
We have developed a simple model system that can be used to evaluate methods of radioimmunomaging of tumors, using human chronic gonadotropin (hCG) as a model antigen and a monoclonal antibody against hCG as a model antibody. HCG was coated on a polystyrene spherical bead with a quarter inch in diameter and CNBr activated Sepharose 4B beads. Before in vivo studies, in vitro radioimmunoassay were performed. And specific binding to the both beads were obtained. Then hCG coated beads (a polystyrene bead or Sepharose beads) were put into the subcutaneous tissue on the back of mice. At 24hr after the transplantation, when the serum hCG was not detectable by the conventional RIA, radiolabeled antibodies were injected and its biodistribution was monitored. The percent injected dose per gram (%ID/g) for hCG coated polystyrene beads increased to a maximum at 48hr. In case of Sepharose beads, the %ID/g for hCG coated beads increased continuously, whereas the accumulation for most organs decreased with time. As an irrelevant antigen, beads coated with bovine serum albumin were transplanted and its uptake was as low as one third of that for hCG coated polystyrene beads, and as low as one third of hCG coated Sepharose beads.


The effects of phospholipid components on tumor uptake and blood clearance of Ga-67-liposomes were studied. Ga-67-liposomes were composed of various phospholipids, that is, egg yolk phosphatidylcholine (eggPC), phosphatidylcholine/dimyristoyl, dipalmitoyl, distearoyl (DMPC, DPPE, DSPC, respectively), and sphingomyelin (SM), with cholesterol (molar ratio 2:1). Mice bearing Ehrlich solid tumor were used as a tumor model.

When using SM-Ga-67-liposomes, Ga-67 accumulation in tumor was the largest and blood clearance of Ga-67 radioactivity was the lowest of the five types liposomes. As for DSPC-Ga-67-liposomes, tumor accumulation was a little lower and blood clearance was faster than those with SM-liposomes. When using eggPC, DMPC or DPFC liposomes, Ga-67 was rapidly eliminated from polystyrene beads accumulation and tumor uptake was not so much. The highest tumor to blood ratio of Ga-67 radioactivity at 24 hr after i.v. injection was obtained using DSPC liposomes. These results suggest that the longer retention of Ga-67-liposomes in the circulation increases tumor uptake of Ga-67. SM-Ga-67-liposomes are the most excellent of the five with regard to the tumor uptake, but DSPC-Ga-67-liposomes are more suitable for tumor imaging because of their good tumor to blood ratio.

53 HIGH ACCUMULATION OF Tc-99m(V)-DMS IN MTC 6-23 BEARING NUDE MICE. I. Yokomizo, K. Morihuchi, K. Yokoyama, H. Sakahara, H. Ohta, K. Endo, K. Torizuka. Faculty of Pharmaceutical Sciences, School of Medicine, Kyoto University, Kyoto.

As reported, Tc-99m(V)-dimercaptoposuccinate (DMS) has shown its usefulness as a tumor imaging, specifically in patients with medullary thyroid carcinoma (MTC) (JNM 25:325, 1984). To investigate the accumulation of Tc(V)-DMS in MTC nude mice bearing MTC 6-23 tumor, originated in rats were prepared as an animal model. Biodistribution studies of Tc(V)-DMS were comparatively carried out in non-treated nude mice and Ehrlich ascites tumor bearing ddY mice. Results indicated the Tc(V)-DMS accumulation in MTC was higher than in Ehrlich tumor. At 3 hours post-injection, %dose/g tissue in MTC reached 3.5 times higher value than in Ehrlich tumor. This accumulation and serum calcitonin (CT) levels increased along with MTC tumor growth. At 2 weeks after transplantation, %dose/g tumor tissue was 0.61 (3 hours post-injection) and CT level was 90 pg/ml, while at 6 weeks after transplantation, %dose/g was 1.33 and CT level was 400 pg/ml (normal CT level was 63 pg/ml). Thus, gathered data demonstrated the high MTC accumulation of Tc(V)-DMS detected in clinical studies was well reflected in animal bearing MTC 6-23 tumor. Studies on relevant factors associated with Tc(V)-DMS uptake and the level of CT is now under progress.

54 METAL COMPLEX DISSOCIATION OF Tc(V)-DMS, A COMPATIBLE PHENOMENON IN TUMOR IMAGING AGENT: Tc-CITRATE. K. Horiuchi, I. Yokomizo, Y. Onishi, and A. Yokoyama. Fac. of Pharmaceutical Sciences, Kyoto University, Kyoto.

A new tumor imaging agent, Tc(V)-dimercaptosuccinate (DMS) has been designed based on occurrence of metal complex dissociation in polynucleate Tc-complex*. Tc-citrate (Cit) also a polynucleated complex has been reported as an imaging agent. Using a dilution methodology, compatibility of those Tc-complexes dissociation with tumor accumulation was tested in-vitro, with Ehrlich ascites tumor cells. A test with double labeled Tc-C-14-Cit, showed lack of ligand involvement, but of radiometal Tc in tumor cell accumulation. Under dilution stimulus, increasing uptake of Tc was detected. This phenomenon traced by TLC (n-BuOH:AcOH:H2O=3:2:1, 100% acetone) showed the generation of fast moving peak. Tc-Cit being more dissociable caused, over 10 times dilution, the formation of another peak of lower mobility, well correlated with poor cell uptake. This was better reflected in in-vivo biodistribution, under hemodilution, higher stability of Tc(V)-DMS lead to higher target/non-target ratio than Tc-Cit with undesirable distribution to stomach, liver. Validity of polynuclear Tc-complex dissociation as a phenomenon inducing tumor uptake and the compromise between Tc-complex stability and ability to dissociate are discussed.