EMB EFFECT OF METHOTREXATE-ALBUMIN-MONOCLONAL ANTIBODY CONJUGATES ON METHOTREXATE-RESISTANT CELLS

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Human osteogenic sarcoma cells were selected in vitro for resistance to methotrexate (MTX) by treatment with 12-O-tetradecanoylphorbol-13-acetate and increasing concentrations of MTX. In some cases it was possible to obtain variants which grew in concentrations 8-10 times the IC_{50} for parental cells. Parental and resistant cells were tested in vitro for their susceptibility to MTX, and to conjugates of MTX linked by human serum albumin to a monoclonal antibody (791T/36) which recognises an antigen on the osteogenic sarcoma cells. These conjugates have previously been shown to be cytotoxic selectively for antibody-reactive cells (Garnet et al, Int. J. Cancer, 31, 661, 1983).

Cells which displayed resistance to free MTX in comparison with the parental cells were susceptible to the toxic effects of the drug-antibody conjugates, cytotoxicity with the conjugates approaching that seen against the parental cells. It is suggested that targeting by means of monoclonal antibody might offer a means of overcoming resistance of cancer cells towards conventional cytotoxic drugs.

ERD METABOLISM OF DIACETYL-DIANHYDROGALACTITOL (DADAG) BY RAT LIVER MICROSOMES

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DADAG is a new alkylating hexitol derivative developed in Hungary. It was incubated in various concentrations with rat liver microsomes in the presence or absence of the NADPH generating system. The parent drug and its metabolites were determined by GLC methods. The formation of the pharmacologically active metabolite dianhydrogalactitol (DAG) is characteristically connected with esterase activity of the system. In addition three other metabolites were detected. In the presence of the NADPH generating system the disappearance of DADAG decreased.

ERH 3-METHYLCHOLANTHRENE-INDUCED CHANGES IN NUCLEOLAR STRUCTURE AND NUCLEOLAR SILVER STAINING PROTEINS OF RAT LIVER CELLS

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The present experiments were carried out on liver cells of ten-day-old rats. The animals were treated with a single i.p. dose of 3-methylcholanthrene (3-MC) and killed after 24, 48, 72 and 96 hr. The livers were exmained by conventional and cytochemical (silver staining) electron microscopic methods. The investigations showed that treatment with 3-MC was followed by nucleolar hypertrophy, nucleolar segregations and the frequent occurrence of fibrillar centres. Higher amounts of the end-products of silver staining were observed in the nucleoli after 3-MC administration and the reaction was stronger in the fibrillar components than in the fibrillar centres. The highest level of nucleolar hypertrophy and the appearance of silver deposits were observed at 72 hr after 3-MC treatment. The results suggest that the 3-MC treatment brought about increased functional activity of nucleoli and the increased activity of nucleolar genes was detectable at ultracytochemical level.
