

**TUMOR LOCALIZATION OF TECHNETIUM-99m-ALPHA-D-
GLUCOSE-1-PHOSPHATE USING DUAL RADIOLABELLED
STEALTH LIPOSOME ENGINEERED WITH IOR CEA-1
MONOCLONAL ANTIBODIES**

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Tc-99m was complexed with alpha-D-glucose-1-phosphate (DGP) using stannous chloride as a strong reducing agent. Stealth liposomes were prepared using Sphingomyelin (SM), Phosphatidylcholine (PC), Cholesterol (CH) and Monosialogangliosides (GM-1) in the ratio of SM: PC: CH: GM-1: 1:1:1:0.2 by the method of sonication. Tc-99m-DGP was entrapped in these vesicles and the radiolabelling efficiency was found to be greater than 90% as ascertained by size exclusion chromatography. The stability of Tc-99m-DGP labeled stealth liposomes were determined by incubating a 0.1 ml aliquot of the liposome preparation in 1.0 ml serum or saline and counting the activity still bound to the liposome layer at various time intervals (0-24 hr). About 35-40% of the radioactivity was released over 24 hr.

Immunostealth liposomes were prepared by coupling I-125 labeled murine anti carcino embryonic antigen (CEA) monoclonal antibody (IOR-1) with N-hydroxysuccinimide ester of palmitic acid followed by conjugation of this IOR-1 on the surface of stealth liposomes. The rationale behind dual radiolabelling is that Tc-99m is a monoenergetic gamma emitter (150 KeV), whereas I-125 possess x-rays emitter in the range of 27-35 KeV. This unique difference in energies does not interfere during evaluation by scintillation gamma camera. Organ distribution and blood kinetics were also studied in tumor bearing C(3)H Jax mice. In contrast to stealth liposomes, immunostealth liposomes exhibited increased accumulation of radioactivity in tumor (9.85% injected dose/gram), whereas it was significantly decreased in liver (1.72% injected dose/gm) at 24 hr after intravenous administration in tumor bearing C(3)H Jax mice. Organ distribution of immunostealth liposomes in tumor bearing C(3)H Jax mice indicated high tumor to blood ratio after 24 hr indicating its preferential accumulation in tumor. Excised tumor indicated that labeled immunostealth liposomes injected intravenously in C(3)H Jax mice were concentrated maximally at 1 hr (16.6%) which decreased slowly with time and 13.9% and 9.85% was detected at 3 hr and 24 hr respectively. Blood showed 6.42% activity

at 1 hr followed by 5.35% and 1.62% at 3 hr and 24 hr respectively. Muscles showed 12.7% activity at 1 hr followed by 9.72% and 6.25% at 3 hr and 24 hr respectively.

The effect of liposome size on tumor localization of label may be related to the interaction of liposome with tumor cells. The greater uptake of SUVs label may also be the measure of increased half time of such liposomes in the blood. This is supported by the scintigraphic studies, which show that increased uptake of radioactivity is found with stealth SUVs (20-50 nm). Furthermore, carcinoembryonic antigen specificity of our immunostealth liposomes suggests their potential application in understanding the nature of a tumor.