

^{99m}Tc direct labeling of a new anti-MUC1 monoclonal antibody, PR81, as a potential agent for imaging of human breast cancer in nuclear medicine

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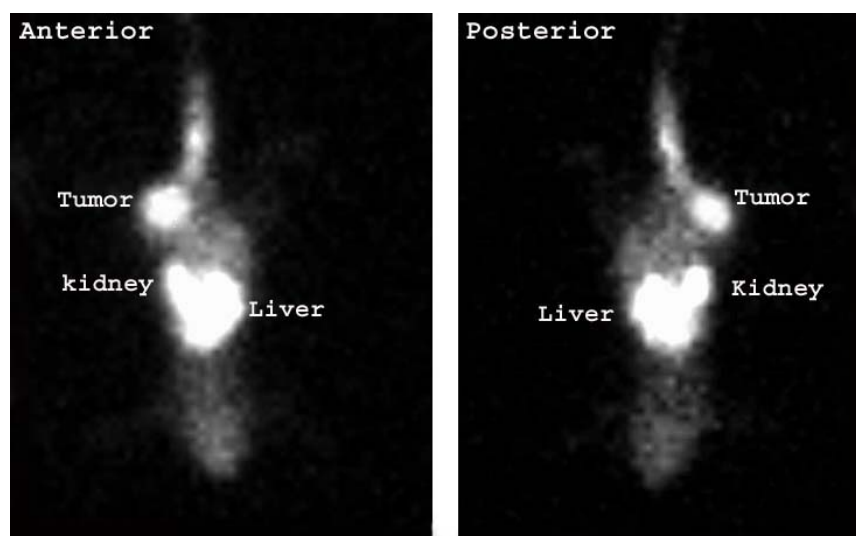
Radioimmunoscintigraphy (RIS) is a technique which uses radiolabeled antibodies to visualize tumors, taking advantage of antigens preferentially expressed by malignant tissues. Human epithelial mucin, MUC1, is commonly over expressed in adenocarcinomas including 80% of breast cancers and represents a useful target for RIS. The PR81 is a new murine anti-MUC1 monoclonal antibody that was found to react with the membrane extracts of several human breast cancer tissues and the cell surface of MUC1 positive cell lines. In this study we have developed a direct method for labeling of this MAb with ^{99m}Tc which is simple, rapid, efficient and particularly suitable for development of a 'kit'. The quality control of new radiopharmaceutical and immunoscintigraphy studies in BALB/c mice bearing breast tumor xenografts were also performed.

Materials and Methods

The Ab reduction was performed with 2-mercaptoethanol (2-ME) at a molar ratio of 2000:1 (2-ME:MAb). The reduced Ab was labeled with ^{99m}Tc *via* methylene diphosphonate (MDP) as a transchelator. The labeling efficiency was determined by ITLC. The amount of radiocolloids was measured by cellulose nitrate electrophoresis. Stability of labeled product was checked by incubation at 37° C for 24 hrs in fresh human serum and analyzed by gel filtration chromatography (FPLC). The integrity of labeled MAb was checked by means of SDS-PAGE. Cell-binding assay was used to test binding ability of ^{99m}Tc-PR81 to MCF 7 cells. Biodistribution was studied in normal BALB/c mice at 4 and 24 hr post-injection. The tumor imaging was performed in female BALB/c mice with breast tumor xenografts at 24 hr after the radiolabeled compound injection.

Results

The labeling efficiency was 94.2%±2.3 and radiocolloids were 2.5%±1.7. *In vitro* stability was 70%±5.7 in fresh human serum over 24 hr. There was no significant Ab fragmentation due to labeling procedure. Both labeled and unlabeled PR81 were able to compete for binding to MCF 7 cells. Biodistribution studies in normal BALB/c mice showed that there were no specific accumulations in any organs. The immunoscintigraphy studies demonstrated definite localization of the preparation at the site of tumors with high sensitivity (Figure 1).



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Figure1. Anterior and posterior whole-body scintigraphy images of a representative female BALB/c mouse with breast tumor xenograft in the left side of abdomen were taken at 24 hr after intravenous injection of ^{99m}Tc -PR81.

Conclusion

The findings show that the new preparation can be considered as a promising radiopharmaceutical for imaging of human breast cancer in nuclear medicine.

Key Words

Breast cancer; MUC1; Monoclonal antibody; ^{99m}Tc -radiolabeling, Radioimmunoscintigraphy

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