STUDIES ON PROMOTION BY CROTON OIL IN RAT SKIN CARCINOGENESIS

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Male inbred Wistar and Lister rats and (WixBN)F_1 hybrids were treated on the dorsal skin with 7,12-dimethylbenz (a)anthracene (DMBA) (2.5 mg once weekly for 3 weeks) followed after 1 week by croton oil (CO, 5 mg twice weekly) to study initiation-promotion in rats of different strains and the possible importance of the fact that two main tumour types are induced in rat skin: squamous cell tumours (SQCT) and basal cell/adnexal tumours (BCAT).

Over a 1 year period, DMBA/CO produced lower total tumour incidences in Wistar and (WixBN)F_1 rats than DMBA -initiation alone, but SQCT appeared only after CO-promotion in the hybrids and had a shorter latent period in the CO-treated Wistars, while BCAT seemed to be inhibited by CO. Current experiments on Lister rats show after 6 months higher total tumour incidences and shorter latent periods after CO-promotion, especially after increasing the DMBA applications to 6 in 3 weeks.

Thus CO-promotion was active in rat skin carcinogenesis, but the response varied with strain and initiator dose, and the results indicate that CO promoted SQCT, not BCAT.

CELL POPULATION KINETICS OF 12-O-TETRADECANOYLPHORBOL-13-ACETATE (TPA) INDUCED HYPERPLASIA. Erle Grieg Astrup and Olav Hilmar Iversen, Institute of Pathology, University of Oslo, The National Hospital, Oslo 1, Norway.

Alterations in cell population kinetics of mouse epidermis after a single topical application of 17 nmol TPA was studied by recording the replication and proliferation rates of basal cells, the number of basal and suprabasal (maturing) cells and the number of squamous layers in the stratum corneum. From 0-12 hr there was a temporary block of cells in S-phase and mitosis, followed from 12-96 hr by several waves of partially synchronized basal cells displaying increased rates of DNA-synthesis and cell division. These changes were accompanied by concomitant waves of increased rates of cell maturation and cell loss that reduced considerably the epidermal transit time.

The promoter induced hyperplasia results from a considerably enhanced cell proliferation that exceeds concomitant increases in the rates of cell maturation and cell loss. There is no delayed maturation. Thus the alterations in cell population kinetics after TPA treatment is equal to the regenerative response following felt wheel abrasion and wounding.

CHEMOPREVENTIVE EFFECT OF RETINOL ON THE HEPATIC METAPLASTIC CHANGES INDUCED IN VIVO IN THE MOUSE BY DIETHYLNITROSAMINE AND PHENOBARBITAL. M.Audette and M.Pagé. Départmente de Biochimie, Faculté de Médecine, Université Laval, Québec, Canada.

Vitamin A and retinoid derivatives were found to exert a chemopreventive action on the neoplastic transformation of various epithelial tissues. Attempts were made to verify the retinol action on the hepatic preneoplastic transformation induced in C3HeB/FeJ mice treated with diethylnitrosamine and phenobarbital and fed with various retinol supplemented diet. Histological examination revealed that after 30 and 45 weeks, a Vitamin A supplementation of 500 µM/kg of diet decreased the severity of metaplastic changes found in treated animals fed with normal chow. A higher dose of 1000 µM/kg of diet induced severe hepatic and systemic intoxication and was discontinued. Estimation of the percentage of binucleated cells has revealed that the incidence was higher in deficient mice, it increased between 30 and 45 weeks for normal and Vitamin A (-)-fed animals but decreased in retinol supplemented mice.

It seems that retinol in the diet may play a chemopreventive role in the occurrence of early liver perturbations following administration of subcarcinogenic doses of DEN.

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