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## CYTOGENETIC CHANGES OF MOUSE KERATINOCYTES IN PRIMARY CULTURES AND DERIVED CELL LINES: A POSSIBLE MECHANISM FOR MALIGNANT TRANSFORMATION

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Chromosome changes were followed in primary cultures of mouse keratinocytes (PEC) under conditions leading to spontaneous transformation and compared with cytogenetic characteristics of 10 transformed keratinocyte cell lines. Numerical and structural aberrations were the first changes observed in PEC, before any morphological alteration occurred. Hypodiploid metaphases were already seen in 2 day cultures, and chromosomes 4 and 7 were most frequently under-represented. Hyperdiploid metaphase appeared with culture time. The level of structural aberrations increased progressively, but marker chromosomes were only discovered in the cell lines. The transformed keratinocyte lines were aneuploid (near-tetraploid) and possessed stable individual markers, mostly consisting of translocations. Three lines shared a common marker 15, a duplication of the c-myc oncogene containing region. However, a consistent loss of 1 to 2 copies of numbers 7 and 14 respectively, was a common feature. Homogeneously staining regions (HSR) and double minute chromosomes (DM) were present in 50% and 100% of the lines respectively. In conclusion, the chromosomal loss, leading to hemizygosity, the gene amplification (DM and HSR) and gene translocation may represent a mechanism for transformation of mouse keratinocytes.

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## CYTOCHEMICAL STUDIES IN ADENYLYL CYCLASE IN PRENEOPLASTIC AND NEOPLASTIC LIVER LESIONS

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Changes in glycogen content and in the activity of various enzymes, including key enzymes of carbohydrate metabolism, have been shown in focal hepatic lesions during liver carcinogenesis induced in the rat by chemicals (Adv. Enzyme Reg. 22, 97, 1984). The primary biochemical lesion responsible for these metabolic aberrations remained unclear. We therefore investigated the activity of adenylate cyclase (AC), which plays an important role in the regulation of cellular metabolism, in preneoplastic and neoplastic lesions induced in rat liver by N-nitrosomorpholine (NNM). AC was demonstrated histochemically in cryostat sections according to the method of Howell and Whitfield using AMP-PCP as a substrate. As a rule, the activity of AC was strongly reduced in preneoplastic glycogen storage foci and in mixed cell foci which were composed of both hepatocytes rich and hepatocytes poor in glycogen. Rarely unclassified foci were observed which showed an increase in the activity of AC. In neoplastic nodules and in hepatocellular carcinomas the activity of AC remained decreased or reappeared. Sometimes it was even increased over the activity of normal hepatocytes. We conclude that changes in the activity of AC are closely related to the alterations in carbohydrate metabolism described earlier.

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## ASSESSMENT OF IMMUNE STATUS OF BREAST CANCER PATIENTS BY THE LEUKOCYTE ADHERENCE INHIBITION TEST

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The leukocyte adherence inhibition (LAI) assay was used to study specific cell-mediated antitumour immune reactions in 84 breast cancer patients at different stages of disease. A control group consisted of 28 healthy women, 25 patients with benign breast tumours and 6 with malignant melanoma. Leukocytes of breast cancer patients were exposed to a soluble antigenic preparation obtained after a high-speed centrifugation of a tissue homogenate from a freshly excised breast carcinoma. The breast cancer extract significantly inhibited the adherence of allogeneic leukocytes from almost all patients with breast carcinoma. At the same time, the leukocyte adherence was not affected by identically prepared extracts from benign breast tumour tissue (fibroadenoma) or a colorectal carcinoma ( $P<0.01$ ). It is to be emphasized that this reactivity was maintained up to 6 months in Stage I and III patients, but in the same instance, there was a significant drop in reactivity of Stage II patients two weeks after surgery.