MULTIFACTORIAL TRANSFORMATION OF HUMAN B LYMPHOCYTES IN VITRO
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The incidence of Burkitt lymphomas (BL) has been linked to a massive and early infection of African children with Epstein-Barr virus (EBV). Other carcinogens are thought to be required for the emergence of BL tumourigenic clones. We have attempted to reproduce this malignant progression in vitro: human lymphocytes were first immortalized by the B95-8 strain of EBV and then treated with sub-toxic doses of 2 carcinogens (NQO and R7000).

We chose first to utilize the lymphocytes of an Ataxia-Telangiectasia patient, this autosomal recessive genetic disease being known to be correlated with a great genetic instability. The supertransformation of these EBV-immortalized carcinogen-treated lines was demonstrated by the rapid appearance of new properties in vitro in suspension in liquid or semi-solid medium and in vivo by an increased tumourigenicity in nude mice, some clones being more tumourigenic than Daudi and Namalva BL lines. Still, by their morphology and by the histological characteristics of the tumours obtained, the supertransformed clones were different from BL cell lines. In a second series of experiments, normal human adult lymphocytes were treated in the same way with EBV and carcinogen. An identical evolution, though requiring a longer delay was observed.

DIFFERENTIAL REPAIR OF O^6-METHYLGUANINE (O^6-meG) FROM DNA OF PARENCHYMAL AND NON-PARENCHYMAL RAT LIVER CELLS AFTER CHRONIC ADMINISTRATION OF DIMETHYLNITROSAMINE (DMN).
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Previous studies have demonstrated that chronic administration of DMN to rats is followed by considerable increase in repair of O^6-meG in liver DNA. To explore the role of various liver-cell populations in induction of an increased repair of this adduct, male BDIV rats were given DMN (2 mg/kg daily) for 3 weeks, the final dose being of [^{14}C]DMN (controls received only [^{14}C]DMN). Rats were killed 2 to 10 hr thereafter; DNA was isolated from parenchymal (PC) and non-parenchymal (NPC) cells, separated by elutriation centrifugation, and normal and alkylated purines were determined after hydrolysis by chromatography on HPLC or Sephadex G-10. The levels of 7-methylguanine in PC and NPC DNA were the same as or slightly higher than those in control animals, and the persistence of this product was similar in both groups. In contrast, the initial amount of O^6-meG in PC DNA was considerably lower and the rate of its loss from PC DNA higher in pretreated than that in control rats. However, no substantial difference in the initial concentrations of O^6-meG and its subsequent loss occurred in NPC DNA of either pretreated or control animals. The inability of NPC to respond to chronic administration of DMN by an increased repair of O^6-meG in DNA correlated with appearance of haemangiosarcomas, but not hepatomas, in a corresponding long-term study.

BENZO(a)PYRENE AND ALDRIN METABOLISM IN CULTURED HUMAN AND RAT HEPATOMA CELL LINES.
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Five established hepatoma cell lines, 4 derived from human hepatoma and one of rat origin, have been compared for their capacity to metabolize one cyclodiene chlorinated insecticide, aldrin, one polycyclic aromatic hydrocarbon, benzo(a)pyrene (BP) and one aromatic amine, 2 acetylaminofluorene (2AAF). The metabolic conversion of aldrin to dieldrin, assayed by electron-capture gas liquid chromatographic analysis, was found to be much more efficient in the rat hepatoma line than in any human lines. Two human hepatoma lines displayed the highest BP metabolizing activity and one of the others can advantageously replace the hamster fibroblasts (V79) used up to now as a target partner in cell-mediated cytotoxic assays for BP. The wide individual variation observed between the 4 human lines towards their BP metabolizing capacities, whether measured as the amounts of water soluble products or estimated by cell-mediated cytotoxic assays, did not appear when the same human lines were tested, by the same methods, for their 2AAF metabolizing activities. The lack of correlation between aldrin, BP and 2AAF metabolism suggests that these metabolizing activities are under different genetic controls. Our data also show that, in screening tests, the use of human and rat carcinoma cells, either as target or as metabolizing cells, has an important value.