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BASIC STUDIES ON ACCUMULATION OF In-111-LABELED MONOCLONAL ANTIBODIES TO TUMOR.

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By using In-111 labeled F(ab')2 fragments of monoclonal antibodies(19-9,17-1A) against human colorectal carcinoma,we studied their availability for radioimmunodetection of malignant tumors in in vitro and in tumor bearing nude mouse. In vitro binding of 19-9 and 17-1A to human colorectal adenocarcinoma cells (SW948. SW1417) was 5-20%/$10^6$ cells and markedly greater than that to HeLa S3 cells which were examined as a control. In vitro binding to tumor tissues (SW948) of 1.5-2mm cubes which were excised from the nude mouse was 3-12 times as much as normal tissues (liver,kidney,muscle,etc.) of the nude mouse. In the study of in vitro binding to cryo-preserved surgical explants of tissues in 10 patients with colorectal carcinoma,a significant binding was recongnized in 4 tumor tissues with 19-9,and 8 tumor tissues with 17-1A. However,binding of 19-9 and 17-1A to some of surrounding normal colorectal tissues was also significantly greater than that of In-111 laveld control antibody. In the study of imaging in SW948 bearing nude mice,tumor sites were visualized from 1 day after injection of 19-9 or 17-1A. However, nonspecific uptake of radioactivity was seen in liver and kidney. These results indicate that the clinical application of radio-immunoimaging with 19-9 and 17-1A might be limited.

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STUDY OF RADIOIMMUNODETECTION WITH In-111 LABELED MONOCLONAL ANTI-COLORECTAL CARCINOMA ANTIBODY FRAGMENTS 19-9 $F(ab')_2$ AND 17-1A $F(ab')_2$ .

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Monoclonal antibodies 19-9 and 17-1A react with tumor associated antigens found on human colorectal and gastric and other carcinomas.$F(ab')_2$ fragments of 19-9 and 17-1A were conjugated with DTPA and labeled with In-111.To evaluate the utility for radioimmunodetection,we studied the binding affinities of In-111 labeled 19-9 $F(ab')_2$ and 17-1A $F(ab')_2$ to human cancer tissues,compared with that of In-111 labeled control IgG $F(ab')_2$ in vitro.In 33-85% of colorectal and gastric cancer tissues, In-111 19-9 $F(ab')_2$ or 17-1A $F(ab')_2$ showed the affinity more than 1.5 times as much as that of In-111 control IgG $F(ab')_2$ . Scintiphos of athymic mice xenografted human gastric cancer demonstrated tumor localization 8 hours after injection of In-111 19-9 $F(ab')_2$ .Biodistribution 72 hours after injection showed tumor/blood ratio of 45.8 and tumor/liver ratio of 1.37.These results indicated In-111 19-9 $F(ab')_2$ and 17-1A $F(ab')_2$ may be useful for radioimmunoimaging of human colorectal and gastric cancers.

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Binding of In-111 labeled 17-1A and 19-9 antibody to human gastric and colon cancers.

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MoAb 17-1A and 19-9 have been shown to react specifically to human gastro-intestinal tract cancers. In order to use In-111 labeled F(ab) fragment of the two MoAb for the radioimmunoimaging, we studied the quantitative assessment of antigen density of surgical specimens of human gastric and colon cancers. The crude membrane fraction was prepared from the materials obtained at surgery and incubated for one hour at 4 C with In-111 labeled 17-1A and 19-9 F(ab) . Of 17 colon cancers studied, all showed positive binding with 17-1A, whereas 7(64%) of 11 gastric cancers gave positive results. 19-9 was positive in 9(53%) of 17 colon cancers and 4(36%) of 11 gastric cancers.

In-111 labeled MoAb 17-1A and 19-9 F(ab) were injected into nude mice xenografted with human colon cancer cells SW-1116 and Co-3. The MoAbs preferentially localized in transplanted tumors, although liver and kidney showed high non-specific Ab accumulation.

The results suggest the clinical usefulness of In-111 labeled 17-1A and 19-9 antibodies in the radioimmunoimaging of colon and gastric cancers.

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COMPARISON OF LABELING METHODS OF MONOCLONAL ANTIBODY; In-111 and I-125

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To evaluate improved methods of radio-immunodetection, In-111 and I-125 labeled antibodies and fragments of antibody were compared. $F(ab')_2$ and Fab of Anti-carcino-emblyonic antigen antibody;28A (IgG) were radiolabeled. The labeling method of In-111 labeled MAb was conjugated with cDTPA, molar ratio of Ab:DTPA were 1:0.6-0.8 after purification.
Radioiodination of MAb; Chloramine-T method, Iodo-Gen method and IODO-BEAD method were compared. These radiolabeled MAb were injected to tumor bearing nude mice, Tumor concentration,blood level and tumor/blood ratio were calculated. Blood clearance; T1/2 of In-111 Mab were Intact 51hrs, $F(ab')_2$ 20 hrs and Fab 13 hrs, these of I-125 MAb were Intact 77hrs, $F(ab')_2$ 37hrs and Fab 21hrs. Tumor/blood ratio of In-111 labeled antibodies were twice as I-125 labeled antibodies. The results of fragments on tumor/blood ratio were Fab > $F(ab')_2$ > Intact in both radionuclides. In other organs, liver, kidney and spleen were showed high concentration by In-111 labeled antibodies.