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The interaction between 5-fluoropyrimidines and DNA was investigated using an approach by which cells are lysed in dilute alkali to reveal drug-induced fragmentation of DNA. One mechanism used to induce DNA lesions is the incorporation of drug into DNA, resulting in the induction of alkali-sensitive DNA lesions. The presence of lesions results in fragmentation of DNA, which is visualized by agarose gel electrophoresis.

The second mechanism does not involve incorporation of drug into DNA. This mechanism is in all probability due to inefficient DNA repair of normally occurring defects in nucleotides.

In human colon adenocarcinoma cells treated with 5-FU one can detect both mechanisms. In cells treated with 5-FdU one can detect only the second mechanism.

Ref: Cancer Res. 44: 3414, 1984; Cancer Res., 46: 3866, 1986.

LOCALIZATION OF RADIOLABELLED MONOCLONAL ANTI-CEA ANTIBODIES AND FRAGMENTS IN COLON CARCINOMA, - DIAGNOSTIC AND THERAPEUTIC APPROACHES

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Thirty-one patients with known colorectal carcinomas were injected with Fab and F(ab')2 fragments from the monoclonal anti-CEA antibody (MAb) 35 labelled with 3 to 6 mCI of [123]I and tested by emission computerized tomography (ECT) 6, 24 and sometimes 48 hr after injection. All 23 primary tumours and local recurrences except one were clearly visualized. Interestingly, 9 of these patients had almost normal circulating CEA levels and 3 of the visualized tumours weighed only 3 to 5 g. Among 19 known metastatic tumour involvements 14 were correctly localized by ECT (Delaloye et al., J.Clin.Invest., 77: 301-311, 1986). For therapeutic purposes, seven patients with liver metastases were injected in the hepatic artery with MAbs and anti-CEA labelled with 100 mCi of [131]I. None of the 7 patients showed any significant side effects for a period of observation of 5 to 10 months. We observed good localization of intact [131]I MAb in liver metastases, as documented by ECT obtained 4 days after injection, and an estimated radiation dose to the tumour of 1000 rads, but we have not yet obtained definite evidence of tumour regression.

VACCINATION AGAINST EPSTEIN BARR (EB) VIRUS ASSOCIATED MALIGNANCIES

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We have investigated the possibility of using vaccinia virus recombinants expressing EB virus genes as potential vaccines to prevent EBV associated tumours. EB virus membrane antigen gp340 was inserted into and expressed in several strains of vaccinia virus. The gp340 produced by the vaccinia recombinants was indistinguishable from authentic gp340 by the criteria examined. Rabbits vaccinated with one of the recombinants produced antibodies that neutralized EB virus. We have also inserted the EB virus glycoprotein gB into vaccinia virus either as the authentic protein or as an in frame fusion with Hepatitis B virus surface antigen. These two constructs should present the EBgB to the immune sytem of vaccinated animals in different ways. Vaccination of rabbits is underway and should tell us whether the EBgB gene product is capable of raising EB virus neutralising antibody and also give us an idea how best to present antigens to the immune system.

RFLP ANALYSES OF c-Ha-ras LOCUS IN HUMAN TUMOURS

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A restriction fragment length polymorphism (RFLP) of the human c-Ha-ras locus has been analysed in DNA from breast tumours, leukaemic cells and lymphocytes from normal individuals by agarose gel electrophoresis and Southern blot hybridization. Examination of the allele frequencies showed three "common" alleles (6.8, 7.5, 8.3 kb) occurring with frequencies 38.2%, 36.5% and 19.2%, respectively, and several "rare" alleles (about 6%). More Ha-ras homozygotes were noted in DNA isolated from tumours than from white blood cells in normal individuals. No