Symposium IV

Clinical usefulness of monoclonal antibodies for the radioimmunoassay of tumor markers

(1) Radioimmunoassay for tumor marker

Keigo Endo, Dept of Nuclear Medicine, Kyoto University, Kyoto

By the establishment of hybridoma technology by Kohler and Milstein in 1975, who were awarded Nobel prize of 1984, opened its new era in the oncology of Nuclear Medicine. Monoclonal antibodies (Ab) have been utilized in the 1) radioimmunoassay of tumor markers, 2) the radioimmunoimaging and 3) the radioimmunotherapy of cancer.

CA 19-9 is the first tumor marker of pancreatic carcinoma developed by hybridoma technology in 1979 and demonstrated the superiority of monoclonal Ab to conventional polyclonal serum. Serum 19-9 levels were elevated in more than 80 % of patients with pancreatic cancer but in less than 10 % of chronic pancreatitis and none in 98 heatly control subjects. Thus, RIA of CA 19-9 proved to be useful in the differential diagnosis between pancreatic carcinoma and chronic pancreatitis, and for follow the patients after the surgery. However serum CA 19-9 values correlated with the size of tumor. CA 19-9 was negative in almost all pancreatic carcinomas of less than 3 cm in diameter and may not be useful for the early diagnosis or the screening of pancreatic cancer, as was the case in the α-fetoprotein (AFP) and Carcinoembryonic antigen (CEA).

Since the success of CA 19-9 as a tumor marker, the production and usage of these reagents in oncology has expanded dramatically. Up to now a variety of monoclonal antibodies against human tumor antigens are produced, such as melanoma, osteogenic sarcoma, breast, lung, stomach, prostate, and colorectal cancers, and so on.

CA-125 is the second tumor marker of monoclonal Ab clinically studied. CA-125 was also very useful in the ovarian carcinomas and more tumor marker, developed by hybridoma technology, will become available soon. These unique specificities and homogeneity, that is, monoclonal Ab consists of immunoglobulins recognizing the tumor specific antigens, have inspired the use of monoclonal Ab as a radiotracer for the radioimmunoimaging and radioimmunotherapy of cancer.

The production of monoclonal Ab to human tumor antigens has only begun. The clinical usefulness of these reagents in the radioimmunoassay of tumor markers is highly promising.

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(2) Radioimmunodetection

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MELANOMA ANTIGEN.

K.Kusakabe. Tokyo Women's Medical College, Tokyo.

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TUMOR LOCALIZATION STUDIES USING RADIOANTIBODIES TO AFP AND CEA.

N. Ishii, T. Koji and S. Nagataki. Nagasaki University, Nagasaki.

Radioimmunolocalization of tumors which produce AFP or CEA was studied using polyclonal or monoclonal antibodies to AFP or CEA. In animal studies, radioantibodies to AFP or CEA localized in tumors which produced AFP or CEA by total body scintigraphy. In clinical applications, positive images were obtained in about 50% of patients with hepatoma or CEA producing tumors. The results of imaging of hepatoma using antibodies to AFP correlated with tumor/serum ratios of AFP. The radioactive antibodies to AFP bound to cellulose discs coated with AFP even when excessive amounts of AFP existed in medium in vitro, and in animal experiments, labeled antibodies in the form of immune complexes were accumulated selectively to AFP discs transplanted into the peritoneal cavities of rats in proportion to the amounts of AFP coating the discs.

From the studies using cultured human colon carcinoma cells which produce CEA, monoclonal antibodies to CEA specifically bound to cell surface CEA, and rapidly disappeared from the cell surface after incubation at 37°C probably due to endocytosis.