susceptible to attack by AAAF than the rest of the SV40 genome. When naked DNA was labeled with ^{3}H-AAAF in vitro no hyperreactive region was seen. The hyperreactive region may represent a stretch of DNA which is nucleosome-free or has another unusual chromosomal structure.
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HYPERTROPHY AND HYPERPLASIA OF MOUSE EPIDERMIS INDUCED BY 3-METHYLCHOLANTHRENE AND PHORBOL ESTER ARE STRAIN DEPENDENT AND MAY CORRELATE WITH SUSCEPTIBILITY TO TUMOR INDUCTION

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In two-stage carcinogenesis models (tumor-"initiation" and -"promotion") of mouse skin cell proliferation and subsequent epidermal hyperplasia (HP) are implicated in the concept of tumor promotion. The possible importance of cell hypertrophy (HT), however, is unclear. Epidermal lesions induced by 3-methylcholanthrene (MCA) and by 12-0-tetradecanoylphorbol-13-acetate (TPA) were analyzed by means of morphometry in mouse strains differing in susceptibility to tumor induction. In all strains MCA, a complete carcinogen (i.e. which in addition to a tumor initiating-property also possesses promotorlike activity) caused epidermal thickening peaking between the 2nd and 5th day after a single treatment. This thickening was due to both increase in average cell size (HT) and an increase in the number of cells (HP) per unit of length of interfollicular epidermis. After MCA HP as well as HT were significantly greater in carcinogen susceptible BALB/c (HP 135 %, HT 300 %) and C57BL (HP 140 %, HT 330 %) than in more resistant DBA (HP 120 %, HT 150 %) and AKR (HP 120 &, HT 175%) mice. From these values it appears that HT was more marked than HP and that the difference in the hypertrophiogenic effect of MCA between high and low responders was more obvious than the difference in the hyperplasiogenic effect of the carcinogen. Similar strain-specific differences in HP as well as HT between high responders and low responders of tumorigenesis were noted using the tumor promoting agent TPA which needs no metabolic conversion for its action. The present studies rise the possibility that - in addition to possible differences in the initiation phase and/or DNA repair processes - strain-specific differences of epidermal reactions in the promoting phase might be important in susceptibility to tumor induction.

HEAVY WATER : EFFECTS ON PROLIFERATION OF NORMAL AND NEOPLASTIC CELLS IN MICE

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In 1938, Barbour and Allen observed reduced growth rates of transplantable carcinoma or lymphosarcoma in nine deuterated mice. In the fifties and sixties, it appeared from the results of several similar experiments that moderate body deuteration of mice and rats may slow down tumor growth and sometimes prolong survival. We found only one study focussing on the combined effects of heavy water and cytostatic drugs on a small number of mice inoculated with Krebs-2 ascites tumor; in spite of reduced tumor growth rates, these animals died earlier than the controls.
In the present study, young adult DBA/2 mice bearing transplantable tumors were treated with different concentrations of heavy water and with repeated injections of methotrexate (MTX). We used several lymphoid tumors, and the mastocytoma P 815.