566

Tc-99m LABELING OF MONOCLONAL ANTIBODY USING CE-DTS AS A BIFUNCTIONAL CHELATING AGENT: TUMOR IMAGING STUDY IN ATHYMIC MICE.

Y. Arano, T. Furukawa, T. Yahata, A. Yokoyama, K. Endo, H. Sakahara, T. Nakashima and K. Torizuka. Faculty of Pharmaceutical Sciences and School of Medicine, Kyoto University, Kyoto.

A stable Tc-99m labeled monoclonal antibody with preserved its original immunoreactivity has been obtained through the use of p-carboxyethylphenylglyoxal-di(N-methylthiosemicarbazone) (CE-DTS), a new bifunctional chelating agent with selectivity for Tc-99m.

In the present study, Fab fragment of the monoclonal antibody against hCG (56C) was coupled to CE-DTS and labeled with Tc-99m at pH 6.2 using stannous chloride methodology. Then, tumor imaging study was carried out in athymic mice transplanted with hCG producing human testicular tumor.

Stable Tc-99m labeled CE-DTS-Fab with preserved immunoreactivity was made available. Tumor visualization was obtained as early as 6 hours, and at 24 hours post-injection, tumor/blood and tumor/muscle ratio reached 1.46 and 5.10, respectively.

These results showed the validity of using CE-DTS method for the Tc-99m labeling of monoclonal antibody as well as the possibility of tumor imaging within the half life of Tc-99m.

567

RADIOIMMUNODETECTION OF HUMAN HEPATOCELLULAR CARCINOMA USING ANTI-AFP MONOCLONAL ANTIBODY

T.Hashimoto,K.Nakamura,I.Nishiguchi,A.Kubo,S.Hashimoto. Dept.Radiology,School of Medicine,Keio University. S.Hosokawa,M.Yasuda,K.Nagaike.Res.Center,Mitsubishi Chem.Ind.

[Introduction]Radioimmunodetection is to be expecting as the method to detect the localization of cancer using the monoclonal antibody.This time We have discussed the probability of radioimmunodetection of human hepatocellular carcinoma using anti-AFP monoclonal antibody.[Materials and Methods]1)anti-AFP monoclonal antibody(19F12)was prepared by the method of B cell hybridoma.2)19F12 was labeled by the iodine-125 using chloramine T method.3)Male athymic mice (nu/nu,BALB/c, 6 week)were inoculated with hepatoma(NuE)or gastric cancer(MKN45 and MKN28).4)Nude mice hosting hepatoma were intravenously injected of labeled 19F12 50~100 μCi (13~18mCi/mg prot),and were imaged at daily intervals. 5)8 days post injection,the mice were killed and biodistribution was determined.[Results]Tumor localization was clearly visible 24hr after administration of radioiodinated antibody,and became increasingly clear as body background cleared.Tumor to liver ratio of hepatoma was prominently higher than that of gastric cancer. Although,the liver was strongly visiualized in the mice given the Ga-67 citrate,high tumor to liver ratio was acquired in the mice given the radioiodinated monoclonal antibody.Therefore,this method is thought to be very promising to detect the localization of hepatoma in the liver,and to visiualize the metastatic lesions.

568

RADIOIMMUNO-IMAGING OF HUMAN MAMMARY TUMOR BY MONOCLONAL ANTIBODIES

. Y.Mori, H.Sekine, K.Kawakami and T.Ohono. Jikei university school of Med,Tokyo.

For many clinicians to manage malignancy, it is desired to detect a small primary lesion or micrometastases of malignancy in early stage. In theory the radiolabeled tumor specific monoclonal antibodies(MoAb) could be one of the ideal signales. However clinical use of radiolabeled MoAb for human tumors has not been established.

In attempting to radioimmunodetection for human malignancy, we established the experimental animal model as a 1ststep. The nude mice bearing human mammary carcinoma were examined.
The MoAb JB100 against human mammary carcinoma which has been established its specific reactivity by mean of ELIS assay and tissue staining, was radiolabeled with I-131 by iodogen method and used to image in vivo. After the intraperitoneal injection of radiolabeled MoAb(24-120h) the mouse was imaged by γ-camera with pinholecollimeter.
As a result, progressive accumulation of radiolabeled antibody was observed in mammary carcinoma during 96h after injectionon γ-camera images.
As 2nd experiment, to comfirm the charactalistics of binding specificity of the radio-labeled MoAb to only human mammary carcinoma (not other human malignancy) , a nude mouse was implanted two kinds of human tumors- mammary carcinoma & gastric carcinoma. The mice bearing two tumors were given intraperitoneal injection of radiolabeled MoAb and imaged as above discribedor their tissues were removed and counts/weight were muasured to caluculate the ratios. As a result after injection 96h the highest accumulation wasnoted in mammary carcinoma whereas no accumulationin the control gastric carcinoma. This study demonstrated that this I-131 labeled MoAb well presurved its binding specificity to human mammary carcinoma in vivo as well as in vitro assay.

569

RADIOIMMUNOIMAGING OF OSTEOGENIC SARCOMA XENOGRAFTS BY A MONOCLONAL ANTIBODY (Ab); COMPARISON OF In-111 LABELED Ab WITH RADIOIODINATED Ab.

H.Sakahara, K.Endo, M.Koizumi, T.Nakashima, M.Kunimatsu, H.Ohta, S.Hosoi, H.Tanaka, T.Yamamuro, S.Toyama, T.Nakamura, and K.Torizuka. Kyoto University, Kyoto.

We have developed several monoclonal antibodies (Ab) against human osteogenic sarcoma, one of which OST7 selectively localized in osteogenic sarcoma xenograft (KT005) in nude mice. To compare In-111 labeled Ab with radioiodinated Ab for radioimmunoimaging, whole IgG and $F(ab')_2$ fragment of OST7 labeled with these radionuclides were injected into nude mice bearing KT005. All radiolabels retained their antigen-binding activity and clearly visualized transplanted tumors. Net tumor concentration of In-111 labeled OST7 was 30% of injected dose per gram and higher than that of radioiodinated one (about 23% of dose per gram) but In-111 labeled Ab showed high accumulation in the liver and kidney. In radioiodinated OST7, $F(ab')_2$ fragment provided much better images than intact Ab. Using $F(ab')_2$ fragment as a carrier for In-111, little improvement of images was obtained due to high background activity in the kidney and liver.

Since localization of OST7 in KT005 is excellent, this model system gives a good basis for evaluating in vivo characteristics of radiolabeled Ab.