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Preparation and Preclinical Evaluation of 64Cu-NOTA-anti MUC1 as a Radioimmunoconjugate for Diagnosis of MUC1+ breast cancer by PET

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Background: Radioimmunoscintigraphy (RIS) has attracted considerable clinical application in tumor detection. Underglycosylated MUC1 antigen is one of the early hallmarks of tumor genesis and is overexpressed in more than 80% of breast cancers. PR81 is a new murine anti-MUC1 monoclonal antibody (mAb). In this study, as the first step, we have developed an efficient indirect labeling method of PR81 with 64Cu (T1/2 = 12.8 h, β+ = 17%, β− = 39%, EC = 43%) through using NOTA (p-SCN-Bn-NOTA) bi-functional chelator and performed preliminary biodistribution studies in mouse bearing breast adenocarcinoma.
Methodology: PR81 was conjugated with NOTA (Macrocyclics B-605), the average number of the chelator conjugated per mAb was calculated and total concentration was determined by spectrophotometrically. NOTA–antiMUC1 was labeled with 64Cu then Radiochemical purity and immunoreactivity, internalization study by MCF7 cell line and serum stability of 64Cu–NOTA–anti MUC1 were determined. The biodistribution studies and radioimmunoscintigraphy were performed in female BALB/c mouse bearing breast carcinoma tumor (64Cu–NOTA–antiMUC1 i.v., 100 µl, 20±5 µg mAb , 6, 12, 24 and 48 h).
Results and Discussion: 64Cu–NOTA–anti MUC1 was prepared (RCP >98% ± 0.4, Specific activity 5.2 ± 1.2 µCi/µg). Conjugation reaction of chelator (50 molar excess ratio) to antibody resulted in a product with the average number of chelators attached to a mAb (c/a) of 4.1 ± 0.5. Labeling yield with 64Cu in 400µg concentration of bioconjugate was 96.5% ± 2.1. Immunoreaction of 64Cu–NOTA–anti MUC1 complex towards MUC1 antigen was determined by RIA and the complex showed high immunoreactivity towards MUC1. In vitro and in vivo stability of radioimmunoconjugate was investigated respectively in PBS and blood serum by RTLC method. In vitro stability showed more than 94% ± 1.26 in the PBS and 81% ± 2.62 in the serum over 24 h. The Immunoreactivity of the radiolabeled PR81 towards MCF7 cell line was done by using Lindmo assay protocol. Under these conditions, the immunoreactivity of the radioimmunoconjugate was found to be 0.82. The biodistribution of 64Cu–NOTA–anti MUC1 complex in the mice with normal and breast tumor at 6, 12, 24 and 48 h after intravenous administration, expressed as percentage of injected dose per gram of tissue (%ID/g). Biodistribution and imaging studies at 24 and 48 h post-injection revealed the specific localization of complex at the site of tumors.
Conclusion: 64Cu–NOTA–anti MUC1 is a potential compound for molecular imaging of PET for diagnosis and follow up of MUC1 expression in oncology.
Keywords—anti MUC1, Copper-64, Monoclonal Antibody, Bio-distribution, Breast Cancer.

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