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Targeting of Borontreated anti-AFP MoAb to hepatoma cells; application of borontreated MoAb for BNCT.

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In past our study, we have described that ^{10}B atoms delivered by monoclonal antibodies (MoAb) exhibited cytotoxic effect on AH-66 cells in a dose dependent manner by *in vitro* thermal neutron irradiation (Takahashi et al., Japan. J. Exp. Med. 57 : 83, 1987). The aim of the present study was the *in vivo* evaluation of the delivery capacity of ^{10}B atoms using borontreated-anti AFP MoAb to alpha-fetoprotein (AFP) producing tumor xenografts in nude mice. Borontreated MoAb was prepared by conjugating with ^{10}B compounds to an anti AFP MoAb using N-succinimidyl-3 (2-pyridyldithio) propionate (SPDP). The number of ^{10}B atoms conjugated directly to MoAb was estimated to be 442 per antibody through prompt gamma ray spectrometry. The biodistribution data obtained at 12hrs, 24hrs, 72hrs and 120hrs after injection of 1.5 mg ^{10}B conjugated anti AFP MoAb showed 1.27 ± 0.30, 2.38 ± 0.76, 2.59 ± 0.18 and 2.20 ± 0.06 (ppm). In using a control of ^{10}B conjugated anti-dinitro-phenol (DNP) MoAb, the data showed 0.89 ± 0.01, 0.92 ± 0.27, 1.20 ± 0.07 and 1.16 ± 0.18 (ppm). The ^{10}B concentration in blood samples was 0.40 ± 0.10 (ppm) using anti-AFP MoAb and 0.51 ± 0.14 (ppm) using anti-DNP MoAb. The number of ^{10}B atoms delivered to the tumor cell was caluculated to be 0.72×10^9 at 12hrs, 1.10×10^9 at 24hrs, 2.39×10^9 at 72hrs and 0.94×10^9 at 120hrs after the injection of ^{10}B-anti-AFP MoAb. Alam et al. estimated the necessary amount of ^{10}B atoms for effective BNCT to be 10^9 per tumor cell. We were able to accumulate 2.39×10^9 ^{10}B atoms to AH-66 tumor cell by using ^{10}B-anti-AFP MoAb. Maximum accumulation was 72hrs after injection. These data indicated that the ^{10}B conjugated MoAb could deliver sufficient quantities of ^{10}B atoms to the tumor cells which should achieve the appropriate cytotoxic effect at 72hrs after injection with thermal neutron irradiation.

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EARLY DIAGNOSIS OF MALIGNANT TUMOR IN MICROCIRCULATION

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Microcirculatory examination was performed in 143 patients with advanced malignant tumors. Of them, 102 had circulatory white microthrombi, 19 had trace amount, 50 were of mild degree, 29 moderate and 4 severe, the severity being related to clinical manifestations. All the four severe cases had obvious metastatic lesions. The platelet adhesion rate in most cases were not so high and the white counts were normal. In 64 patients tumor cells were examined with positive results in 7 and 20 had retrograde cells. So it was considered that white thrombi were associated with the circulating tumor cells. In the series 34 were of the stasis type of microcirculatory disturbances, associated with red thrombi and slow blood flow; 71 were of the spastic type of microcirculatory disturbances. The former type showed poor results while the latter type showed better results to radiotherapy and chemotherapy.

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Detection of c-erbB-2 expression in breast cancer: Comparison of an immunocytochemical assay with a new tissue extract enzyme immuno assay.

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The protooncogen c-erbB-2 encodes a 185 KDa transmembrane glycoprotein that is a member of the growth factor receptor family exhibiting tyrosin kinase activity. The activation of the c-erbB-2 protooncogene is most often accomplished by gene amplification and results in the overexpression of the protein. This overexpression can be found in about 20% of all breast carcinomas and seems to be an independent prognostic indicator for shortened disease free interval and overall survival.

In this study an immunocytochemical method ("Triton Diagnostics´ c-erbB-2 ICA Kit") was compared to an enzyme immunoassay ("Triton Diagnostics´ c-erbB-2 Tissue Extract EIA Kit"). For ICA frozen tissue sections were used. For the EIA tumor samples were processed according to the procedure for steroid receptor measurement in cytosol.

From 40 tissue samples analyzed (37 carcinomas, 3 benign tumors) 22% gave a positive result in ICA. These data correlated statistically significant ($p = 0.0003$, Mann-Whitney U Test) to the results obtained by EIA. Also 9 samples form normal tissue were analyzed by EIA and gave significantly lower results ($p = 0.007$) compared to malignant tissue. Besides we found an inverse correlation between c-erbB-2 ICA and steroid receptors (ER: $p = 0.027$, PR: $p = 0.016$). ER and PR showed a highly significant positive correlation ($p < 0.00001$).

It can be concluded that both the EIA and the ICA give comparable results. Thus a method is available for routine analysis of c-erbB-2 expression in tumor samples.